Detection of Coronary Stenoses at Rest With Myocardial Contrast Echocardiography

Kevin Wei, MD; Khim Leng Tong, MD; Todd Belcik, RDCS; Patrick Rafter, BS; Michael Ragosta, MD; Xin-Qun Wang, MS; Sanjiv Kaul, MD

Background—We hypothesized that autoregulatory changes in arteriolar blood volume (aBV) that develop distal to a stenosis can be measured with myocardial contrast echocardiography, allowing coronary stenosis detection at rest without recourse to stress.

Methods and Results—Patients with varying degrees of coronary artery stenosis on quantitative angiography underwent high-mechanical-index myocardial contrast echocardiography at 15 Hz to allow measurement of phasic changes in aBV in large intramyocardial vessels using either Definity (group 1; n=22) or Imagent (group 2; n=22). Progressive increases in the background-subtracted systolic/diastolic aBV signal ratio were noted between each level (none, mild [<50%], moderate [50% to 75%], and severe [>75%]) of stenosis severity for both group 1 (0.09±0.13, 0.13±0.08, 0.58±0.22, and 0.77±0.40; P<0.001) and group 2 (0.10±0.05, 0.27±0.18, 0.39±0.28, and 0.74±0.37; P<0.0001) patients. A systolic/diastolic aBV signal ratio of >0.34 provided a sensitivity and specificity of 80% and 71%, respectively, for the detection of >75% coronary stenosis in group 1 patients, whereas a ratio of >0.43 provided a sensitivity and specificity of 89% and 74%, respectively, for the detection of >75% stenosis in group 2 patients.

Conclusions—Both the presence and severity of a physiologically significant coronary stenosis can be detected at rest by measuring the increase in aBV on myocardial contrast echocardiography that occurs distally to the stenosis without recourse to any form of stress. (Circulation. 2005;112:1154-1160.)

Key Words: contrast media ■ coronary disease ■ diagnosis ■ echocardiography ■ imaging

Because of coronary autoregulation, resting myocardial blood flow (MBF) remains normal despite the presence of up to 85% lumen diameter narrowing of the coronary artery.1 If there is adequate collateral-derived MBF, resting perfusion and function can be normal even in the presence of total coronary occlusion.2,3 Therefore, in the absence of prior myocardial infarction, noninvasive detection of coronary artery disease (CAD) relies on exercise or pharmacological stress to unmask abnormal flow reserve of the native coronary and/or the coronary collateral system, which manifests as reversible perfusion defects or wall thickening (WT) abnormalities on cardiac imaging.

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The normal coronary system has ≈45 mL of blood, which is divided almost equally between the arterial, venous, and capillary compartments.2 Within the myocardium, ≈90% of blood is present in capillaries during systole (the rest being resident in arterioles and venules), which is called the myocardial blood volume (MBV). When a pure intravascular tracer such as microbubbles is administered as a continuous intravenous infusion, the backscatter signal received during steady state on myocardial contrast echocardiography (MCE) represents the MBV.5

The current method for quantifying MBF with MCE uses high-energy ultrasound to destroy microbubbles in the myocardium during steady state and to measure the rate of microbubble replenishment at progressively longer intervals between destructive ultrasound pulses (Figure 1).6 Because the mean velocity of microbubbles (or erythrocytes) in capillaries is 1 mm·s⁻¹ at rest and the ultrasound beam elevation is 4 to 5 mm, it takes 4 to 5 seconds to replenish the beam.6 Part of this replenishment also occurs from microbubbles moving at faster velocities in larger vessels within the myocardium such as the arterioles. The pulsing interval versus microbubble backscatter relation is therefore curvilinear; faster velocities depict more rapid filling. A tangent drawn on any part of the curve (Figure 1) represents the mean velocity of microbubbles during that part of myocardial replenishment.

Because the blood in myocardial arterioles comprises only a small proportion of MBV, microbubble signals from these vessels are usually negligible when the ultrasound beam is fully replenished. However, if imaging is performed with a...
very short pulsing interval between destructive ultrasound pulses, the signal obtained is derived only from vessels that fill in this short period of time (Figure 1) because neither capillaries nor venules have adequate time to fill. Thus, signals representing arteriolar blood volume (aBV) can be obtained from the myocardium with this technique.7 Because forward flow in large intramyocardial vessels occurs during diastole, aBV signals on MCE are seen predominantly during diastole.

As stated, autoregulation maintains normal resting MBF in the presence of a stenosis, which involves dilatation of 150- to 300-μm-diameter arterioles and an increase in arteriolar and total coronary blood volumes.8 The more severe the stenosis is, the greater the increase in arteriolar dimensions and their volume is.9,10

During systole, a change in myocardial elastance causes retrograde displacement of the aBV into large intramyocardial vessels,11 resulting in a small systolic signal on MCE.7 In the presence of a stenosis, because aBV is larger, there is likely to be greater retrograde displacement of microbubbles from smaller arterioles and an increase in the systolic myocardial signal.7 Because the larger intramyocardial arteries do not participate in autoregulation, the diastolic signal remains unchanged. We have shown in an animal model that the systolic-to-diastolic (S/D) aBV signal ratio measured at rest increases in the presence of stenosis and that the degree of increase is proportional to coronary stenosis severity.7 In this study, we hypothesized that this approach could be used to detect the presence of CAD at rest in humans without recourse to any form of stress.

Methods

Patient Population

The study protocol was approved by the Human Investigation Committee at the University of Virginia. Patients >18 years of age with known or suspected CAD scheduled for diagnostic coronary angiography were approached for enrollment in the study. All patients provided written informed consent. Patients with abnormal resting WT on echocardiography were excluded. Cardiac catheterization was performed immediately after MCE. The patients were divided into 2 groups based on the ultrasound contrast agent used and its method of administration.

In group 1 patients, 0.5 mL Definity (Bristol-Myers Squibb Medical Imaging) was administered as an intravenous bolus, followed by a 5-mL saline flush for each acquired view. The large dose was required to produce backscatter signals from the small intramyocardial aBV. Consequently, imaging was limited to the apical segments because significant far-field shadowing precluded the assessment of mid and basal segments.

In group 2 patients, 9 mL Imagent (IMCOR Pharmaceuticals) was diluted in 50 mL saline and administered as an intravenous infusion at 8 mL/min.12 These microbubbles are fragile and can be destroyed by ultrasound with the use of an intermediate mechanical index (MI) to produce adequate myocardial signals. The smaller concentration of microbubbles in the infusion precludes attenuation from occurring and allows myocardial signals to be discerned even in basal segments.

Echocardiography

Echocardiography was performed with a Sonos 7500 system (Philips Ultrasound) coupled with a 2.5-MHz transducer capable of power modulation imaging. Compression was set at 51 dB, and gain settings were optimized at the beginning of each study and then held constant throughout. The MI was set at 0.7; higher MI’s were avoided to minimize microbubble destruction within the left ventricular cavity, which would have resulted in lower myocardial signals. A frame rate of 15 Hz (pulsing interval, 67 ms) was used to allow microbubble replenishment of only larger intramyocardial arterioles with high flow velocities. The destructive MI ensured that capillary replenishment did not occur at this short pulsing interval.

Baseline images were obtained before administration of microbubbles from the apical 4-, 2-, and 3-chamber views, followed by contrast-enhanced images in the same views. The transmit focus was adjusted to the apex and the mitral annulus for imaging apical and basal segments, respectively. Apical and basal segments of each wall were therefore examined separately, so multiple digital cine loops were acquired in each view. The entire imaging procedure took ≤15 minutes in all patients.

In the group 1 patients who received Definity, only the anterior territory (anterior septum, anterior wall, and apex) was analyzed because the mid and basal segments were shadowed; both territories were analyzed in the group 2 patients who received Imagent. For group 2 patients, the heart was divided into anterior and posterior (basal, mid inferior, and posterolateral) territories.

All contrast-enhanced frames from 2 to 3 contiguous cardiac cycles were selected offline.7 A region of interest was drawn over the mid myocardium on an end-diastolic frame. The mid myocardium from all other selected frames was then manually aligned to the same region of interest, from which myocardial aBV signals were derived. We have previously shown that myocardial aBV signals using this approach are linearly related to the myocardial microbubble concentration for the dose of microbubbles used.12

Diastole and systole were identified by the direction of endocardial movement on echocardiography. Contrast-enhanced images from 2 or 3 end-diastolic and end-systolic frames from each cardiac cycle were averaged to reduce noise. The precontrast tissue signal from similar frames was then subtracted from the respective contrast-enhanced aBV value before deriving the background-subtracted S/D aBV ratio.

To correlate MCE with quantitative coronary angiography (QCA) data, the highest S/D aBV ratio from the anterior territory was correlated to the most severe stenosis in the left anterior descending coronary artery in both groups of patients. Additionally, in the group 2 patients, the highest S/D aBV ratio from the posterior territory was assigned to the most severe stenosis in either the right or left circumflex coronary artery. Because the magnitude of retrograde displacement of aBV is also related to myocardial contractility, left ventricular WT was quantified with this equation: systolic wall thickness minus diastolic wall thickness divided by diastolic wall thickness times 100.
TABLE 1. Patient Demographics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group 1 (n=22)</th>
<th>Group 2 (n=22)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, n (%)</td>
<td>16 (73)</td>
<td>15 (68)</td>
</tr>
<tr>
<td>Median age (range), y</td>
<td>68 (27–81)</td>
<td>58 (42–77)</td>
</tr>
<tr>
<td>History of smoking, n (%)</td>
<td>4 (18)</td>
<td>8 (36)</td>
</tr>
<tr>
<td>History of diabetes, n (%)</td>
<td>7 (32)</td>
<td>4 (18)</td>
</tr>
<tr>
<td>History of hypertension, n%</td>
<td>14 (64)</td>
<td>18 (82)</td>
</tr>
<tr>
<td>History of hypercholesterolemia, n (%)</td>
<td>15 (68)</td>
<td>15 (68)</td>
</tr>
</tbody>
</table>

QCA Study
Digital cineangiographic images acquired in orthogonal projections were used for QCA. Calibration was performed using the coronary guiding catheter as a reference (6F = 2.0 mm, 7F = 2.33) with the image magnified × 4. The coronary artery segment of interest was selected, and the minimal lumen and proximal normal vessel segment diameters were measured with digital calipers. Percent diameter stenosis was computed in a standard manner with single-plane, “worst-view” angulation.¹³

Statistical Analysis
Data are expressed as mean ± 1 SD. An ordinary least-squares linear regression model was used to assess whether there was a strong association between aBV ratios and levels of stenosis. ANOVA was used to test for any differences in aBV ratio between the 4 stenosis levels. A value of P < 0.05 was considered significant, and all tests were 2 sided. Analyses were also adjusted for all pairwise comparisons between levels of stenosis using Bonferroni’s correction, which was derived by multiplying the probability value by number of comparisons.

To account for correlations between multiple observations (anterior and posterior regions) within the same group 2 subject, the Huber and White sandwich estimator was used to estimate the variance-covariance matrix.¹⁴,¹⁵ Using this method, we assumed a “working independence model” to derive estimates of the coefficients and then obtained unbiased robust estimates of variances and covariances of these estimates by adjusting for the correlation between multiple observations from cluster samples. Echocardiographic studies (for background-subtracted S/D aBV ratio and WT) and coronary angiograms (for QCA) from 6 randomly selected patients were analyzed by the same observer at least 1 month apart and coronary angiograms (for QCA) from 6 randomly selected patients were analyzed by the same observer at least 1 month apart and by 2 independent observers for intraobserver variability and by 2 independent observers for interobserver variability. Pearson correlations between the data were assessed from least-squares-fit linear regression analysis.

TABLE 2. MCE and WT Data at Rest

<table>
<thead>
<tr>
<th>Variable</th>
<th>No Stenosis</th>
<th>Mild Stenosis (&lt;50%)</th>
<th>Moderate Stenosis (51%–75%)</th>
<th>Severe Stenosis (&gt;75%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>5</td>
<td>6</td>
<td>6</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Stenosis on QCA, %</td>
<td>0 ± 0</td>
<td>36 ± 13</td>
<td>66 ± 5</td>
<td>85 ± 5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>WT, %</td>
<td>33 ± 8</td>
<td>38 ± 8</td>
<td>39 ± 7</td>
<td>34 ± 3</td>
<td>0.51</td>
</tr>
<tr>
<td>S/D aBV ratio</td>
<td>0.09 ± 0.13</td>
<td>0.13 ± 0.08</td>
<td>0.58 ± 0.22†</td>
<td>0.77 ± 0.40‡</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Group 2*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>5</td>
<td>13</td>
<td>16</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Stenosis on QCA, %</td>
<td>0 ± 0</td>
<td>37 ± 12</td>
<td>61 ± 6</td>
<td>87 ± 9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>WT, %</td>
<td>34 ± 5</td>
<td>36 ± 10</td>
<td>33 ± 8</td>
<td>33 ± 7</td>
<td>0.71</td>
</tr>
<tr>
<td>S/D aBV ratio</td>
<td>0.10 ± 0.05</td>
<td>0.27 ± 0.18</td>
<td>0.39 ± 0.28†</td>
<td>0.74 ± 0.37‡</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

*All 22 group 2 patients had ≥2 measurements (anterior and posterior territories) except 1 patient who had only posterior territory measurement.
†Bonferroni-corrected P < 0.05 vs no stenosis.
‡Bonferroni-corrected P < 0.05 vs mild stenosis.

Results
Patient Characteristics
A total of 48 patients were enrolled in the study, 24 in each of the 2 groups. Echocardiographic images were not of adequate quality for quantitative analysis in 1 patient from each group. Digital images were not recorded in a group 1 patient because of technical failure, and a group 2 patient did not undergo cardiac catheterization. Baseline characteristics of the remaining 44 patients by 2 different contrast agents are shown in Table 1. Stenoses were divided into 4 levels based on QCA: none (0%), mild (1% to 50%), moderate (51% to 75%), and severe (>75%). The mean stenosis value for each level from both patient groups is shown in Table 2. Among the 22 territories in group 1 patients and the 43 territories in group 2 patients (1 anterior territory was of inadequate quality) available for analysis, 10 were supplied by normal coronary arteries.

Echocardiographic Results
WT was normal and similar between all segments regardless of the level of stenosis (Table 2). Figure 2 depicts time versus aBV plots derived from 2 contiguous cardiac cycles at a 15-Hz frame rate (interval between ultrasound pulses, 67 ms) obtained from an apical region of interest in a group 1 patient with a normal left anterior descending coronary artery. Rapid diastolic anterograde replenishment of large intramyocardial vessels with microbubbles produced appreciable myocardial contrast enhancement and high diastolic aBV signals. During systole, however, the retrogradely displaced aBV was small so that the number of microbubbles within the imaging field during systole was barely above the detection threshold of the system, and the myocardium appeared to be devoid of aBV signals. Consequently, marked differences in phasic aBV signals are seen in this patient with normal coronary arteries.

Figure 3 illustrates time versus aBV plots derived from a group 2 patient with a 75% right coronary artery stenosis from a region of interest drawn over the inferior wall. Retrograde displacement of microbubbles from the large aBV (secondary to autoregulation) into intramyocardial vessels...
produced significant contrast enhancement of the inferior wall during systole, so systolic aBV signals almost equal the diastolic values in this patient.

The S/D aBV ratios across the 4 levels of stenosis from all patients are shown in Table 2. No differences in WT, heart rate, or systolic and diastolic blood pressures were found between the 4 levels of stenosis. Furthermore, no differences in any of these variables were found in patients with S/D aBV ratios above compared with below the median value within each stenosis level.

Figure 4 illustrates the relation between stenosis severity and the S/D aBV ratios for the group 1 (Figure 4A) and group 2 (Figure 4B) patients. A progressive and highly significant difference in this ratio was found with increasing stenosis severity. For both groups, the S/D aBV ratios for moderate and severe stenoses were significantly higher than that for no stenosis (Bonferroni-corrected $P < 0.05$ and $P < 0.01$, respectively), and the ratios for severe stenoses were significantly higher than those for mild stenoses (Bonferroni-corrected $P < 0.01$). A test of trend indicated that as severity of stenosis increased, aBV ratio increased for both groups of patients ($P < 0.0001$). After adjustment for potential confounding variables—including age, sex, and histories of hypertension, hypercholesterolemia, smoking, and diabetes—the difference between the degree of stenosis and S/D aBV ratio was no longer statistically significant using ANOVA. However, the trend toward a higher mean aBV ratio was still noted with more severe stenosis.

With receiver-operating characteristics curves, an aBV signal ratio $> 0.34$ provided a sensitivity and specificity of 80% and 71%, respectively, for detection of $> 75\%$ coronary stenosis in group 1 patients (Figure 5); a ratio $> 0.43$ provided a sensitivity and specificity of 89% and 74%, respectively, for the detection of $> 75\%$ stenosis in group 2 patients (Figure 6).
Table 3 depicts interobserver and intraobserver variability for measurement of percent WT, S/D aBV ratio, and QCA-determined percent diameter stenosis. Excellent correlations were found for all variables.

### Discussion

In this study, we have shown for the first time that coronary stenoses can be detected by imaging the myocardium at rest in patients with suspected CAD using MCE. This is based on the ability of MCE to measure changes in the volume of blood within the resistance arterioles that participate in coronary autoregulation distal to a noncritical epicardial coronary stenosis. We have shown that both the presence and severity of a physiologically significant coronary stenosis can be determined with this approach. Further studies are required to determine the feasibility and reliability of this approach in unselected patients with known or suspected CAD.

#### Physiological Basis of the Approach

Changes in myocardial elastance during the cardiac cycle determine the rate, amount, and direction of blood displacement within the myocardium.16 During diastole, myocardial elastance is low, and the high pressure gradient between the aorta and right atrium allows rapid anterograde filling of the intramyocardial vessels. The increase in myocardial elastance early in systole results in closure of smaller, more compliant myocardial arterioles and small venules that effectively partition off the capillary bed from the rest of the intramyocardial circulation via a valvelike effect. Consequently, when the myocardial elastance increases further later in systole, the capillary blood volume does not change significantly.7,17 Compression of intramyocardial arterioles and veins, however, causes blood in these vessels to be “milked out” in mid and late systole. In the case of venules, blood is propelled anterogradely into the coronary sinus,18 whereas in arterioles, blood is displaced retrogradely into larger intramyocardial arteries.11 Thus, unlike the coronary artery, anterograde coronary sinus flow occurs predominantly in systole.11 The retrograde displacement of blood into larger intramyocardial coronary arteries results in systolic flow reversal in these vessels.

In the presence of a noncritical coronary stenosis, 150- to 300-μm coronary arterioles dilate in proportion to the severity of stenosis.9,10 The increase in coronary resistance from the presence of a stenosis is offset by a decrease in arteriolar resistance, so total coronary vascular resistance and resting MBF remain unchanged.19 When a stenosis exceeds 85% or the coronary perfusion pressure is <45 mm Hg, coronary arterioles can no longer dilate, and MBF starts decreasing.19 The dilatation of 150- to 300-μm coronary arterioles causes total coronary blood volume to increase in proportion to the severity of stenosis.9,10 Blood in these 150- to 300-μm coronary arterioles makes up a very small fraction of MBV,4 and changes in their dimensions are usually obscured by backscatter from the capillaries (which constitute 90% of the MBV during systole) on routine MCE.

If capillary microbubble replenishment is prevented and the microbubble dose is increased, signals from larger intramyocardial vessels can be detected.7 This is accomplished by taking advantage of the slow blood flow velocity (~1 mm · s⁻¹) of capillaries compared with that of the larger intramyocardial arterioles. By transmitting ultrasound at an MI that destroys microbubbles and a frame rate of 15 Hz, only microvessels with a high flow velocity that can either fully or substantially replenish with microbubbles in ~67 ms are detected. Because capillaries do not replenish appreciably in this interval, high-MI imaging at 15 Hz allows evaluation of the phasic changes of the larger intramyocardial arteries into which blood from 150- to 300-μm arterioles is displaced retrogradely in systole.
The magnitude of retrograde displacement of blood increases in the presence of a stenosis and is based on the increase in aBV of resistance arteries from autoregulation and a decrease in coronary arterial afterload (lower mean coronary artery pressure distal to the stenosis). The more severe the stenosis is, the greater the retrograde displacement is. Because filling of the ultrasound beam is not influenced by the direction of microvascular flow, even retrograde flow is detected by our method as an increase in systolic aBV signal in the presence of stenosis.

If the heart were stationary, high-MI continuous imaging would destroy all the microbubbles in the ultrasound beam, so none would reach the distal vessels. Because the beating heart exhibits base-to-apex motion, rotation, and respiration-induced translation, the ultrasound beam intersects myocardial tissue at different locations during each pulse, which precludes complete microbubble destruction and allows them to reach distal portions of the coronary microcirculation. These microbubbles are then propelled retrogradely with the blood that is milked from the endocardium to the epicardium in systole and can be detected on ultrasound imaging.

**Limitations of the Method**

The S/D aBV ratio can be affected by variables other than stenosis severity. Tachycardia shortens diastolic filling times, causing a decrease in the diastolic aBV and a spurious increase in the S/D aBV ratio. By increasing cardiac contractility, catecholamines could increase the retrograde systolic displacement of blood, and myocardial dysfunction could decrease it. However, the presence of segmental myocardial dysfunction often implies the presence of CAD (prior myocardial infarction, stunning, or hibernation), and there is generally no need to perform a noninvasive test for coronary stenosis detection.

The finding of a low S/D ratio in some patients despite the presence of an angiographically severe stenosis is possibly related to the presence of collateral-derived MBF. The collateral-supplied regions are generally not subverted by stenotic vessels and therefore exhibit normal S/D ratios. In fact, we have recently demonstrated this in a canine model. Such effects could potentially be minimized by analyzing only the central portions of a perfusion bed, which are least likely to be affected by collateral flow. However, while the presence of collateral flow might limit the ability of our method to detect a physiologically significant stenosis, the S/D aBV ratio might be prognostically more important than the degree of stenosis on QCA because it might represent myocardium less likely to experience severe ischemia. Long-term studies are required to prove this point.

QCA is an inadequate gold standard in many respects because this single measure of lesion morphology does not take into account the physiological effects of factors like multiple stenoses in tandem, long stenoses, or the presence of diffuse coronary narrowing. Although we could not incorporate invasive measures such as fractional flow reserve, coronary flow reserve derived with intracoronary Doppler flow wire, or intravascular ultrasound in the present study, these measures could provide assessments of the physiological significance of stenoses that may correlate even better with S/D aBV ratio than QCA.

The number of patients used in the study is small. They were carefully selected from among those already scheduled for coronary angiography. Consequently, both insufficient power and selection bias are possible drawbacks. The mean S/D aBV ratios at different stenoses levels were different for the 2 ultrasound contrast agents, which was probably related to their characteristics and the mode of administration. Furthermore, a single ultrasound system was used for this study. The absolute values for different stenosis levels also are likely to differ between ultrasound systems. Therefore, this study provides only proof of principle, and the results need substantiation from a larger number of unselected patients and different contrast agents and ultrasound systems.

**Acknowledgments**

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**Disclosure**

Dr Wei has received a research grant from IMCOR Pharmaceuticals; has received other research support from Philips Ultrasound; has served on the speakers’ bureau of and/or received honoraria from Bristol-Myers Squibb Medical Imaging; and has served as a consultant to and/or on the advisory board of IMCOR Pharmaceuticals.

**References**

CLINICAL PERSPECTIVE

Coronary artery disease (CAD) is currently the leading cause of death in the western hemisphere. The World Health Organization predicts that in <20 years it will be the leading cause of death worldwide. In many patients, the first manifestation of CAD is sudden death or acute myocardial infarction. A reliable, robust, inexpensive, and simple test that could be used to detect physiologically significant CAD would be very useful worldwide. The current means of noninvasively diagnosing CAD are either inaccurate (exercise electrocardiography) or expensive and not widely available (nuclear imaging, ultrafast CT, and MRI). They are also tedious and inefficient because most of them require some form of pharmacological or exercise stress. Myocardial contrast echocardiography could offer the ability to detect the presence and severity of physiologically relevant CAD at rest using a relatively inexpensive procedure that takes no more than 15 minutes to perform. The novel and simple approach described in this article merits further investigation.
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