Myocardial Viability Detected by Dobutamine Echocardiography in Patients With Chronic Coronary Artery Disease, and Long-Term Outcome After Coronary Angioplasty

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Viable but dysfunctional myocardium detected by dobutamine echocardiography (DE) predicts early improvement in regional left ventricular (LV) function after percutaneous transluminal coronary angioplasty (PTCA). Whether DE can predict the long-term (>2 years) outcome after PTCA is still unclear. Thus, 50 patients (age 60.4 ± 9.5 years) with chronic coronary artery disease and regional LV dysfunction who underwent DE 1 week before PTCA to assess myocardial viability were followed for 4.0 ± 0.8 years. Regional LV function and LV ejection fraction (LVEF) were evaluated by 2-dimensional echocardiography in patients who remained event-free (cardiac death or myocardial infarction or unstable angina pectoris) after PTCA. At late follow-up (>2 years after PTCA), 29 patients showed regional LV function improvement, 15 showed no improvement, 3 showed worsening and 3 patients had cardiac events (1 nonfatal myocardial infarction and 2 unstable angina pectoris). LVEF improved (0.53 ± 0.09 to 0.60 ± 0.09 , $p < 0.001$) in patients with improved regional LV function, but deteriorated (0.38 ± 0.03 to 0.30 ± 0.03) in the 3 patients with worsened regional LV function. Of the 29 patients with improvement, 27 (93%) had viable myocardium, whereas only 3 (20%) of the 15 with no improvement had viable myocardium and all 6 of those with poor outcomes (3 with cardiac events and 3 with worsening) had viable myocardium ($\chi^2 = 28.9$, $p < 0.001$). Patients with viable myocardium and a poor outcome had a lower mean LVEF before PTCA, and at 1 week and 3 months after PTCA ($p = 0.004$, < 0.001 , and $= 0.001$, respectively), and a higher restenosis rate ($p = 0.007$) than patients with viable myocardium and without a poor outcome. It is concluded that viable myocardium detected by DE may predict long-term improvement in regional and global LV function after PTCA. However, patients with viable myocardium and persistent low LVEF are at risk for cardiac events or worsening of LV function. (Jpn Circ J 2000; 64: 183–190)

Key Words: Dobutamine echocardiography; Long-term outcome; Percutaneous transluminal coronary angioplasty (PTCA); Viable myocardium

Dobutamine echocardiography (DE) is a simple and potentially widely available imaging modality for detecting viable yet dysfunctional myocardium in patients with coronary artery disease (CAD) and for predicting improvement in regional left ventricular (LV) function after coronary artery revascularization.^{1–4} In our previous study we demonstrated that, in comparison with thallium-201 reinjection imaging, DE reliably predicts functional recovery of dysfunctional myocardium after coronary artery revascularization.⁵ Most of the published reports have shown improved wall motion within 3 months after revascularization in dysfunctional LV regions detected viable by DE.^{2–5} A recent report showed that in patients with stable CAD, the improvement in wall motion in dysfunctional regions detected viable by DE is incomplete at 3 months after surgical revascularization, and that more improvement occurs at 1 year after revascularization.⁶

On the other hand, recently published reports show that viable myocardium detected by DE is a predictor of a worse prognosis in patients with chronic CAD treated medically.^{7,8} Successful percutaneous transluminal coronary angioplasty (PTCA) improves reversibly depressed regional LV systolic function,^{3,4} which persists unless severe restenosis develops.⁹ Although a large multicenter study showed a better outcome for PTCA in patients with preserved LV function compared with patients with depressed LV function,¹⁰ the relationship between myocardial viability detected by DE in dysfunctional regions and long-term (>2 years) outcome, including LV function, after PTCA remains unclear. Therefore, the present study was performed to investigate whether DE can predict the long-term outcome after PTCA in patients with chronic CAD by detecting dysfunctional yet viable myocardium.

Methods

Patient Selection

From April 1992 to March 1996, all patients with CAD and resting wall motion abnormalities in any LV segment related to a stenosed coronary artery as revealed by 2-dimensional (2-D) echocardiography and who were sched-

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uled for PTCA were screened with DE. Of 118 patients selected by the initial inclusion criteria 52 were excluded for the following reasons: (1) acute myocardial infarction (MI) or unstable angina pectoris (AP) within the past 6 weeks (17 patients), (2) history of sustained ventricular tachycardia or atrial fibrillation (5 patients), (3) therapy with a β -adrenergic blocker (17 patients), (4) poor echocardiographic quality (10 patients), and (5) refusal to participate (3 patients). Of the remaining 66 patients who underwent DE, 63 were revascularized by PTCA and selected for this prospective study. In each patient, the stenosed coronary artery supplying the LV segments with resting wall motion abnormalities (dysfunctional myocardium) were dilated by PTCA. The PTCA procedure was considered successful when the residual luminal narrowing immediately after PTCA was less than 50% and when no major complication, ECG or enzymatic evidence of MI, the need for bypass surgery during hospitalization or in hospital death occurred. Cardiovascular risk factors and clinical status were recorded at the time of DE. The indications for PTCA were significant stenosis ($\geq 75\%$ reduction in luminal diameter) of any major coronary artery and provokable ischemia by an exercise tolerance test, or based on clinical considerations or viability information from thallium-201 scanning. The study protocol was approved by the institutional ethical committee on clinical investigations and informed consent was obtained from all patients.

Dobutamine Echocardiography

DE was performed approximately 1 week before PTCA according to our previously described protocol.⁵ Briefly, all patients underwent 2-D echocardiography at rest with 3.5-MHz and 2.5-MHz transducers and a commercially available scanner (Toshiba SSH-160A, Tokyo, Japan or Hewlett Packard SONOS 1500, Andover, MA, USA). Parasternal long- and short-axis, and apical 4- and 2-chamber images were recorded on 12-mm S-VHS videotape and simultaneously stored on an off-line computer analyzer using a Prism 5000 system (Tomtec Imaging, Boulder, CO, USA) for subsequent analysis. Atropine sulfate (0.5 mg) was injected into a peripheral vein and echocardiography was repeated in a similar manner. Dobutamine was then infused in an incremental regimen of 4, 8, 12 and $20 \mu\text{g kg}^{-1} \text{min}^{-1}$ at 4-min intervals with continuous ECG monitoring. Blood pressure was recorded at the third minute of each stage of dobutamine infusion. Repeated images were obtained at the last minute of each dose of infused dobutamine and were recorded as described before.

Follow-up Studies

Early Follow-up Clinical status was recorded and follow-up 2-D echocardiography at rest was performed at 1 week and 3 months after successful PTCA. Image acquisition was identical to the DE protocol described earlier.

Follow-up coronary artery angiography (CAG) was performed 3 months after successful PTCA. When follow-up CAG revealed restenosis (defined as $>50\%$ reduction in the gain in luminal diameter achieved at the previous PTCA)¹¹ and repeat PTCA was indicated, follow-up echocardiography was repeated 1 week and 3 months after repeat PTCA.

Late Follow-up Follow-up information was obtained by a review of medical records, a mailed questionnaire, and telephone interviews with the patient or the treating physician after a minimum interval of 2 years. Cardiac events

were defined as death of cardiac origin, or MI or unstable AP that required myocardial revascularization. In patients who died in hospital or at home, the cause of death was determined from the medical record, the family or the local physician who signed the death certificate. A designation of cardiac death required documentation of significant arrhythmia or cardiac arrest, or both, or death attributable to congestive cardiac failure or MI in the absence of any other precipitating factors. Myocardial infarction was defined as a cardiac event requiring admission to hospital, with the development of new electrocardiographic changes and an increase in the cardiac enzyme level.

To evaluate regional and global LV function late after PTCA, 2-D echocardiography was performed in patients who remained event-free and agreed to come to the outpatient clinic for follow-up echocardiography. Image acquisition was identical to that in the DE protocol and early follow-up echocardiography.

Analysis of Echocardiograms

Echocardiographic image analysis was performed by the consensus of 2 experienced investigators who were unaware of the patient's clinical and angiographic data. The interpretation was based on a side-by-side comparison of images in the quad-screen digital display, as well as by a review of other cardiac cycles, including off-axis projections, from videotaped images. Regional wall motion was assessed according to the recommendations of the American Society of Echocardiography (ASE), using a 16-segment model where one could conveniently relate the various segments to coronary artery distribution.¹² A four-grade wall motion scoring system was used, where 1 represented normal or hyperkinesis, 2 represented hypokinesis, 3 represented akinesis and 4 represented dyskinesis.¹² We found that this scoring system gave good reproducibility (92% inter- and 91% intra-observer agreement) in a previous study of part of the present study population.¹³

All segments were scored at baseline, during each dose of infused dobutamine, and during each follow-up echocardiography. Viable myocardium was defined as an improvement of systolic thickening in the central portion of at least one asynergic segment at any dose of infused dobutamine. The wall motion score index for each patient was calculated from the total segmental score divided by the number of segments evaluated. Regional LV function after PTCA was considered to be improved if there was a decrease in the regional wall motion score index (RWMSI) in the revascularized area compared to the baseline value before PTCA. Worsening was defined as an increase in RWMSI compared with the baseline value. The LV ejection fraction (LVEF) at the baseline DE (before atropine and dobutamine infusion) and at rest during each follow-up echocardiography were calculated from apical views using the modified Simpson's rule.

Statistical Analysis

Data are presented as mean $\pm$ standard deviation. The paired t test and chi-square test were used to compare data, as appropriate. Differences within continuous variables over time were evaluated by analysis of variance for repeated measures. A p value less than 0.05 was considered statistically significant.

Table 1 Patients Data

	Dob-viable (n=36)	Dob-non viable (n=14)	p
Age (years, mean $\pm$ SD)	60.8 $\pm$ 9.8	59.6 $\pm$ 8.9	0.7
Sex (male %)	31 (86.1%)	12 (85.7%)	0.97
Vessel disease			
Single	23 (63.9%)	6 (42.9%)	0.4*
Double	10 (27.8%)	6 (42.9%)	
Triple	3 (8.3%)	2 (14.3%)	
Diabetes mellitus	12 (33.3%)	2 (14.3%)	0.18
Hypertension	20 (55.6%)	5 (35.7%)	0.21
Hypercholesterolemia	14 (38.9%)	6 (42.9%)	0.8
Smoking	27 (75%)	11 (78.6%)	0.79
Family history of CAD	13 (36.1%)	6 (42.9%)	0.66
Medications (%)			
Long-acting nitrates	33 (91.7%)	14 (100%)	0.27
Calcium channel antagonist	32 (88.9%)	12 (85.7%)	0.76
ACE inhibitor	9 (25%)	3 (21.4%)	0.79
Baseline mean LVEF	0.51 $\pm$ 0.1	0.44 $\pm$ 0.07	0.02

*p is of chi-square test (df=5). Dob, dobutamine; CAD, coronary artery disease; ACE, angiotensin converting enzyme; LVEF, left ventricular ejection fraction.

Fig 1. Schematic representation of late outcomes of the patients with and without viable myocardium by dobutamine echocardiography (DE). RWMSI, regional wall motion score index; LVEF, left ventricular ejection fraction.

Results

Patients

Of the 63 patients who underwent DE and were revascularized by PTCA, 5 were lost to follow-up. Follow-up information was available for 58 (92%) after 4.0 $\pm$ 0.8 years. Of these 58 patients, 3 patients died of noncardiac causes (1 from a traffic accident, 1 from malignant lymphoma and 1 from pneumonia) and 5 refused to come for late follow-up echocardiography because they had moved to a different location. The remaining 50 patients, (43 male, 7 female; 41–78 years old, mean 60.4 $\pm$ 9.5 years) who underwent both early and late follow-up, including 2-D echocardiography, constituted the final study population. Before PTCA, of these 50 patients, 10 patients were asymptomatic, 30 had stable AP and 10 had dyspnea on effort. Myocardial infarction had occurred previously in 38 patients. Twenty-nine patients had 1-vessel disease, 16 had 2-vessel disease and 5

had 3-vessel disease. The LVEF ranged from 0.32 to 0.69 (0.49 $\pm$ 0.1).

Dobutamine Echocardiography

Of the 50 patients who comprised the final study population, 36 (72%) had viable myocardium and 14 (28%) had nonviable myocardium by DE. The mean LVEF was higher in patients with viable myocardium than in those with nonviable myocardium, whereas other co-morbidities and medical therapies were evenly distributed between the 2 groups (Table 1).

Follow-up

Early Follow-up Anginal symptoms improved in 29 patients (24 with viable and 5 with nonviable myocardium) and symptoms of congestive heart failure improved in 6 patients (2 with viable and 4 with nonviable myocardium) within 3 months after PTCA.

Table 2 Relationship Between Outcomes and Viability by Dobutamine Echocardiography (DE)

	Improvement (n=29)	No improvement (n=15)	Event/worsening (n=6)
DE-viability (+)	27 (93%)	3 (20%)	6 (100%)
DE-viability (-)	2 (7%)	12 (80%)	0

$p < 0.001$ by chi-square test.

Table 3 Clinical Characteristics of Dobutamine-Viable Patients With and Without Poor Outcome (Event/Worsening in Wall Motion)

	With poor outcome Event (+) /worsening (+) (n=6)	Without poor outcome Event (-) & worsening (-) (n=30)	p
Age (years, mean $\pm$ SD)	61.2 $\pm$ 9.9	60.7 $\pm$ 1.0	0.92
Sex (male %)	4 (66.7%)	27 (90%)	0.19
Vessel disease			
Single	2 (33.3%)	21 (70.0%)	
Double	4 (66.7%)	6 (20%)	0.06*
Triple	—	3 (10%)	
Diabetes mellitus	1 (16.7%)	11 (36.7%)	0.34
Hypertension	4 (66.7%)	16 (53.3%)	0.55
Hypercholesterolemia	2 (33.3%)	12 (40%)	0.76
Smoking	4 (66.7%)	23 (76.7%)	0.61
Family history of CAD	1 (16.7%)	12 (40%)	0.28
Mean LVEF			
Before PTCA	0.40 $\pm$ 0.05	0.53 $\pm$ 0.09	0.004
1 week after PTCA	0.40 $\pm$ 0.06	0.57 $\pm$ 0.09	<0.001
3 months after PTCA	0.42 $\pm$ 0.08	0.58 $\pm$ 0.08	0.001
Restenosis	6 (100%)	12 (40%)	0.007
Long acting nitrates	5 (83.3%)	27 (90%)	0.64
Calcium channel antagonist	6 (100%)	25 (83.3%)	0.28
ACE inhibitor	1 (16.7%)	13 (43.3%)	0.22
β -blocker	1 (16.7%)	1 (3.3%)	0.19

*p is of chi-square test (df=5). CAD, coronary artery disease; LVEF, left ventricular ejection fraction; PTCA, percutaneous, transluminal coronary angioplasty; ACE, angiotensin converting enzyme.

Of the 36 patients with viable myocardium, RWMSI improved (1.9 ± 0.5 to 1.4 ± 0.4 , $p < 0.001$) in 26 (72%) within 3 months after PTCA and LVEF improved (0.52 ± 0.1 to 0.58 ± 0.09 , $p < 0.001$) in 21 (58%). Of the 14 patients with nonviable myocardium, only 1 (7%) showed RWMSI improvement (2.6 to 1.0) and LVEF improvement (0.43 to 0.70) at early follow-up.

Restenosis was diagnosed in 27 (49%) of 55 dilated vessels. The restenosis rate was 59% (20/34) of left anterior descending (LAD) arteries dilated, 36% (5/14) of right coronary arteries dilated and 29% (2/7) of circumflex coronary arteries dilated. Regional wall motion improved in 11 patients with restenosis, in 10 patients with significant restenosis ($\geq 75\%$ reduction in luminal diameter, range 75–100%) and in the remaining patient with 50% restenosis. Repeat PTCA was indicated in 12 vessels in 12 patients, and was successful in 10 vessels in 10 patients. In the remaining 2 patients with total occlusion, repeat PTCA failed and these patients were followed with medical treatment. Repeat PTCA improved anginal symptoms in symptomatic patients. The rates of restenosis and repeat PTCA were similar between patients with viable and nonviable myocardium (restenosis, 50% vs 36% and repeat PTCA 19.4% vs 21.4%, $P = \text{NS}$).

Late Follow-up Late outcomes of the patients with and without viable myocardium by DE are summarized in Fig 1. Three patients with viable myocardium had cardiac events (1 nonfatal MI and 2 unstable AP). The remaining 33 (92%) of the 36 patients with viable myocardium remained event-free. No cardiac events occurred in any of

the patients with nonviable myocardium.

Of the 38 symptomatic patients before PTCA (27 with viable and 11 with nonviable myocardium) who remained event-free, 36 (95%, 25 with viable and 11 with nonviable myocardium) were free from anginal pain or dyspnea at the late follow-up. The remaining 2 patients with viable myocardium had persistent dyspnea on effort.

Of the total 50 patients, 29 patients showed RWMSI improvement (1.9 ± 0.5 to 1.4 ± 0.4 , $p < 0.001$), 15 showed no improvement (2.2 ± 0.8 to 2.2 ± 0.8), 3 showed worsening (2.6 ± 0.2 to 2.9 ± 0) and 3 had cardiac events. LVEF improved (0.53 ± 0.09 to 0.60 ± 0.09 , $p < 0.001$) in patients with improved RWMSI, but deteriorated (0.38 ± 0.03 to 0.30 ± 0.03) in 3 patients with worsened RWMSI. Of the 29 patients with improvement, 27 (93%) had viable myocardium, whereas of the 15 with no improvement, only 3 (20%) had viable myocardium and all 6 of those with poor outcomes (3 cardiac events and 3 worsening) had viable myocardium ($\chi^2 = 28.9$, $p < 0.001$) (Table 2).

Of the 36 patients with viable myocardium, 27 (75%) showed regional wall motion improvement, 3 (8%) showed no improvement and 6 (17%) had a poor outcome. Of the clinical characteristics considered in patients with viable myocardium, mean LVEF was lower before PTCA and at 1 week and 3 months, and the restenosis rate at the 3-month CAG was higher in patients with a poor outcome than in patients without a poor outcome (Table 3). Among the 3 patients with viable myocardium who showed wall motion and LVEF deterioration at late follow-up, 2 had re-occlusion of a coronary artery at the 3-month CAG, and repeat

Fig 2. (A) Regional wall motion score index (mean $\pm$ standard deviation) at pre-PTCA (before coronary angioplasty), 1 week and 3 months after PTCA and at late follow-up in event free patients with viable myocardium and improved regional wall motion. (p is for analysis of variance for repeated measures.) (B) Left ventricular ejection fraction (mean $\pm$ standard deviation) at pre-PTCA (before coronary angioplasty), 1 week and 3 months after PTCA and at late follow-up in event free patients with viable myocardium and improved regional wall motion. (p is for analysis of variance for repeated measures.)

PTCA failed.

When regional LV function and LVEF at the late follow-up in event-free patients were compared with those at the early follow-up, 24 patients with viable and 1 with nonviable myocardium had a sustained improvement in regional LV function (ie, the follow-up RWMSI was the same as the RWMSI at 3 months). Additional improvement in regional LV function and LVEF was noted in 3 patients with viable myocardium and 1 with nonviable myocardium. With regard to the 3 patients with viable myocardium who showed worsening at the late follow-up but remained event free, improvement in RWMSI was noted in 1 of these 3 patients at 3 months (2.4 to 1.6) and no change was

detected during the early follow-up in another (2.7 to 2.7). In the remaining patient, wall motion improved at 1 week (2.7 to 2.1), then deteriorated at 3 month (2.5), but was still better than the pre-PTCA RWMSI, although the RWMSI at late follow-up (2.9) was worse than the pre-PTCA value. Fig 2A, B shows the time course of improvement of the mean RWMSI and mean LVEF after PTCA in patients with viable myocardium who remained event free.

Discussion

To our knowledge, this is the first study in which patients with chronic CAD and regional wall motion abnor-

malities who underwent DE and were revascularized by PTCA were followed for a long period (4.0 ± 0.8 years) and in which LV function was evaluated at late follow-up. Our results show that 75% of the patients with viable myocardium by DE had long-term improvement in regional and global LV function after PTCA, whereas 17% of the patients had a poor outcome (cardiac events or worsening of LV function). Patients with viable myocardium and a poor outcome had a significantly lower mean LVEF before and after PTCA and a higher restenosis rate than patients with viable myocardium and without a poor outcome. On the other hand, all the symptomatic patients with nonviable myocardium by DE were relieved of symptoms and remained event-free after PTCA.

Clinical Significance of Viable but Dysfunctional Myocardium

Because dysfunctional but viable myocardium may recover function if blood flow is restored,^{4,15} it is conceivable that in patients with ventricular dysfunction related to CAD, revascularization may improve ventricular function and consequently the prognosis.

Recently, many investigators have shown interest in techniques for detecting myocardial viability and for predicting recovery of regional and/or global LV function after coronary artery revascularization. In our previous study of a part of the present study population,³ we demonstrated that, in comparison with thallium-201 reinjection imaging, DE reliably predicted functional recovery of dysfunctional myocardium after coronary artery revascularization. Recent editorials have analyzed and summarized the accuracy of the various techniques used to predict the recovery of ventricular function^{16,17} and low-dose DE and positron emission tomography (PET) seem to have similar positive and negative predictive values, whereas thallium-201 single-photon emission tomography is more sensitive, but less specific. Most previous studies have considered that regional or global LV function within 3 months after revascularization determines the diagnostic accuracy of the technique in predicting post-revascularization functional recovery. Only one recent study using DE considered regional and global LV function at 14 months after revascularization, and showed that DE predicted the functional recovery of 63% of dysynergic segments at 3 months and of 75% of dysynergic segments at late follow-up.⁶ Thus, the present study addressed the importance of late follow-up for increasing the diagnostic accuracy of DE to predict post-revascularization functional recovery.

Despite the increasing diagnostic accuracy of these imaging techniques, the identification of myocardial viability remains an academic exercise unless it translates into a better prognosis or quality of life. Our present study shows that viable myocardium detected by DE is predictive of regional functional recovery in 75% of patients at a median follow-up period of 4 years. The rate of cardiac events was only 8% in our patient population with viable myocardium who were revascularized by PTCA. Williams et al's study using DE, showed that 43% of their patients with evidence of viability or ischemia who were treated medically had subsequent cardiac events at 16 months of follow-up.⁷ Thus, our present results show a prognostic benefit of revascularization in patients with viable myocardium. A few previous studies using PET¹⁸⁻²¹ and low-dose DE^{7,8} have investigated the prognostic significance of viable myocardium, and have shown that the presence of viable

myocardium, if left unrevascularized, leads to a greater number of events. This should dictate revascularization in these patients to improve the prognosis; myocardial viability may act as an unstable substrate for further events. However, in contrast to this theory, Yoshida and Gould²² showed a higher mortality rate in patients without viable myocardium, and no differences were observed between patients who underwent revascularization and those who did not.²² Furthermore, none of the medically treated patients in their study died, whereas 2 of 18 patients without viable myocardium who were revascularized died. It is well known that in patients with severe LV dysfunction, high morbidity and mortality often accompany surgical revascularization procedures, and cardiac transplantation might be an alternative treatment strategy.²³ However, this is the same population that ultimately may benefit from revascularization,²⁴ because the mortality rate is very high when they are treated medically.^{25,26} Nesto et al showed an increased 5-year survival rate and improved postoperative LVEF in patients with CAD and reduced LVEF who had inotropic contractile reserve before surgery.²⁷ Our present results showed improved regional wall motion and LVEF 4 years after PTCA in patients who had myocardial viability detected by DE before PTCA. Therefore, the preoperative selection of patients with inotropic reserve and myocardial viability is crucial.

In the present study, 3 (6%) patients with viable myocardium showed regional wall motion and LVEF deterioration at late follow-up. Cornel et al recently observed that resting wall motion had deteriorated at 14 months after revascularization in 9% of dysynergic segments.⁶ They did not mention any events or any changes in LVEF in patients with wall motion deterioration at late follow-up. Dahl et al showed that patients with viable myocardium by PET before revascularization and no restenosis at 5 ± 2 months after revascularization had improved regional and global LV function, whereas wall motion did not change in patients with viable myocardium and restenosis.²⁸ Melgares et al in their study without viability assessment, showed sustained improvement in wall motion from 1 to 5.5 months after PTCA in patients without restenosis and a significant deterioration of wall motion from 1 to 5.5 months after PTCA in patients with restenosis.⁹ These data suggest that coronary restenosis limits the recovery of regional LV dysfunction achieved after successful PTCA. However, in our present study and in the study of Melgares et al,⁹ a number of patients with restenosis showed better regional wall motion than before angioplasty. It is not easy to explain why regional dysfunction did not return to the same baseline value despite a similar degree of recurrent restenosis. It is possible that the differential histopathology of primary and restenotic lesions may explain the different functional behavior between them despite similar angiographic severity.²⁹ In the present study, 2 of 3 patients with viable myocardium who showed wall motion and LVEF deterioration at late follow-up had re-occlusion of a coronary artery at the 3-month CAG, and repeat PTCA failed. Sustained and chronic hypoperfusion due to restenosis may be the main factor that contributed to the reduction in myocardial contractile function in these patients. In the remaining patient, restenosis was 50% at the 3-month CAG and wall motion and LVEF were improved at 3 months. Progression of stenosis or a silent event may have led to the deterioration in wall motion and EF in this patient. LVEF decreased in all 3 of these patients with wall motion deteri-

oration, and as low LVEF is a marker of a poor prognosis,^{30,31} we considered worsening of LVEF to be a poor outcome, as with the cardiac events, after PTCA.

In the present study, the restenosis rate was high in patients with PTCA of the LAD and other series have identified this procedure as a risk factor for restenosis.^{9,32,33} In the present study, LVEF was lower in patients without viable myocardium than in patients with viable myocardium, and the restenosis rate was similar between the 2 groups. However, only patients with viable myocardium and a low LVEF before and after PTCA and restenosis had a poor outcome. Thus, in patients with chronic CAD and regional LV dysfunction, myocardial viability in dysfunctional segments detected by DE before PTCA, as well as low LVEF before and after PTCA and restenosis, identify patients at risk for a poor outcome.

In the present study, all of the patients without viable myocardium by DE who were revascularized by PTCA remained event-free and all symptomatic patients without viability were relieved of symptoms. Anselmi et al showed that surgical revascularization led to a worse prognosis in patients with severe LV dysfunction and without viable myocardium.⁸ In their study, patients without viable myocardium who underwent surgical revascularization had a mortality rate of 22% (4/18), whereas none of the 7 patients treated with PTCA died. Their finding and our present results suggest that when revascularization is indicated on clinical grounds and angiographic findings, PTCA could be used to revascularize patients without viability to relieve symptoms and to prevent future cardiac events.

Study Limitations

The present study comprised a small number of patients who were revascularized by PTCA, so we could not demonstrate a prognostic benefit of PTCA compared with medical treatment. However, the rate of cardiac events in our present study population was lower compared with those reported in the literature in patients with viable myocardium detected by DE who were treated medically,^{7,8} which indirectly shows a prognostic benefit of PTCA in our patients with viable myocardium.

In the present study, the DE protocol was designed for detecting myocardial viability in terms of contractile reserve in dysfunctional LV segments, not to diagnose inducible ischemia. We believe that this point is not crucial, because myocardial viability and ischemia are often present at the same time, and renewed episodes of ischemia and repetitive stunning have been postulated as causative in the pathophysiology of hibernation.³⁴ In fact, studies using low- and high-dose DE have shown that the 'biphasic response' (defined as improvement at low dose and worsening at peak stress) predicts recovery of function after revascularization.⁷

In the present study, the degree of LV dysfunction was not a criterion for inclusion and 18 (36%) of our patients had preserved LVEF (>0.50) and thus, by definition, had a low risk of death and following events. Thus, our data can not be extrapolated to a patient population with markedly depressed LVEF.

In the present study, follow-up 2-D echocardiography was not performed between 3 months and 2 years. Therefore, we cannot comment on the optimal timing of follow-up studies for the detection of complete recovery of contractile function after PTCA. Detailed and larger studies are needed to answer this question.

Conclusions

DE is a useful imaging modality for detecting viable but dysfunctional myocardium in patients with chronic CAD and regional LV dysfunction. The present results suggest that viable myocardium detected by DE may predict long-term improvement in regional and global LV function after PTCA. However, patients with viable myocardium and a persistent low LVEF are at risk for cardiac events or worsening of LV function. On the other hand, although the absence of viability by DE predicted 80% of no improvement in regional LV function after PTCA, all of these patients remained event free and symptomatic patients without viability by DE were relieved of symptoms. These data suggest that when revascularization is indicated on clinical grounds and angiographic findings, PTCA could be used to revascularize patients not showing viability on DE in order to relieve symptoms and to prevent future cardiac events.

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