● *Original Contribution*

ULTRASONIC TISSUE CHARACTERIZATION FOR CORONARY CARE UNIT PATIENTS WITH ACUTE MYOCARDIAL INFARCTION

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Abstract—The ultrasonic integrated backscatter of myocardium changes in infarction and ischemia. On the third day after acute myocardial infarction, 30 patients underwent ultrasonic tissue characterization from the parasternal short-axis view. With a composite parameter, the phase-weighted variation, sensitivity, specificity, and accuracy for diagnosing multivessel coronary artery disease were 84.6%, 52.9% and 66.6%, respectively. Using 67° as the cutoff value for the phase deviation of the backscatter power curve, the recanalization of the infarct-related artery could be detected with a positive predictive value of 77.7% and a negative predictive value of 66.6%. Ultrasonic tissue characterization is a feasible technique for detecting the multivessel coronary artery diseases and the recanalization of infarct-related artery for patients with acute myocardial infarction. The diminished cardiac cycle-dependent variation in integrated backscatter and increased phase deviation can differentiate patent coronary arteries from those coronary arteries with anatomically significant stenoses. © 1998 World Federation for Ultrasound in Medicine & Biology.

Key Words: Ultrasonic tissue characterization, Acute myocardial infarction, Multivessel coronary artery disease, Reperfusion.

INTRODUCTION AND LITERATURE

The identification of multivessel coronary artery disease in patients with acute myocardial infarction (AMI) has important prognostic implications (Schulman et al. 1988; Muller et al. 1991). Although coronary angiography is still regarded as the “gold standard” for the assessment of coronary artery disease, many noninvasive approaches, including exercise electrocardiography, stress ²⁰¹thallium myocardial perfusion scanning and dobutamine stress echocardiography have been developed to predict multivessel coronary artery disease in AMI (Abraham et al. 1986; Berthe et al. 1986). Some limitations, however, have been noted. To begin with, all these methods are performed under stress conditions and are not very suitable for use during the acute stage. Next, exercise electrocardiography and ²⁰¹thallium scintigraphy are not feasible for patients admitted to the coronary care unit. Also, the protocol of dobutamine stress echocardiography states that the first-induced new regional

wall motion abnormality is the absolute end-point. Therefore, the sensitivity of this test in identifying coronary artery disease is limited only to finding the most severe lesions demonstrating low-threshold asynergies; thus, leaving less severe lesions undetected (Bigi et al. 1995).

Over the past decade, the ultrasonic tissue characterization of myocardium using integrated backscatter has been validated to detect acutely infarcted and stunned myocardium (Milunski et al. 1989). By lower cyclic variation and phase reversal, Saeian et al. (1994) have recently used ultrasonic tissue characterization to diagnose AMI in coronary care unit patients. However, reperfusion and remote ischemia were not mentioned. Because both acute myocardial ischemia and infarction result in increased integrated backscatter and blunting of cardiac cycle-dependent variation in backscatter (Mimbs et al. 1981; Glueck et al. 1985; Fitzgerald et al. 1987; Milunski et al. 1989; Barzilai et al. 1990; Lythall et al. 1992), we hypothesized that ultrasonic tissue characterization could also be used to detect the remote coronary artery lesions, other than the infarct-related arteries. The purpose of this study was: (a) To compare the amplitude

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and phase-shift of the cardiac cycle-dependent variation in backscatter between the myocardium perfused by the patent, stenotic and infarct-related coronary arteries; (b) to verify the use of ultrasonic tissue characterization in detecting multivessel coronary artery disease after acute myocardial infarction; and (c) to determine if ultrasonic tissue characterization is capable of predicting recanalization after reperfusion therapy.

MATERIALS AND METHODS

Patients

From February to May in 1996, 37 consecutive patients were admitted to our coronary care unit for AMI with 2 of the 3 following criteria: prolonged ischemic chest pain, characteristic electrocardiographic changes and an increase in serum creatine phosphokinase-MB. Criteria for the electrocardiographic localization of infarction were adapted from the standardized terminology proposed by Surawicz et al. (1978). Creatine phosphokinase-MB detected in an amount of more than 5% of an elevated total creatine phosphokinase was considered diagnostic for AMI. A Q-wave myocardial infarction was diagnosed by the development of a new Q-wave ≥ 0.04 in more than one lead, and a non Q-wave infarction was diagnosed by the elevated creatine phosphokinase-MB isoenzymes with deep and symmetric T-wave inversion. Two patients who refused coronary angiography and 2 patients with unsatisfactory precordial echocardiographic imaging were excluded. ^{99m}Tc Technetium pyrophosphate imaging was done to confirm and locate the myocardial infarction in 32 patients. Three patients with previous myocardial infarctions were excluded. No patients had any of the other criteria of exclusion: atrial fibrillation, multiple ventricular premature contractions, or cardiomyopathy.

Thirty patients were included in this study; 13 patients received recombinant tissue-type plasminogen activator as the reperfusion therapy. Primary percutaneous transluminal coronary angioplasty was performed in the other 2 patients. When ultrasonic tissue characterization was performed, no patient was given any inotropic agent or experienced postinfarction angina. At the discretion of the attending physician, β -blockers were administered.

Echocardiographic studies

Patients received echocardiographic studies with a Hewlett Packard (HP) system (Sonos 1500) on the third day after their acute myocardial infarction. A 64-element ultrasound transducer operating at a center frequency of 2.5 MHz was used in this study. Standard two-dimensional (2-D) views were obtained and independently reviewed by 2 observers who had no knowledge of the clinical and ultrasonic tissue characteriza-

tion data, to identify the presence of regional wall-motion abnormalities. Wall motion was graded as normal, hypokinetic, akinetic, or dyskinetic. The coronary lesions were predicted by using conventionally defined wall segments (Schiller et al. 1989) and a schema correlating the segmental wall motion abnormalities with the coronary artery distribution (Sawada et al. 1991; Segar et al. 1992). Agreement among the 2 observers was achieved in 96% (29 of 30) of the studies. Any disagreement among the 2 observers was resolved through discussion.

Backscatter data acquisition and analysis

The backscatter data were collected immediately after obtaining the 2-D images. Ultrasonic tissue characterization examinations were performed by a third observer with a real-time 2-D prototype imaging system (77025A, Hewlett Packard, Andover, MA) capable of providing images in which gray-levels were displayed proportional to the integrated backscatter amplitude obtained. When operating in the integrated backscatter mode, the received ultrasound signals were amplified, mixed with the intermediate frequency and, finally, totaled with appropriate time delay. The imaging frame rate was automatically set to 30 Hz and the dynamic range of the integrated backscatter signal was approximately 44 dB. Despite the substantial anisotropy in the parasternal short-axis view, which can be compensated for with lateral gain compensation (Recchia et al. 1993), we used the view at the papillary muscle level to obtain the 2-D image of integrate backscatter for evaluating all the three vessel territories simultaneously. The transmit power, time gain compensation and lateral gain compensation were adjusted to optimize image presentation and remained constant throughout the study. Sixty frames of the left ventricular short-axis view were displayed and captured in digital format for each examination period. The integrated backscatter was quantified by placing a region-of-interest (ROI) in the myocardium on the frozen image. The ROI was configured with a different shape, size and orientation to fit within the boundaries of the myocardial wall at end-diastole. For most patients, the 21×21 pixel ROI was used. The location of the ROI was adjusted frame by frame to keep it well within the subendocardial myocardium (Wickline et al. 1985a; Sagar et al. 1987) and to avoid specular endocardial and epicardial echoes throughout the cardiac cycle. For each patient, three ROIs were chosen in the same parasternal short axis image. One was at the mid-anteroseptal area to represent the myocardium perfused by left anterior descending coronary artery (LAD); another was at the junction of mid-posterior with mid-lateral area to represent the myocardium perfused by left circumflex artery (LCX); the other was at the mid-inferior area for the

Fig. 1. The ultrasonic tissue characterization in a 71-y-old female with inferior wall myocardial infarction. (a) The backscatter data acquisition over the junction of midposterior and midlateral segments to represent the myocardium perfused by the left circumflex artery. (b) The curve of integrated backscatter vs. time (from top to bottom, representative of the integrated backscatter from myocardium perfused by the left circumflex artery, the right coronary artery, and the left anterior descending artery, respectively). In every curve, the baseline was adjusted individually to reveal the phase shift from every coronary artery. (c) The coronary angiography showed stenosis over the proximal portion of the left anterior descending artery (white arrow) that was classified as remote diseased coronary artery. (d) The coronary angiography showed a culprit lesions (black arrow) over the right artery with TIMI Grade 2 flow.

myocardium perfused by right coronary artery (RCA). On the frozen frame of parasternal short axis image, those ROIs were approximately at the 12, 4, 8 o'clock direction to the center of the left ventricle, respectively. The serial time-varying changes in the magnitude of integrated backscatter (in dB) within the ROI were then obtained from each frame during the cardiac cycle and displayed as a curve of integrated backscatter vs. time with electrocardiographic R wave as a reference (Fig. 1a). The images and data sets were stored in the optic disk for off-line analysis. For most patients, the curve included more than two consecutive beats. The power amplitude of the integrated backscatter was obtained by averaging all the values corresponding to the same time point in each cardiac cycle. The power curve for a full cardiac cycle was plotted as amplitude vs. time with

frame of 33- μ s interval. We wrote a program with the MATLAB (the Math Works, Inc.) and the first harmonic Fourier fitting of the power curve (Mottley *et al.* 1984) was obtained promptly.

Two basic measurements were obtained from the first harmonic Fourier fitting of the integrated backscatter curve: the amplitude and phase. Along with the two measures, Fig. 2 demonstrated a typical integrated backscatter power curve and its first harmonic Fourier fitting overlay. We designated the variation, by doubling the amplitude, to represent the difference between maximal and minimal values of integrated backscatter. By using the electrocardiographic R wave as the trigger reference, the phase-weight variation was derived from the variation and the phase (Wickline *et al.* 1986; Fitzgerald *et al.* 1987). The following criteria were used to decide the

Fig. 2. The integrated backscatter power curve vs. time for a cardiac cycle. The thick solid curve represents the results of the first Fourier harmonic fitting. The phase and doubling amplitude (variation) of the first Fourier harmonic fitting are indicated.

phase-weighted variation, the phase angle and the weighting factor (Vitale et al. 1995):

$$\text{Factor} = -1 \quad \text{if } (0^\circ \leq \text{phase} \leq 45^\circ) \quad (1)$$

$$-\cos[2(\text{phase} - 45^\circ)]$$

$$\text{if } (45^\circ \leq \text{phase} \leq 135^\circ) \quad (2)$$

$$1 \quad \text{if } (135^\circ \leq \text{phase} \leq 225^\circ) \quad (3)$$

$$\cos[2(\text{phase} - 45^\circ)]$$

$$\text{if } (225^\circ \leq \text{phase} \leq 315^\circ) \quad (4)$$

$$-1 \quad \text{if } (315^\circ \leq \text{phase} \leq 360^\circ) \quad (5)$$

The criteria used in weighting variations were such that the variation with a phase value of approximately 180° (135° to 225°) was normal and had a weight factor of 1. On the contrary, variations with a phase value progressively smaller than 135° or $> 225^\circ$ were reduced by a factor gradually changing toward -1 . According to the assumption that the normal phase value was 180° , the phase deviation could be obtained by the absolute value of phase value minus 180° and designated as the difference between the phase value and the conceptualized normal ones. It took about 1 h to acquire the ultrasonic tissue characterization, analyze the backscatter data and arrive at the final parameters.

The presence of interpatient acoustic variability (such as miscellaneous attenuation across the chest wall on transthoracic approach) and different gain setting to optimize the image in each patient made the standardization of integrated backscatter power difficult. By a dog study, however, Naito et al. (1995) disclosed that

there was no significant difference in the amplitude of cyclic variation in integrated backscatter between the open chest and closed chest setting. Our analysis was derived from the values of variation, phase-weighted variation and phase deviation.

Data reproducibility

To test the reproducibility, we performed ultrasonic tissue observers characterization by two observers in another 20 subjects. One of the two doctors did the test twice to evaluate the intraobserver variability. All the examinations started from the integrated backscatter data acquisition (Stuhlmüller et al. 1992). The mean absolute variabilities for variation were 0.7 ± 0.5 dB (intraobserver) and 1.3 ± 1.0 dB (interobserver). For phase, these were $5 \pm 7^\circ$ (intraobserver) and $7 \pm 9^\circ$ (interobserver). Performing correlation analysis of the repeated measurements by the linear regression method, the coefficients of correlation for variation were 0.95 (intraobserver) and 0.79 (interobserver). The standard errors of the estimate were 0.8 dB (intraobserver) and 1.4 dB (interobserver). As to phase, the coefficients of correlation were 0.90 (intraobserver) and 0.81 (interobserver). The standard errors of the estimate were 8° (intraobserver) and 10° (interobserver). These were considered as the reproducibility of our laboratory.

Coronary angiography

After obtaining consent forms from the patients, coronary angiography was performed with routine technique between 7 and 10 days after the onset of AMI. For the 2 patients who received emergent percutaneous transluminal coronary angioplasty, follow-up coronary angiography was done 1 week later. A computer-aided quantitative angiographic analysis system (DCI-S Automated Coronary Analysis System, Philips Medical Systems, Eindhoven, The Netherlands) was used. After identifying the infarct-related artery, the patency was assessed by 2 observers with no knowledge of the treatment for reperfusion. The reperfusion status was reported as thrombolysis in myocardial infarction (TIMI) flow grades (The TIMI Study Group 1985). A $> 70\%$ diameter stenosis was considered significant. The stenotic lesions of vessels other than infarct-related arteries were classified as remote coronary artery disease. Because the ultrasonic tissue characterization study was only executed at mid ventricular level, the two lesions at the distal portion of LAD were not considered as significant coronary stenosis in this study.

Statistical analysis

All results were given as mean $\pm$ standard deviation. The 2-sample *t* test was used to compare continuous data between 2 different groups. The chi-square test was

Table 1. Basic characteristics

	Single-vessel disease	Multivessel disease	<i>p</i> value
Number	17	13	
Men	12 (71%)	9 (69%)	NS
Age	66 ± 10	63 ± 10	NS
Risk factors			
Hypertension	10 (59%)	8 (62%)	NS
Diabetes mellitus	3 (18%)	4 (31%)	NS
Smoking	9 (53%)	7 (54%)	NS
Hyperlipidemia	1 (6%)	1 (8%)	NS
Reperfusion therapy	10 (59%)	5 (38%)	NS

NS = not statistically significant.

used to compare categoric data. One-way analysis of variance (ANOVA) was used to compare continuous data among ≥ 3 different groups. A *p* value < 0.01 (2-tailed) was considered statistically significant. The specificity, sensitivity and accuracy for predicting coronary artery disease were plotted vs. various values of phase-weighted variation to determine the significant cutoff value. Furthermore, the receiver operating characteristic curve analysis (Wanger *et al.* 1995) was also applied to evaluate the cutoff value of phase-weighted variation. The same analysis was done for the phase deviation to determine the cutoff value in predicting recanalization.

RESULTS

Patients and coronary angiography

All the 30 patients (21 men and 9 women with a mean age of 60 ± 7 y) had Q-wave myocardial infarction and 13 of the 30 patients had multivessel disease. Seven patients had 3-vessel disease and the other 6 had 2-vessel disease. There was no statistically significant difference in the basic clinical characteristics between the patients with single and with multivessel disease (Table 1). Fifteen patients received reperfusion therapy (2 patients with primary percutaneous transluminal coronary angioplasty and 13 patients with thrombolytic therapy). The TIMI Grade 3 flow was noted in 13 of these 15 patients. There were statistically significantly fewer patients with TIMI Grade 3 flow in those who did not receive reperfusion therapy (5 of 15 vs. 13 of 15, *p* = 0.009).

Conventional 2-D echocardiography

The regional wall motion abnormalities could be detected by 2-D echocardiography in all the infarct-related artery territories. Of the 13 patients with multivessel disease, 4 (31%) demonstrated remote asynergy as defined by wall-motion abnormalities in a vascular territory outside the infarct-related artery. On the other

hand, 4 of the 5 patients with remote asynergy had multivessel disease (positive predictive value, 80%).

Parameters from backscatter data analysis

The vascular territories were classified in 3 groups: (a) Supplied by the infarct-related artery; (b) supplied by the remote-diseased coronary artery with lesions of more than 70% stenosis in diameter; and (c) supplied by the patent coronary arteries. In Table 2, the variation, phase-weighted variation and phase deviation of these 3 groups are shown. There were statistically significant differences of variation, phase-weighted variation and phase deviation between the myocardial territories having patent coronary arteries and those with infarct-related arteries (all *p* < 0.0001). The phase deviation in the territories supplied by remote diseased coronary arteries was similar to those in patient coronary arteries (*p* = 0.97). The variation and phase-weighted variation, however, were significantly lower in the territories supplied by remote-diseased coronary arteries (both *p* = 0.0003). The curves of the sensitivity, specificity, and accuracy in predicting the presence of coronary artery disease (including both infarct-related artery and $> 70\%$ stenotic coronary artery) vs. different values of phase-weighted variation are shown in Fig. 3. The optimal result was obtained when the cutoff value of phase-weighted variation was 5.8 (Table 3). The area under the receiver operating characteristic curve was 0.857 (Fig. 3).

Recchia *et al.* (1993) have shown that the lateral gain compensation could reduce the influence of anisotropy on 2-D integrated backscatter images. They also used parasternal short-axis view in their study. We analyzed ultrasonic tissue characterization on the 40 patent coronary vessel territories. The difference of phase in the 3 groups (classified by the different locations of ROI, on LAD, LCX and RCA territories, respectively) was insignificant (*p* = 0.346, by ANOVA). The difference of variation was of some

Table 2. Parameters in ultrasonic tissue characterization for patent, remote diseased, and infarct-related artery

	Variation	Phase deviation	Phase-weighted variation
PCA	7.2 ± 2.8	$27.5 \pm 15^\circ$	7.2 ± 2.8
RDA	$4.4 \pm 2.5^+$	$27.7 \pm 19.5^\circ$	$4.3 \pm 2.6^+$
IRA	$4.5 \pm 2.0^\ddagger$	$56.1 \pm 29.1^{\circ**}$	$2.5 \pm 1.9^\ddagger$
TIMI = 3	$4.2 \pm 1.7^\ddagger$	$44.2 \pm 27.2^\circ$	$3.2 \pm 1.7^\ddagger$
TIMI ≤ 2	4.9 ± 2.4	$73.9 \pm 22.6^{\circ**\S}$	$1.3 \pm 1.6^{\ddagger**\S}$

IRA = infarct-related artery; PCA = patent coronary artery; RDA = remote diseased coronary artery; TIMI = the TIMI flow grade of infarct-related artery.

$^+p < 0.001$, compared to that of PCA; $^\ddagger p < 0.0001$, compared to that of PCA; $^*p < 0.001$, compared to that of RDA; $^\S p < 0.005$, comparison between TIMI = 3 and TIMI ≤ 2 .

Fig. 3. The sensitivity, specificity, accuracy, and the receiver operating characteristics curve for the phase-weighted variation in detecting the coronary lesions. Left: Variation in sensitivity (open squares), specificity (open rhombi), and accuracy (open triangles) are plotted as a function of different values of the phase-weighted variation. The optimal cutoff point is marked. Right: The corresponding receiver operating characteristic curve with the arrowhead indicating the optimal cutoff point.

significance ($p = 0.16$, by ANOVA). It was attributed to the lower variation of the LCX territories (5.9 ± 2.8 dB) than that of LAD (7.6 ± 3.5 dB) and of RCA (7.6 ± 2.8 dB). It also reduced the specificity in detecting coronary artery disease in the LCX territories (57.9%) and in predicting multivessel disease (52.9%, see below). The variation of the RCA and LAD territories, however, was similar ($p = 0.99$). Thereafter, we thought that the angle between ultrasound beam and myocardial fiber orientation was not the major factor resulting in the difference of variation

because it might be similar for RCA and LCX territories. The lung tissue might have significant influence on the acquisition of integrated backscatter data from the LCX territories.

Detection of multivessel disease

The sensitivity in detecting remote coronary artery disease with more than 70% stenotic lesions was reevaluated by the phase-weighted variation with the cutoff value of 5.8 and was listed in Table 3. When we excluded the 2 patients with distal lesions in the LAD, the sensi-

Table 3. Sensitivity, specificity, and accuracy for phase-weighted variation in detecting individual coronary artery disease and remote disease

	LAD	LCX	RCA	Total
Sensitivity	100% (19 of 19)	81.8% (9 of 11)	85% (17 of 20)	90% (45 of 50)
Specificity	81.8% (9 of 11)	57.9% (11 of 19)	80% (8 of 10)	70% (28 of 40)
Accuracy	93.3% (28 of 30)	66.7% (20 of 30)	83.3% (25 of 30)	81.1% (73 of 90)
Sensitivity for remote disease	100% (5 of 5)	80% (8 of 10)	60% (3 of 5)	80% (16 of 20)

LAD = left anterior descending artery; LCX = left circumflex artery; RCA = right coronary artery; the numbers in parentheses represent the number of patients.

Fig. 4. The sensitivity, specificity, accuracy, and the receiver operating characteristic curve of the phase deviation for predicting TIMI Grade 3 flow. Left: Variation in sensitivity (open squares), specificity (open rhombi), and accuracy (open triangles) are plotted as a function of different values of the phase deviation. The optimal cutoff point is marked. Right: The corresponding receiver operating characteristic curve with the arrowhead indicating the optimal cutoff point.

tivity for this vessel was very high (100%). For predicting multivessel disease, the sensitivity, specificity and accuracy were 84.6%, 52.9% and 66.6%, respectively.

Reperfusion identification

The infarct-related arteries were classified into 2 groups, according to whether or not TIMI Grade 3 flow was present. In these two groups, the phase-weighted variation and phase deviation were statistically significantly different ($p = 0.0047$ and $p = 0.0032$, respectively). There was, however, no statistically significant difference in the variation ($p = 0.41$). By using different values of the phase deviation, the curves of the sensitivity, specificity, and accuracy in predicting the presence of TIMI Grade 3 flow are shown in Fig. 4. The cutoff value of 67° was chosen and the sensitivity, specificity, accuracy, positive predictive value, and negative predictive value were 77.7%, 66.6%, 73.3%, 77.7% and 66.6%, respectively. The area under the receiver operating characteristic curve was 0.808 (Fig. 4).

DISCUSSION

Previous studies (Wickline *et al.* 1985a, 1985b) have shown a cardiac cycle-dependent variation of inte-

grated backscatter from the myocardium with maximal values at the end-diastole and minimal values at the end-systole. The backscatter power variability can be modified by ischemia or infarction. Induction of ischemia in animals or humans causes an increase in time-averaged integrated backscatter and a reduction in backscatter cyclic variation (Glueck *et al.* 1985; Wickline *et al.* 1986; Fitzgerald *et al.* 1987; Milunski *et al.* 1989; Barzilai *et al.* 1990; Lythall *et al.* 1992; Vitale *et al.* 1995). The phase value obtained by the first harmonic Fourier fitting or the QT delay increases when ischemia or infarction is induced experimentally. Such changes parallel the modifications induced in myocardial wall kinesis and correlate with the severity of the ischemia (Wickline *et al.* 1986). Reperfusion can restore the amplitude of cyclic variation and the phase delay to some extent and cause the time-averaged backscatter to diminish a little (Glueck *et al.* 1985; Wickline *et al.* 1986; Milunski *et al.* 1989). Because these restorations develop before the recovery of regional wall motion abnormalities, ultrasonic tissue characterization has been assumed to be a useful tool in detecting the stunned myocardium (Milunski *et al.* 1989). Recently, O'Brien *et al.* (1995b)

have verified the acoustic propagation properties capable of identifying stunned and infarcted myocardium.

According to a physiologically based model for the behavior of ultrasonic backscatter proposed by Wickline et al. (1985b), the time-varying change in backscattered energy during the cardiac cycle results from a changing acoustic impedance that is caused by variations in tissue elastic modulus during sarcomere shortening and is influenced by ischemia. Recently, a "geometric" model has been proposed by O'Brien et al. (1995a) to account for the cyclic backscatter, that is based primarily on change in the density of scatters with contraction. On the other hand, Glueck et al. (1985) have found that the backscatter changes parallel those of myocardial systolic function more closely than they parallel changes in perfusion per se. According to the models or findings mentioned above, we assumed that ultrasonic tissue characterization could provide a useful measure of regional intramural contractile function that was relatively independent of wall motion or wall thickening.

Saeian and his coworkers (1994) have used ultrasonic tissue characterization for diagnosing AMI in the coronary care unit. When this technique is compared with 2-D echocardiography, both have a comparable sensitivity, specificity, and accuracy. Ultrasonic tissue characterization is superior when left bundle branch block or non Q-wave AMI is present. However, the influence of reperfusion therapy was not mentioned. In this study, the difference in the variation, phase-weighted variation and phase deviation between those territories with patent coronary arteries and infarct regions was very significant and indicated that these parameters could help distinguish healthy from injured myocardium. On the contrary, 2 patients (one receiving thrombolytic therapy during the third h and the other with primary percutaneous transluminal coronary angioplasty during the fourth h after onset of chest pain) had similar parameters in infarct-related arteries as those in patent coronary arteries. In these 2 patients, although the regional wall motion belonging to the infarct-related artery territories was still asynergic, the integrated backscatter power curve had been restored to a nearly normal pattern. This phenomenon has been cited by Milunski et al. (1989) and indicates the existence of stunned myocardium. Therefore, the identification of myocardial infarction through ultrasonic tissue characterization would be influenced by the reperfusion therapy, to some extent.

Grouping the infarcted myocardium into 2 categories according to the presence of TIMI Grade 3 flow, the difference of phase-weighted variation was significant ($p = 0.0047$) and might be attributed to the phase deviation ($p = 0.0032$). It has been shown by Milunski et al. that increased QT delay index (similar to the phase deviation in this study) indicated marked asynchrony of

the mechanical function in infarct regions. On the other hand, the improvement in QT delay index after recanalization may be due to more synchronous systolic shortening in the injured, but recovering, myocardium (Milunski et al. 1989). In addition, the variations in these 2 groups were comparable ($p = 0.41$) and different from that in patent coronary arteries (both $p < 0.001$). It was similar to the findings of Milunski's study about the early phase after reperfusion (Milunski et al. 1989) and implicated the substantial anisotropy in the infarct regions. (Wickline et al. 1992). Therefore, although the magnitude of cyclic variation of integrated backscatter has not been restored, the diminished phase deviation can be considered as a early marker for recanalization of the infarct-related artery.

Two-dimensional echocardiography is a valid method to localize and quantify the extent of myocardial involvement early after the onset of AMI. (Nixon et al. 1980; Gibson et al. 1982). It can also detect areas of ischemia (Nixon et al. 1980). By identifying remote asynergy, Gibson et al. (1982) has demonstrated that the sensitivity for detecting multivessel disease in patients without prior infarction is 58% (8 of 14) and slightly higher than what we found (31% in our survey). Many investigators have discovered the modifications of myocardial reflectivity during ischemia preceding the regional dyssynergy (Vitale et al. 1995; Marini et al. 1996). In this study, the sensitivity for detecting multivessel coronary artery disease after AMI by ultrasonic tissue characterization was higher than that by standard 2-D echocardiography. We could identify the jeopardized myocardium with grossly normal contractile function by this method. Furthermore, no pharmacological stimuli or additional stress test was needed for ultrasonic tissue characterization. It is very convenient and safe for coronary care unit patients. The phase deviation in the patent coronary arteries and remote-diseased coronary arteries were similar ($p = 0.968$) because no obvious regional dyssynergy was noted in either group. However, the variation and phase-weighted variation of regions belonging to remote diseased coronary arteries were smaller than that in patent coronary arteries (both $p < 0.0003$). It might result from remote ischemia. The compensatory hyperkinesia of segments perfused by patent coronary arteries might also accentuate the difference.

There was no statistically significant difference in the variation, phase-weighted variation and phase deviation between the remote diseased coronary arteries and the infarct-related arteries with TIMI Grade 3 flow ($p = 0.828$, $p = 0.138$ and $p = 0.041$, respectively). The detection and localization of AMI, therefore, could be influenced both by reperfusion and remote diseases. Making a comparison of the variation, phase-weighted variation and phase deviation among these groups listed

in Table 2, we found a tendency that reperfusion could restore these parameters in infarct-related arteries to the level in remote-diseased coronary arteries, even to patent coronary arteries just like the 2 patients mentioned above. The degree of restoration may be correlated with the time interval between the onset of infarction and the development of reperfusion (Wickline *et al.* 1986). A large-scale study, however, is warranted to disclose the statistical significance. If the restoration implicates the myocardial viability, ultrasonic tissue characterization appears to sensitively delineate the reversibility of ischemic injury in response to reperfusion.

Study limitations

This study has several limitations. First, the result of ultrasonic tissue characterization was only correlated to the angiographic findings in this study. The correlation between the angiographic stenosis and the existence of remote or silent ischemia, however, is left to be ratified. Similarly, we used the phase deviation in predicting the recanalization of infarct-related artery. However, it does not necessarily indicate the salvage of the risk area. Long-term follow-up study and other modalities for viability assessment are mandatory to verify our observation. Second, in this study, the ultrasonic tissue characterization could not afford a comprehensive view of the whole ventricle because of anisotropy and difficult delineation of the endocardium in the apical segments (Saeian *et al.* 1994). Only the midventricular myocardium was evaluated. In our study, there was no patient in whom the infarct area was too small to be delineated in this image. Third, the overlap segments between individual vascular territory will also influence the prediction for the vascular lesions. It was specially difficult to differentiate the vascular involvement between the left circumflex and right coronary arteries. It would decrease the diagnostic sensitivity and specificity in this study. Fourth, the magnitude of ultrasonic energy backscattered from myocardial tissue, as well as the attenuation suffered by the ultrasonic waves, depends on the angle of insonification with respect to the predominant orientation of the myofibers at selected intramural levels. Although the property of ultrasonic anisotropy can be compensated by clinically applicable techniques, such as lateral gain compensation and time gain compensation (Recchia *et al.* 1993), a large-scale study is necessary to disclose the ultrasonic angle dependency of the measurement obtained in the three different areas of the short axis image. Finally, the magnitude of cardiac cycle-dependent variation of integrated backscatter is reduced in the patients with pressure-overload ventricular hypertrophy (Masuyama *et al.* 1989b) and diabetes mellitus (Perez *et al.* 1992). The magnitude is also affected by aging (Masuyama *et al.* 1989a). These factors are common in

patients with AMI. Our study was too small in scale to reveal the possible effects of these factors, although there was no statistically significant difference in the basic clinical characteristics between the patients with single and with multivessel disease. Further investigation is warranted.

SUMMARY

Ultrasonic tissue characterization with integrated backscatter is readily applicable in the coronary care unit. The diminished cardiac cycle-dependent variation in integrated backscatter and increased phase deviation can differentiate patent coronary arteries from those coronary arteries with anatomically significant stenosis. The presence of multivessel disease can be diagnosed by using the composite parameter, the phase-weighted variation. The existence of TIMI Grade 3 flow of those infarct-related arteries can be predicted by using the phase deviation. Ultrasonic tissue characterization may serve as a useful adjunct in evaluating the presence of multivessel disease and in detecting potentially salutary effects of prompt reperfusion of the acutely ischemic myocardium. Further studies are mandatory, first to elucidate the implications of the cyclic variation of integrated backscatter in remote or silent ischemia, and second to assess the feasibility of the method for myocardial viability.

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