Detection of Functionally Significant Coronary Artery Disease: Role of Regional Post Systolic Shortening

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Abstract

Background: The main goal of this manuscript was to evaluate the diagnostic value of the global and regional postsystolic shortening (PSS) parameters, assessed by two-dimensional (2D) speckle-tracking echocardiography, at rest and during dobutamine stress for the detection of functionally significant coronary artery stenoses in patients with moderate pretest probability of stable coronary artery disease (CAD).

Methods: Dobutamine stress echocardiography (DSE) and adenosine stress myocardial perfusion imaging by cardiac magnetic resonance (CMR-MPI) were performed on 83 patients with moderate pretest probability of stable CAD and left ventricle ejection fraction ≥55%. CAD was defined as ≥50% diameter stenoses on invasive coronary artery angiography (CAA) validated as hemodynamically significant by CMR-MPI. According to invasive CAA and CMR-MPI results, patients were divided into two groups: Nonpathologic CAD (−) group: 38 (45.8%) and pathologic CAD (+) group: 45 (54.2%). Results: There were no significant differences in clinical characteristics, conventional 2D echocardiography between the two groups at rest and during low dobutamine dose. Regional postsystolic index (PSI) during recovery phase had the highest area under the receiver operating characteristic curve (AUC) (AUC 0.882, sensitivity 87%, specificity 92%) for the detection of functionally significant one-vessel disease. During high dobutamine dose, regional PSI had sensitivity 78% and specificity 81% (AUC 0.78) to detect significant CAD. Regional PSI remained the same tendency remains for the detection of multiple-vessel CAD. Other myocardial deformation parameters were less sensitive and specific during high dobutamine dose and recovery phase. Conclusions: PSS parameters showed to be sensitive and specific in detecting hemodynamically significant coronary artery stenosis in patients with stable CAD with moderate pretest probability. The study revealed that the assessment of regional PSI performed during recovery improves the diagnostic accuracy of DSE for the detection of functionally significant CAD.

Keywords: Adenosine stress magnetic resonance imaging, speckle tracking imaging, stable coronary artery disease, stress echocardiography

INTRODUCTION

Despite therapeutic advances, the optimal diagnostic and treatment strategy of coronary artery disease (CAD) remains controversial. The decision about the management of stable CAD should rely on the hemodynamic significance of coronary artery stenosis. Invasive coronary artery angiography (CAA) is believed to be the gold standard to detect coronary artery stenosis, but it does not show functionally significant CAD. Dobutamine stress echocardiography (DSE) is a widely accepted and cost-effective noninvasive clinical test with established diagnostic accuracy to detect left ventricle (LV) myocardial ischemia, myocardial viability and extent of scar. However, the accuracy of the DSE method strongly depends on the operator experience and interpretation. Recent clinical studies proposed postsystolic shortening (PSS) parameters as important markers of LV myocardial ischemic memory. The main goal of this manuscript was to evaluate the sensitivity and specificity of the PSS measured by speckle-tracking echocardiography (STE) during DSE for the detection of functionally significant CAD.

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### METHODS

#### Study population

We prospectively enrolled 83 patients who were referred to the Department of Cardiology of Lithuanian University of Health Sciences for investigation of stable chest pain and had moderate pretest probability of obstructive CAD. The risk was assessed according to clinical pretest probability score: The type of chest pain (typical angina, atypical angina, and nonchest pain), age, and sex was evaluated. The study was approved by the regional bioethics committee and all patients gave written informed consent. The study protocol included DSE, myocardial perfusion imaging by cardiac magnetic resonance (CMR-MPI), and invasive CAA. CMR-MPI and invasive CAA were performed on average 4 ± 1 weeks after DSE. Patients’ inclusion criteria were adult age, patients with a moderate pretest probability of CAD, LV ejection fraction (EF) ≥55% measured by echocardiography at rest. Patients’ exclusion criteria were poor echocardiography image quality, patients with previous myocardial infarction or unstable angina pectoris, patient with a history of coronary artery bypass surgery or percutaneous coronary intervention, significant valve pathology; atrial fibrillation/flutter, conduction disturbances, severe renal impairment (estimated glomerular filtration rate ≤30 ml/min/1.73 m²), contraindications to CMR-MPI (heart pacemaker or defibrillator, metal implants, claustrophobia), and iodine allergy.

Patients were divided into two main groups: Patients assigned to pathological (CAD [+]) group, who had at least one hemodynamically significant stenosis, whose hemodynamic significance was confirmed by the presence of a perfusion defect detected by the CMR-MPI. Patients, who have been classified without having hemodynamically significant CAD, were assigned into a nonpathological group (CAD [−]).

#### Image acquisition and analysis

All patients were imaged in the left lateral decubitus position using a commercially available system (Vivid 7, GE Healthcare, Horten, Norway) with a 1.5–4.6 MHz transducer. Standard two-dimensional (2D) images and Doppler data were acquired from parasternal long and short axis views and apical (four, three, and two chambers) views, which were acquired at rest, at a dobutamine dose of 20 mg/kg/min, at peak stress, and early recovery 1 min after stress. DSE was performed using a standard protocol. Beta-blockers were discontinued 48 h, nitrates-12 h before the study.

#### Speckle-tracking echocardiography analysis

Off-line speckle-tracking analysis (EchoPac, GE Healthcare, Horten, Norway) was performed using images obtained during DSE. To achieve optimal imaging quality for subsequent analyses, frame rate ranged from 60 to 90 frames per second. To ensure correct tracking of speckles investigator visually assessed the automatically defined region of interest (ROI). If speckles were inadequately visualized, the ROI was manually readjusted. Average strain values were calculated for the whole LV (global) and for the myocardial regions subtended by major coronary arteries (left anterior descending, left circumflex, or right coronary artery). Stenosis in the left main coronary artery was considered to affect both the left anterior descending and left circumflex coronary artery regions.

The postystolic strain was derived from the difference between the strain at aortic valve closure (AVC) (the end of ejection time) and the postystolic peak of the longitudinal strain (PLS) curve. The postystolic index (PSI) was derived from the strain curve, as follows: ((Maximum strain in cardiac cycle − peak systolic strain)/[maximum strain in cardiac cycle]) × 100. For analysis, the average of PSI from all myocardial walls was used. PSS was assessed qualitatively and regarded as present if postystolic strain index was >20%. This cut off value was based on the previous evidence evaluating PSS.[8,9]

#### Cardiac magnetic resonance

CMR images were acquired using a 1.5 T MRI scanner (Magnetom Aera, Siemens AG Healthcare, Erlangen, Germany) with a dedicated 18-channel phased-array receiver coil in the supine position. Cine images were obtained with a balanced steady-state-free precession (bSSFP) sequence in three long-axis views, followed by a contiguous stack of short-axis views covering the entire LV from base to apex. The following imaging parameters were used: Repetition time (TR) =5.1 ms, echo time (TE) =1.3 ms, flip angle = 80°, in-plane spatial resolution 0.9 mm × 0.9 mm with a slice thickness of 8 mm and 25 phases per cardiac cycle. First-pass stress perfusion imaging was performed using a saturation-recovery prepared bSSFP sequence (TR = 2.5 ms, TE = 1.3 ms, flip angle = 12° and voxel size 2.4 mm × 2.4 mm × 8.0 mm) over 50 consecutive heart beats. The images were acquired after 4 min of 140 µg/kg/min adenosine infusion and high rate injection of 0.1 mmol/kg gadobutrol (Gadovist®, Bayer Schering Pharma AG, Berlin, Germany). In cases of the inadequate hemodynamic response, the adenosine dose was increased up to 210 µg/kg/min.[10] Rest first-pass perfusion images were acquired >15 min after stress perfusion imaging. The late gadolinium enhancement (LGE) images were obtained 10 min after gadolinium injection in long-and short-axis planes. Cine and LGE images were acquired at the identical long- and short-axis orientation.

All images were analyzed using dedicated software (Syngo. via, Siemens AG Healthcare, Erlangen, Germany) following a recent consensus document for quantification of LV function and mass using CMR.[11] Perfusion defects were defined as subendocardial or transmural visually dark myocardial areas when compared with remote myocardium, persisting for at least 10 frames. The stress and rest perfusion scans were reviewed simultaneously, and areas of hypoperfusion were assigned to the ventricular segments, using the standard American Heart Association 18-segment model.[12] Myocardial tissue was considered infarcted if the signal intensity on LGE images was >5 standard deviations above that of the remote myocardium.
Invasive coronary angiography

After DSE and CMR-MPI all patients underwent invasive CAA. Angiography was performed using a standard protocol with a minimum of two projections obtained per vessel. Angiographic data were analyzed by two experienced investigators blinded to the DSE and CMR-MPI results.

Statistical methods and analysis

Statistical analysis was performed using the SPSS version 25.0 (IBM, Armonk, NY, USA) software package. Categorical variables were expressed with their frequency and relative frequency rate (%). Categorical variables homogeneous distribution was evaluated by the Chi-square ($\chi^2$) test ($\chi^2$ or Fisher’s exact test – in case of small expected values). For comparison of continuous variables, the Mann–Whitney U, Student’s t-test, paired Student’s t-test, and nonparametric Kruskal–Wallis test were used.

The time between AVC and PLS and PSI as CAD indicators was evaluated using receiver operating characteristic (ROC) curves. A subject was assessed as positive or negative according to whether the parameter value was greater, less or equal to a given cut off value. Associated with any cut off value was the probability of a true positive (sensitivity) and a true negative (specificity). A used index of accuracy is the area under the ROC curve (AUC), with values close to 1.0 indicating high diagnostic accuracy.

Intra-observer and inter-observer variability values were calculated as the absolute difference between the corresponding two measurements as a percentage of the mean.

Results

Study population

The current study group consisted of 83 individuals (55% men). Based on CMR-MPI and CAA outcomes, patients were divided into groups: The nonpathologic CAD (–) group: 38 (46%) and pathologic CAD (+) group: 45 (54%). Detailed clinical characteristics are demonstrated in Table 1. Fifty-one (61.4%) patients had pathologic and 32 (38.6%) patients – nonpathologic DSE results. The sensitivity and specificity of DSE to detect hemodynamically significant coronary artery stenosis was 78% and 83%, respectively. LV EF was normal and did not differ in both pathologic and nonpathologic groups. Other conventional echocardiographic parameters did not differ between groups and all parameters were within the normal range [Table 2].

Cardiac magnetic resonance-myocardial perfusion imaging findings

CMR-MPI was performed to validate perfusion defects. Conventional CMR measurement results are presented in

| Characteristics | CAD (−) group | CAD (+) group | P |
|-----------------|---------------|---------------|---|
| LVEDD (mm) (+SD) | 45.4±5.3 | 46.5±6.9 | 0.74 |
| LVEDV index (mm/m²) (+SD) | 23.1±2.5 | 23.6±3.5 | 0.71 |
| LVESD (mm) (+SD) | 32.6±6.3 | 30.2±5.7 | 0.36 |
| LVESD index (mm/m³) (+SD) | 16.7±3.5 | 15.6±3.5 | 0.43 |
| LVEDV (mL) (+SD) | 93.5±25.7 | 89.5±25.4 | 0.32 |
| LVESV (mL) (+SD) | 45.6±10.4 | 44.8±13.3 | 0.74 |
| LVEF (%) (+SD) | 38.4±14.5 | 36.7±15.3 | 0.42 |
| Mm (g/m²) (+SD) | 19.5±6.6 | 18.4±7.0 | 0.46 |
| IVS (mm) (+SD) | 59.3±6.1 | 60.4±6.5 | 0.64 |
| Wt (±SD) | 84.3±20.4 | 79.8±20.1 | 0.54 |
| RWT (±SD) | 0.37±0.11 | 0.39±0.13 | 0.71 |
| PW (±SD) | 11.4±3.2 | 12.4±4.3 | 0.68 |
| E/A ratio* (±SD) | 0.9±0.3 | 0.9±0.4 | 0.61 |
| E peak rate (m/sec) (±SD) | 60.5±14.4 | 64.6±18.5 | 0.43 |
| A peak rate (m/sec) (±SD) | 70.3±25.1 | 74.4±12.4 | 0.11 |
| e' lateral (m/sec) (±SD) | 9.2±1.6 | 9.4±2.4 | 0.62 |
| e' septal (m/sec) (±SD) | 7.7±1.7 | 9.0±5.5 | 0.44 |
| E/e' (±SD) | 3.3±1.3 | 4.1±2.1 | 0.26 |
| DT (ms) (+SD) | 273.4±55.1 | 270.9±92.1 | 0.49 |
| LA volume (mL/m²) (+SD) | 28.2±4.3 | 29.8±3.5 | 0.33 |

*Median (Q1;Q3). A=Left atrial systolic velocity; DT=Deceleration time; E=Early diastolic transmural flow velocity; e'=Early diastolic mitral annular velocity; E/e'=Early diastolic transmitral flow velocity and early diastolic mitral annular velocity; EA=Early diastolic transmural flow velocity (E) and atrial systolic velocity (A) ratio; IVS=Interventricular septum; LA=Left atrium; LVEDD=Left ventricular end-diastolic diameter; LVEDV=Left ventricular end-diastolic volume; LVEF=Left ventricular ejection fraction; LVESD=Left ventricular end-systolic diameter; PW=Posterior wall; LVESV=Left ventricular end-systolic volume; MMI=Myocardial mass index; RWT=Relative wall thickness; WMISI=Wall motion score index; CAD=Coronary artery disease; ACE=Angiotensin-converting-enzyme; ARB=Angiotensin II receptor blockers.
Table 3: Conventional cardiac magnetic resonance parameters

| Characteristics                        | CAD (−) group | CAD (+) group | P   |
|----------------------------------------|---------------|---------------|-----|
| LVEDD (mm) (±SD)                       | 43.6±5.1      | 45.8±5.2      | 0.47|
| LVESD (mm) (±SD)                       | 34.8±6.3      | 35.5±6.5      | 0.68|
| MMI (g/m²) (±SD)                       | 82.8±18.7     | 80.6±20.6     | 0.63|
| LVEF (%) (±SD)                         | 59.4±6.3      | 60.8±6.9      | 0.74|
| LV diastolic volume index (ml/m²) (±SD)| 74.2±18.9     | 80.6±20.2     | 0.32|
| LV systolic volume index (ml/m²) (±SD) | 31.4±6.4      | 32.7±7.3      | 0.67|
| LV systolic volume (ml) (±SD)          | 96.7±21.1     | 101.6±23.5    | 0.34|
| LA area (cm²) (±SD)                    | 24.6±4.8      | 23.4±4.4      | 0.69|

CAD=Coronary artery disease, LA=Left atrium, LV=Left ventricular, LVEDD=Left ventricular end-diastolic diameter, LVEF=Left ventricular ejection fraction, LVESD=Left ventricular end-systolic diameter, MMI=Myocardial mass index, SD=Standard deviation

Table 4: Characteristics of coronary arteries stenosis on invasive coronary artery angiography among study patients

| Characteristics                        | CAD (n=47) |
|----------------------------------------|------------|
| One-vessel disease, n (%)              | 26 (55.3)  |
| Two-vessel disease, n (%)              | 14 (29.8)  |
| Three-vessel disease, n (%)            | 7 (14.9)   |
| Location of stenosis, n (%)            |            |
| Right coronary artery                  | 18 (38.3)  |
| Left main coronary artery              | 4 (8.5)    |
| Left circumflex artery                 | 13 (27.7)  |
| Left anterior descending artery        | 28 (59.6)  |

CAD=Coronary artery disease

Table 5: Global post systolic index during different stages of dobutamine stress echocardiography in Coronary artery disease (−) and Coronary artery disease (+) groups

| Variables                              | CAD (−) group | CAD (+) group | P   |
|----------------------------------------|---------------|---------------|-----|
| Global PSI at rest (%)                 |               |               |     |
| One-vessel disease                     | 4.07±1.37     | 4.59±3.04     | 0.32|
| Multiple-vessel disease                | 4.33±1.58     | 4.89±2.56     | 0.43|
| Left anterior descending artery disease| 4.77±1.62     | 5.29±2.11     | 0.24|
| Right coronary artery disease          | 4.43±1.82     | 5.41±2.34     | 0.27|
| Circumflex artery disease              | 4.94±1.77     | 5.61±2.74     | 0.51|
| Global PSI at low dobutamine doses (%) |               |               |     |
| One-vessel disease                     | 4.42±1.79     | 5.96±3.14     | 0.22|
| Multiple-vessel disease                | 4.59±1.65     | 5.48±2.31     | 0.53|
| Left anterior descending artery disease| 4.98±1.68     | 6.89±2.58     | 0.14|
| Right coronary artery disease          | 4.71±1.70     | 6.11±2.44     | 0.24|
| Circumflex artery                      | 4.98±1.86     | 5.88±2.17     | 0.66|
| Global PSI at high dobutamine doses (%)|               |               |     |
| One-vessel disease                     | 5.23±1.96     | 10.46±3.42    | 0.02|
| Multiple-vessel disease                | 6.26±2.48     | 10.72±3.17    | 0.03|
| Left anterior descending artery disease| 6.12±2.18     | 10.88±3.47    | 0.02|
| Right coronary artery                  | 6.24±2.33     | 11.21±3.41    | 0.008|
| Circumflex artery                      | 6.48±2.46     | 8.12±3.32     | 0.17|
| Global PSI at recovery (%)             |               |               |     |
| One-vessel disease                     | 4.32±1.93     | 9.42±4.12     | 0.01|
| Multiple-vessel disease                | 4.78±1.64     | 9.75±3.24     | 0.02|
| Left anterior descending artery disease| 5.14±2.41     | 10.02±3.27    | 0.01|
| Right coronary artery                  | 5.47±2.31     | 10.34±3.48    | 0.02|
| Circumflex artery                      | 6.38±2.76     | 7.98±3.22     | 0.24|

CAD=Coronary artery disease, PSI=Post-systolic index

No significant differences were found of conventional parameters between the groups. After CMR-MPI, perfusion defects were found in 45 (52%), meanwhile, no defects in 41 (48%) patients. Although 3 patients had ≥70% stenosis on CAA, they had no perfusion defects when evaluated by CMR-MPI and they there excluded from the study. The 27 (60%) patients had perfusion defects in the left anterior descending coronary artery territory, 12 (27%) in the left circumflex artery territory, and 18 (40%) in the right coronary artery territory.

Coronary artery angiography results

CAA detected stenosis ≥70% in 61 vessels (47 patients). In the 4 cases, CAA confirmed ≥50% stenosis of the left main stem. Single-vessel disease dominated by the left anterior descending artery. The distribution of diseased coronary arteries in the pathologic CAD (+) group is shown in Table 4.

Speckle-tracking echocardiography analysis

Post systolic shortening parameters at rest

Global, regional PSI and time between AVC and PLS with and without CAD during the rest phase are shown in Tables 5-7. There was no difference between the pathologic and nonpathologic groups during the rest.

Post systolic shortening parameters at low dobutamine doses

After the low dobutamine doses injection, the differences of the groups were not detected among the analyzed parameters [Tables 5-7].

Post systolic shortening parameters at peak stress

At high dobutamine doses, global PSI became significantly higher in one- and multiple-vessel disease in CAD (+) group patients compared with nonpathologic CAD (−) group [Table 5]. The same tendency was found in regional PSI [Table 6]. The time between AVC and PLS demonstrated a significant difference between the groups only in one-vessel disease [Table 7]. Global and regional PSS parameters were specific to establish the difference of the left anterior descending and right coronary arteries disease.

Post systolic shortening parameters at the recovery phase

During the recovery phase, global PSI remained significantly higher in pathologic CAD (+) [Table 5]. The same tendency
was found in regional PSI [Table 6]. Results show that differences of one-and multiple-vessel disease increased between the patients, with and without hemodynamically significant stenosis, during the recovery phase compared with high dobutamine stress in all examined parameters (especially in regional PSI of one-vessel disease). Furthermore, results of an investigation performed on the left anterior descending and right coronary arteries demonstrated significant differences between the groups in all parameters during the recovery phase.

**Comparison of global, regional postsystolic index, and time between aortic valve closure and peak of the longitudinal strain diagnostic accuracy to detect significant coronary artery disease**

Regional PSI at high dobutamine doses had the greatest AUC for both one-and multiple-vessel disease during the high dobutamine doses with AUC of 0.751. Compared with global PSI and time between AVC and PLS, regional PSI had the best diagnostic value for the left anterior descending artery disease (AUC 0.774) and right CAD (AUC 0.722) [Table 9].

To detect one-vessel disease, regional PSI had the highest AUC of 0.882 with sensitivity 87%, specificity 92% [Figure 1] during recovery and was even more precise compared to high dobutamine doses (AUC 0.784). Other parameters, following time between AVC and PLS (AUC 0.838) and global PSI (AUC 0.826) was less accurate [Figure 1]. The regional PSI (AUC 0.773) and global PSI (AUC 0.762) were more precise methods compared to the time between AVC and PLS (AUC 0.740) to detect multiple-vessel disease.
Moreover, regional PSI (AUC 0.840) and time between AVC and PLS (AUC 0.791) display better prognostic results than the global PSI (AUC 0.786) for detecting left anterior descending artery disease. During the recovery phase, PSS parameters of stenosis measured in the left anterior descending artery showed more significant prognostic value compared with measurement performed during the high doses of dobutamine.

Intra-observer and inter-observer variability of postsystolic shortening parameters

Inter-observer variability of global PSI, regional PSI and time between AVC and PLS were 5.3%, 5.9%, and 5.5% at rest, 6.4%, 7.0%, and 6.6% at peak stress, and 5.5%, 6.2%, and 6.0% at recovery. Intraobserver variability of global PSI, regional PSI, and time between AVC and PLS was 4.9%, 5.4%, and

### Table 8: ROC analysis of post-systolic index in Dobutamine stress echocardiography during high dobutamine doses and recovery

| Strain, SR parameters | Cut off value (%) | Sensitivity (%) | Specificity (%) | AUC | P  |
|-----------------------|-------------------|----------------|-----------------|-----|----|
| **Global PSI**        |                   |                |                 |     |    |
| At high dobutamine doses |                  |                |                 |     |    |
| One-vessel disease    | 6.46              | 70             | 74              | 0.724 | 0.04 |
| Multiple-vessel disease | 6.97             | 66             | 75              | 0.712 | 0.04 |
| Left anterior descending artery disease | 6.85 | 72           | 77              | 0.755 | 0.03 |
| Right coronary artery  | 6.53              | 69             | 73              | 0.714 | 0.03 |
| Circumflex artery     | 6.67              | 62             | 65              | 0.678 | 0.12 |
| At recovery            |                   |                |                 |     |    |
| One-vessel disease    | 5.56              | 82             | 77              | 0.826 | 0.01 |
| Multiple-vessel disease | 5.89             | 73             | 79              | 0.762 | 0.03 |
| Left anterior descending artery disease | 6.42 | 76           | 74              | 0.786 | 0.02 |
| Right coronary artery  | 6.22              | 70             | 73              | 0.720 | 0.04 |
| Circumflex artery     | 6.41              | 66             | 62              | 0.686 | 0.12 |
| **Regional PSI**      |                   |                |                 |     |    |
| At high dobutamine doses |                  |                |                 |     |    |
| One-vessel disease    | 6.82              | 78             | 81              | 0.784 | 0.02 |
| Multiple-vessel disease | 7.45             | 73             | 77              | 0.751 | 0.03 |
| Left anterior descending artery disease | 7.38 | 76           | 83              | 0.774 | 0.01 |
| Right coronary artery  | 7.17              | 72             | 74              | 0.722 | 0.04 |
| Circumflex artery     | 6.72              | 68             | 64              | 0.694 | 0.09 |
| At recovery            |                   |                |                 |     |    |
| One-vessel disease    | 6.76              | 87             | 92              | 0.882 | <0.001 |
| Multiple-vessel disease | 6.92             | 79             | 85              | 0.773 | 0.02 |
| Left anterior descending artery disease | 6.68 | 76           | 81              | 0.840 | 0.01 |
| Right coronary artery  | 6.37              | 71             | 68              | 0.734 | 0.02 |
| Circumflex artery     | 6.43              | 65             | 60              | 0.668 | 0.17 |

AUC=Area under the curve, PSI=Post-systolic index

### Table 9: ROC analysis of Time between Aortic valve closure and Peak longitudinal strain in Dobutamine stress echocardiography during high dobutamine doses and recovery

| Strain, SR parameters | Cut off value(ms) | Sensitivity (%) | Specificity (%) | AUC | P  |
|-----------------------|-------------------|----------------|-----------------|-----|----|
| **At high dobutamine doses** |                  |                |                 |     |    |
| One-vessel disease    | 99.79             | 73             | 79              | 0.763 | 0.03 |
| Multiple-vessel disease | 98.46             | 64             | 67              | 0.642 | 0.23 |
| Left anterior descending artery disease | 96.63 | 69           | 78              | 0.748 | 0.03 |
| Right coronary artery  | 90.14             | 58             | 63              | 0.627 | 0.31 |
| Circumflex artery     | 85.98             | 52             | 54              | 0.587 | 0.44 |
| **At recovery**       |                   |                |                 |     |    |
| One-vessel disease    | 101.43            | 82             | 90              | 0.838 | 0.002 |
| Multiple-vessel disease | 99.67             | 74             | 83              | 0.740 | 0.02 |
| Left anterior descending artery disease | 100.19 | 78           | 83              | 0.791 | 0.01 |
| Right coronary artery  | 96.16             | 70             | 76              | 0.716 | 0.03 |
| Circumflex artery     | 86.95             | 55             | 63              | 0.614 | 0.42 |

AUC=Area under the curve
4.8% at rest, 5.6%, 6.1%, and 5.4% at peak stress, and 5.5%, 6.5%, and 4.9% at recovery, respectively.

**Discussion**

We prospectively studied the value of 2D STE PSS parameters in the detection of hemodynamically significant myocardial ischemia in patients with an intermediate pretest probability of CAD. The main finding of our research was that PSS parameters, especially at the recovery phase, are specific and sensitive methods to define the CAD in patients with an estimated intermediate probability of CAD. Furthermore, our study shows that the regional PSI during the recovery stage had the strongest diagnostic value to detect myocardial ischemia.

Echocardiographic parameters to detect global and regional systolic myocardial deformation during DSE in patients with CAD have been evaluated and presented in previous studies. However, DSE is believed to be a significant amount of time and experienced professionals requiring noninvasive diagnostic methods, which approach into clinical practice is still doubtful. According to Liou et al., meta-analysis results, LV deformation measurements performed at rest show only average clinical value for the diagnosis of significant stable CAD. However, only a few small reports were made about the accuracy of LV deformation parameters during the recovery phase. Our results support the results from previous studies indicating that PSS parameters during DSE are useful for the detection of hemodynamically significant CAD. Voigt et al. suggested that strain rate (as a parameter to detect PSS) can be used for the detection of myocardial ischemia as a prognostic parameter (AUC 0.95) and is proven to be more precise compared with myocardial tissue velocity imaging (AUC 0.77). Certainly, the different method that was used to define functionally significant CAD in these studies, could have contributed to the differences between the present study and results reported by Voigt et al. They used CAA to detect the coronary stenoses, meanwhile, in our study, all patients had confirmation of hemodynamically significant coronary stenoses measured by CMR-MPI. According to the latest meta-analysis, CMR-MPI has the highest performance for the diagnosis of functionally significant CAD, confirmed by FFR. Both studies showed similar features, however, different justification criteria were used to establish the diagnosis. Even though the authors found...
the high prognostic value of parameters measured during high dobutamine doses, they did not submit the results at the recovery phase. Our study results suggest that regional PSI had a higher diagnostic accuracy to detect CAD if measured during recovery than during the high-dobutamine dose (AUC 0.882 vs. 0.784; compared to one-vessel disease). Furthermore, while comparing strain measurements from different studies, we should take into consideration the intervendor differences in accuracy. Oana Mirea et al.[21] propose that to distinguish differences between segments with and without scar among vendors, accuracy range from poor to excellent (AUC between 0.68 and 0.85).

Previous researchers[22-24] established that PSI and time between AVC and PLS are sensitive, however, not specific parameters to detect hemodynamically significant CAD.[6,25] Along with the conventional DSE, our results suggest that the assessment of PSS by STE during recovery phase should be considered in the daily practice, as it provides a noninvasive technique for defining patients with functionally significant CAD, moreover, the diagnostic accuracy of PSS may result in decreased number of invasive CAA for stable CAD patients.[26] Ozawa et al.[26] in their study evaluated PSI and time between AVC and PLS as prognostic markers to detect significant CAD. They defined groups using the criteria of pathologic PSS. The time between AVC and PLS had relatively low prognostic value with AUC 0.55, meanwhile, PSI had AUC 0.68. Authors of this study agree that LV hypertrophy, ventricular overload is associated with clearly reduced PSS parameters and could influence their results, as these factors, as well reduced LVEF, were already indicated previous research.[24] However, Uusitalo et al.[27] managed to prepare a study protocol that excluded patients who might distort the data. Therefore, their results of global and regional PSI can be compared with the study we performed (thus the exclusion criteria were likewise ours). Regional PSI at Uusitalo et al. investigation was 9.8% ± 9.6%, very similar to our study-10.32% ± 5.41%. The standard deviation indicates that the study had a relatively small number of patients. Even though present outcomes proved regional PSI prognostic value to define the CAD in patients with an intermediate pretest probability of CAD, the ROC analysis of Uusitalo et al.’s study displayed that increased PSI at recovery provided the best AUC for detection of significant coronary stenosis (AUC 0.72). Our performed analysis showed greater AUC value-0.882. Uusitalo et al. compared the conventional DSE and strain-based measurements during DSE and concluded that one-vessel-based analysis, strain, PSI, and visual analysis of wall motion provided comparable diagnostic accuracy, whereas the combination of strain or PSI with visual analysis provided incremental value over visual analysis alone. The study that we performed suggest that PSS parameters, especially regional PSI, offers high accuracy on the one-vessel-based analysis, not to mention the significance for detection of multi-vessel disease.

Study limitations

First, one of the main limitations of this study was that the protocol did not include FFR as a reference standard for the functional assessment of coronary artery stenosis. Thus, the analysis relied on a CMR-MPI for the evaluation of the functional severity of coronary stenosis. Second, this was a single-center nonrandomized study with a small number of patients (N = 83) and the significance should be tested in a multi-center, randomized cohort. Furthermore, the contrast imaging during DSE, which could improve the diagnostic value, was not used in the analysis. As well, isolated evaluation of the left circumflex artery was complicated due to the multiple stenoses of other vessels, therefore, the analysis results of this artery are not significant in our study.

Conclusions

During the recovery phase, PSS parameters demonstrated to be sensitive and specific to the exposure of CAD. The regional postystolic strain index has the strongest diagnostic value for the detection of functionally significant stenoses. Consequently, the assessment of strain performed during and after dobutamine stress is valuable due to the improving diagnostic accuracy and guiding a decent treatment of obstructive CAD.

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Conflicts of interest

There are no conflicts of interest.

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