Doppler Assessment of Left Ventricular Diastolic Filling Pattern during the Convalescent Stage of Acute Myocardial Infarction

Effects of Infarct Size and Coronary Thrombolysis

Tohru MASUYAMA, M.D.,[1] Satoshi NAKATANI, M.D.,[2]
Masaaki UEMATSU, M.D.,[1] Kazuhiro YAMAMOTO, M.D.,[1]
Akira KITABATAKE, M.D.,* *and* Kazuhisa KODAMA, M.D.

SUMMARY

Pulsed Doppler echocardiography was used to study left ventricular diastolic filling pattern (LVDFP) over the convalescent stage of acute myocardial infarction (AMI) in 25 patients. Twelve normal subjects served as a control group. The patients were divided on the basis of enzymatically estimated infarct size into 2 groups: 7 as the large AMI group, and the other 18 as the small AMI group. Peak early diastolic filling velocity (E) and the ratio of E to peak filling velocity at atrial contraction (E/A ratio) were determined from the Doppler transmitral flow velocity recordings at 1 and 4 weeks after the onset of AMI. At 1 week E and E/A ratio were significantly lower in the small AMI group compared to the control and the large AMI groups, however, there was no significant difference in E and E/A ratio between the control and the large AMI groups. E/A increased with cumulative CK release among the patients ($r=0.54$, $p<0.01$). In the following 3 weeks E and E/A ratio decreased only in the large AMI group, and E and E/A ratio at 4 weeks weakly correlated with pulmonary capillary wedge pressure ($r=0.63$, $p<0.01$ and $r=0.65$, $p<0.01$) and ejection fraction ($r=0.50$, $p<0.05$ and $r=0.62$, $p<0.01$) among the patients. There was no significant difference in E or E/A ratio between patients with and without coronary thrombolysis.

Thus, LVDFP in the early convalescent stage of AMI was characterized by low E and E/A ratio in patients with small AMI, however, a " pseudonormalized " pattern was observed in patients with large AMI. The effect of the infarct size on LVDFP diminished in the late convalescent stage of AMI. LVDFP in patients with AMI appears to be influ-

From the Cardiovascular Division, Osaka Police Hospital, and *the First Department of Medicine, Osaka University School of Medicine, Osaka, Japan.

1) Present address: The First Department of Medicine, Osaka University School of Medicine, Osaka.

2) Present address: National Cardiovascular Center, Suita, Osaka.

Address for correspondence: Tohru Masuyama, M.D., First Department of Medicine, Osaka University School of Medicine, 1-1-50 Fukushima, Fukushima-ku, Osaka 553, Japan.

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enced by the infarct size and by the time of study. The effect of coronary thrombolysis on LVDFP was not evident throughout the convalescent stage of AMI in this study.

Key Words:
Acute myocardial infarction Pulsed Doppler echocardiography Transmitral flow velocity pattern Diastolic function Infarct size Coronary thrombolysis

THE size of a myocardial infarct is an important determinant of left ventricular (LV) systolic function and prognosis in patients with acute myocardial infarction (AMI).[1] Coronary thrombolysis and/or coronary angioplasty, which are performed in patients with AMI with the hope of their beneficial effects on the infarct size, appear to improve prognosis and LV systolic function in the chronic stage.[2)-5)] Because changes in LV diastolic filling pattern are sometimes observed in advance of deteriorations in LV systolic function even in patients with coronary artery disease, it is interesting to study LV diastolic filling pattern and its changes during the convalescent stage of AMI. However, LV diastolic filling pattern has not been studied in patients with AMI yet. In this study, LV diastolic filling pattern was studied in the early and late convalescent stages of AMI using pulsed Doppler echocardiography. The objectives of this study were (1) to characterize LV diastolic filling pattern in patients with AMI, (2) to explore whether LV diastolic filling pattern changes during the convalescent stage of AMI, and (3) to examine whether LV diastolic filling pattern and its changes during the convalescent stage are affected by the infarct size and/or successful coronary reperfusion.

METHODS

Patients selection: Twenty-two patients were selected from 36 consecutive patients with AMI using the following criteria: (1) no history of previous myocardial infarction (6 patients excluded for this reason); (2) coronary angiography was performed and coronary thrombolysis was tried within 6 hours of the onset of chest pain (coronary thrombolysis was successful in 17 of the 22 selected patients); (3) 2 patients were excluded due to inadequate Doppler recordings; (4) intravenous medication, even if used, was not running at 1 week after the onset of AMI (2 patients excluded for this reason); (5) moderate to severe mitral regurgitation was not detected using pulsed Doppler echocardiography at 1 week or 4 weeks after the onset of AMI (3 patients excluded for this reason); (6) cardiac rhythm was sinus rhythm and heart rate

was less than 95 bpm (none excluded); (7) post-infarction angina did not develop within 4 weeks after the onset of AMI (none excluded); (8) valvular heart disease or congenital heart disease was not detected by echocardiography and cardiac catheterization (none excluded); (9) coronary angiography obtained at 4 to 6 weeks after the onset of AMI showed patency (in patients with successful coronary thrombolysis) or occlusion (in patients with failed coronary thrombolysis) of the infarct-related coronary artery (1 patient excluded for this reason). In addition to the 22 patients, 3 patients without coronary thrombolysis were studied. These 3 patients fulfilled the aforementioned criteria of (2) to (7) but their coronary angiograms obtained within 24 hours from the onset of AMI and at 4 to 6 weeks after the onset of AMI evidenced total occlusion of the infarct-related coronary artery. Thus, the study population consisted of 25 patients, 21 males and 4 females, ranging in age from 42 to 79 years (mean 60).

The infarct-related coronary artery was the left anterior descending artery in 14 patients, the right coronary artery in 8, and the left circumflex artery in 3 patients. At 1 week after the onset of AMI, nitrates, calcium antagonists, diuretics and/or angiotensin converting enzyme inhibitors were used in 24 of the 25 patients. At 4 weeks, the same doses of the medications were continued in the same patients. In addition, all patients with coronary thrombolysis received anticoagulant and/or antiplatelet agents. Medication was not routinely discontinued prior to testing.

Enzymatic studies were done in all patients by measuring creatine kinase (CK) activity every 4 or 6 hours in the initial 3 days. Time-activity curves were constructed for each patient. Total CK release was calculated according to the method of Norris et al.[6] The patients were divided into 2 groups on the basis of cumulative CK release: 7 patients with cumulative CK release of $\geq$6,000 U/l were classified as the large AMI group, and 18 patients with cumulative CK release of $<$6,000 U/l, as the small AMI group.

Left ventriculography was performed in 22 of the 25 patients, and LV end-diastolic and end-systolic volumes were determined using the area-length method to provide ejection fraction. Pulmonary capillary wedge and LV pressures were measured in 20 of the 25 patients.

Twelve subjects without apparent heart diseases served as control and constituted a control group. Ten were male and 2 were female, and age ranged from 43 to 75 years (mean 60). Two Doppler examinations were performed in these subjects at an interval of 2 weeks.

Doppler examination: Doppler examinations were performed at 1 week after the onset of AMI in the early convalescent stage and were repeated at 4 weeks after the onset in the late convalescent stage in all patients using

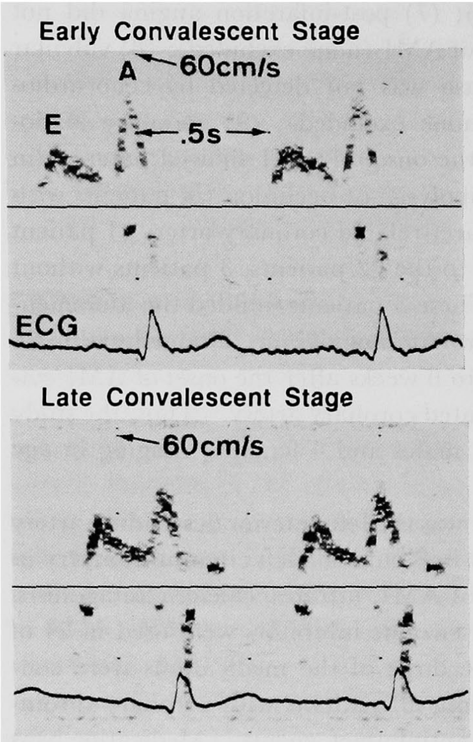

Fig. 1. Representative Doppler recordings of transmitral flow velocity pattern at 1 week (top) and 4 weeks (bottom) after the onset of acute myocardial infarction in a 51-year-old male patient with small inferior myocardial infarction (cumulative creatine kinase release of about 1,400 U/l) and coronary thrombolysis. Doppler recordings of transmitral flow velocity pattern were obtained at the level of the mitral anulus in the left atrium as done in the other patients, which partially account for the extremely low value of the peak early diastolic filling velocity (E) in this patient.[34] In this case E and the peak atrial filling velocity (A) slightly increased and decreased during the convalescent stage, respectively, although the changes in the parameters were minimal. Abbreviations: ECG= electrocardiogram; s=second.

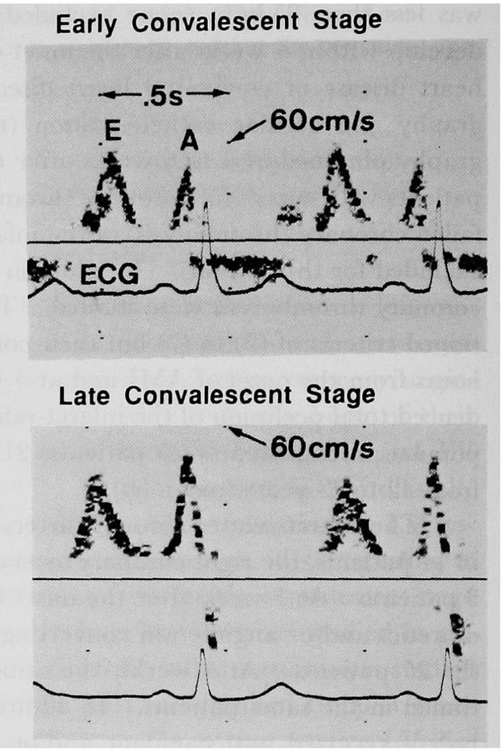

Fig. 2. Representative Doppler recordings of transmitral flow velocity pattern at 1 week (top) and 4 weeks (bottom) after the onset of acute myocardial infarction in a 56-year-old male patient with large anteroseptal myocardial infarction (cumulative creatine kinase release of about 12,200 U/l) and coronary thrombolysis. It is noted that in the early convalescent stage the peak early diastolic filling velocity (E) is higher and the peak atrial filling velocity (A) is lower in this patient compared to the patient with small infarction (Fig. 1). E markedly decreased during the convalescent stage. Abbreviations: ECG =electrocardiogram; s=second.

a duplex Doppler echocardiograph (Toshiba SDS-21B with SSH-40A) and a transducer array of 2.4 MHz. Each patient rested in a left lateral position and breathed in a relaxed fashion during ultrasound examination. The Doppler sample volume with a length of approximately 2 mm was carefully posi-

tioned just at the level of the mitral anulus in the left atrium with the guidance of the apical long axis view. The Doppler signals of the transmitral inflow were optimized by using audio output and with a high-pass filter of 400 Hz, and were recorded at a paper speed of 50 or 100 mm/sec on a strip-chart recorder. We determined the peak early diastolic filling velocity (E), the peak filling velocity in the atrial contraction phase (A), and the ratio of E to A (E/A ratio) as Doppler parameters of LV diastolic filling (Figs. 1 and 2). Flow velocity was not corrected for the angle. The average values of eight consecutive cardiac cycles were used for the analysis. We further determined changes in E, A and E/A ratio using the patients' own values at 1 week after the onset of AMI as controls.

Statistical analysis: All values are expressed as mean$\pm$SD. The first and second measurements of Doppler parameters in the control group were used as controls for the data obtained at 1 week and 4 weeks after the onset of AMI in the patients groups, respectively. Analysis of variance and Scheffe's F test were used to compare data among groups. Relations between two variables were studied using a simple linear regression analysis.

Results

Comparison of Doppler parameters of LV diastolic filling between controls and patients with AMI (effects of the infarct size) (Table I): E and E/A ratio at 1 week after the onset of AMI were smaller in the small AMI group compared to the control group ($p<0.05$ and $p<0.01$, respectively) and the large AMI group ($p<0.05$ and $p<0.01$, respectively). However, there was no significant difference in E or E/A ratio between the control group and the large AMI group. In the following 3 weeks E and E/A ratio decreased in the large AMI group but not in the small AMI group. There was a significant difference in E and E/A ratio at 4 weeks after the onset between the control group and the small AMI group ($p<0.01$ and $p<0.01$, respectively), but there was no longer a significant difference in E or E/A ratio at that time between the small and large AMI groups. The relation between cumulative CK release and Doppler parameters of LV diastolic filling obtained at 1 week and 4 weeks after the onset of AMI were studied among the 25 patients (Fig. 3). Cumulative CK release did not correlate with E ($r=0.29$, p=N.S.) but did correlate with E/A ratio ($r=0.54$, $p<0.01$) at 1 week after the onset of AMI. However, cumulative CK release did not correlate with E or E/A ratio ($r=0.01$, p=N.S., $r=0.25$, p=N.S., respectively) at 4 weeks after the onset of AMI.

Doppler parameters of LV diastolic filling in relation to coro-

Table I. Doppler Parameters of Left Ventricular Diastolic Filling in Controls and Patients with Acute Myocardial Infarction

Group	Control	Small infarction (∑CK<6,000 U/l)	Large infarction (∑CK≥6,000 U/l)
Number	12	18	7
Gender	10M, 2F	15M, 3F	6M, 1F
Age (years)	60±10	62±11	56±10
HR (1w) (bpm)	71±8	71±10	76±10
E (1w) (cm/sec)	58±11	38±14*	60±26†
A (1w) (cm/sec)	53±11	53±10	46±6
E/A (1w)	1.16±0.43	0.72±0.22**	1.29±0.46††
HR (4w) (bpm)	72±9	68±11	69±17
E (4w) (cm/sec)	59±11	38±11**	47±14
A (4w) (cm/sec)	54±10	51±12	46±6
E/A (4w)	1.15±0.42	0.77±0.23**	1.01±0.21
ΔE (cm/sec)	1±5	0±10	−12±17**†
ΔA (cm/sec)	1±4	−1±10	1±6
ΔE/A	−0.01±0.16	0.05±0.21	−0.28±0.39†

Values are reported as mean values±SD. *P<0.05 and **p<0.01 versus controls. †p<0.05 and ††p<0.01 versus the small infarction group. The first and second measurements of Doppler parameters in the control group were used as controls for the data obtained at 1 week and 4 weeks after the onset of acute myocardial infarction in the patient groups, respectively. Abbreviations: A=peak filling velocity at atrial contraction; ∑CK=cumulative creatine kinase release; E=peak early diastolic filling velocity; HR=heart rate; w=week(s).

nary thrombolysis (Table II): Successful coronary thrombolysis was obtained in 6 of the 7 patients of the large AMI group and in 11 of the 18 pateints of the small AMI group. Doppler parameters were compared between 11 patients with and 7 without coronary thrombolysis in the small AMI group, but no significant differences were observed in any Doppler parameters at the early or late convalescent stages of AMI.

Comparison of Doppler parameters of LV diastolic filling with hemodynamic parameters (Table III): Doppler parameters of LV diastolic filling at 4 weeks after the onset of AMI were compared with pulmonary capillary wedge pressure and angiographically determined ejection fraction. E and E/A ratio correlated significantly with pulmonary capillary wedge pressure ($r=0.63$, $p<0.01$, $n=20$; $r=0.65$, $p<0.01$, $n=20$, respectively) and with ejection fraction ($r=0.50$, $p<0.05$, $n=22$; $r=-0.62$, $p<0.01$, $n=22$, respectively) (Figs. 4 and 5).

Discussion

Pulsed Doppler echocardiography was used to study the LV diastolic fill-

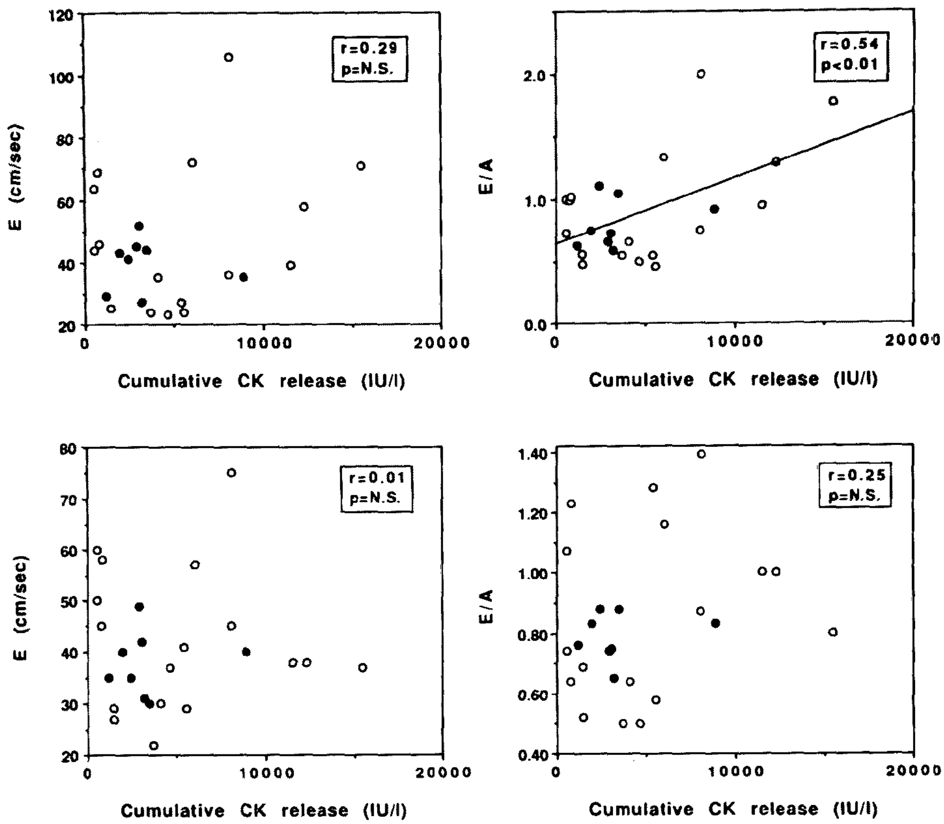

Fig. 3. The relations between cumulative creatine kinase (CK) release and Doppler parameters at 1 week (top panels) and 4 weeks (bottom panels) after the onset of acute myocardial infarction were studied. Open circles stand for patients with coronary thrombolysis, and closed circles stand for those without coronary thrombolysis. Abbreviations: E=peak early diastolic filling velocity); E/A=the ratio of the peak early diastolic filling velocity to the peak filling velocity at atrial contraction.

ing pattern over the convalescent stage in patients with AMI. LV diastolic filling pattern in the early convalescent stage of AMI was characterized by low E and E/A ratio in patients with small AMI, but a " pseudonormalized " pattern was observed in patients with large AMI. The effect of the infarct size on the diastolic filling pattern diminished in the late convalescent stage, but the abnormalities or " normalities " in the LV diastolic filling pattern in late convalescent stage appear to be dependent on the LV systolic function and filling pressure, both of which are largely affected by the infarct size. Effects of coronary thrombolysis on the diastolic filling pattern were not evident throughout the convalescent stage of AMI.

Table II. Effects of Coronary Thrombolysis on Doppler Parameters of Left Ventricular Diastolic Filling at 1 Week and 4 Weeks after the Onset of Acute Myocardial Infarction in Patients with Small Myocardial Infarction

Recanalization	Success	Failure	p-Value
Number	11	7	n.s.
Age (years)	61±12	63±10	n.s.
HR (1w) (bpm)	71±12	70±7	n.s.
E (1w) (cm/sec)	37±17	40±9	n.s.
A (1w) (cm/sec)	53±9	52±13	n.s.
E/A (1w)	0.68±0.22	0.79±0.21	n.s.
HR (4w) (bpm)	70±14	65±3	n.s.
E (4w) (cm/sec)	39±13	37±7	n.s.
A (4w) (cm/sec)	53±13	48±10	n.s.
E/A (4w)	0.76±0.29	0.78±0.09	n.s.
ΔE (cm/sec)	2±11	−3±8	n.s.
ΔA (cm/sec)	0±11	−4±7	n.s.
ΔE/A	0.08±0.26	−0.01±0.14	n.s.

Value are reported as mean values±SD.
Abbreviations: A=peak filling velocity at atrial contraction; E=peak early diastolic filling velocity; HR=heart rate; n.s.=not significant; p=probability; w=week(s).

Table III. Correlation Coefficient Matrix of Doppler Parameters of Left Ventricular Diastolic Filling at 4 Weeks after the Onset of Acute Myocardial Infarction versus Hemodynamic Parameters

	E	A	E/A	Sample size (n)
PCWP	0.63**	−0.14	0.65**	20
LVEDP	0.57**	−0.01	0.51*	20
LVSP	−0.16	−0.14	−0.13	20
LVEDV	0.08	−0.11	0.17	22
LVESV	0.32	−0.19	0.46*	22
EF	−0.50*	−0.17	−0.62**	22

*P<0.05, **p<0.01.
Abbreviations: A=peak filling velocity at atrial contraction; E=peak early diastolic filling velocity; EF=ejection fraction; LVEDP=left ventricular end-diastolic pressure; LVEDV=left ventricular end-diastolic volume; LVESV=left ventricular end-systolic volume; LVSP=left ventricular systolic pressure; n=number; PCWP=pulmonary capillary wedge pressure.

LV diastolic filling pattern in the early convalescent stage of AMI: In the early convalescent stage lower E and E/A ratio were observed in the small AMI group compared to the control group, but there was no significant difference in E and E/A ratio between the control group and the large AMI group. E and E/A ratio have been used to anticipate LV relaxation abnormalities in patients with coronary artery disease or hypertrophied

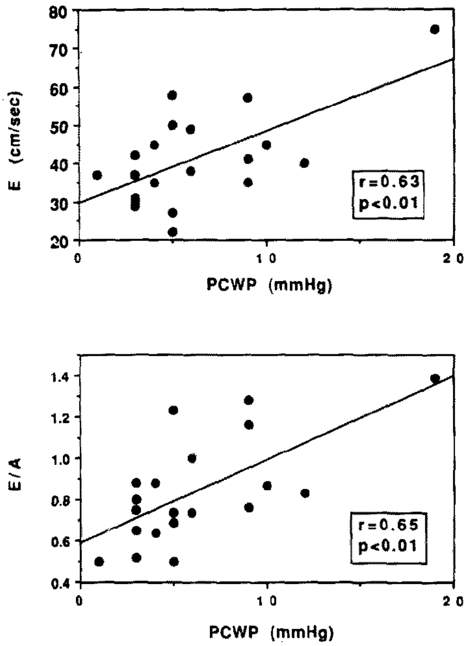

Fig. 4. Relation between pulmonary capillary wedge pressure (PCWP) and Doppler parameters obtained at 4 weeks after the onset of acute myocardial infarction. Abbreviations: E=peak early diastolic filling velocity; E/A= the ratio of the peak early diastolic filling velocity to the peak filling velocity at atrial contraction.

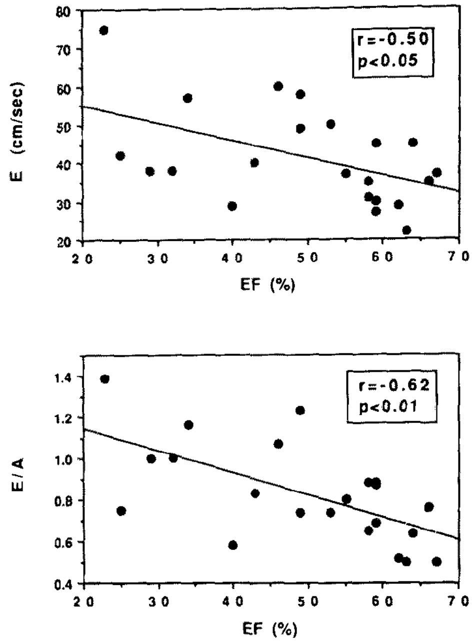

Fig. 5. Relation between angiographically determined left ventricular ejection fraction (EF) and Doppler parameters obtained at 4 weeks after the onset of acute myocardial infarction. Abbreviations: E=peak early diastolic filling velocity; E/A=the ratio of the peak early diastolic filling velocity to the peak filling velocity at atrial contraction.

hearts,[7)-12)] and they are more likely to decrease than to increase in association with impaired LV relaxation.[13)-15)] Thus, the lower than normal values of E and E/A ratio in the small AMI group may be explained by the abnormalities in LV relaxation and/or compliance. However, "pseudonormalized" E and E/A ratio were observed in patients with large AMI. Further, there was a significant positive correlation between cumulative CK release and E/A ratio among the patients. The larger AMI is considered to produce more impairment in LV systolic function as well as in LV relaxation, causing effects expected to be opposite to those found in this study. Thus, the abnormalities in LV relaxation and/or compliance cannot account for the increased E and E/A ratio in the large AMI group. E and E/A ratio are related to the pressure gradient between the left atrium and the left ventricle at early diastole; therefore, changes in these Doppler parameters may not necessarily reflect changes in LV relaxation, but can be produced by altered left atrial pres-

sure.[14),16)-18)] The Stanford Group has shown that mitral flow velocity patterns can be "pseudonormalized" even in patients with LV relaxation abnormalities by an increase in left atrial pressure.[18)] Although left atrial or pulmonary capillary wedge pressure was not measured in the early convalescent stage in this study, it is likely to be higher in patients with large AMI compared to the other patients. Other possible factors that may affect LV diastolic filling pattern include aging,[19)] heart rate,[20)] blood pressure[10)] and PQ interval,[21),22)] but these factors were intentionally or accidentally matched among the groups.

LV diastolic filling pattern in the late convalescent stage of AMI: Mean values of E and E/A ratio at 4 weeks after the onset of AMI were still lower in the small AMI group than in the control group; however, there was no longer a significant difference in E and E/A ratio between the small and large AMI groups. Further, there was no significant correlation between cumulative CK release and E or E/A ratio. Thus, effects of the infarct size on the LV diastolic filling pattern diminished because of the decreases in E and E/A ratio during the convalescent stage only in the large AMI group. Coronary thrombolysis was obtained in 7 of the 8 patients with large AMI, and improved LV systolic function due to coronary thrombolysis may account for the large decreases in E and E/A ratio in this group.[2)-5)] Alternatively, this finding may be explained by an alteration in LV compliance with healing of the infarction. It is noted that the Doppler parameters of LV diastolic filling correlated with LV ejection fraction and pulmonary capillary wedge pressure in the late convalescent stage, indicating that infarct size is still one of the determinants of LV diastolic filling pattern even in the late convalescent stage.

Effects of coronary thrombolysis on LV diastolic filling pattern: Over the convalescent stage of 4 weeks, there was no difference in the Doppler parameters of LV diastolic filling between patients with and without successful coronary thrombolysis. Thus, our data do not support the idea that coronary thrombolysis improves LV diastolic filling pattern. Although the possible beneficial effects of coronary thrombolysis on LV diastolic filling pattern in the early convalescent stage might have been masked in this study by other factors that were not perfectly matched between the groups, the present study indicates the absence of at least obvious effects of coronary thrombolysis on LV diastolic filling pattern in the convalescent stage.

Limitations of the study: Several limitations of the study are noted. First, enzymatic estimation of the infarct size is influenced by coronary thrombolysis, probably reflecting enhanced washout of enzyme from the infarct zone.[23)] Thus one might think that larger CK release in patients with coro-

nary thrombolysis only suggests more enhanced washout of enzyme with the same or even smaller infarct size, and that the possible same or even smaller infarct size accounts for the "pseudonormalized" LV diastolic filling pattern in the early convalescent stage of the patients with cumulative CK release of ≥6,000 U/l (large AMI group). However, the relation between cumulative CK release and Doppler parameters of LV diastolic filling was little affected by the results of coronary thrombolysis as evidenced in Fig. 3, and the possible effect of coronary thrombolysis on the cumulative CK release cannot invalidate enzymatic estimation of infarct size in our patients.

Second, Doppler studies were not performed before coronary thrombolysis or within a week after the onset of AMI. It is certainly hard to study LV diastolic filling pattern in patients with AMI at the acute stage, because important factors that affect LV diastolic filling pattern can easily change with the therapeutic plan, especially in this interim. For example, heart rate, blood pressures and LV preload are included in the determinants of LV diastolic filling pattern,[10),14),16),17),20)] and they are very fragile to frequent administration of antihypertensive drugs and intravenous drip of fluid and/or vasodilating and inotropic agents that are necessary in at least some patients.

Third, the potential effect of the infarct vessel on Doppler parameters of LV diastolic filling in patients with AMI should be addressed. Although this effect is still unclear in patients with AMI, it has been demonstrated to be minimal in patients with old myocardial infarction and in patients with effort angina.[7),9)]

Finally, Doppler parameters at 1 week after the onset of AMI were not compared with hemodynamic measurements because these were not available in this study. Further, no reference of LV relaxation was measured in this study. It is clear, however, that our findings cannot be explained by LV relaxation abnormalities, per se, of our patients as described above.

Clinical implications: The findings of this study suggest Doppler parameters of LV diastolic filling in the convalescent stage of AMI are affected by the infarct size. Abnormal LV diastolic filling pattern was observed in patients with small AMI; however, the filling pattern was "pseudonormalized" in patients with large AMI. These findings suggest that apparently normal LV diastolic filling pattern does not necessarily mean reserved LV relaxation or diastolic function in patients with AMI, although the large infarct size may account for the apparently normal pattern. It is also noted that the "pseudonormalization" of the LV diastolic filling pattern was evident in the early convalescent stage rather than in the late convalescent stage.

This study also showed that Doppler parameters change from the early to late convalescent stage, especially in patients with large AMI. These find-

ings suggest that not only the infarct size but also the timing of Doppler examination should be taken into consideration when Doppler parameters are used to assess LV diastolic function in patients with AMI.

Finally, the effects of coronary thrombolysis on the filling pattern were not evident throughout the convalescent stage in the comparative analysis of the Doppler parameters between patients with and without coronary thrombolysis. Thus, Doppler parameters of LV diastolic filling in the convalescent stage may not be used as a predictor of coronary thrombolysis, but may be used to assess global function of the left ventricle.

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