Two-Dimensional Speckle-Tracking during Dobutamine Stress Echocardiography in the Detection of Myocardial Ischemia in Patients with Suspected Coronary Artery Disease

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Background: Two-dimensional speckle-tracking applied to dobutamine stress echocardiography (DSE) may aid in the detection of coronary artery disease (CAD). The aim of this study was to determine the value of strain, strain rate, and postsystolic strain index (PSI) measured by speckle-tracking during DSE in the evaluation of the presence, extent, and severity of myocardial ischemia.

Methods: Fifty patients 63 ± 7 years of age with intermediate probability of CAD were prospectively recruited. All patients underwent DSE, quantitative positron emission tomographic perfusion imaging, and invasive angiography. Regional peak systolic longitudinal strain, strain rate, and PSI were measured at rest, at a dobutamine dose of 20 μg/kg/min, at peak stress, and at early recovery (1 min after stress). Obstructive CAD was defined as >75% stenosis or 40% to 75% stenosis combined with either fractional flow reserve < 0.80 or abnormal findings on myocardial perfusion positron emission tomography.

Results: Obstructive CAD was detected in 22 patients and in 36 of 150 coronary arteries. Strain analyses showed the highest reproducibility at rest, at a dobutamine dose of 20 μg/kg/min, and at early recovery. Increased PSI and reduced strain during early recovery were the strongest predictors of obstructive CAD and were associated with the extent, localization, and depth of myocardial ischemia by positron emission tomography. On 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.

Conclusions: Assessment of systolic or postsystolic strain by speckle-tracking echocardiography during early recovery after DSE can help in the detection of hemodynamically significant coronary stenosis compared with visual wall motion analysis alone. (J Am Soc Echocardiogr 2016;■:■-■.)

Keywords: Speckle-tracking, Coronary artery disease, Dobutamine stress echocardiography, Myocardial perfusion imaging, Postsystolic strain

Dobutamine stress echocardiography (DSE) is a well-established imaging modality in the detection of coronary artery disease (CAD) on the basis of regional wall motion abnormalities induced by myocardial ischemia.[1,2] Numerous studies have shown the high accuracy and prognostic value of DSE for obstructive CAD.[1,2] However, wall motion analysis during DSE is subjective, and considerable expertise is required to achieve the published levels of accuracy.

Quantitative analysis of myocardial deformation by strain and strain rate (SR) imaging may help in the detection of ischemic wall motion abnormalities during DSE.[3-5] Two-dimensional (2D) speckle-tracking enables the quantification of myocardial deformation on frame-to-frame tracking of ultrasonic speckles in grayscale images with automated software.[6-9] In addition to ease of application and angle independence, the strength of speckle-tracking compared with Doppler tissue imaging is that strain can be measured in any direction within the imaging plane.[7-9] Despite a lower frame rate compared with Doppler techniques, experimental validation has shown good agreement between speckle-tracking strain and sonomicrometry at high heart rates during dobutamine stress.[8] Furthermore, experimental and clinical studies have indicated potential value for 2D speckle-tracking strain and SR during DSE in the detection of CAD.[8-12] In addition to systolic deformation, postsystolic shortening has been proposed as a sensitive marker of myocardial ischemia.[13] However, previous studies have been limited by the use of an anatomic

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Abbreviations

AUC = Area under the curve

CAD = Coronary artery disease

CV = Coefficient of variation

DSE = Dobutamine stress echocardiography

FFR = Fractional flow reserve

PET = Positron emission tomographic

PSI = Postsystolic strain index

ROC = Receiver operating characteristic

SR = Strain rate

2D = Two-dimensional

angiographic definition of CAD (i.e., >50% or >75% stenosis)[10,11] or small sample size.[12] Therefore, there is a need for studies validating regional systolic and postsystolic strain measured by speckle-tracking during different phases of DSE for the detection of functionally significant CAD and severity of myocardial ischemia. We hypothesized that speckle-tracking can provide incremental diagnostic information and increase the sensitivity to conventional wall motion analysis during DSE in the evaluation of patients with suspected CAD.

We prospectively compared the value of systolic strain, SR, postsystolic strain, and visual wall motion analysis in the detection of myocardial ischemia during DSE in patients with intermediate pretest probability of CAD.[14] All patients underwent invasive coronary angiography with fractional flow reserve (FFR) and positron emission tomographic (PET) myocardial perfusion imaging to detect significant CAD. Furthermore, the extent and severity of myocardial ischemia were assessed using quantitative PET perfusion. Obstructive CAD was defined as >75% stenosis or in the presence of intermediate stenosis (40%-75%) as FFR ≤ 0.80 or in the absence of FFR measurement as abnormal myocardial perfusion by PET.

METHODS

Study Population and Design

We prospectively recruited 52 patients who were referred for investigation of stable chest pain and had intermediate pretest likelihood of obstructive CAD on the basis of the type of symptoms, age, sex, and findings on exercise electrocardiography from 2009 to 2013.[14,15] The referring centers were informed of the exclusion criteria of the study, which were age <30 or >75 years, low or high pretest probability of CAD, pregnancy, acute coronary syndrome, known diagnosis of CAD, ejection fraction <35%, asthma, significant valvular disease, congenital heart disease, cardiomyopathy, severe hypertension, recent (<6 months) cerebral ischemic attack, active cancer, persistent atrial fibrillation, and atrioventricular block. The study was performed according to the Declaration of Helsinki and was approved by the local ethics committee, and each patient gave written informed consent.

The study protocol included DSE, PET perfusion imaging during adenosine stress, and invasive coronary angiography, which was performed on average 5 ± 3 weeks after DSE. One patient was excluded because of a poor echocardiographic window and one because of known CAD. Thus, the final study group consisted of 50 patients, whose clinical characteristics are presented in Table 1.

Table 1 Clinical characteristics of patients (n = 50)

Variable	Value
Men	26 (52%)
Age (y)	63 ± 7
Patients with CAD	22 (44%)
One-vessel disease	12 (24%)
Two-vessel disease	6 (12%)
Three-vessel disease	4 (8%)
Obstructive coronary stenoses	36 (24%)
Stenosis > 75%	19 (52%)
FFR < 0.8 and 40%–75% stenosis	5 (14%)
Ischemic PET and 40%–75% stenosis	12 (33%)
Location of stenosis	
LM	1 (3%)
LAD	14 (39%)
Proximal or middle	10 (71%)
Distal	4 (29%)
LCX	9 (25%)
Proximal or middle	7 (78%)
Distal	2 (22%)
RCA	11 (31%)
Proximal or middle	7 (64%)
Distal	4 (36%)
Risk factors	
Hypertension	29 (58%)
Hypercholesterolemia	31 (62%)
Diabetes	7 (14%)
Current smoker/previous smoker	4 (8%)/8 (16%)
Family history of CAD	7 (14%)
Medication	
Aspirin	38 (76%)
β-blocker	33 (66%)
Statin	40 (80%)
ACE inhibitor/ARB	23 (46%)
Calcium channel blocker	7 (14%)
Long-acting nitrate	2 (4%)

ACE, Angiotensin-converting enzyme; *ARB*, angiotensin receptor blocker; *LAD*, left anterior descending coronary artery; *LCX*, left circumflex coronary artery; *LM*, left main coronary artery; *RCA*, right coronary artery.
Data are expressed as number (percentage) or as mean ± SD.

Dobutamine Stress Echocardiography

DSE was performed using a standard staged protocol.[2] Dobutamine was infused through a peripheral infusion line intravenously with a mechanical pump starting at dose of 10 μg/kg/min. The dose was increased at 3-min intervals to 20, 30, and 40 μg/kg/min with intravenous atropine up to 2 mg given if necessary to augment the heart rate response. Blood pressure and electrocardiogram were monitored continuously. Criteria for terminating the test were achieving a target heart rate response of 85% of the age-predicted maximum, development of wall motion abnormality, angina pectoris, severe ischemic electrocardiographic changes, systolic blood pressure >240 mm Hg, abnormal blood pressure reaction during stress, or significant arrhythmia. Beta-blockers were withdrawn for 2 days and long-acting nitrates the morning of the study.