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Original article

Prediction of coronary artery stenosis using strain imaging diastolic index at rest in patients with preserved ejection fraction

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Summary
Background: Post-ischemic myocardial diastolic stunning persists for a long time after transient ischemia even after systolic function has recovered. We sought to identify coronary artery stenosis in clinical patients using strain imaging diastolic index (SI-DI) at rest.
Methods: We retrospectively examined 85 patients with suspected coronary artery disease and preserved ejection fraction (EF; >50%) who underwent both echocardiography and coronary angiography. Speckle tracking strains were measured in 3 apical views and parasternal left ventricular (LV) short-axis views at the papillary muscle level. LV segments with inadequate image quality and deficit segments in the movie were excluded by the blinded observer. After strain analysis, LV segments were classified into no stenosis (≤50%), mild stenosis (51—75%), and severe stenosis (>75%) groups on the bases of the coronary angiogram.
Results: SI-DI decreased significantly in severe stenosis segments ($p < 0.05$, ANOVA), but none of the peak strains showed significant difference. The area under the curve for predicting severe stenosis in radial, longitudinal, and transverse SI-DI was 0.72, 0.74, and 0.80, respectively. A cut-off value of 49 for transverse SI-DI can predict LV segments with severe stenosis with sensitivity of 0.79 and specificity of 0.73. A screening cut-off value of 63 for transverse SI-DI shows sensitivity of 0.95 and specificity of 0.50.

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Conclusion: SI-DI at rest is a novel marker in predicting coronary stenosis even in patients with preserved EF. This index can be used to screen patients with suspected coronary artery disease in routine echocardiography and does not require stress provocation.

Introduction

Echocardiographic detection of coronary artery disease usually requires stress tests because visible systolic dysfunction is not always evident at rest, unless myocardial infarction is present [1—3]. Recently, use of strain imaging derived from 2D speckle tracking analysis has been validated for quantitative evaluation of regional wall motion abnormalities in ischemic heart disease [4—6]. Strain analysis is a method for assessing regional systolic function and diastolic function [7,8]. It has also been reported that post-ischemic left ventricular (LV) delayed relaxation (diastolic stunning) persists for a long time (at least 24 h) after recovery from transient ischemia even when systolic function has recovered [9,10]. The purpose of this study was to clarify the diagnostic utility of strain imaging diastolic index (SI-DI) in identifying coronary artery disease in patients with preserved ejection fraction (EF).

Methods

Patients

From November 2006 to January 2010, we retrospectively examined 142 consecutive patients with suspected angina pectoris who underwent both echocardiography and coronary angiography within a 24-h period. Patients were excluded if they had EF < 50%, myocardial infarction, previous cardiac surgery, non-sinus rhythm, conduction abnormalities, left main trunk stenosis, or significant valvular heart disease. The remaining 85 patients were enrolled in the study analysis. Baseline patient characteristics are listed in Table 1. The study was approved by the institutional review board and informed consent was obtained.

Coronary angiography

All patients underwent standard coronary angiography. The coronary artery segments and stenoses were visually assessed by the first operator according to the recommendation of the American Heart Association [11]. The degree of stenosis was classified as ''no stenosis'' (≤50% diameter stenosis), ''mild stenosis'' (51—75% diameter stenosis), and ''severe stenosis'' (>75% diameter stenosis). Coronary artery segments 1—3 were regarded as culprit lesions for right coronary artery (RCA) territories. Coronary artery segments 6 and 11 were regarded as culprit lesions for left anterior descending (LAD) and left circumflex (LCX) coronary arteries, respectively. Segments perfused by coronary arteries with no stenosis in the proximal segments (segments 1, 2, 3, 6, and 11) and significant stenosis in the distal segments (segments 4, 7, 8, 13, and 14) were excluded from the analysis because distal stenosis may influence myocardial function. To simplify the protocol, other branch lesions were exempted from the analysis.

Table 1 Baseline characteristics.

Number of patients	85
Male/female	66/19
Age (years)	63 ± 12
Interventricular septal thickness (mm)	10 ± 1
LV end-diastolic diameter (mm)	48 ± 5
LV posterior wall thickness (mm)	10 ± 1
LV end-systolic diameter (mm)	30 ± 5
Ejection fraction (%)	67 ± 9
Systolic blood pressure (mm Hg)	129 ± 22
Diastolic blood pressure (mm Hg)	67 ± 11
Heart rate (BPM)	64 ± 11

Values are presented as mean ± SD except number of patients.
LV, left ventricular.

Echocardiography and speckle tracking analysis

All patients underwent standard echocardiography within 24 h of coronary angiography [12]. Digital recordings were converted to audio video interleaved movies and transferred to a personal computer workstation for offline analysis. Retrospective 2D speckle tracking analysis was performed by one observer who was blinded to the coronary angiographic results. The analysis was performed using 2D speckle tracking software (Toshiba Medical Systems, Tochigi, Japan) as previously described [6,9,13]. LV myocardial segments with poor images for speckle tracking and deficit segments were excluded by the blinded observer.

The LV segments perfused by the 3 major coronary arteries were defined according to the guideline of the American Society of Echocardiography [12]. In the parasternal LV short-axis image at the papillary muscle level, anterior septum and anterior segments, lateral and posterior segments, and the inferior and inferior septum, were regarded as segments perfused by LAD, LCX, and RCA, respectively. In the apical LV images, anterior septum and anterior segments, antero-lateral and infero-lateral segments, as well as inferior septum and inferior segments at the papillary muscle level, were regarded as segments perfused by LAD, LCX, as well as RCA, respectively. Apical segments were not analyzed in the current study because most of the apical segments were inadequate for the speckle tracking analysis.

The radial strain of the total LV wall thickness was calculated in each segment of the LV short-axis image. The transverse strain of the total LV wall thickness and longitudinal strain were calculated in each segment of the apical 2-chamber, long-axis, and 4-chamber images. Peak strain was defined as the highest strain value throughout the cardiac cycle. End-systole was automatically defined by the tracking software as the timing of the minimum LV cavity. SI-DI was calculated as (strain value at end-systole minus strain value at one-third of diastole duration) divided by the strain value at end-systole (%) as shown in Fig. 1 [9].

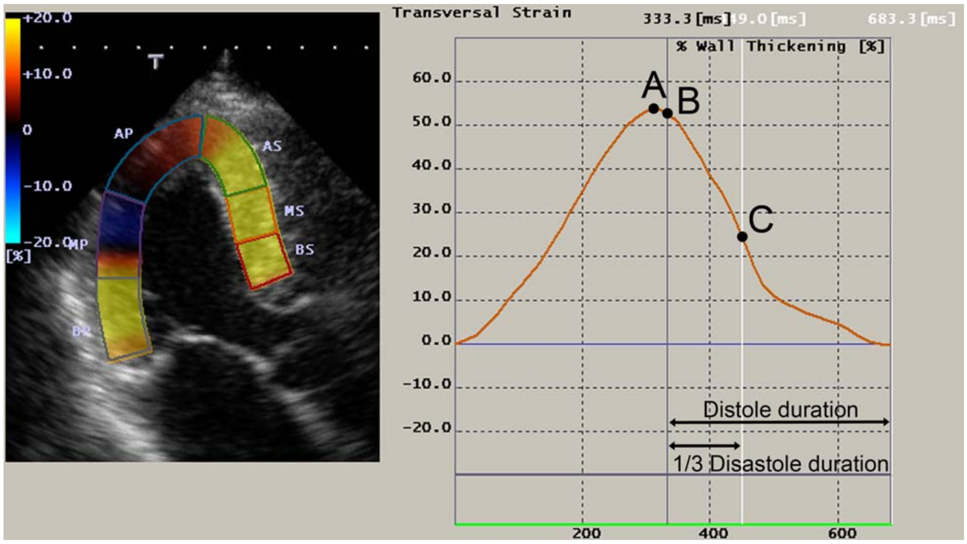

Figure 1 Systolic and diastolic index measured from regional LV strain curve. Peak strain (*A*) was defined as the highest strain value throughout the cardiac cycle. Strain values at end-systole (*B*) and at one-third of diastole duration (*C*) were measured. Strain imaging diastolic index (SI-DI) was calculated as: $[100 \times (B - C)]/B$ (%).

Statistical analysis

Values are presented as mean ± standard deviation (SD). Differences among groups were evaluated by one-way ANOVA followed by Scheffe's multiple comparisons. Receiver operating characteristics curve (ROC) was created using SI-DI in the discrimination of segments with severe stenosis, and the area under the curve (AUC) was calculated. All *p*-values were considered statistically significant at less than 0.05.

Results

In blinded speckle tracking analysis, 183 myocardial segments in the LV short-axis view and 129 myocardial segments in the apical LV long-axis views could be accurately analyzed. Other segments were excluded owing to inadequate images for speckle tracking or deficient segments in the movie. According to the coronary angiographic results, 137 segments had no stenosis, 17 segments had mild stenosis, and 15 segments had severe stenosis in the parasternal LV short-axis view. In the apical view, 88 segments had no stenosis, 15 segments had mild stenosis, and 19 segments had severe stenosis.

Each study subject had a normal EF. Speckle tracking analysis revealed that peak strains (systolic index) had no significant differences among groups with different degrees of coronary artery stenosis. In contrast, even in echocardiography at rest, all SI-DI (diastolic index) values were significantly different among the 3 groups (Table 2). Although the SI-DI values of segments with mild stenosis were lower than those of segments with no stenosis, the difference was not statistically significant. However, SI-DI values were significantly different between segments with no stenosis and those with severe stenosis.

ROC curve analysis was performed for the discrimination of segments with severe stenosis. The AUC in the case of radial, longitudinal, and transverse SI-DI was 0.72, 0.74, and 0.80, respectively. A cut-off value of 49 for transverse SI-DI can predict LV segments with severe stenosis with sensitivity of 0.79 and specificity of 0.73. A screening cutoff value of 63 for transverse SI-DI shows sensitivity of 0.95 and specificity of 0.50 (Fig. 2).

Discussion

Echocardiographic identification of ischemic myocardial abnormalities is crucial and often influences treatment and prognosis. Stress echocardiography remains the current standard for predicting coronary artery stenosis although it is still mainly based on subjective visual interpretation, relatively time-consuming, costly, and dependent on the observer's skill [14—17]. The current study revealed that SI-DI at rest is another novel strategy for identifying severe coronary stenosis.

Recent studies have shown that ischemic injury persists much longer than previously thought. Ishii et al. have revealed that use of transverse SI-DI can demonstrate post-ischemic diastolic stunning despite complete systolic functional (peak transverse strain) recovery, and that the change can persist for more than 24 h after reperfusion [9]. Moreover, Azevedo et al. reported that the ischemic diastolic dysfunction detected by cardiac magnetic resonance imaging (MRI) persists for at least 24 h even when systolic function has recovered [10]. Neizel et al. reported that regional diastolic dysfunction detected by cardiac MRI persists even 6 months after successful reperfusion of acute myocardial infarction [18]. Regional diastolic index showed better accuracy than regional systolic index in predicting persistent myocardial dysfunction even at 6-month follow-up.

Accordingly, patients with transient ischemic attack such as angina pectoris may have regional stunned myocardium accompanied by ''invisible'' diastolic dysfunction even long

Table 2 Systolic and diastolic strain values in each stenosis.

	No stenosis (≤50%)	Mild stenosis (51–75%)	Severe stenosis (>75%)	*p*-Value (ANOVA)
Radial strain				
Peak strain (%)	56.3 ± 22.6	47.7 ± 20.2	53.6 ± 24.4	0.317
SI-DI (%)	64.9 ± 17.9	59.4 ± 26.4	49.4 ± 18.9*	0.009
Longitudinal strain				
Peak strain (%)	−16.5 ± 3.7	−16.3 ± 3.7	−16.5 ± 5.4	0.977
SI-DI (%)	49.4 ± 20.5	40.7 ± 20.6	30.6 ± 15.6*	0.001
Tranverse strain				
Peak strain (%)	31.2 ± 13.8	27.1 ± 14.8	29.3 ± 13.1	0.541
SI-DI (%)	69.8 ± 37.8	50.3 ± 60.9	37.7 ± 24.2*	0.012

Values are presented as mean ± SD. SI-DI, strain imaging diastolic index calculated as (strain value at end-systole minus strain value at one-third of diastole duration) divided by the strain value at end-systole (%).
* $p < 0.05$ vs. strain value in no stenosis by Scheffe's multiple comparison.

after the symptoms have disappeared. Our results also showed regional LV diastolic dysfunction despite normal systolic function (peak strain and EF). These results indicated that many patients with suspected coronary artery disease have regional stunned myocardium at the time of routine echocardiography.

SI-DI values were significantly different between the no stenosis and severe stenosis groups. On the other hand, SI-DI values did not significantly differ between the no stenosis and mild stenosis groups. These findings suggest that mild stenosis may not cause ischemic changes, even in diastolic function, or perhaps the number of segments with mild stenosis was too small for detection of subtle ischemic changes.

The accuracy of the current study results was not strong enough for predicting coronary stenosis. However, with the use of suitable screening cut-off values, SI-DI can show high sensitivity. Thus, SI-DI can be used to rule out severe coronary stenosis in routine rest echocardiography.

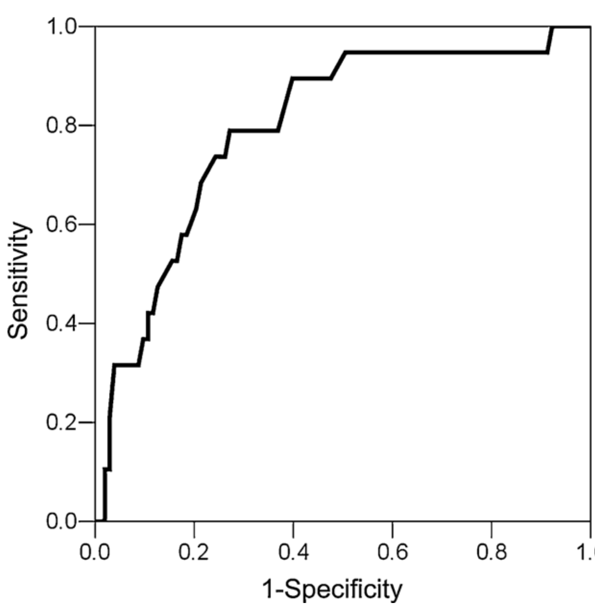

Figure 2 Receiver operating characteristics curve analysis of transverse strain imaging diastolic index (SI-DI) for identifying severe coronary artery stenosis.

Limitations

To simplify the definition, we ignored coronary stenosis in the coronary branch arteries. These stenoses might influence perfused myocardial function. Moreover, there are many coronary variations that could affect the distribution of myocardial perfusion. We did not take these into account in the current study. In addition, the time period from the last chest pain to echocardiography varied widely. Other conditions, such as diffuse lesions with less significant stenosis, myocardial hypertrophy, and hypoxia, may cause myocardial ischemia. Further studies are needed to confirm our results under these specific conditions.

Another limitation was the image quality of the echocardiograms. Because of the retrospective nature of the analysis, many images were excluded due to poor quality for speckle tracking analysis. Since the speckle tracking technique is dependent on image quality, we had to exclude many myocardial segments. As a result, a limited number of segments were analyzed. However, despite these limitations, our results indicate that SI-DI is a useful non-invasive marker for ruling out severe coronary artery stenosis.

Conclusions

The diastolic index, SI-DI at rest, is a novel marker for ruling out severe coronary artery stenosis in routine echocardiography, even in patients with preserved EF.

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