

# Pulsed Doppler Assessment of Left Ventricular Diastolic Filling in Coronary Artery Disease Before and Immediately After Coronary Angioplasty

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To determine if left ventricular (LV) diastolic filling abnormalities are detectable by Doppler echocardiography in patients with coronary artery disease (CAD), 34 patients with CAD and 24 normal, age-matched control subjects underwent mitral valve pulsed Doppler examination. At catheterization, all CAD patients had typical angina, at least 70% diameter narrowing of 1 major coronary artery, ejection fraction of 50% or more and no valvular heart disease. Seventeen CAD patients underwent coronary angioplasty and had a Doppler examination 1 day before and 1 day after the procedure. Doppler diastolic time intervals, peak velocities at rapid filling (E velocity), atrial contraction (A velocity) and the ratio peak E/peak A velocities were measured. The following areas under the Doppler velocity envelope and their percentage of the total area were calculated: first third of diastole (0.33 area), triangular area under the peak E velocity (E area), and triangular area under the peak A velocity (A area). Patients with CAD and normal subjects were significantly different ( $p < 0.01$ ) in peak E velocity (CAD

$0.60 \pm 0.12$  m/s, normal  $0.68 \pm 0.12$  m/s), peak A velocity (CAD  $0.59 \pm 0.12$  m/s, normal  $0.48 \pm 0.11$  m/s), ratio peak E/peak A velocities (CAD  $1.0 \pm 0.27$ , normal  $1.5 \pm 0.32$ ), A area (CAD  $0.052 \pm 0.015$  m, normal  $0.036 \pm 0.010$  m), ratio E area/A area (CAD  $1.7 \pm 0.53$ , normal  $2.5 \pm 0.69$ ), and all area fractions. In the CAD patients who had undergone coronary angioplasty, no differences were found in any Doppler index before and immediately after the procedure. Thus, abnormal patterns of LV diastolic filling occur in patients with CAD and normal global systolic function. The decreased percentage of the Doppler area occurring during rapid filling and the increased percentage of the Doppler area occurring in late diastole suggest that CAD patients have impaired early diastolic filling. These diastolic filling abnormalities are unimproved 24 hours after successful coronary angioplasty. Doppler echocardiography provides a useful, noninvasive technique for assessment of LV diastolic filling in patients with CAD.

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**R**ecent radionuclide angiographic studies show that abnormalities in left ventricular (LV) diastolic filling occur in patients with coronary artery disease (CAD) and often precede the development of systolic dysfunction.<sup>1-4</sup> These studies demonstrated prolonged time to peak filling rate, decreased LV relaxation rates, and a decreased percentage of the total diastolic volumetric flow occurring during rapid filling in patients

with CAD. Pulsed Doppler echocardiography is another noninvasive technique that has recently been used to evaluate LV diastolic filling.<sup>5-9</sup> Doppler diastolic filling indexes have correlated closely with those measured from cineangiography<sup>5</sup> and radionuclide angiography.<sup>8</sup> Diastolic time intervals, peak flow velocities, and the proportion of flow in the various phases of diastole can be accurately measured from the mitral valve Doppler recording. This study determines if abnormal patterns of LV diastolic filling are detectable on the pulsed Doppler examination of patients with CAD and, if so, whether these abnormal patterns are altered immediately after coronary angioplasty.

## Methods

**Patients:** Pulsed Doppler echocardiograms were recorded in 34 patients (22 men, 12 women) with CAD and 24 normal adults (10 men, 14 women). The normal

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adults had no evidence of cardiovascular disease by history, physical examination or 2-dimensional echocardiography. Normal participants were selected so that their ages matched those of the CAD group. They were 42 to 76 years old (mean 51) and weighed 59 to 104 kg (mean 76). At the time of the Doppler examination, the systolic blood pressure of the normal group was  $117 \pm 13$  mm Hg (mean  $\pm$  standard deviation) and diastolic blood pressure was  $71 \pm 12$  mm Hg.

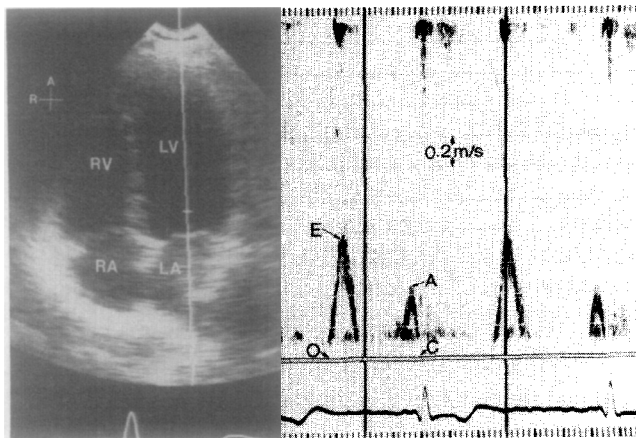
From June 1984 to January 1986, patients with CAD were selected from the total patient population undergoing cardiac catheterization to participate in the study. The selection criteria were (1) a history of typical angina, (2) at least 70% diameter narrowing of 1 major coronary artery or a large branch, (3) LV ejection fraction of 50% or more by cineangiography or radio-nuclide ventriculography, and (4) absence of valvular heart disease. The CAD patients were 36 to 75 years old (mean 54) and weighed 43 to 114 kg (mean 78). Eleven patients had evidence of a prior myocardial infarction by Q waves on the electrocardiogram and wall motion abnormalities, and 12 patients had a history of systemic hypertension. At catheterization, 22 patients had 1-vessel disease, 9 had 2-vessel disease and 3 had 3-vessel disease. Eleven patients had segmental wall motion abnormalities in the distribution of the affected coronary artery. At the time of the Doppler examination, 4 patients were receiving no medications, 28 were taking nitrates, 24 were taking calcium channel-blocking drugs and 15 were receiving  $\beta$ -blocking drugs. No patient had angina immediately before or during the Doppler recording. At examination, the systolic blood pressure of the CAD group was  $111 \pm 18$  mm Hg and diastolic blood pressure was  $64 \pm 12$  mm Hg.

Of the CAD group, a subgroup of 17 patients (13 men and 4 women, 36 to 75 years old) underwent coronary angioplasty. These patients had pulsed Doppler

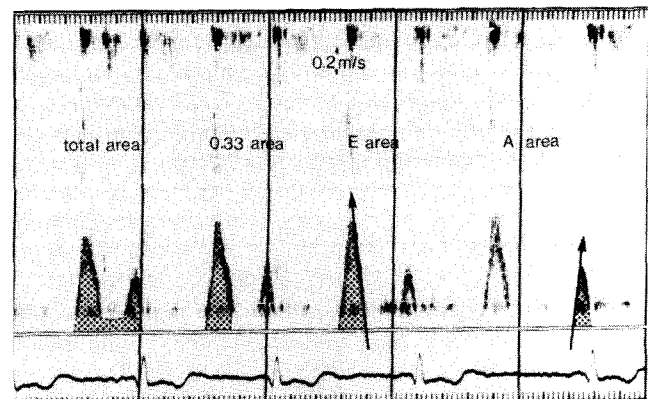
examinations 1 day before and 1 day after angioplasty. At catheterization before angioplasty, 14 patients had 1-vessel disease and 3 had 2-vessel disease. Mean LV ejection fraction was 65% (range 50 to 85), and a translesional gradient of at least 40 mm Hg was seen across each stenosis before dilatation. After angioplasty, all residual stenoses were 40% or less and all residual gradients were 18 mm Hg or less. In the 6 weeks after angioplasty, all patients underwent thallium exercise treadmill testing; no evidence of ischemia was noted and no patient had an anginal episode, although all antianginal medications were continued.

**Pulsed Doppler studies:** Pulsed Doppler examinations of the LV inflow were performed using an Advanced Technology Laboratories Mark 600 ultrasound system with a 2.25-MHz transducer. With use of the apical 4-chamber view, the Doppler sample volume was placed in the mitral valve funnel just on the LV side of the mitral annulus<sup>8</sup> (Fig. 1). The sample volume position was then adjusted so as to position the ultrasound beam as parallel to LV inflow as possible. The opening and closure points (O and C points) of the mitral valve Doppler and the peak velocities during rapid ventricular filling (E velocity) and during atrial contraction (A velocity) were recorded for at least 3 cardiac cycles at a paper speed of 50 mm/s. The following intervals and velocities were measured from the Doppler spectral recording: (1) heart rate (measured as 60/RR interval); (2) O to C time (this time interval represents the diastolic flow period); (3) O to E time (this interval represents the rapid filling period); (4) peak E velocity; (5) peak A velocity; and (6) ratio of peak E velocity/peak A velocity.

Using techniques previously described,<sup>6</sup> we assessed the patterns of LV filling by integrating several areas under the mitral valve velocity curve (Fig. 2). The integrated areas were (1) the total area under the Doppler velocity envelope, (2) the area under the Doppler curve for the first 33% of diastole (0.33 area), (3) the E area or the triangular area formed by drawing a straight line down from the peak E velocity to the baseline, and (4) the A area or the triangular area formed by drawing a straight line down from the peak A velocity to the baseline. Also, the ratio of E and A



**FIGURE 1.** Apical 4-chamber view (left) showing the position of the sample volume (crossbar) at the time of the mitral valve Doppler examination. On the normal mitral valve Doppler tracing (right), O and C represent opening and closure points of the mitral valve and E and A the peak velocities during rapid filling and atrial contraction. A = apex; LA = left atrium; LV = left ventricle; R = right; RA = right atrium; RV = right ventricle.



**FIGURE 2.** Mitral valve Doppler recording showing the areas that were measured.

**TABLE I Doppler Time Interval and Velocity Data in Normal and Coronary Artery Disease (CAD) Groups**

Measurement	Normals (n = 24)	Patients with CAD (n = 34)	p Value
O to E (s)	0.069 ± 0.014	0.076 ± 0.015	0.08
O to C (s)	0.49 ± 0.15	0.48 ± 0.13	0.73
Peak E (m/s)	0.68 ± 0.12	0.60 ± 0.12	<0.01*
Peak A (m/s)	0.48 ± 0.11	0.59 ± 0.12	<0.01*
Peak E/peak A	1.5 ± 0.32	1.0 ± 0.27	<0.0001*

\*Statistically different between groups at the 5% level.

Values are mean ± standard deviation.

A = velocity at atrial contraction; C = time point of mitral valve closure; E = velocity during rapid ventricular filling; O = time point of mitral valve opening.

areas was calculated. Each Doppler area was divided by the total area under the Doppler curve to obtain the area fractions. The area fractions were calculated to describe the percentage of the total velocity envelope occupied by the individual areas and to normalize the data for differences in preload and cycle lengths between the patients.

A Microsonics CAD 888 microprocessor system and a hand-held crosswire cursor were used to measure the Doppler areas. For the area measurements, the Doppler recordings were traced along the darkest portion of the spectral curve (the modal velocity), through the area of the wall filter, and to the baseline at the point where the velocity recorded from the motion of the valve leaflet crossed the baseline. For the peak velocity measurements, the highest value at the outer-most border of the Doppler curve was used.

**Statistical analysis:** Doppler measurements reported are the average values of 3 or more cardiac cycles. Statistical comparisons between the normal and CAD patients were made using an unpaired t test. Statistical comparisons between the CAD patients before and after angioplasty were made using a paired t test. A 2-tailed probability value <0.05 was used to indicate a significant intergroup difference.

The beat-to-beat variation coefficients for selected Doppler diastolic measurements have been reported as follows<sup>6</sup>: total area under the Doppler curve 2.4%, 0.33 area 4.9%, A area 3.8%, and peak A velocity 4.2%. Also, the interobserver variability for selected Doppler diastolic measurements has been reported previously as follows<sup>6</sup>: total area under the Doppler curve 2.8%, 0.33 area 2.4%, A area 3.8%, and peak A velocity 2.1%.

**Results**

**Patients:** The normal and CAD patients did not differ in age, weight, heart rate or systolic blood pressure. The diastolic blood pressure of the CAD group was slightly less than that of the normal group (64 ± 12 vs 71 ± 12 mm Hg, p = 0.03). No differences were found in heart rate and blood pressure at the time of the 2 Doppler examinations in the CAD patients who underwent coronary angioplasty.

**Doppler ultrasound findings:** Comparisons of normal and coronary artery disease groups: On qualitative inspection, the mitral valve Doppler recordings of

**TABLE II Doppler Area Data in Normal and Coronary Artery Disease (CAD) Groups**

Measurement	Normals (n = 24)	Patients with CAD (n = 34)	p Value
Total area (m)	0.14 ± 0.029	0.15 ± 0.022	0.22
0.33 area (m)	0.076 ± 0.020	0.069 ± 0.019	0.21
E area (m)	0.086 ± 0.018	0.082 ± 0.018	0.66
A area (m)	0.036 ± 0.010	0.052 ± 0.015	<0.01*
E area/A area	2.5 ± 0.69	1.7 ± 0.53	<0.0001*
0.33 area/total area	0.53 ± 0.062	0.46 ± 0.095	<0.01*
E area/total area	0.62 ± 0.070	0.55 ± 0.076	<0.01*
A area/total area	0.26 ± 0.071	0.35 ± 0.11	<0.001*

\*Statistically different between groups at the 5% level.

Values are mean ± standard deviation.

Abbreviations as in Table I.

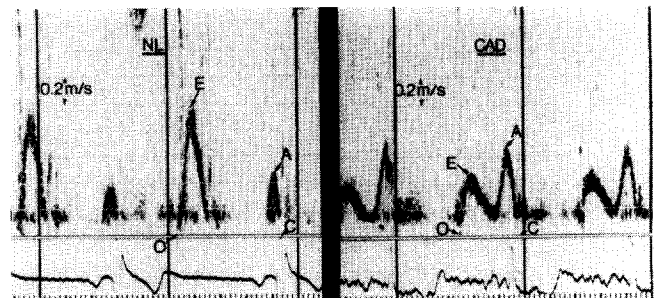
**TABLE III Doppler Area Data in Coronary Artery Disease Patients Before and After Coronary Angioplasty (n = 17)**

Measurement	Before	After	p Value
Total area	0.14 ± 0.021	0.14 ± 0.026	0.58
0.33 area	0.065 ± 0.020	0.063 ± 0.022	0.74
E area	0.079 ± 0.016	0.072 ± 0.012	0.11
A area	0.050 ± 0.015	0.047 ± 0.016	0.13
E area/A area	1.7 ± 0.52	1.7 ± 0.46	0.86
0.33 area/total area	0.46 ± 0.11	0.46 ± 0.09	0.92
E area/total area	0.56 ± 0.074	0.54 ± 0.086	0.09
A area/total area	0.36 ± 0.11	0.35 ± 0.11	0.30

Values are the mean ± standard deviation.

Abbreviations as in Table I.

the CAD patients had a much different appearance than those of the normal subjects (Fig. 3). The CAD patients had a higher peak A velocity, a lower peak E velocity and a larger area under the A wave than did normal subjects. The Doppler time intervals and velocity measurements are listed in Table I. No differences were found in O to E and O to C times. The peak E velocity of the CAD group was significantly lower



**FIGURE 3.** Examples of mitral valve Doppler tracings obtained from a normal patient (left) and a CAD patient (right). CAD patients tended to have a higher peak velocity during atrial contraction (peak A velocity), a reduced peak velocity during rapid filling (peak E velocity), a higher percentage of the total under the Doppler curve occurring during atrial contraction, and a lower percentage of the total area under the Doppler curve occurring during rapid filling. C = mitral valve closure; CAD = coronary artery disease; NL = normal; O = mitral valve opening.

than that of the normal subjects. The peak A velocity of the CAD group was significantly higher; therefore, the ratio peak E velocity/peak A velocity was significantly lower in the CAD patients.

The Doppler areas and area fractions of the 2 groups are shown in Table II. No differences were found between the 2 groups in the total area under the Doppler curve, the 0.33 area and the E area. The A area of the CAD patients was significantly larger than that of the normal patients; therefore, the ratio E area/A area was significantly lower in the CAD patients. Of the area fractions, the percentage of the total Doppler area occurring in the first third of diastole and the percentage of the total Doppler area occurring under the E wave were significantly lower in the CAD patients. The percent of the total Doppler area occurring under the A wave was significantly greater in the CAD patients. The Doppler indexes that distinguished normal subjects from CAD patients are shown in Figures 4 and 5.

*Comparison of coronary artery disease patients before and after angioplasty:* In the CAD patients who

underwent angioplasty, no differences were found in O to E time, O to C time, peak E velocity, peak A velocity, and the ratio peak E velocity/peak A velocity immediately after the procedure

The Doppler areas and area fractions for the CAD patients who underwent angioplasty are shown in Table III. As with the velocity data, no differences were observed in any of the Doppler areas or area fractions 1 day after coronary angioplasty.

*Subgroup analysis:* To determine if variables such as hypertension, wall segment abnormalities and disease severity influenced the results, CAD patients were classified into several subgroups for additional statistical analysis. First, the 12 patients with systemic hypertension were omitted from the CAD group and comparisons were made between the remaining 22 CAD patients and the 24 normal subjects. Omission of patients with hypertension did not change the study results. Second, the CAD group was separated into 2 subgroups. One subgroup consisted of 11 patients with evidence at catheterization of segmental wall motion abnormalities and the other subgroup consisted of 23

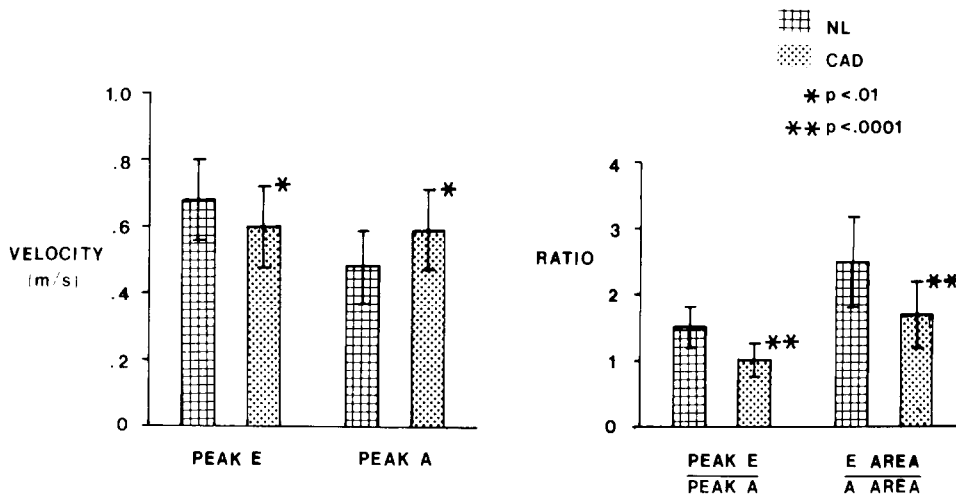


FIGURE 4. Doppler measurements that separated normal subjects from CAD patients. Abbreviations as in Figure 3.

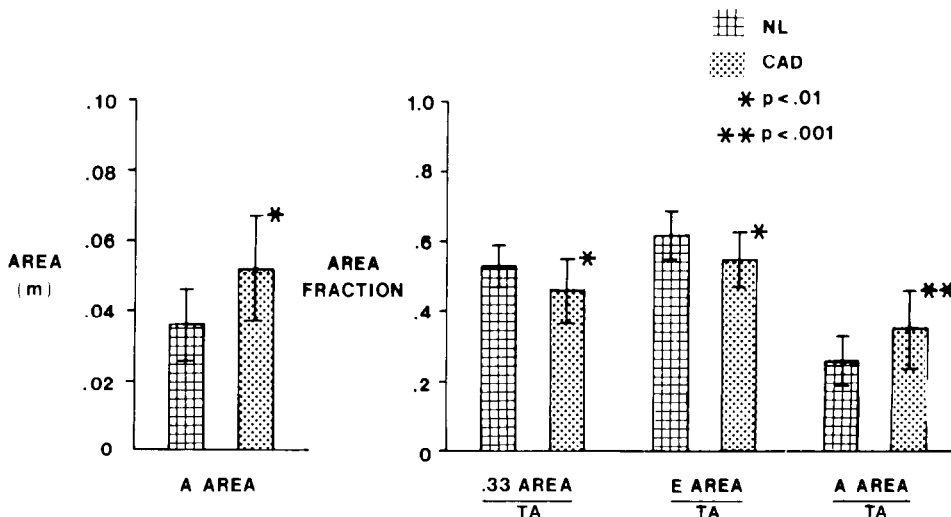


FIGURE 5. Doppler areas and area fractions that separated normal subjects from CAD patients. TA = total area under the Doppler curve; other abbreviations as in Figure 3.

patients with no segmental wall motion abnormalities. The Doppler time intervals, velocity data and area measurements of the 2 subgroups were compared using unpaired *t* tests. No differences were found in any of the Doppler measurements among the subgroups. Also, when the Doppler measurements from each subgroup were compared with those of the normal group, the results were the same as when comparisons were made between the entire CAD group and the normal group. Third, the CAD group was classified into 2 subgroups based on the extent of involvement of the coronary circulation. One subgroup consisted of 22 patients with 1-vessel disease and the other subgroup consisted of 12 patients with either 2- or 3-vessel disease. The Doppler time intervals, velocity data and area measurements of the 2 subgroups were compared using the unpaired *t* test, and no differences were found between subgroups. Doppler measurements from each subgroup were compared with those of the normal group. The results of these comparisons were the same as those made between the entire CAD group and the normal subjects.

## Discussion

This study indicates that CAD patients have an abnormal pattern of LV diastolic filling detectable by mitral valve Doppler examination. The decreased percent of the Doppler area occurring during rapid ventricular filling and the increased percentage of the Doppler area occurring in late diastole suggest that CAD patients have impaired LV early diastolic relaxation. These diastolic filling abnormalities are detectable by mitral valve Doppler examination in patients at rest and in patients with normal global systolic function. The ratio peak E velocity/peak A velocity, the ratio E area/A area, and the percentage of the total Doppler area occurring under the A wave of the mitral valve Doppler measurements were the most useful for distinguishing normal subjects from CAD patients.

Our mitral valve Doppler findings are consistent with previous radionuclide angiographic reports of diastolic filling abnormalities in CAD patients. Diastolic filling abnormalities reported in the radionuclide studies include decreased peak filling rate in early diastole, prolonged time to peak filling rate, decreased percentage of LV stroke counts in early diastole, and increased percentage of LV stroke counts in atrial systole.<sup>1-4</sup> Our Doppler findings of a decreased percentage of the total Doppler area under the E wave, increased percentage of the total Doppler area under the A wave, and a decreased ratio E area/A area are comparable to the radionuclide finding of decreased early-to-atrial LV filling ratio in patients with CAD. Although the radionuclide time to peak filling rate is prolonged in patients with CAD, the Doppler time to peak filling velocity (O to E time) is normal. This difference exists because the radionuclide time to peak filling rate is measured from end systole and thus includes the isovolumic relaxation period. The Doppler time to peak filling velocity is measured from the mitral valve opening and does not include isovolumic

relaxation. The finding of normal O to E time suggests that CAD patients have a normal rapid filling period and supports the concept that the prolongation of LV filling noted in these patients is due to prolongation of isovolumic relaxation time alone.

**Other factors affecting the mitral valve Doppler measurements:** LV diastolic filling is an important indicator of the diastolic properties of the ventricle; however, LV filling can be influenced by several factors other than the diastolic function of the ventricle. These factors include heart rate, age, blood pressure, ventricular loading conditions and systolic function.<sup>10-13</sup> Miyatake et al<sup>14</sup> and Gardin et al<sup>15</sup> reported an increase in the mitral valve peak A velocity with aging. This finding has been attributed to an increase in LV stiffness with aging, leading to impaired LV distensibility in early diastole and a compensatory augmentation of atrial contraction.<sup>14</sup> Our normal subjects were selected so that their ages matched those of the CAD patients; therefore, it is unlikely that age could explain the differences we observed in the Doppler measurements between patients groups. However, the variation of the Doppler indexes of LV diastolic filling with age must be taken into account when an individual patient is being evaluated. Differences in diastolic filling patterns between normal subjects and CAD patients cannot be explained on the basis of heart rate because the heart rates of the 2 groups were not different at the time of the Doppler examination. Also, the 2 groups did not differ in systolic function or ventricular loading conditions because only patients with normal ejection fractions and no evidence of mitral or aortic insufficiency were included in the CAD group.

Recent radionuclide studies have shown abnormalities in LV diastolic filling in patients with systemic hypertension that are similar to those seen in patients with CAD.<sup>16-18</sup> Mitral valve Doppler examinations of children with systemic hypertension revealed increased peak A velocity, decreased percentage of the total Doppler area in the first third of diastole, and increased percentage of the total Doppler area occurring under the A wave.<sup>6</sup> Abnormalities seen on Doppler examinations of CAD patients were similar to but of much greater magnitude than changes seen on Doppler examinations of hypertensive children. Exclusion of the 12 hypertensive patients from the CAD group did not alter the study results; therefore, we do not believe that the differences in Doppler examinations of normal and CAD patients can be explained solely on the basis of inclusion of patients with systemic hypertension in the CAD group.

The Doppler abnormalities noted in the CAD patients did not correlate with the presence of segmental wall motion abnormalities or the extent of involvement of the coronary circulation. No differences were found in the Doppler measurements of CAD patients with segmental wall motion abnormalities and CAD patients with no segmental wall motion abnormalities. Similarly, no differences were found in the Doppler measurements of CAD patients with 1-vessel disease and those with either 2- or 3-vessel disease.

Most CAD patients were receiving drug therapy at the time of the Doppler examination. We do not know what effect nitrates and  $\beta$ -blocking and calcium channel blocking drugs have on the Doppler measurements of diastolic filling; however, we detected significant abnormalities in LV diastolic filling despite clinically acceptable drug regimens. Further studies are necessary before and after drug therapy to determine if additional abnormalities are present on Doppler examination in untreated patients, and if Doppler indexes of diastolic filling will be useful for serial assessment of a patient's response to drug therapy.

**Doppler measurements before and after coronary angioplasty:** The Doppler diastolic filling abnormalities observed in CAD patients were unimproved 24 hours after coronary angioplasty despite angiographic, pressure gradient, thallium stress test, and clinical evidence for successful dilatation of the lesion and abolition of ischemia. This finding suggests that CAD alters diastolic filling in a manner that is not immediately reversible after successful angioplasty. Using radionuclide angiography, Bonow et al<sup>19,20</sup> showed improved LV diastolic filling indexes (decreased time to peak filling rate, increased peak filling rate) in CAD patients examined 2 days to 1 month after angioplasty. Several catheterization studies performed in CAD patients several months after coronary angioplasty or surgical revascularization also showed improved LV diastolic function, especially during exercise.<sup>21,22</sup> A possible explanation for the different results found in our study compared with the previous studies is that our CAD patients were examined within 24 hours of coronary angioplasty and while at rest. In a recent radionuclide study, Lewis et al<sup>23</sup> observed no improvement in the LV peak filling rate in CAD patients examined at rest 2 to 5 days after coronary angioplasty. During exercise, however, peak filling rate increased significantly. Further studies are necessary in CAD patients who have undergone angioplasty to determine if the Doppler indexes of LV diastolic filling improve during exercise or with time.

**Clinical use of the Doppler technique for evaluating diastolic filling:** This study suggests that Doppler echocardiography is useful in identifying diastolic filling abnormalities in patients with CAD. Diastolic filling abnormalities were detectable by mitral valve Doppler examination in CAD patients with normal global systolic function and in CAD patients with no history of previous myocardial infarction or segmental wall motion abnormalities. Doppler examination can be performed quickly, at the bedside, and with minimal discomfort to the patient.

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