**Noninvasive Assessment of Left Ventricular
Diastolic Filling in Coronary Artery Disease
by Doppler Dipyridamole-Stress Testing**

Shinobu TOMIMOTO, M.D., Motoshi TAKEUCHI, M.D.,
and Hisashi FUKUZAKI, M.D.

SUMMARY

To evaluate left ventricular diastolic function during dipyridamole-provoked myocardial ischemia, transmitral flow was studied in 73 patients with coronary artery disease and 8 normal subjects using pulsed Doppler echocardiography. Coronary vasodilating agents like dipyridamole can provoke myocardial ischemia in patients with coronary artery disease. The peak flow velocity of left ventricular rapid filling (R), that of atrial contraction (A) and the ratio of A to R (A/R) in each cardiac cycle were measured. The rapid filling phase was divided into two subphases at the point of R. The integral of the two subphases and atrial contraction were computed and designated IR1, IR2 and IA. The time intervals of the two subphases of rapid filling were designated TR1 and TR2. Of the 73 patients with coronary artery disease, 41 patients developed ischemia (positive responder=PR) and 32 patients did not (negative responder=NR) after dipyridamole infusion. In PR, A/R increased ($p<0.05$), IR2 decreased ($p<0.01$) and TR2 shortened ($p<0.01$) significantly. In NR and normal subjects, these indices remained unchanged. We observed mitral regurgitation (MR) in 13 PR patients during acute myocardial ischemia. A/R increased in patients without MR but A/R remained unchanged in patients with MR. These results suggest that in acute myocardial ischemia, changes in Doppler indices (A/R, IR2 and TR2) reflect a left ventricular diastolic abnormality, and that the masking of the diastolic abnormality was ascribed to the presence of MR.

Additional Indexing Words:

Pulsed Doppler echocardiography	Transmitral flow	Dipyrida-
mole	Myocardial ischemia	Coronary artery disease

From the First Department of Internal Medicine, Kobe University School of Medicine, Kobe, Japan.

Address for reprints: Shinobu Tomimoto, M.D., Section of Internal Medicine, Kobe Steel Hospital, Kakogawa, 797-295 Isshiki, Hiraoka-cho, Kakogawa, Hyogo 675-01, Japan.

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MANY investigators have suggested that intravenous dipyridamole is useful for detecting myocardial ischemia or significant coronary artery stenosis by utilizing electrocardiography, thallium-201 myocardial scintigraphy and two-dimensional echocardiography.^{1)–4)} Recently, various parameters of left ventricular filling were described as useful indicators of coronary artery disease.^{5)–9)} Noninvasive pulsed Doppler echocardiographic techniques, which allow a real-time and direct measurement of left ventricular function, have been applied to identify diastolic abnormalities by changes in left ventricular filling patterns.^{10)–13)} Left ventricular diastolic dysfunction may be demonstrated by pulsed Doppler echocardiography during acute myocardial ischemia in patients with chronic coronary artery disease.^{14)–17)} Doppler experimental studies have shown early abnormalities in left ventricular filling occurring following coronary artery occlusion.^{18),19)}

In this study, we used pulsed Doppler echocardiography before and after dipyridamole infusion in patients with significant coronary artery disease and normal subjects. We observed three Doppler-derived indices. They are velocity parameters (A, R, A/R), time integral area parameters (IR1, IR2, IA) and time interval parameters (TR1, TR2). This study was designed to compare the changes in transmitral flow parameters during anginal attack induced by dipyridamole infusion using pulsed Doppler echocardiography to assess impaired left ventricular filling.

METHODS

Study patients: Subjects were 81 (57 men, 24 women, mean age 56 ± 10 years) consecutive patients who underwent both right and left cardiac catheterization, including left ventriculography and coronary arteriography, for evaluation of coronary artery disease. Seventy-three patients who were classified as the coronary artery disease group had coronary artery stenosis greater than 75% in at least one major coronary artery. Eight patients who had normal coronary arteriograms and normal left ventriculograms were classified as normal subjects. In all patients, treatment with calcium antagonists or nitrates had been discontinued for at least 48 hours and treatment with beta-receptor blockers for at least 7 days. We excluded patients with unstable angina, left main trunk or 3-vessel disease, congestive heart failure, congenital or valvular heart disease and cardiomyopathy from this study.

Dipyridamole echocardiography test: The dose of dipyridamole was 0.56 mg/kg. The dipyridamole was diluted in 20 ml of saline solution and infused over 4 min. During the dipyridamole-stress test, the blood pressure and 12-lead electrocardiogram were recorded before and every minute after the start

of the dipyridamole intravenous infusion. On the basis of the response of the electrocardiogram to infusion of dipyridamole, the patients were classified into 2 groups; negative responder, those patients with coronary artery disease not presenting ischemic electrocardiographic changes after dipyridamole infusion, and positive responder, those patients with coronary artery disease developing ischemic electrocardiographic changes after dipyridamole infusion. To treat side effects due to dipyridamole such as chest pain, nausea, vomiting and/or electrocardiographic changes, intravenous aminophylline (100 to 250 mg), which promptly resolved the effect of dipyridamole, was ready for immediate use.²⁰⁾ All standard echocardiographic views (parasternal long and short axis, apical four-chamber and two-chamber) were obtained when possible. Two-dimensional echocardiography was continuously recorded by videotape recorder (Victor, BR8600) during the dipyridamole infusion and up to 20 min after the end of dipyridamole infusion.

Pulsed Doppler technique: A commercially available pulsed Doppler flow-meter combined with an electronic beam sector-scanning echocardiography (Toshiba, SSH 40A/SDS 21A and SSH 65A) was used to measure the trans-mitral flow pattern. The ultrasonic frequency used was 2.4 MHz and the pulse repetition rate was 4 KHz. A "Doppler filter" setting of 400 Hz was used. The system has a movable cursor that allows Doppler searching anywhere on the simultaneous two-dimensional echocardiographic image. When the Doppler mode is selected, the sector scanning is stopped and the last visualized two-dimensional echocardiographic image is frozen. The detected Doppler signals were recorded on a strip-chart recorder. The paper speed was 100 mm/sec in this study. Pulsed Doppler echocardiograms were taken during held-mid expiration in all patients, who were placed in the left lateral decubitus position. The transducer was placed nearly at the point of the apical impulse to obtain the best visualization of an apical two-chamber view (long axis). The Doppler sampling beam was perpendicular to the mitral anulus for the two-dimensional echocardiographic apical two-chamber view (long axis) of the heart. We attempted to maximize Doppler shift by small position changes of the sampling volume so as to be close to parallel to mitral inflow. Pulsed Doppler echocardiographic data were sampled in two phases during this study, the first before dipyridamole infusion (control) and the second after dipyridamole infusion.

Data analysis: The normal transmitral flow pattern consisted of rapid filling in early diastole and an atrial contraction wave. The peak flow velocity of the left ventricular rapid filling phase (R), that of the atrial contraction phase (A) and the ratio of A to R (A/R) in each cardiac cycle were calculated. The rapid filling phase was divided into two subphases at the point of R, and

Fig. 1. Transmittal flow velocity profile and the two variables derived from the transmittal velocity pattern. The measurements of transmittal flow velocity used in this study are 1) velocity parameters: R (cm/sec)=the peak velocity in the rapid filling phase, A (cm/sec)=the peak velocity in the atrial contraction phase, A/R =the ratio of peak velocity in the atrial contraction phase to that in the rapid filling phase. 2) Doppler integrated area parameters: $IR1$ (cm)=the area of time to peak rapid filling, $IR2$ (cm)=the area of time from peak rapid filling to the end of rapid filling, IR (cm)= $IR1+IR2$, IA (cm)=the area of atrial contraction phase, I (cm)= $IR+IA$. 3) Doppler time interval parameters: $TR1$ (msec)=the time interval to peak rapid filling, $TR2$ (msec)=the time interval from peak rapid filling to the end of rapid filling, TR (msec)= $TR1+TR2$.

the integral of the subphases and the atrial contraction phase was measured by a computerized area curve meter system (Ushikata, X-PLAN 360iR). These integrals, $IR1$, $IR2$ and IA , refer to the indices of filling volume of each phase. The time intervals of the rapid filling subphases are $TR1$ and $TR2$, respectively (Fig. 1). Time interval data were divided by the square root of the R-R interval to normalize them ($c-TR1$, $c-TR2$ and $c-TR$).

The presence of mitral regurgitation (MR), defined as a holosystolic turbulent flow through the mitral valve into the left atrium, was sought from pulsed Doppler echocardiographic examination in the apical four- and two-chamber views. The Doppler sampling volume was carefully and progressively moved throughout the entire left atrium to identify the regurgitant jet. All echocardiographic images were recorded by videotape for subsequent analysis.

Rate-pressure products (heart rate $\times$ systolic blood pressure) were measured before dipyridamole infusion (control) and at the onset of ischemia in positive responders and at the point of hyperkinesia in negative responders.

Statistics: Significance of difference was obtained by Student's t-test for paired data. Results are expressed as mean $\pm$ standard deviation. A p value <0.05 was considered significant.

RESULTS

Seventy-three patients with coronary artery disease were divided into 2 groups according to the presence or absence of a dipyridamole-induced anginal attack (positive responder, PR and negative responder, NR, respectively). NR consisted of 32 patients and PR consisted of 41 patients. The details of the normal subjects, NR and PR are listed in Table I. Anginal attack and electrocardiographic changes developed over a period ranging from 1 to 5 min after the end of dipyridamole infusion in PR. Patients with NR and normal subjects had no anginal attack or electrocardiographic changes after dipyridamole infusion.

Results of hemodynamic variables (Table II): In all groups, there were no differences in systolic blood pressure between the control period and after dipyridamole infusion, but in the latter period heart rate increased significantly in all groups, resulting in augmentation of the rate-pressure product (Table II).

Pulsed Doppler echocardiographic data (Tables III-V): Filling indices in each group during the control period and after dipyridamole infusion are summarized in Tables III and IV. Doppler velocity data are in Table III. In all groups, A and R increased significantly after dipyridamole infusion. In nor-

Table I. Summary of Clinical and Catheterization Data

	Normal subjects	Coronary artery disease			
		Negative responders		Positive responders	
Patients	8	32		41	
Age	51 $\pm$ 8	58 $\pm$ 9		59 $\pm$ 10	
Sex	6M 2F	24M	8F	27M	14F
CAD					
LAD	0	28		29	
LCX	0	5		6	
RCA	0	7		13	
MR	0	2		4	
Previous MI	0	12		19	

CAD=coronary artery disease with luminal stenosis $>75\%$; M=male; F=female; MR=mitral regurgitation; MI=myocardial infarction; LAD=left anterior descending artery; LCX=left circumflex artery; RCA=right coronary artery. Values represent mean $\pm$ SD.

Table II. Comparison of Hemodynamic Variables in the Control and Dipyridamole Studies

Measurement	Normal subjects (n=8)	Coronary artery disease	
		Negative responders (n=32)	Positive responders (n=41)
HR (beats/min)			
CNT	60±10	62±11	60±11
DPR	70±12*	71±10**	74±11**
S-BP (mmHg)			
CNT	122±16	130±19	140±21
DPR	115±18	125±20	142±20
RPP (beats·mmHg/min)×10 ⁻²			
CNT	72±15	81±18	82±19
DPR	80±17	90±21*	104±31**

CNT=control; DPR=dipyridamole infusion; HR=heart rate; S-BP=systolic blood pressure; RPP=rate-pressure product.

CNT vs DPR: * p<0.05, ** p<0.01.

Table III. Doppler Velocity Data in Normal Subjects and Patients with Coronary Artery Disease

Measurement	Normal subjects (n=8)	Coronary artery disease	
		Negative responders (n=32)	Positive responders (n=41)
R (cm/sec)			
CNT	63.3±8.96	54.3±13.5	53.0±13.1
DPR	69.8±10.8**	60.5±13.6**	58.9±18.2**
A (cm/sec)			
CNT	47.9±6.35	59.2±12.7	60.2±13.2
DPR	56.4±9.69*	71.0±14.6**	69.6±17.1**
A/R			
CNT	0.78±0.15	1.16±0.53	1.18±0.36
DPR	0.81±0.11	1.30±0.52	1.29±0.50*

CNT=control; DPR=dipyridamole infusion.

CNT vs DPR: * p<0.05, ** p<0.01.

mals and NR, A/R remained unchanged. In PR, A/R increased significantly during dipyridamole-induced anginal attack (1.18 ± 0.36 to 1.29 ± 0.50 , $p<0.05$). Doppler area data are in Table IV. In NR, IR1, IR2, IR and I remained unchanged after dipyridamole infusion. In PR, IR2 decreased significantly during dipyridamole-induced anginal attack (5.36 ± 1.88 to 4.32 ± 1.75 cm, $p<0.01$), but IR1, IR1+IR2 (IR) and IR1+IR2+IA (I) remained unchanged. In all groups, IA increased significantly after dipyridamole in-

Table IV. Doppler Area Data in Normal Subjects and Patients with Coronary Artery Disease

Measurement	Normal subjects (n=8)	Coronary artery disease	
		Negative responders (n=32)	Positive responders (n=41)
IR1 (cm)			
CNT	4.43±1.11	3.78±1.30	3.26±1.12
DPR	4.46±1.15	3.87±1.32	3.63±1.27
IR2 (cm)			
CNT	6.04±1.09	5.59±2.05	5.36±1.88
DPR	5.79±2.12	5.42±2.25	4.32±1.75**
IR (cm)			
CNT	10.5±1.97	9.36±2.93	8.60±2.78
DPR	10.2±2.84	9.28±3.24	7.98±2.88
IA (cm)			
CNT	4.65±1.04	6.07±1.82	5.81±1.83
DPR	5.56±1.43**	6.97±2.04**	6.31±2.20*
I (cm)			
CNT	15.2±2.71	15.5±4.00	14.6±4.13
DPR	15.8±3.87	16.2±4.33	14.1±4.02

CNT=control; DPR=dipyridamole infusion; IR=IR1+IR2; I=IR+IA.

CNT vs DPR: * <0.05, ** p<0.01.

Table V. Doppler Time Interval Data in Normal Subjects and Patients with Coronary Artery Disease

Measurement	Normal subjects (n=8)	Coronary artery disease	
		Negative responders (n=32)	Positive responders (n=41)
c-TR1 (msec)			
CNT	98±18	109±26	90±20
DPR	117±28	117±27	109±21**
c-TR2 (msec)			
CNT	150±17	150±27	150±34
DPR	131±44	139±34	122±28**
c-TR (msec)			
CNT	248±25	259±43	247±46
DPR	248±46	252±42	237±42

c=1/square root of the R-R interval; CNT=control; DPR=dipyridamole infusion.

CNT vs DPR: ** p<0.01.

fusion. Doppler time interval data are presented in Table V. In PR, c-TR1 was prolonged and c-TR2 shortened significantly after dipyridamole infusion (c-TR1; 90±20 to 109±21, c-TR2; 150±34 to 122±28 msec). C-TR re-

Fig. 2. Pulsed Doppler recording of transmitral flow shown from the apical position in patients with coronary artery disease. Left panel is control and right panel is dipyridamole-induced anginal attack. Top, A/R increased in a patient without mitral regurgitation (MR) during acute myocardial ischemia (73-year-old female). Bottom, A/R remained unchanged in a patient with MR (58-year-old male).

Table VI. Comparison of Doppler-Derived Indices in Patients with or without MR

Measurement	MR (-) (n=28)		MR (+) (n=13)	
	CNT	DPR	CNT	DPR
R (cm/sec)	52.6±12.6	55.0±16.6	54.0±14.5	65.8±21.5*
A (cm/sec)	59.5±12.3	70.0±16.5**	61.2±15.5	69.6±19.0*
A/R	1.19±0.39	1.37±0.50**	1.16±0.29	1.10±0.46
IR1 (cm)	3.11±0.99	3.33±1.16	3.58±1.33	4.30±1.26
IR2 (cm)	5.18±1.91	4.12±1.90**	5.76±1.82	4.72±1.33*
IR (cm)	8.82±2.70	7.49±2.98	9.31±2.95	9.03±2.47
IA (cm)	5.88±1.63	6.44±2.04*	5.69±2.27	6.02±2.56
I (cm)	14.3±3.89	13.7±4.19	15.1±4.45	14.9±3.41
c-TR1 (msec)	97.3±22	107±17**	107±31	114±24
c-TR2 (msec)	150±38	127±31**	147±23	118±24*
c-TR (msec)	246±50	234±44	249±35	233±39

CNT=control; DPR=dipyridamole infusion; IR=IR1+IR2; I=IR+IA; c-TR=c-TR1+c-TR2; MR=mitral regurgitation. CNT vs DPR: * $p < 0.05$, ** $p < 0.01$.

maintained unchanged after dipyridamole infusion. In normal subjects and negative responders, Doppler time interval data remained unchanged after dipyridamole infusion. The changes in A/R ratio, IR2 and c-TR2 in each individual patient are shown schematically in Fig. 2.

MR was present in 13 patients during dipyridamole-induced angina in

Fig. 3. Atrial / Rapid (A/R) peak flow velocity ratio, the area of time from peak rapid filling to the end of rapid filling (IR2) and the time interval from peak rapid filling to the end of rapid filling (c-TR2) at rest (control) and after dipyridamole infusion in 41 positive responders (PR=dipyridamole-induced anginal attack) and 32 negative responders (NR=no ischemic change). A/R, IR2 and c-TR2 did not change significantly in NR, whereas these indices did demonstrate significant changes in PR.

PR. We divided PR into 2 subgroups according to the presence (13 patients) or absence of MR (28 patients) in PR. Six had MR in the control state and in 7 ischemic MR was observed during acute myocardial ischemia. There were no significant differences in heart rate, blood pressure, degree of chest pain or electrocardiographic changes between the 2 subgroups. These Doppler data are shown in Table VI. A/R increased significantly (1.19 ± 0.39 to 1.37 ± 0.50 , $p < 0.01$) in patients without MR, but A/R remained unchanged (1.16 ± 0.29 to 1.10 ± 0.46 , $p = \text{NS}$) in patients with MR. IR2 decreased significantly in both subgroups with MR (5.76 ± 1.82 to 4.72 ± 1.33 cm, $p < 0.01$) and without MR (5.18 ± 1.91 to 4.12 ± 1.90 cm, $p < 0.01$). C-TR1 was prolonged significantly in patients without MR. C-TR2 was shortened significantly in patients with MR and without MR. C-TR remained unchanged in both

groups. A representative case of Doppler signals taken from a control study and from the corresponding dipyridamole study is illustrated in Fig. 3.

In PR, A/R increased in 24 patients and IR2 decreased in 37 patients. In NR, A/R increased in 17 patients and IR2 decreased in 4 patients. The overall sensitivity of A/R for myocardial ischemia was 42% and specificity was 65%. The sensitivity of IR2 for myocardial ischemia was 90% and the specificity 84%.

DISCUSSION

Effect of dipyridamole administration: The diagnostic value of intravenous dipyridamole in comparison with the findings of exercise testing³⁾ for coronary artery disease has been reported. Picano et al reported that a dipyridamole two-dimensional echocardiographic test (assessment of wall motion abnormality) is feasible and useful for detecting coronary artery disease and has a higher specificity than exercise-stress testing.⁴⁾ In this study, we assessed left ventricular filling during dipyridamole-provoked myocardial ischemia using pulsed Doppler echocardiography. Intravenous dipyridamole acted as an arteriolar dilator, causing mildly reduced blood pressure, increased heart rate, cardiac output and coronary sinus flow.^{1),21),22)} In this study, heart rate and rate pressure product increased after dipyridamole infusion. Of 81 patients undergoing dipyridamole-stress testing, 25% had some side effects of dipyridamole. These were transient headache, transient facial flushing and transient nausea. There were no cardiac side effects or deaths. The chest pain and side effects were promptly resolved by intravenous injection of aminophylline.

Doppler echocardiography: In this study, we observed three Doppler-derived indices. These are velocity parameters (A, R and A/R), time integral area parameters (IR1, IR2 and IA) and time interval parameters (TR1, TR2 and TR). The velocity parameters R and A, and IA increased after dipyridamole infusion in all groups, probably due to the hyperkinetic state present after peripheral vasodilation due to dipyridamole. During acute myocardial ischemia, A/R increased, IR2 decreased, c-TR1 was prolonged and c-TR2 shortened significantly. During ischemia, the integrated trans-mitral flow in the former phase of rapid filling remained unchanged and in the latter phase of rapid filling decreased significantly. Our data showed that this difference after dipyridamole infusion was due to a difference between changes in each duration. Left ventricular filling is proportional to the magnitude of the left atrial-left ventricular pressure gradient, as previously proposed by Yellin et al²³⁾ and the pressure gradient may be maximized at the

left ventricular minimum pressure. Courtois et al reported that the mitral flow starts in close proximity to the time of the first left atrial-left ventricular pressure crossover point, and the transmitral pressure gradient is zero at or near peak flow velocity (R) at the rapid filling phase (second left atrial-left ventricular pressure crossover point).²⁴⁾ Minimum left ventricular pressure also appears to be associated with an inflection point in the early diastolic Doppler-velocity signal. Previous studies have reported that diastolic pressure increases with ischemia and that the elevation of early diastolic pressure is caused by the impaired left ventricular relaxation clearly shown during ischemic conditions by prolongation of decay.^{6),7),25)} Accordingly, an extended time interval to peak velocity of rapid filling induced by acute myocardial ischemia is believed to indicate the time interval from mitral valve opening to the second crossover point of the left atrial-left ventricular pressure (pressure gradient is zero), which may be caused by impaired left ventricular relaxation in acute myocardial ischemia. It is reasonable to suggest that in the former phase of rapid filling, the filling volume was unchanged in acute myocardial ischemia, since the delay in left ventricular pressure fall to minimum pressure associated with impaired relaxation may cause prolonged filling time as well as reduction in filling velocity. On the other hand, when the duration from peak velocity of rapid filling to the end of rapid filling was shortened in acute myocardial ischemia, its filling volume was reduced. If the left atrial-left ventricular pressure gradient is a major factor in reducing ventricular filling in the rapid filling phase, it is suggested that the duration of the latter phase of rapid filling may be shortened in acute myocardial ischemia, since elevation of left ventricular diastolic pressure induced by ischemia can delay left ventricular pressure fall to minimum pressure and rapidly minimize the left atrial-left ventricular pressure gradient after reaching the second crossover point of left atrial-left ventricular pressure. The reduced peak rapid filling flow velocity decreased in the latter phase of rapid filling and changes in time interval of the rapid filling phase during acute myocardial ischemia can be explained by the decrease in the early left atrial-left ventricular pressure gradient and the extended time interval to peak velocity of rapid filling after the acute increase in early diastolic pressure.

We observed MR in 13 patients in PR. A/R increased in patients without MR, while A/R remained unchanged in patients with MR. Thus, velocity parameters (A, R, A/R) did not clearly change in patients with MR during acute myocardial ischemia. In these patients, who were assumed to have a left ventricular diastolic abnormality, the masking of the diastolic abnormality was ascribed to the presence of MR. An elevation in left atrial pressure due to MR increased the left atrial-left ventricular pressure gradient,

and can mask a left ventricular diastolic abnormality when assessed by peak rates of filling or filling patterns. The use of velocity parameters to evaluate left ventricular function may be misleading if patients with MR are analyzed together with those who have more normal filling patterns. In patients with MR, it is suggested that the integrated transmitral flow in the latter phase of rapid filling may be decreased, since the duration of the latter phase of rapid filling is shortened. Previous studies have shown that MR can cause increases in left ventricular peak filling rate and mitral flow velocity.^{23),25)–28)}

The overall sensitivity of A/R in detecting myocardial ischemia was 42% and the specificity 65%. The IR2 sensitivity for myocardial ischemia was 90% and the specificity 84%. It is necessary to consider not only velocity indices but also time velocity integral indices from the viewpoint of evaluating left ventricular filling using pulsed Doppler echocardiography and also to consider MR.

Limitation of the study: It is important for evaluating left ventricular filling using pulsed Doppler echocardiography to consider the influence of heart rate. Dipyridamole may induce an increase in heart rate, and transmitral flow will show a monophasic filling pattern when heart rate exceeds 100 beats/min. The monophasic filling pattern produced by the fusion of early rapid filling and atrial contraction makes the analysis of left ventricular filling difficult.^{5),7)} According to several previous reports, dipyridamole-stress testing has higher specificity but lower sensitivity for the diagnosis of coronary artery disease.^{2)–4)} We performed this study noninvasively. Therefore we cannot provide definitive hemodynamic explanations for the alterations observed. Left ventricular filling is influenced by multiple factors, such as left ventricular relaxation, compliance and filling pressure. Because peak filling velocities are determined by the pressure differences between the atrium and ventricle, A, R and A/R can be influenced by left ventricular filling pressure.²⁹⁾ For further understanding of left ventricular filling, it may be necessary to measure hemodynamic parameters in addition to changes in transmitral flow.

Clinical implication: This study was designed to compare the changes in pulsed Doppler echocardiographic indices of diastolic ventricular filling during dipyridamole-provoked acute myocardial ischemia in patients with coronary artery disease. Coronary vasodilating agents like dipyridamole can provoke ischemia in patients with coronary artery disease. Pulsed Doppler echocardiography can perform the beat-by-beat measurement of transmitral flow quickly and noninvasively. Doppler dipyridamole-stress testing is not limited by the physical condition of the patients and can be performed at the bed side without severe side effects. In a detailed phase analysis of the transmitral flow we also showed that the reduction of the integration of velocity of trans-

mitral flow during the rapid filling phase with dipyridamole-stress testing was mainly caused by that from the peak velocity of rapid filling to the end of rapid filling. These results suggested that rapid filling was restricted during acute myocardial ischemia and its restriction was mainly caused by impairment of the latter phase of rapid filling. When assessing left ventricular filling during angina using velocity parameters of pulsed Doppler echocardiography, MR must be taken into account. MR can mask a left ventricular diastolic abnormality when assessed by peak rates of filling or filling patterns.

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