

Sensitive Detection of Myocardial Viability in Chronic Coronary Artery Disease by Ultrasonic Integrated Backscatter Analysis

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Background: Myocardial viability is not synonymous with contractile reserve and identifiable in a significant percentage of dysfunctional myocardial segments without contractile reserve. The usefulness of ultrasonic tissue characterization by the phase-corrected magnitude of cyclic variation of integrated backscatter (MVIB) in chronic coronary artery disease is not fully validated. Thus, whether MVIB predominantly reflects the contractile reserve or myocardial viability of chronically dysfunctional myocardium was determined.

Methods: The MVIB of severely dysfunctional interventricular septum or posterior wall was measured in 34 consecutive patients with previous myocardial infarction. Dobutamine stress echocardiography and fluorine-18 fluorodeoxyglucose positron emission tomography were used as the standards of contractile reserve and myocardial viability, respectively.

Results: Among 44 dysfunctional segments, only 15

were judged as having contractile reserve and 29 were judged as not by dobutamine stress echocardiography, whereas 26 segments showed myocardial viability using fluorine-18 fluorodeoxyglucose positron emission tomography and 18 did not. MVIB was greater in segments with than in those without contractile reserve (4.7 ± 2.2 vs -1.4 ± 4.9 dB, $P < .0001$), but there was considerable overlap between the groups. On the other hand, MVIB of segments with and without myocardial viability (4.1 ± 2.6 vs -4.3 ± 3.3 dB, $P < .0001$) was distinctly different and predicted myocardial viability with a sensitivity of 92% and a specificity of 94%.

Conclusions: For patients with chronic coronary artery disease, MVIB better reflects myocardial viability than it does contractile reserve. Ultrasonic tissue characterization, in concordance with fluorine-18 fluorodeoxyglucose positron emission tomography, is a sensitive method for detecting myocardial viability. (J Am Soc Echocardiogr 2005;18:26–31.)

Dobutamine stress echocardiography (DSE) is widely used to determine myocardial contractile reserve and has been shown to be outstandingly accurate in predicting functional recovery after coronary revascularization.^{1–3} On the other hand, recent studies suggested that radionuclide studies such as myocardial scintigraphy or fluorine-18 fluorodeoxyglucose positron emission tomography (FDG-PET) can sensitively identify even subtly viable myocardium in which the degree of viability may not be enough to contribute to contractile

reserve or functional recovery.^{4–10} Thus, the integrity of cell membrane or cell metabolism recognized using radioactive tracers does not necessarily imply functional contractile reserve. However, the identification of smaller amounts of viable myocytes may have important clinical implications independent of contractile reserve, in that it may be beneficial in preventing left ventricular (LV) remodeling and electrical instability.^{7,11–13}

Ultrasonic tissue characterization with integrated backscatter (IB) can detect stunned myocardium after a revascularization procedure in the early stage of acute myocardial infarction.^{14–16} IB analysis, a far simpler technique than DSE or FDG-PET, is attractive from both a clinical and an economic point of view. However, the role of myocardial IB analysis for patients with chronic coronary artery disease has not been fully investigated. In this study, we aimed to determine whether the magnitude of cyclic variation of IB (MVIB) predominantly reflects the contractile reserve or the myocardial viability of chronically dysfunctional myocardium. For this purpose

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we designed the study using two standards: DSE as the standard for contractile reserve and FDG-PET as the standard for myocardial viability.

METHODS

Patients

The study enrolled 34 consecutive patients admitted to our institution who fulfilled the following inclusion criteria: (1) severe asynergy in the anterior portion of the interventricular septum and/or in the LV posterior wall on routine 2-dimensional (2D) echocardiographic examination; and (2) history of myocardial infarction or presence of $\geq 75\%$ coronary stenosis on coronary angiogram (left anterior descending artery stenosis in patients with asynergy in the anteroseptum, and left circumflex artery stenosis in patients with asynergy in the posterior wall). The diagnosis of myocardial infarction was based on a clinical history consistent with acute myocardial infarction and ST segment elevation in two or more electrocardiographic leads in a standard 12-lead tracing. Patients with unstable angina and recent myocardial infarction (< 1 month) were excluded. Other exclusion criteria were severe ventricular arrhythmia and relevant organic heart disease other than coronary artery disease. Our institutional review board approved the study. Informed consent was obtained from all patients. Dividing the LV wall into the standard 16 segments based on the 2D echocardiographic examination at rest, 43 (14 basal and 29 midventricular) anteroseptal segments and 7 (5 basal and 2 midventricular) posterior segments that showed severe hypokinesis, akinesis, or dyskinesis were defined as dysfunctional segments.

DSE

Patients were allowed to take their prescribed medicines with the exception of β -blockers, which were withdrawn for 48 hours or more before the investigation. Using a diagnostic ultrasound system (Sonos 5500, Philips Medical Systems, Andover, Mass) equipped with an S4 transducer (2–4 MHz), gray-scale 2D echocardiograms in standard planes were acquired at baseline, and during 5- and 7.5- $\mu\text{g/kg/min}$ dobutamine infusion. These echocardiographic images were recorded digitally in a quadscreen, cine-loop format using an echocardiographic image analysis system (Prism 5000, TomTec Imaging Systems, Boulder, Colo). Electrocardiograms were continuously monitored, and blood pressure was recorded at 1-minute intervals. Dividing the LV wall into 16 segments, two experienced observers qualitatively classified the segmental wall motion before and during dobutamine infusion with the use of the following scoring system: 5 = dyskinetic; 4 = akinetic; 3 = severe hypokinetic; 2 = hypokinetic; and 1 = normal. Except for the dyskinetic segments, dysfunctional segments were judged to have contractile reserve when the wall motion score improved

by at least 1 grade after 7.5- $\mu\text{g/kg/min}$ dobutamine administration. The contractile reserve for the dyskinetic segments was defined as the improvement in wall motion score of 2 grades or more. If segmental wall motion was worsened by dobutamine stress as compared with that at previous stage, the segment was judged to develop myocardial ischemia.

FDG-PET

FDG-PET was performed using a whole body scanner (Ecat Exact HR+, Siemens Medical Systems/CTI, Knoxville, Tenn) equipped with germanium-68/gallium-68 retractable line sources for transmission scans. Transmission images were obtained using an external ring of gallium-68 so that the emission images could be corrected for photon attenuation. The intrinsic resolution was 4.5-mm full width at half maximum. To increase myocardial glucose uptake, each patient received a solution of 50 g of glucose 30 minutes before the injection of fluorodeoxyglucose. If glucose intolerance was apparent, hyperinsulinemic-euglycemic clamping was performed. Images were corrected for attenuation using coefficients obtained during a 20-minute transmission scan. At 30 minutes after glucose loading, or 1 hour after the start of the insulin clamp, 555 MBq of fluorodeoxyglucose was injected. Forty minutes later, exogenous myocardial glucose use was determined from a 20-minute static scan. Quantitative assessment of segmental fluorodeoxyglucose uptake was performed using two short-axis and vertical long-axis tomographic images in which the LV wall was divided into 16 segments corresponding to the echocardiographic evaluation. A segment was accepted as having myocardial viability when segmental fluorodeoxyglucose uptake was $\geq 50\%$ of the maximal uptake.

IB Analysis

Two-dimensional IB images of the LV were obtained using the same system as in the DSE with an online acoustic densitometry software package. This system provides either fundamental or second harmonic 2D images (30 frames/s) in which the gray level is displayed proportional to the IB intensity. In this study, the second harmonic IB images (transmission frequency 2.1 MHz/receive frequency 4.2 MHz) in the parasternal long-axis plane were obtained at rest, and stored on the magneto-optical disk.

IB analysis was performed by retrieving the previously stored cine-loop data from the magneto-optical disk. Loops including any premature beats were excluded from the analysis. In the dysfunctional segments, the largest possible ellipsoidal region of interest was placed, avoiding bright specular echoes from the endocardium (Figure 1). Location of the region of interest was manually adjusted on a frame-by-frame basis to keep it at the target site throughout a cardiac cycle. The mean value of IB in the region of interest was measured in decibels. These data were used to generate the temporal profile of cyclic variation of IB. MVIB was calculated as the difference between the minimum and

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