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Echocardiography

Coronary Flow Reserve, Strain and Strain Rate Imaging during Pharmacological Stress before and after Percutaneous Coronary Intervention: Comparison and Correlation

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Introduction: Coronary flow reserve (CFR) could apply reliable information about the coronary circulation, and strain (S) and strain rate imaging (SRI) are able to quantify the left ventricular myocardial performance. The aim of this study was to assess myocardial performance in relation to the function of the coronary circulation before and after successful percutaneous coronary intervention (PCI) of the left anterior descending artery. Material and Method: Fourteen patients (10 men, 4 women, mean age 53.2 ± 11.4 years) with severe left anterior descending stenosis who had a successful selective PCI were recruited into this study. CFR and myocardial deformity indices (S and SR) were recorded before and after percutaneous intervention, both at rest and during stress echo test. Results: CFR, S, and SR increased after intervention significantly. There was significant correlation between CFR ratio and poststress systolic strain (SS) ratio and early diastolic strain rate (ESR) ratio ($P < 0.05$ and $r > 0.6$). Also CFR improvement had significant relationship with changes of poststress Systolic SR and poststress Systolic S ($P < 0.05$ and $r > 0.6$). Based on regression analysis the amount of change in CFR was independently associated with change in SS during stress and systolic SR. Conclusion: PCI improves CFR (a marker of coronary perfusion), strain, and strain rate (markers of regional cardiac wall deformation). The independent association between CFR improvement and poststress systolic strain and strain rate means that SRI parameters can independently predict CFR changes after PCI. (Echocardiography 2011;28:570-574)

Key words: transthoracic echocardiography, strain, strain rate imaging, coronary flow reserve

Coronary flow reserve (CFR) is defined as difference between stress and resting flow velocity of coronary vessels and represents the amount of increased blood flow associated with myocardial demand. It is a useful index for coronary artery stenosis severity and can be measured by transthoracic echocardiography at a relatively low cost.[1,2] The noninvasive measurement of left anterior descending artery (LAD) critical stenotic lesions by transthoracic echocardiography is found to be effective even in emergency settings.[3] However, this method has some limitations.[4]

The ultrasonic strain rate (SR) and strain (S) measurement has been suggested recently as a new noninvasive method for evaluation of regional myocardial deformation. SR is defined as the gradient of local myocardial tissue velocities between two points; S is time integral of SR over time and represents the local magnitude of deformation. Strain and strain rate imaging (SRI) can objectively quantify the left ventricular (LV) myocardial wall motion. These parameters are more accurate in measuring local contractility than tissue Doppler imaging, and can provide additional information compared to visual qualitative wall motion evaluation.[5] However, the relationship between changes in CFR and SRI before and after percutaneous coronary intervention (PCI) and its clinical implications have not been investigated before.

The aim of this study is to investigate the relationship between SRI-derived myocardia performance both at rest and during pharmacological stress and coronary circulation determined

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by CFR, measured by transthoracic Doppler echocardiography; both before and after successful PCI to the left anterior descending artery (LAD).

Material and Method:

Study Population:

From a total of 18 patients with significant (>75% luminal narrowing) LAD stenosis by quantitative coronary angiography who were going to undergo selective PCI, 14 patients with successful PCI were recruited into this study. Exclusion criteria were history of myocardial infarction (MI), unstable angina, congestive heart failure, atrioventricular block, atrial fibrillation, and obstructive pulmonary disease. All patients were in stable sinus rhythm and had normal resting LV function. Patients fasted for at least 4 hours and xanthines containing beverages or medications were discontinued 12 hours before the tests. PCI was considered successful if there was less than 30% residual stenosis without troponin rising in lab exam and no ECG changes. Coronary flow velocity was measured by transthoracic Doppler echocardiography: once in 24–48 hours before and once in the first week following PCI. After completion of pharmacological stress test, S and SR were obtained both at rest and during the maximal coronary flow velocity. The study protocol was approved by the institutional Ethics Committee, and informed consent was obtained from all the patients.

Transthoracic Echocardiography:

To perform transthoracic Doppler echocardiography, a Vivid 7 (GE Medical System, Horten, Norway) digital ultrasonographic system with a M3S transducer (frequency of 1.5–3 MHZ) in Coronary flow mode was used. Coronary blood flow velocity measurements were stored digitally and were analyzed offline by an expert investigator. All measurements were calculated by the same investigator, blinded to the patients' clinical status and other relevant documents.

Coronary Flow Reserve:

Coronary flow velocities in the LAD were recorded using a M3S transducer with color flow mapping guidance. The ultrasound beam direction was aligned in parallel with the LAD flow as much as possible. The digitized coronary flow velocity spectrum provided velocity time integral (VTI). An average of the measurements in three cardiac cycles was obtained.

CFR ratio was Defined as CFR (post-PCI/pre-PCI):

CFR change was defined as CFR (Δpost – pre-PCI).

Drug Infusion:

Dipyridamole was injected with a dose of 0.56 mg/kg in 4 minutes through an in-dwelling 20G cannula in the left antecubital vein. Throughout Dipyridamole infusion, the conduction system was continuously monitored by electrocardiography. Blood pressure and heart rate were assessed at baseline and at the time of peak action of Dipyridamole. At the end of the test, the patients were given 125 mg of Aminophyline.

Strain and SRI:

After performing conventional echocardiography, SRI images were obtained with commercially available echocardiography equipment (Vivid 7, GE Medical System) both at rest and at maximal coronary flow velocity (4–8 minutes after the completion of Dipyridamole infusion). Apical four-, three-, and two-chamber color Doppler tissue imaging were taken at a high frame rate (150–200 fps) and analyzed using Echo Pac 3.0 (GE Medical System). The region of interest was placed at mid and basal segments of septal, anterior and anteroseptal walls.

To determine strain and strain rates, data were averaged from three consecutive cardiac beats at each site. An offset to measure strain and strain rate was set at 9–11 mm. Manual tracking throughout the cardiac cycle was used for all the patients. Aortic valve closure was preserved as a marker for end systole. Systolic strain (SS) and systolic strain rate (SSR) were defined as the magnitude of the deformation measured from end diastole to end systole. From the averaged SR and strain data, peak SS and SSR were calculated. The average of values of the measurements from five sites in the LAD territory (mid and base of the anteroseptal, mid and base of the anterior and mid septal segments) was determined. The ratios of post-PCI to pre-PCI systolic were calculated for SS, SSR, and early diastolic SR.

Statistics:

All of the statistical analyses were performed using the SPSS Software package, version 16 (SPSS Inc. Chicago, IL, USA). Descriptive data were presented as mean ± SD. Paired *t*-test was used to compare the mean differences before and after PCI. After performing a correlation test, linear regression analysis was employed to assess independent relationship between the continuous variables. P-value < 0.05 was considered statistically significant.

Results:

Fourteen patients (10 men, 4 women) with mean age of 53.2 ± 11.4 years took part in our study. LV ejection fraction (LVEF) was above 50% in

TABLE I

Clinical, Echocardiographic, and Hemodynamic Characteristics of Study Subjects

Variable	Value (Mean ± SD or Number)
Age (years)	53.2 ± 11.4
Male/female	10/4
Body mass index (kg/m^2)	26.3 ± 2.4
CCS angina grade 1	2
CCS angina grade 2	8
CCS angina grade 3	4

BP = blood pressure; CCS = Canadian Cardiovascular Society.

all cases. There were no major side effects during Dipyridamole infusion, but minor side effects such as headache, flushing and dyspnea were noted in six (43%) patients. The baseline characteristics of the patients are shown in Table I. The baseline and peak heart rate and blood pressure were not significantly different in the patients pre- and post-CFR measurements.

Before-after PCI Comparison:
There was a statistically significant increase in CFR after PCI in all cases. Furthermore, all patients showed statistically significant elevation in recorded SS, SSR, and ESR, both at rest and during stress test after PCI (Table II).

Correlation between CFR and SRI Measurements:
The recorded SS, SSR, and ESR were not significantly correlated with at rest or stress CFR, either before or after PCI (P value > 0.05 and nonsignificant r).

Correlation between Ratios (post-Divided to Pre-PCI):
There was significant correlation between CFR ratio and post stress SS ratio and ESR ratio (P = 0.002 [r = 0.76] and P = 0.011 [r: 0.66], respectively) (Fig. 1).

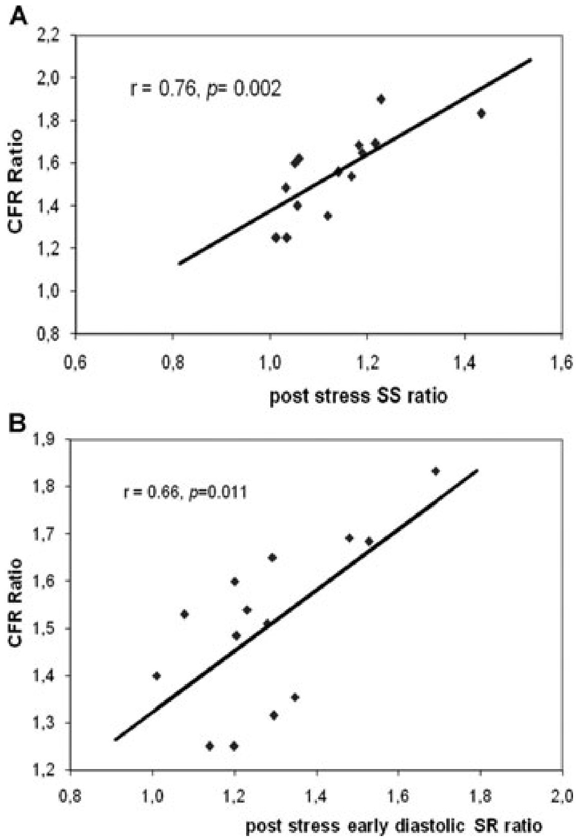

Figure 1. Correlation between coronary flow reserve (CFR) and strain (S) and strain rate (SR) parameters. Coronary flow reserve ratio and **A.** poststress SS ratio **B.** poststress early diastolic SR ratio.

TABLE II

Comparison of Recorded Measurement before and after PCI

Index	Before (mean ± SD)	After (Mean ± SD)	P value
CFR (cm/s)	1.61 ± 0.39	2.44 ± 0.50	<0.001
At rest			
SS (%)	13.58 ± 2.88	15.90 ± 2.77	<0.001
SSR (1/S)	0.84 ± 0.23	1.23 ± 0.18	<0.001
ESR (1/S)	0.88 ± 0.21	1.22 ± 0.18	<0.001
During stress test			
SS (%)	15.37 ± 2.98	17.23 ± 2.97	<0.001
SSR (1/S)	1.10 ± 0.23	1.41 ± 0.22	<0.001
ESR (1/S)	1.16 ± 0.26	1.44 ± 0.25	<0.001

CFR = coronary flow reserve; SS = end systolic strain; SSR = peak systolic strain rate; ESR = early diastolic strain rate.

Correlation between Change Amounts (post minus pre-PCI):
CFR improvement had significant relationship with changes of poststress SSR and poststress SS (P = 0.002 [r: 0.7] and P = 0.013 [r: 0.64], respectively) (Fig. 2).

Regression:
Based on regression analysis, the amount of change in CFR was associated with change in SS during stress test (beta coefficient = 0.0.64, P = 0.014, adjusted R^2 = 0.36, R^2 = 41%, P = 0.014). Also CFR improvement was shown to be independently associated with SS change (beta coefficient = 0.7, P = 0.005, adjusted R^2 = 0.45, R^2 = 49%, P = 0.005).

Discussion:

The capacity of a coronary artery to increase its flow under conditions of maximum resistance has been recognized by physiologists for decades.

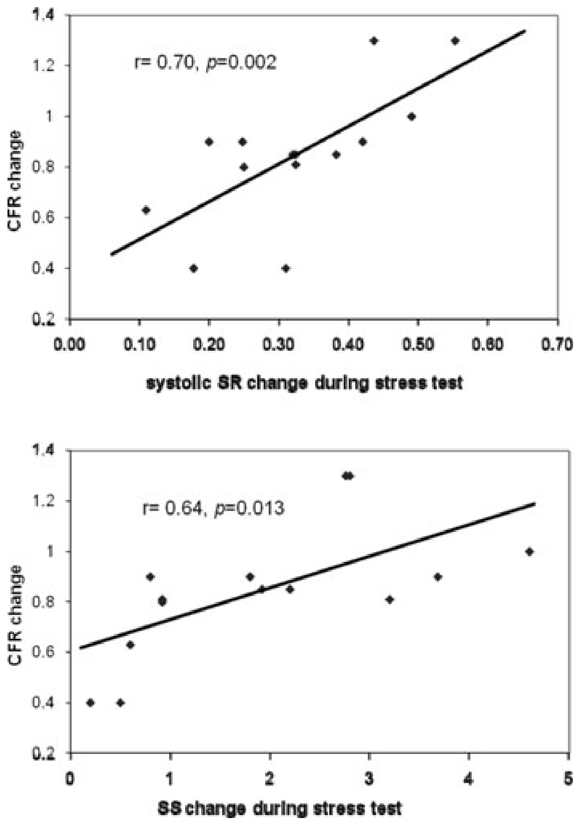

Figure 2. Correlation between coronary flow reserve (CFR) and strain (S) and strain rate (SR) parameters. Coronary flow reserve improvement and **A.** SS change during stress test **B.** systolic SR change during stress test.

Technological advances have enabled cardiologists to measure this change selectively in the major coronary vessels of humans under a wide variety of physiological and pathophysiological conditions.[6] Recently, the usefulness of transthoracic Doppler echocardiography to assess CFR has been reported in various clinical settings. CFR adds quantitative support to the exquisitely quantitative assessment of wall motion analysis in the stress echo lab.[7,8]

Transthoracic Doppler echocardiography can be used as a noninvasive tool to measure CFR both in stenosed and normal epicardial coronary arteries (predominantly in LAD coronary artery). Comparing the accuracy of transthoracic Doppler with intracoronary measurement of CFR provides highly satisfying results.[9,10] Poststenotic CFR measurement is helpful in functional assessment of moderate stenosis, detection of significant or critical stenosis and monitoring restenosis after revascularization.[11] It can also be used to predict cardiac function. In this study a significant improvement in CFR after PCI was found in patients with severe coronary artery disease, which was compatible with the clinical status of the patients.

SRI can reliably be used to measure regional myocardial deformation and deformation rate, both at rest and during pharmacological stress.[12] Resting S and SR can also be used to evaluate and predict tissue damage and cardiac wall motion abnormalities in patients with coronary artery disease after PCI.[13,14] The quantification of regional myocardial deformation by using Dobutamine Stress Echocardiography has been shown to be useful in detecting the ischemic dysfunctional segment of myocardium.[15] Based on our results, the myocardial deformities assessed by S and SR significantly improve after PCI; which can be attributed to the increase in blood supply of the affected region. Weidemann et al. have reported similar results. However, it should be emphasized that predicting value of S and SR for the further tissue damages strongly depends on the viewed part of the cardiac wall.[13]

According to this study, poststress SS and CFR changes after PCI are correlated. Considering this association, SRI could be used as an alternative and complementary index for CFR evaluation in patients with severe LAD stenosis, especially when technical weaknesses or pitfalls do not allow accurate assessment, or when there is suspicion about the obtained results. For instance, CFR must be measured distally to stenosis, because erroneous CFR assessment at stenosis site is underestimated due to increased baseline flow velocity. Additionally, the flow in LAD branches could be erroneously interpreted as the flow in LAD main trunk.[4] Other imaging pitfalls can result from confusion associated with fluid in pericardial space, extracardiac thoracic arteries, and thoracic veins.[10]

The independent association between CFR improvement and poststress systolic strain and strain rate, based on regression, means that SRI parameters can independently predict CFR changes after PCI.

Conclusion:

PCI improves both CFR (a marker of coronary perfusion) and strain and strain rate (markers of regional deformation). There is statistically significant association between CFR, strain and strain rate. Improvement in CFR after PCI to LAD could be independently predicted with strain and strain rate. The achieved result is applicable only to patients with severe LAD stenosis.

Study Limitations:

This study evaluated the immediate effects of PCI within 1 week, but the long-term effects of PCI on CFR and myocardial function were not examined. Further studies should determine whether PCI can induce persistent improvements in CFR and myocardial function. Post-PCI ejection fraction was not recorded in this study so we could not report any association between recorded characteristics of regional myocardial deformation and CFR with ejection fraction.

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