Doppler Echocardiographic Assessment of Left Ventricular Systolic and Diastolic Function in Mild Hypertension

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SUMMARY Abnormalities in left ventricular (LV) wall thickness and mass have been demonstrated in patients with mild hypertension utilizing M-mode echocardiography. In addition, studies using radionuclide angiography have demonstrated abnormalities in early diastolic LV filling in asymptomatic hypertensive patients with normal ejection fraction and cardiac output. Recently, Doppler recordings of flow velocity in the ascending aorta and through the mitral valve have been shown to provide useful information about LV function. To determine whether flow abnormalities could be detected in patients with mild hypertension, we recorded Doppler aortic and mitral valve flow velocities in 21 men with mild hypertension. Casual systolic blood pressure was 147 ± 18 mm Hg (mean ± SD) and diastolic blood pressure was 96 ± 9 mm Hg. LV mass (310 ± 75 g) was elevated (i.e., above the 95% normal prediction interval) in 8 of 19 patients who underwent M-mode echocardiography; LV ejection fraction was normal in all patients (mean, 80%). As in previous studies in normal subjects, we found in these hypertensive patients an inverse correlation between age and both aortic peak flow velocity (r = -0.51, p<0.05) and transmitral early diastolic peak flow velocity (r = -0.44, p<0.05) and a positive relationship between age and mitral valve late diastolic peak flow velocity (r = 0.73, p<0.001). Compared to age-corrected normal data, the following mitral flow velocity parameters were abnormal: early diastolic deceleration time (mean, 28% above predicted normal; p<0.005), rate of deceleration of early diastolic flow velocity (mean, 14% below predicted normal; p<0.005), and late diastolic flow time (mean, 17% above normal; p<0.005). Neither aortic peak flow velocity nor mitral early or late diastolic peak flow velocity correlated with echocardiographic LV mass or with casual or 24-hour average systolic or diastolic blood pressure. Only transmitral late diastolic flow velocity integral (area under flow velocity curve) was significantly correlated with LV mass (r = 0.54, p<0.02). We conclude that patients with mild hypertension have normal aortic and transmitral peak flow velocities despite the presence of increased echocardiographic LV muscle mass. However, Doppler evidence of LV filling abnormalities — including a diminished rate of deceleration of early diastolic transmitral flow velocity and increased early diastolic deceleration time and late diastolic flow time — can be detected in these patients.

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KEY WORDS • hypertension • Doppler echocardiography • aortic flow velocity • mitral flow velocity

NONINVASIVE techniques have been utilized to evaluate left ventricular (LV) anatomy and function in asymptomatic patients with mild hypertension. A number of investigators have demonstrated changes in echocardiographic LV dimensions, wall thickness and mass, as well as in left atrial and aortic root dimensions, in asymptomatic patients with hypertension — often occurring prior to the detection of electrocardiographic abnormalities diagnostic for LV hypertrophy.1-5 In addition, studies using radionuclide angiography have demonstrated that slowing of the maximal rate of LV filling occurs before alterations in either LV ejection fraction or cardiac output in asymptomatic patients with hypertension.6-7 Studies using Doppler echocardiography have suggested that measurements of transmitral flow velocity might provide useful information about LV diastolic filling.8-10 In addition, Doppler aortic flow velocity measurements have shown applicability in the assessment of LV function and in the estimation of stroke volume.11-16 We, and others, have shown that age affects both Doppler mitral and aortic flow velocity parameters in adult normal subjects.17,18 In this study, we evaluated a group of asymptomatic patients with mild hypertension by using Doppler echocardiography. The goals were to detect possible abnormalities in aortic and mitral Doppler flow velocity measurements and to evaluate possible effects of age, blood pressure, and LV mass on the Doppler flow velocity parameters in mild hypertension.
Methods

Patient Population

Our study population consisted of 21 adult male subjects, aged 24 to 75 years (mean age, 53 years), who had been accepted for follow-up in the Hypertension Center of the Veterans Administration Medical Center, Long Beach, California. Criteria for inclusion were a normal diastolic blood pressure of 90 to 110 mm Hg and the absence of overt evidence of cardiac dysfunction. No specific echocardiographic LV wall mass was used as a criterion for inclusion. In all but one case, subjects were either never begun on antihypertensive medication or had had such medication discontinued at least 2 weeks prior to being studied by Doppler echocardiography. All subjects gave informed consent according to institutional guidelines prior to participation in this study.

Blood Pressure Recording

Patients had blood pressure recordings obtained by cuff sphygmomanometry both as casual readings (in all 21 patients) and as the average of readings obtained on automated ambulatory 24-hour blood pressure monitoring (in 15 patients).20 Casual blood pressure and heart rate were measured with the subject supine after 5 minutes at rest.

M-Mode Echocardiography

M-mode echocardiography was performed in 19 patients with commercially available ultrasound equipment and standard techniques. Measurements were made using leading-edge methods according to the standards suggested by the American Society of Echocardiography.21 LV internal dimensions were measured in systole (LVIDs) and diastole (LVIDd), and ventricular septal (VS) thickness and left posterior wall (PW) thickness were also measured in systole and diastole. LV ejection fraction was estimated using the previously described cubed assumption to estimate ventricular volumes22:

\[
EJ = \frac{[(LVIDd)^3 - (LVIDs)^3]/LVIDd}{100}
\]

LV mass was estimated using a modification of the formula described by Troy and associates,23 namely:

\[
\text{LV mass} = 1.05[(LVIDd + VS + PW)d]^3 - (LVIDd)^3]
\]

Doppler Echocardiography

The Doppler equation dictates that the velocity of red blood cells in the heart and great arteries can be estimated by measuring the frequency shift of the ultrasound reflected from red blood cells. In the Doppler equation,

\[
V = \frac{\Delta f(c)}{2f_0 \cos \theta}
\]

where \(V\) = velocity of blood flow (in meters per second), \(\Delta f\) = the Doppler frequency shift in kilohertz, \(c\) = the velocity of ultrasound in tissue (approximately 1540 m/sec), \(f_0\) = the frequency of ultrasound emitted from the transducer, and \(\theta\) is the angle between the ultrasound beam and the long axis of blood flow. Since the velocity of blood flow recorded is a function of the cosine of the angle between the ultrasound beam and the long axis of flow (Doppler equation), if this angle is less than 20 degrees, the velocity measured will underestimate the maximum flow velocity by less than 6%.24

In our study, Doppler echocardiography was performed using an ultrasound instrument (manufactured by Biosound Corporation, Denver, CO, USA) combining a two-dimensional mechanical sector scanner for imaging and a spectrum analyzer-based velocimeter for pulsed Doppler flow velocity measurements.25

Mitral Flow Velocity Measurements

For mitral flow recording, either a 2.25- or 3.5-MHz transducer was used for imaging and flow velocity recording. Recordings of mitral flow velocity were performed from the apical four-chamber view with a cylindrical sample volume, approximately 1 cm in linear length, aligned nearly parallel to the expected long axis of blood flow at the level of the mitral valve orifice. These Doppler records displayed a spectral output of flow velocities (in centimeters per second on the vertical axis) updated at 5-msec intervals (time displayed on the horizontal axis). The transducer was angulated in order to obtain the flow signals demonstrating the greatest mitral peak flow velocities.

To standardize for the effects of respiration and differences in transducer angulation, we made our measurements from the beats demonstrating the greatest early diastolic mitral peak flow velocity. Measurements were made from stop frames recorded at the equivalent of 100 mm/sec paper speed.

As shown in Figure 1, mitral peak flow velocities were measured in early diastole (PFVE) and in late diastole (PFVA). These peak flow velocities were measured at the midpoint of the darkest portion of the spectrum at the time of peak flow velocity in early and late diastole. In addition, mitral total diastolic flow time, early diastolic flow time (EDFT), late diastolic flow time (ADFT) and early diastolic deceleration time (E-FDFT) were measured. The rate of deceleration of mitral early diastolic flow velocity was calculated by dividing the PFVE by the E-FDFT.

Aortic Flow Velocity Measurements

Ascending aortic flow velocity recordings were performed from the suprasternal notch utilizing a right-angle 2.25-MHz transducer and a previously described nonimaging mapping technique.10,11 Briefly, a sample volume of approximately 1 cm in axial length was positioned stepwise in 1-cm increments starting at 3 cm from the transducer face and ending approximately at the level of the aortic leaflets (as denoted by the Doppler high-frequency aortic closure transient). At each sam-

\[\text{FIGURE 1. Method of making Doppler mitral flow velocity measurements (see Methods section for details). PFVE = peak flow velocity in early diastole; PFVA = peak flow velocity in late diastole (atrial systole); EDFT = early diastolic flow time; ADFT = late diastolic flow time; E-F slope = early diastolic deceleration time. (Reprinted from Gardin et al.18 with permission.)}\]
Aortic Flow Velocity Measurements

Doppler Flow Velocity Parameters

Results

Data Analysis

Clinical Characteristics

Peak Velocities

Flow Times

Early Diastolic Deceleration

Flow Velocity Integrals

M-Mode Echocardiographic Characteristics

Table 1 provides clinical details regarding our hypertensive patients, including age, body surface area, individual casual and average 24-hour blood pressure values, prior medications, and interval off medications prior to Doppler echocardiographic study.

Of the 19 hypertensive patients, 10 patients had a ventricular septal thickness greater than 15 mm or asymmetric septal hypertrophy. The LV mass in our population was 310 ± 75 g (mean ± SD) and the mean body surface area was 2.0 ± 0.1 m². When echocardiographic LV wall mass in each patient was compared to the normal LV mass predicted individually (based on age and body surface area), the mean LV wall mass was 116% of the normal predicted value. In 8 of these 19 patients (42%), the LV wall mass exceeded the 95% normal prediction interval (i.e., fell outside the mean expected LV mass ± 58 g). In 3 patients (16%), the LV wall mass fell below the 95% normal prediction interval. Echocardiographic LV mass had no significant correlation with any of the following blood pressure parameters: casual systolic (r = 0.027) and diastolic (r = 0.025) blood pressure and average 24-hour ambulatory systolic (r = 0.28) and diastolic (r = 0.16) blood pressure.

Echocardiographic LV ejection fractions in our hypertensive patients ranged from 74% to 89% (mean, 80%). The range of normal values for ejection fraction in our laboratory is 66 to 84% (mean, 78%). No patient had an abnormally low ejection fraction.

In normal subjects, aortic peak flow velocity decreases with increasing age (r = -0.54, p < 0.001), whereas aortic acceleration time and ejection time are unaffected by age or body surface area. In our normal subjects and hypertensive patients, early diastolic flow velocity integral did not vary significantly from values corrected using our age-adjusted normal regression equation. In our normal subjects, mitral peak flow velocity in early diastole decreased significantly (r = -0.56, p < 0.001) with increasing age, while mitral peak flow velocity in late diastole increased significantly with age (r = 0.52, p < 0.001). Data for these two mitral peak flow velocity parameters in our hypertensive patients did not differ significantly from values predicted on the basis of these normal regression equations.

In our normal subjects and hypertensive patients, early diastolic flow time, early diastolic deceleration time and late diastolic flow time increased with increasing age. Early diastolic flow time in the hypertensive patients did not differ significantly from the values predicted on the basis of the normal regression equation. On the other hand, early diastolic deceleration time in the hypertensive group was, on average, 28% higher than normal predicted values (p < 0.005). Similarly, late diastolic flow time values were, on average, 17% above normal predicted values (p < 0.005).

The rate of deceleration of mitral early diastolic flow velocity in our hypertensive patients averaged 14% below predicted normal values (p < 0.005). The decrease in rate of deceleration of early diastolic flow velocity in our hypertensive patients with aging was even more striking than the significant age-related decrease in this Doppler parameter noted in our normal subjects.

In normal subjects, the flow velocity integral in late diastole increased with increasing age (r = 0.56, p < 0.001). Measurements for late diastolic flow velocity integral in our hypertensive subjects did not differ significantly from the values predicted on the basis of the normal regression equation. Measurements for early diastolic flow velocity integral did not vary with age in our normal subjects. Furthermore, there was no significant difference between measurements for early diastolic flow velocity integral in the hypertensive and normal subjects.
DOPPLER ECHOCARDIOGRAPHY IN MILD HYPERTENSION/Gardin et al.

TABLE 1. Clinical Characteristics

<table>
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<th>Patient no.</th>
<th>Age (yr)</th>
<th>BSA (m²)</th>
<th>Blood pressure (mm Hg)</th>
<th>Medication Interval off (wk)</th>
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<td>149/93</td>
<td>Aldomet</td>
<td>5</td>
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</table>

BSA = body surface area; LV = left ventricular; predicted = normal mean predicted value; NA = not available; — = not applicable; HCTZ = hydrochlorothiazide; LDLZ = hydralazine.

Effects on the Doppler Parameters in Hypertensive Subjects

Age

In our hypertensive patients, three Doppler flow velocity parameters were related to age: aortic peak flow velocity and mitral early and late diastolic peak flow velocities. Aortic peak flow velocity (AoPFV) in these hypertensive patients was inversely related to age (r = -0.50, p < 0.05) to age by the following regression equation (Figure 3):

AoPFV = -0.66(age) + 104

Mitral valve early diastolic peak flow velocity (PFVE) was also inversely related to age (r = -0.44, p < 0.05) by the following equation (Figure 4):

PFVE = -0.38(age) + 71

Finally, mitral late diastolic peak flow velocity (PFVA) was positively related to age (r = 0.73, p < 0.001) by the following equation (Figure 5):

PFVA = 0.66(age) + 15

None of the other aortic or mitral Doppler flow velocity parameters were significantly affected by age. In addition, there was no significant correlation (r = 0.28) between echocardiographic LV mass and age in our subjects.

Left Ventricular Mass and Septal Thickness

Echocardiographic LV mass was only related to one Doppler aortic or mitral flow velocity parameter: mitral late diastolic flow velocity integral (A FVI). The relationship is described by the following equation (r = 0.54, p < 0.02; Figure 6):

A FVI = 0.01(LV mass) + 0.9

Ventricular septal diastolic thickness was not significantly correlated with any Doppler aortic or mitral flow velocity parameter.

Blood Pressure

Casual and 24-hour ambulatory average measurements of systolic and diastolic blood pressure were compared to the Doppler aortic and mitral flow velocity parameters. The casual systolic blood pressure correlated with none of the aortic flow velocity parameters, but showed a borderline correlation with one mitral flow velocity parameter: late diastolic flow time (r = 0.45, p = 0.05). However, there were no significant correlations between average 24-hour ambulatory systolic blood pressure measurements and any of the Doppler aortic or mitral parameters, including late diastolic flow time. Neither casual nor 24-hour ambulatory average measurements of diastolic blood pressure correlated with any Doppler aortic or mitral flow velocity parameter.

Discussion

Our study has demonstrated that in a group of asymptomatic patients with mild hypertension and normal systolic function, age has a major effect on Doppler aortic and transmitral peak flow velocities. The correlations between Doppler aortic and mitral peak flow velocities and age in our hypertensive patients were similar to the correlations previously noted in our studies of subjects without evidence of cardiovascular disease. In particular, in our hypertensive patients, aortic peak flow velocity correlated inversely with age (r = -0.50, p < 0.05) as did the mitral peak flow velocity in early diastole (r = -0.44, p < 0.05). On the other hand, mitral peak flow velocity in late
diastole varied directly with age \((r = 0.73, \ p < 0.001)\). These Doppler aortic and transmitral peak flow velocities did not correlate significantly with systolic or diastolic blood pressure or echocardiographic measurements of ventricular septal thickness or LV mass.

The decrease in aortic peak flow velocity noted with increasing age in our hypertensive subjects may at least in part be related to an increase in aortic root diameter previously reported to occur with aging.\(^{30,31}\) Doppler LV stroke volume can be estimated by multiplying aortic root area by the product of one half of aortic peak flow velocity times aortic ejection time.\(^{12}\) Since our hypertensive patients all had normal LV ejection fractions and stroke volumes, the decrease in aortic peak flow velocity noted with increasing age was apparently due to an increase in aortic root diameter and not to decreases in LV systolic function.

Preliminary evidence that the decrease in early diastolic mitral peak flow velocity noted with increasing age in our hypertensive patients may be related to impaired early diastolic LV filling has been presented by Dabestani et al.\(^{3} \) In 10 patients studied by both Doppler transmitral flow velocity recordings and videodensitometric analysis of LV filling from digital subtraction left ventriculograms, these workers showed that the percentage of total diastolic filling completed by mid-diastole was directly related to the Doppler early diastolic mitral peak flow velocity. Rokey et al.\(^{10}\) have also reported a significant correlation between early diastolic mitral peak flow velocity and cineangiographic peak filling rate \((r = 0.64)\).

Miyatake et al.\(^{17}\) have postulated that the increase in late diastolic mitral peak flow velocity normally noted with aging reflects a compensatory augmentation of ventricular filling with atrial contraction related to impaired early diastolic ventricular filling.

Comparison of Doppler aortic and mitral flow velocity measurements in our hypertensive patients with age-related normal regression equations revealed a number of abnormal parameters: increased mitral early diastolic deceleration time \((p < 0.005)\), decreased rate of deceleration of early diastolic mitral flow velocity \((p < 0.005)\), and increased late diastolic flow time \((p < 0.005)\).

The rate of Doppler mitral early diastolic flow velocity deceleration may be related to the rate of early diastolic closure of the anterior mitral leaflet (E-F slope) measured by M-mode echocardiography, although the E-F slope is somewhat nonspecific.\(^{32}\) Madeira and associates\(^{33}\) have postulated that with opening of the mitral valve in early diastole, vortices occur behind the leaflets, forcing the valve to close. The manner in which the leaflets close is a function of the amount and velocity of blood flowing through the mitral orifice and also the location of the leaflets with respect to the adjacent walls.\(^{34}\) On the other hand, Yellin et al.\(^{35}\) have emphasized that the mitral flow pattern does not precisely follow true leaflet motion on the M-mode echocardiogram. These workers have noted that peak mitral valve excursion always precedes peak flow and variations in peak flow rate far exceed variations in peak valve motion. Nonetheless, factors postulated to explain the decrease in mitral E-F slope on the M-mode echocardiogram relative to normal, including decreased LV compliance and increased LV or mitral valve stiffness,\(^{32,36-38}\) may explain the increase in Doppler early diastolic deceleration time and the decrease in the rate of early diastolic flow velocity deceleration in our hypertensive patients. The increased late diastolic flow time in our hypertensive subjects — over and above the increase noted with increasing age — probably reflects the increased contribution of atrial filling to transmital flow in patients with decreased LV compliance.\(^{17}\)

Using Doppler echocardiography to measure mitral flow velocity in patients with mild hypertension, Kitabatake and associates\(^{3}\) noted a decrease in mitral early diastolic peak flow velocity in patients with mild hypertension, Kitabatake and associates\(^{3}\) noted a decrease in mitral early diastolic peak flow velocity and cinemangiographic peak filling rate \((r = 0.64)\). Miyatake et al.\(^{17}\) have postulated that the increase in late diastolic mitral peak flow velocity normally noted with aging reflects a compensatory augmentation of ventricular filling with atrial contraction related to impaired early diastolic ventricular filling.

Comparison of Doppler aortic and mitral flow velocity measurements in our hypertensive patients with age-related normal regression equations revealed a number of abnormal parameters: increased mitral early diastolic deceleration time \((p < 0.005)\), decreased rate of deceleration of early diastolic mitral flow velocity \((p < 0.005)\), and increased late diastolic flow time \((p < 0.005)\).
this parameter in our hypertensive patients (350 cm/sec/sec) was somewhat greater than the mean value (265 cm/sec/sec) reported in hypertensive patients by Kitabatake et al. This difference may well be due to slight differences in the methods for measuring the rate of deceleration of early diastolic flow velocity.

Studies using radionuclide angiography have demonstrated that both the average and maximal rate of LV filling and the fast filling fraction are decreased in asymptomatic patients with mild-to-moderate hypertension and LV hypertrophy compared to normal subjects. Furthermore, late diastolic flow velocity integral—an index of late diastolic transmitral filling—appears to be related to LV mass in these patients. Additional studies are necessary to evaluate the utility of Doppler flow velocity measurements in evaluating a larger group of patients, including those with more severe hypertension.

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