Visual assessment vs. strain imaging for the detection of critical stenosis of the left anterior descending coronary artery in patients without a history of myocardial infarction

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Received 9 July 2014; accepted after revision 15 September 2014; online publish-ahead-of-print 21 October 2014

Aims

We sought to determine the prevalence of overt and subclinical LV dysfunction in patients with critical left anterior descending coronary artery (LAD) stenosis but without a history of myocardial infarction and to compare diagnostic value of routine echocardiographic parameters with myocardial strain analysis for detection of critical LAD stenosis.

Methods and results

We retrospectively studied 269 patients with suspected coronary artery disease (CAD)—209 consecutive patients with critical LAD stenosis and 60 consecutive patients with atypical chest pain and without CAD. Conventional visual assessment of LV asynergy in the LAD territory was compared with global, regional, and segmental peak systolic longitudinal strain (PSLS) parameters derived by two-dimensional speckle tracking echocardiography (2D STE). Wall motion abnormalities in the LAD territory were found in 41% of patients with critical LAD stenosis, whereas, depending on the cut-off value, global longitudinal strain (GLS) was impaired in 42–69% of patients. GLS with an area under the receiver operating characteristic curve (AUC) of 0.85 showed better discriminative power for detecting critical LAD stenosis than conventional wall motion score index (AUC 0.73, P < 0.05, for the difference between the AUCs). PSLS values were significantly lower in basal and midventricular segments supplied by critically narrowed LAD, particularly if they also appeared dysfunctional on visual assessment.

Conclusions

Detection of subclinical LV dysfunction by 2D STE might improve identification of patients with critical LAD stenosis, although visually apparent regional LV dysfunction in the LAD territory is not uncommon finding in this subset of patients.

Keywords

Coronary artery disease • Longitudinal strain • Speckle tracking

Introduction

The extent and functional significance of the myocardium supplied by the left anterior descending coronary artery (LAD) makes timely detection of LAD stenosis an appealing task. Despite the high-risk profile, the majority of patients with significant LAD stenoses but without a history of myocardial infarction (MI) have normal resting electrocardiogram (ECG) and echocardiogram.1–3 Yet, in patients with chronic total occlusion or critical narrowing of LAD, regional contractile function may frequently be depressed even in the absence of previous MI, due to silent ischaemia, stunned, or hibernating myocardium.4,5 Overtly dysfunctional but non-infarcted myocardium may be appreciated on a resting echocardiogram as regional wall motion abnormalities (WMA).5,6 More subtle regional myocardial dysfunction, not visible to the bare eye, may be detected by novel methods for assessing LV function, such as myocardial strain analysis by two-dimensional speckle tracking echocardiography (2D STE).8–10 Although previous studies consistently reported lower values of

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strain parameters in patients with obstructive coronary artery disease (CAD) compared with those without CAD,
11–14 diagnostic value of 2D myocardial strain for decision-making in a single patient has not been fully established. While myocardial strain analysis might be obviously redundant in the presence of resting WMA, loosely defined ranges of normal global and segmental longitudinal strain values may further limit its clinical applicability.

Therefore, we sought to determine the prevalence of visually apparent and subclinical LV dysfunction in symptomatic patients with critical LAD stenosis but without a history of MI, and to compare diagnostic value of routine echocardiographic parameters with myocardial strain analysis for the detection of critical LAD stenosis.

Methods
We retrospectively enrolled 269 patients with suspected CAD, referred to our centre for coronary angiography—209 consecutive patients with critical stenosis of the LAD (mean age 62 ± 9 years, 75% male) and 60 with atypical chest pain and without significant CAD (59 ± 10 years, 50% male). Only patients without a history of MI and no Q-waves on ECG were included, whereas those with arrhythmias and more than mild valvular heart disease were not eligible for the study.

Echocardiography and two-dimensional speckle tracking
According to the hospital protocol, patients underwent a standard 2D and Doppler echocardiography the day before coronary angiography. Greyscale images with frame rates of 50–70 frame/s were acquired by five experienced echocardiographers using a Vivid 7 scanner (GE Vingmed Ultrasound, Horten, Norway). Images with lower frame rates were included in the visual assessment of regional LV function and volumetric measurements, but excluded from 2D speckle tracking analyses. Image loops of three consecutive heart cycles were digitally stored for further off-line analysis by an EchoPac workstation (GE Vingmed). Left ventricular ejection fraction (LVEF) were calculated using the modified Simpson biplane method.15

Visual assessment of the regional LV systolic function was performed at the time of examination (before coronary angiography) using an 18-segment model of the left ventricle (with three segments per wall) and a conventional 4-point scale for grading each segment (1—normal, 2—hypokinetic, 3—akinetic, and 4—dyskinetic). Wall motion score index (WMSI) was calculated as the average of the scores of all LV segments.15 WMA in the LAD territory were considered to be present if any of two neighbouring segments of the anterior and anteroseptal wall had scores >1. Regional WMSI in the LAD territory (WMSI_LAD) was calculated as the average wall motion score of six segments (basal anterior, basal anteroseptal, midanterior, midanteroseptal, apical anterior, and apical anteroseptal), since these segments are invariably subtended by the LAD.15

Two-dimensional speckle tracking analysis was done by the investigator blinded to both coronary angiography findings and the assessment of regional WMA. The analysis was performed using the commercially available software (EchoPAC version BT12; GE Healthcare, Milwaukee, WI, USA) and a semi-automatic algorithm for tracking the LV myocardium throughout the heart cycle. The endocardial surface in each of three apical views was manually traced at the end-systole, with a region of interest adjusted to include the entire myocardial thickness. After careful visual inspection of the adequacy of tracking, the region of interest was readjusted in all cases of unsatisfactory tracking. Patients with two or more segments with poor tracking even after manual correction were excluded from further analysis. The software then divided each ventricular wall into three segments and generated longitudinal strain curves with numerical values for deformation parameters for all 18 segments. A peak systolic longitudinal strain (PSLS) value was recorded for each segment and global longitudinal strain (GLS) was calculated as the average of all segmental values.16

GLS of 12 basal and midventricular segments (GLS12) was calculated as the average of these 12 segmental values.8,15 Regional PSLS in the vascular distribution area of the LAD (RLSLAD) was calculated as the average of six (three anterior and three anteroseptal) segmental PSLS values.

Coronary angiography
Coronary angiograms were visually assessed for coronary lesions in two orthogonal planes by an experienced interventional cardiologist. Diagnosis of significant CAD was considered when ≥50% reduction of vessel was observed in at least one major coronary artery.17 Critical stenosis was defined as a coronary artery luminal diameter narrowing ≥90%.

Statistical analysis
Continuous data are expressed as mean ± standard deviation, and categorical data are expressed as percentages. Data were compared between two groups using an unpaired t-test for continuous variables and Fisher’s exact test for categorical variables. For comparison of continuous variables among three groups, analysis of variance was performed, with post hoc pairwise comparisons between the groups, whereby adjustments to the significance level were made using the Tukey–Kramer method. Receiver operating characteristic (ROC) curves and their area under the curve (AUC) were calculated to assess the discriminative power of GLS, GLS12, RLS_LAD, and WMSI. The AUC values were compared using the method proposed by DeLong et al.18

Uni- and multivariable regression analyses were performed to determine the value of traditional risk factors for CAD and regional LV dysfunction (RLSLAD and WMSILAD) to predict critical LAD stenosis. In the multivariable analysis, the predictive value of RLS_LAD was corrected by those variables with a value of P < 0.05 in the univariable analysis.

Finally, 25 patients were randomly selected to test the intra- and interobserver variability for both visual assessment of WMA and PLS using kappa statistics and interclass correlation coefficients (ICCs), respectively. All statistical tests were two-tailed, and a P-value of <0.05 was considered significant. Statistical analysis was performed using the commercially available software (PASW Statistics, version 18, SPSS, Inc., Chicago, IL, USA and Medcalc, version 12.2.1.0, Medcalc Software, Mariakerke, Belgium).

Results
Characteristics of the study population are summarized in Table 1. Patients with critical LAD stenosis (38% with unstable angina) were older, more frequently men, and more often had diabetes mellitus and hypertension than those in the control group (P < 0.05, for all). A total of 112 (42%) patients underwent stress testing prior to coronary angiography—positive stress test had 90% (73/81) patients with critical LAD stenosis and 23% (7/31) patients without significant CAD (P < 0.001). Apart from critical narrowing of the LAD, 45% of patients had at least one additional significant coronary artery stenosis (Table 1).

Feasibility and reproducibility
Regional LV function could be assessed in all patients, while 2D speckle tracking longitudinal strain was obtainable in 181 (67%)
patients. In the remaining patients, speckle tracking analysis was precluded due to suboptimal image quality resulting in inadequate tracking \((n = 21)\) and low frame rates of grey scale images \((n = 67)\). If the latter group was excluded, feasibility of 2D speckle tracking in the present study would be 89%.

Intra- and interobserver agreement for visual assessment of LV asynergy in the LAD territory was good \((r = 0.91 \text{ and } 0.82, \text{ respectively})\). ICCs for intraobserver variability were: 0.93 [95% confidence interval (CI) 0.85–0.97] for GLS; 0.91 [95% CI 0.81–0.96] for GLS\(_{12}\); 0.93 [95% CI 0.84–0.97] for RLS\(_{LAD}\), and 0.98 [95% CI 0.97–0.99] for WMSI \((P < 0.05, \text{ for all})\). ICCs for intraobserver variability were: 0.89 [95% CI 0.76–0.95] for GLS; 0.89 [95% CI 0.75–0.95] for GLS\(_{12}\); 0.83 [95% CI 0.60–0.93] for RLS\(_{LAD}\); and 0.86 [95% CI 0.66–0.93] for WMSI \((P < 0.05, \text{ for all})\).

### Table 1  Characteristics of the study population

<table>
<thead>
<tr>
<th></th>
<th>LAD stenosis ((n = 209))</th>
<th>Controls ((n = 60))</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>62 ± 9</td>
<td>59 ± 10</td>
<td>0.022</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>156 (75)</td>
<td>30 (50)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Smoking, n (%)</td>
<td>16 (27)</td>
<td>77 (37)</td>
<td>0.167</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>77 (37)</td>
<td>12 (20)</td>
<td>0.019</td>
</tr>
<tr>
<td>Dyslipidaemia, n (%)</td>
<td>169 (81)</td>
<td>45 (75)</td>
<td>0.364</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>196 (94)</td>
<td>41 (63)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Family history of CAD, n (%)</td>
<td>90 (43)</td>
<td>28 (47)</td>
<td>0.659</td>
</tr>
<tr>
<td>Coronary angiography, n (%)</td>
<td>One-vessel disease</td>
<td>84 (40)</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>Two-vessel disease</td>
<td>93 (45)</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>Three-vessel disease</td>
<td>32 (15)</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>RCA stenosis</td>
<td>106 (51)</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>LCX stenosis</td>
<td>47 (23)</td>
<td>–</td>
</tr>
</tbody>
</table>

CAD: coronary artery disease; LAD: left anterior descending coronary artery; LCX: left circumflex coronary artery; RCA: right coronary artery.

### Table 2  Conventional echocardiographic and strain parameters

<table>
<thead>
<tr>
<th></th>
<th>LAD stenosis with WMA</th>
<th>LAD stenosis without WMA</th>
<th>Controls</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV EDD, mm</td>
<td>51 ± 8(^*)</td>
<td>47 ± 5(^*)</td>
<td>47 ± 5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LV EDV, mL</td>
<td>99 ± 45(^*)</td>
<td>68 ± 21(^*)</td>
<td>60 ± 18</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LV ESV, mL</td>
<td>54 ± 37(^*)</td>
<td>28 ± 15(^*)</td>
<td>22 ± 8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>49 ± 13(^*)</td>
<td>61 ± 9(^*)</td>
<td>66 ± 6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>WMSI</td>
<td>1.83 ± 0.4(^*)</td>
<td>1.11 ± 0.2(^*)</td>
<td>1.03 ± 0.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>WMSI(_{LAD})</td>
<td>1.90 ± 0.5(^*)</td>
<td>1.03 ± 0.2(^*)</td>
<td>1.00 ± 0.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>GLS</td>
<td>−14.3 ± 4.9(^*)</td>
<td>−19.2 ± 3.5(^*)</td>
<td>−22.5 ± 2.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RLS(_{LAD})</td>
<td>−12.9 ± 5.9(^*)</td>
<td>−18.8 ± 4.2(^*)</td>
<td>−23.2 ± 7.9</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

LAD: left anterior descending coronary artery; LV EDD: left ventricular end-diastolic diameter; LV EDV: left ventricular end-diastolic volume; LV ESV: left ventricular end-systolic volume; LVEF: Left ventricular ejection fraction; GLS: global longitudinal strain; RLS\(_{LAD}\): regional longitudinal strain in the LAD territory; WMSI: wall motion score index; WMA: wall motion score abnormalities, defined as wall motion score of >1 of any two neighbouring segments of the anterior and anteroseptal wall.

\(^*\)P < 0.05 vs. controls.

### Routine echocardiographic and global peak systolic strain data

The echocardiographic features of patients with critical LAD stenosis (with and without asynergy in the LAD territory) and the control group are presented in Table 2.

Comparison between visual assessment and strain imaging was performed only for segments where both analyses were possible.

Regional WMA’s in at least two neighbouring segments of the anterior or anteroseptal wall were present in 85 (41%) of patients with critical LAD stenosis, whereas, depending on the cut-off value, GLS was impaired in 42–69% of patients. Patients with critical LAD stenosis and asynergy in the LAD territory had lower LVEF and GLS than both patients without asynergy and controls \((P < 0.05, \text{ for all})\).

ROC analysis revealed poor discriminative performance of routine echocardiographic parameters for the detection of critical LAD stenosis, particularly in patients without WMA in the LAD territory (Table 3). Comparison of AUC values showed that both global and regional PSLS parameters were better discriminators for the detection of critical LAD stenosis than global and regional WMSI \((Figure 1A)\). Significant differences between AUC values were also observed for GLS and conventional echocardiographic parameters (LVEF, LV end-diastolic diameter, and LV end-systolic volume; \(P < 0.05, \text{ for all comparisons})\). Importantly, both strain parameters retained fair discriminative performance when analysis was confined to patients without visual asynergy in the area subtended by the LAD \((Figure 1B)\) and to those with single-vessel \((Figure 1C)\) and multivessel CAD \((Figure 1D)\). All previously published cut-offs of GLS for predicting significant CAD would detect critical LAD stenosis with a sensitivity ranging from 35 to 64% and a specificity between 86 and 92% \((Table 4)\). Nonetheless, RLS\(_{LAD}\) remained an independent predictor of critical LAD when adjusted for factors known to influence longitudinal strain values (age, gender, diabetes mellitus, and hypertension; \Table 5)\).

### Segmental strain analysis

Visually dysfunctional myocardium subtended by critically narrowed LAD had lower PSLS values in basal, midventricular, and apical
segments than visually normokinetic myocardium, supplied by either a critically narrowed or an unstenosed LAD (Table 6). Furthermore, visually normokinetic basal and midventricular segments supplied by critically stenosed LAD had lower values of PSLs than the corresponding segments supplied by unstenosed LAD. Conversely, visually normokinetic apical segments had similar values of PSLs supplied by either stenosed or unstenosed LAD (Table 6).

As a result, in patients without asynergy in the LAD territory, the average PSLs value of basal and midventricular segments of anterior and anteroseptal wall showed fair discriminative power for the detection of critical LAD stenosis [AUC 0.78, 95% CI 0.70–0.87, \( P < 0.001 \)], in contrast to the average PSLs value of apical anterior and apical anteroseptal segments (AUC 0.56, 95% CI 0.46–0.67, \( P = 0.283 \)). Of note, discriminative power of the average PSLs value of all six apical segments was also poor (AUC 0.54, 95% CI 0.51–0.72, \( P = 0.04 \)).

To test the agreement between visual assessment and segmental strain analysis for identification of dysfunctional segments, we classified segments into normal and abnormal using previously proposed cut-off values for normal segmental PSLs,\(^{1,9}\) and then compared the results of both methods for each segment.

A significantly higher proportion of apical segments was identified as abnormal with visual assessment than with strain analysis (\( P < 0.05 \), for both anterior and anteroseptal apical segments), whereas no statistically significant difference between visual and strain analysis was observed for basal and midventricular segments (\( P > 0.05 \), for all) (Figure 2A). Of note, in all cases of discrepancy between visual WMAs of the apex and PSLS values, only hypokinesia of apical segments was observed, and in almost all cases the terms such as ‘shaking’ or ‘trembling’ were used to describe abnormal contraction. Although mild apical asynergy was highly specific for detecting critical LAD stenosis (98%), it was not always associated with significantly reduced apical PSLS values (see Supplementary data online, Video S1 and Figures S1–S3).

Importantly, in patients without WMAs, up to 26% of visually normokinetic segments would be identified as abnormal with strain analysis in patients with critical LAD stenosis, compared with only 3–5% of segments in the control group (Figure 2B).

**Discussion**

The present study demonstrated that regional asynergy in the LAD territory was not rare finding (41%) in patients with critical stenosis of LAD without a history of MI, whereas, depending on the cut-off value, GLS was impaired in up to two-thirds of patients. All longitudinal strain-derived parameters showed better discriminative power for the detection of critical LAD stenosis than conventional echocardiographic parameters, such as regional WMA, LVEF, and LV end-systolic volume. Finally, visually apparent regional LV dysfunction was associated with lower values of segmental longitudinal strain compared with visually normokinetic segments supplied by either critically narrowed or unstenosed LAD.

Apart from traditional risk factors, several echocardiographic findings such as WMA, mitral annular calcification, and aortic sclerosis, have been identified as independent predictors of CAD in adults without overt cardiovascular (CV) disease.\(^7\) Resting WMA may be encountered in patients without previous MI due to ischaemia, myocardial hibernation, or stunning, and it is associated with 2.4- to 6.1-fold increased risk of future MI and death in patients with no prior MI.\(^{6,23}\) One interesting finding of the present study is that WMAs are similarly frequent in patients with critical LAD stenosis as in patients without CV disease, with the exception of aortic stenosis. All these findings support the potential benefit of standard 2D STE as an efficient diagnostic tool in this patient population.
3.4-fold higher risks of CV morbidity and mortality.\textsuperscript{6} In our study, patients with WMA in the LAD territory more frequently had a multivessel disease and also had a larger LV end-diastolic diameter and lower LVEF than those without WMA.

Although resting WMA was a relatively common finding in patients with critical LAD stenosis in the present study, our data confirm that 2D STE-derived longitudinal strain may help to identify a significant proportion of patients with critically narrowed LAD and subclinical regional LV dysfunction not appreciated by visual assessment. In the present study, both global and regional longitudinal strain parameters had higher diagnostic power for detecting critical LAD stenosis compared with WMSI, and also retained a fair discriminative power in a subset of patients without WMA in the LAD territory, but with single-vessel and multivessel CAD. Nonetheless, given the fact that 60% of the study population had two- or three-vessel disease and better performance of strain parameters in the multivessel group (Table 3), the detection of subclinical LV dysfunction may be a better marker of multivessel than single-vessel disease.

We also compared the discriminative performance of conventional volumetric echocardiographic parameters (LVEF and end-systolic volume) with longitudinal strain parameters for the detection of critical LAD stenosis. Given that subendocardial longitudinal myocardial fibres’ function is more susceptible to ischaemia than midwall radial circumferential fibres’ function, it was not surprising that GLS, as a

![Figure 1](image-url) ROC analysis of LV dysfunction by visual assessment and strain imaging for prediction of critical LAD stenosis. (A) The whole study population. (B) Patients without WMA in the LAD territory. (C) Patients with single-vessel disease. (D) Patients with multivessel disease. Refer to Table 3 for area under the curve values. GLS: global longitudinal strain; RLS\textsubscript{LAD}: regional longitudinal strain in the LAD territory; WMSI: wall motion score index; WMSI\textsubscript{LAD}: regional wall motion score index in the LAD territory; WMSI\textsubscript{apex}: wall motion score index of the apical anterior and anteroseptal segments.

<table>
<thead>
<tr>
<th>Cut-off for abnormal strain (reference number given in superscript)</th>
<th>Sn/Sp (%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GLS (&gt; -18.3\textsuperscript{5})</td>
<td>35/92</td>
<td>0.002</td>
</tr>
<tr>
<td>GLS (&gt; -19\textsuperscript{11})</td>
<td>46/92</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>GLS (&gt; -19.7\textsuperscript{13})</td>
<td>54/89</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>GLS\textsubscript{12} (&gt; -18.4\textsuperscript{13})</td>
<td>64/86</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Table 4** Performance of the published cut-offs for the detection of critical LAD stenosis

LAD: left anterior descending coronary artery; GLS: global longitudinal strain; GLS\textsubscript{12}: global longitudinal strain of 12 basal and midventricular segments; Sn: sensitivity; Sp: specificity.
Detection of LV dysfunction by 2D STE

Table 5  Uni- and multivariate regression analyses to identify predictors of critical LAD stenosis

<table>
<thead>
<tr>
<th></th>
<th>Univariate</th>
<th>P-value</th>
<th>Multivariate</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR [95% CI]</td>
<td></td>
<td>OR [95% CI]</td>
<td></td>
</tr>
<tr>
<td>Age [per 1 year]</td>
<td>1.036 [1.005–1.067]</td>
<td>0.024</td>
<td>1.056 [0.997–1.118]</td>
<td>0.061</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>2.333 [1.168–4.662]</td>
<td>0.016</td>
<td>1.187 [0.331–4.258]</td>
<td>0.016</td>
</tr>
<tr>
<td>Dyslipidaemia</td>
<td>1.408 [0.715–2.775]</td>
<td>0.323</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Male sex</td>
<td>2.943 [1.625–5.333]</td>
<td>&lt;0.001</td>
<td>4.088 [1.469–11.377]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Smoking</td>
<td>1.604 [0.848–3.035]</td>
<td>0.146</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Hypertension</td>
<td>6.987 [3.198–15.267]</td>
<td>&lt;0.001</td>
<td>30.058 [5.584–161.794]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>WMSILAD [per 0.1 point]</td>
<td>1.338 [1.151–1.602]</td>
<td>&lt;0.001</td>
<td>1.392 [0.989–1.961]</td>
<td>0.058</td>
</tr>
<tr>
<td>RLSLAD [per 1%]</td>
<td>1.324 [1.185–1.480]</td>
<td>&lt;0.001</td>
<td>1.375 [1.180–1.602]</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

CI: confidence interval; LAD: left anterior descending coronary artery; OR: odds ratio; RLSLAD: regional longitudinal strain in the LAD territory; WMSILAD: regional wall motion score index in the LAD territory.

Table 6  Segmental PSLS

<table>
<thead>
<tr>
<th>Segments</th>
<th>LAD stenosis with WMA</th>
<th>LAD stenosis without WMA</th>
<th>Controls</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior wall</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Basal (n = 143)</td>
<td>–12.4 ± 5.5§</td>
<td>–14.4 ± 4.2*</td>
<td>–18.4 ± 2.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mid (n = 171)</td>
<td>–13.9 ± 6.9§</td>
<td>–16.9 ± 4.6*</td>
<td>–20.5 ± 2.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Apical (n = 172)</td>
<td>–16.9 ± 8.1§</td>
<td>–21.6 ± 7.4*</td>
<td>–24.5 ± 4.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Anteroseptal wall</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Basal (n = 152)</td>
<td>–12.1 ± 7.6§</td>
<td>–15.0 ± 6.1*</td>
<td>–18.8 ± 8.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mid (n = 174)</td>
<td>–15.0 ± 5.6§</td>
<td>–18.5 ± 5.6*</td>
<td>–22.7 ± 3.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Apical (n = 170)</td>
<td>–16.6 ± 6.1§</td>
<td>–22.2 ± 6.2*</td>
<td>–23.8 ± 5.2</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

LAD: left anterior descending coronary artery; WMSI: wall motion score index.
§P < 0.05 vs. controls.
%P < 0.05 vs. patients with critical stenosis and WMA.

measure of longitudinal function, had a significantly higher power for detecting critical LAD stenosis than LVEF, a measure of radial LV function.

On a segmental level, visually dysfunctional segments had lower PSLS values than both visually normokinetic segments supplied by either critically stenosed LAD or unstenosed LAD. We further investigated the ability of visual assessment and 2D speckle tracking strain imaging to identify dysfunctional segments in the LAD territory, by comparing visual segmental wall motion scores and PSLS values for six LV segments invariably irrigated by LAD. Surprisingly, strain imaging appeared to be inferior to visual assessment due to its failure to identify all visually dysfunctional apical segments as abnormal, whereas no significant differences between the two were observed at the level of basal and midventricular segments. It should be noted that, in all cases of discrepancy between visual inspection and strain imaging of apical segments, only mild apical dysfunction was observed. Admittedly, such mild dysfunction may not be appreciated by non-expert observers, making its detection by strain imaging even more important.

Both in patients and controls, PSLS values in apical segments were higher compared with that of basal segments. Possibly incorrect estimation of longitudinal function of apical segments by 2D speckle tracking strain was also suggested by Choi et al. and Biering-Sørensen et al. who reported better diagnostic performance of GLS for the detection of CAD when apical segments were omitted from GLS calculation. Choi et al. speculated that helical structure of the heart with rather circular than longitudinal alignment of myocardial fibres in the apex may be responsible for suboptimal assessment of longitudinal function of the apical myocardium by 2D speckle tracking strain. In line with this, here we further speculate that, in the apical region, 2D speckle tracking software measures a combination of longitudinal and circumferential strain resulting in higher than expected values of PSLS. Nonetheless, a recent 2D speckle tracking study investigating multilayer strain confirmed the existence of a basal-to-apical gradient in longitudinal strain in the inner and middle myocardial layers, with longitudinal strain being highest in the apex and lowest in the base. While this is in line with our results, it is in discordance with previous studies reporting
fairly constant longitudinal strain across the left ventricle. The existence of longitudinal basal-to-apical strain gradient could be particularly important for establishing robust threshold values for segmental longitudinal strain. Meanwhile, until age- and gender-specific reference values from large population studies become available, not only the absolute numerical value of strain parameters but also the pattern of deformation may help to distinguish between normal and ischaemic myocardium. The potential benefit of assessing postsystolic strain for the detection of CAD may be concluded from previous studies and from experience with individual patients (see Supplementary data online, Figures S1–S3) and warrants further research.

**Study limitations**

Despite technological advances and a growing body of evidence on its clinical utility, echocardiographic strain imaging still does not play a role in routine clinical care of the patient with suspected CAD. A relatively low specificity of subclinical LV dysfunction for diagnosing specific cardiac disorder could be one of the possible reasons for slow transition of 2D strain from research to clinical arena. Subclinical impairment of LV function detectable by 2D strain imaging has been described in a variety of cardiac and non-cardiac disorders, including CAD, arterial hypertension, diabetes mellitus, atrial fibrillation, and amyloidosis. In line with this, although we have conservatively chosen to investigate the impact of chronic ischaemia to regional LV function only in LV segments invariably subtended by a critically narrowed coronary artery, we cannot entirely rule out the impact of conditions other than ischaemia, such as diabetes mellitus and hypertension, on lower strain values observed in patients with critical coronary stenosis compared with the control group. However, when adjusted for covariates of age, gender, hypertension, and diabetes mellitus, RLS in the LAD territory remained an independent predictor of critical LAD stenosis.

It should also be noted that only symptomatic patients scheduled for coronary angiography were included in this study and therefore, the true prevalence of regional LV dysfunction in patients with critical LAD stenosis remains unknown.

Finally, patients with WMA were included in this study, provided that they did not have either a history of MI or Q-waves on ECG. Epidemiological studies have, however, established that 5–20% of MIs go unrecognized at the time of occurrence, whereas ECG Q-waves have a lower sensitivity to rule out silent MI compared with imaging studies. It is, therefore, possible that in some patients WMAs were due to previously unrecognized MI.

**Conclusions**

Detection of subclinical LV dysfunction by 2D STE might improve identification of patients with critical LAD stenosis, although visually apparent regional LV dysfunction in the LAD territory is not uncommon finding in this subset of patients. Segmental longitudinal strain values are significantly lower in basal and midventricular segments supplied by critically narrowed LAD, particularly if they also appear dysfunctional on visual assessment.
The example of discrepancy between visual WMA of the apex and segmental PSLS values in a patient with proximal LAD subocclusion is shown in Supplementary data online, Videos S1 and S2 and Figures S1 – S3. Although longitudinal strain curves of all apical segments did not show significantly reduced peak systolic values, there was prominent post-systolic shortening which was the most likely reason for trembling impression, regarded as hypokinesia of apical segments.

Supplementary material
Supplementary data are available at European Heart Journal – Cardiovascular Imaging online.

Acknowledgements
We appreciate the contribution of Ljiljana Simpraga, RN, for her assistance in data collection.

Conflict of interest: Unrestricted software support was provided by GE Healthcare. The sponsor had no role in the study design, data collection, analysis and interpretation, or writing of the manuscript. For all other authors, there is nothing to declare.

Funding
B.P., T.M., and A.N.N. are partly supported by the Ministry of Science, Republic of Serbia (grant no. 175099).

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