Radionuclide measurements of diastolic function for assessing early left ventricular abnormalities in the hypertensive patient

M CARUANA, I AL-KHAWAJA, A LAHIRI, J LEWIS, E B RAFTERY

From the Department of Cardiology, Northwick Park Hospital and Clinical Research Centre, Harrow, and Edgware General Hospital, Edgware, Middlesex

SUMMARY Three measurements of diastolic filling were compared in 29 patients with essential hypertension and 27 age matched normotensive controls. Systolic function was normal in all but one of the patients. The mean (1SD) first one third filling fraction (a measurement of early diastolic filling) was significantly lower in the hypertensive groups (0.27 (0.24)) than in the control group (0.45 (0.16)). The hypertensive group was subdivided into those with electrocardiographic abnormalities and those without. In the subgroup with a normal electrocardiogram the mean (1SD) first one third filling fraction measurement (0.28 (0.16)) was significantly lower than in the control group. In the subgroup with an abnormal electrocardiogram, the first one third filling fraction was even lower (0.24 (0.9)). In addition, the time to peak filling rate (213 (56) ms) was significantly longer in the subgroup with the abnormal electrocardiogram than in the control group (164 (45) ms). However, the interobserver reproducibility of the time to peak filling measurement was poor. The peak filling rate was low in the subgroup with an abnormal electrocardiogram, but not significantly different from the normal controls. The discriminatory value of the three diastolic measurements did not improve with exercise.

These results showed an early diastolic filling abnormality in essential hypertension that did not appear to be caused by disease of the large coronary vessels as it was present in patients with normal wall motion and a normal exercise electrocardiogram. The occurrence of diastolic abnormalities when systolic function is still normal may mark an early stage in the development of hypertensive heart failure, at a time when the process is still potentially reversible.

The Framingham study^{1 2} demonstrated that some degree of arterial hypertension precedes heart failure in 75% of patients who present with this condition. Furthermore, when cardiovascular events occur, they are more likely to be fatal in hypertensive subjects, particularly in those with coexisting left ventricular hypertrophy. Early detection of the effects of high blood pressure upon the heart may therefore be important in preventive treatment. Although left ventricular angiography allows accurate measurement of wall thickness,^{3 4} this invasive investigation with its attendant risks is clearly not appropriate for most patients with uncomplicated

hypertension. Echocardiography is non-invasive and has been shown to be more sensitive than the electrocardiogram for the detection of structural abnormalities in hypertensive patients.⁵ Measurements of wall thickness correlate well with those obtained at operation⁶ and during contrast angiography⁷ but attempts at measuring left ventricular function by echocardiography have produced contradictory results. For example, one group of investigators found an increased velocity of circumferential fibre shortening in patients with left ventricular hypertrophy,⁸ while another group reported normal left ventricular performance in similar patients.⁹

Echocardiographic abnormalities described in mild hypertension include a delayed increase in diastolic dimensions, late mitral valve opening, and a reduction in left ventricular chamber size despite normal wall thickness.¹¹ Invasive studies in

Requests for reprints to Dr E B Raftery, Northwick Park Hospital and Clinical Research Centre, Watford Road, Harrow, Middlesex HA1 3UJ.

Accepted for publication 3 August 1987

Radionuclide diastolic function in hypertension

comparable patients have shown normal left ventricular systolic function and normal end diastolic pressure.¹² Considered together these observations suggest that reduced left ventricular compliance precedes the development of systolic abnormalities in the development of hypertensive heart disease. The suggestion that ventricular compliance is abnormal in hypertension is supported by studies in animals relating increased collagen and decreased elastin and glycoprotein to impaired diastolic relaxation.¹³

Recently, abnormal indices of left ventricular filling in hypertension have been reported by workers using the non-imaging nuclear probe¹⁴ and the gamma camera.¹⁵ These techniques offer the prospect of serial, non-invasive measurements of diastolic function which would permit the assessment of the effects of interventions such as drug treatment of hypertension.

We have examined the usefulness of radionuclide measurements of diastolic function by comparing the values obtained in normal subjects with measurements from patients with hypertension, at rest and during exercise.

Patients and methods

Twenty nine hypertensive patients with a diastolic blood pressure of > 95 mm Hg on two occasions after two weeks without treatment were recruited from the Harrow Hypertension Clinic. All had essential hypertension, diagnosed by clinical and laboratory exclusion of secondary causes.

Twenty seven normal volunteers were chosen as an age matched control population. All were symptom free with no history of heart disease and a resting blood pressure of $< 140/90$ mm Hg. None was taking any cardioactive medication, and all had a normal 12 lead electrocardiogram, a negative symptom limited exercise test (leads CM5 and CC5), and normal left ventricular wall motion during radionuclide angiography.

Equilibrium gated radionuclide angiography was recorded from patients and volunteers with an Elscint Apex 215 M digital gamma camera fitted with an all purpose collimator. The photopeak was set at 140 keV with a 20% window. The blood pool was labelled by an intravenous injection of stannous pyrophosphate, followed 30 minutes later by 740 MBq of technetium-99m pertechnetate, pre-mixed with the subject's own blood in the syringe. The subjects lay supine on a bicycle exercise system while resting 24 frame anterior views and 32 frame left anterior oblique views were recorded. For the acquisition of left anterior oblique views the camera was positioned with a 10° – 15° caudal tilt (as required) to obtain optimum separation of the ventricles and to

remove overlap caused by the left atrial blood pool. Five million counts were recorded using electrocardiographic gating with a 5% RR interval tolerance to exclude the effects of extrasystoles and sinus arrhythmia. After data collection at rest the subjects underwent graded, symptom limited, bicycle exercise. The initial workload of 25 W was increased by 25 W every three minutes, and a 24 frame left anterior oblique acquisition of at least three million counts was recorded during the last stage of exercise using electrocardiographic gating with a 15% RR interval tolerance. The tests were terminated when the patients complained of fatigue, dyspnoea, or angina, or when the normal subjects developed fatigue or dyspnoea. The electrocardiogram was monitored continuously. Leads CM5 and CC5 were recorded at the end of every three minutes during exercise, at peak exercise, and at the end of each minute during 5 minutes of recovery.

The radionuclide data were analysed by two independent observers. After time correction and smoothing, a continuous loop cineangiogram was constructed and examined for wall motion abnormalities. Individual left ventricular regions of interest were identified in each frame of the left anterior oblique studies by a semiautomatic, second derivative, edge-seeking algorithm which has been shown to produce excellent inter- and intraobserver repeatability.¹⁶ An adjacent background region was identified in the end systolic frame and subtracted from the data before a high resolution time-activity curve was plotted. The 32 frames and narrow electrocardiographic gating tolerance ensured good preservation of the diastolic portion of the curve. This time-activity curve was differentiated to assist with identification of the maximum filling point early in diastole, and the following measurements were calculated as described elsewhere^{15 17}: (a) ejection fraction (end diastolic counts – end systolic counts/end diastolic counts); (b) peak filling rate normalised to end diastolic counts (end diastolic counts/s); (c) time to peak filling (ms); (d) first one third filling fraction (stroke counts in first third of diastole/total stroke counts $\times$ RR interval).

An earlier study in our laboratory showed excellent reproducibility of diastolic function measurements by the semiautomatic radionuclide method developed in the Elscint computer.¹⁷ Seventeen patients with chronic stable angina underwent two radionuclide studies each at the end of two week placebo treatment. The two placebo periods were before and after a four week treatment period with an antianginal agent (carvedilol). Indices of diastolic left ventricular function for the two placebo periods were: peak filling rate 1.9 (0.2) and 1.9 (0.2) end diastolic volumes per second; early filling rate 0.9

Table 1 Mean (SD) interobserver difference of radionuclide measurement of left ventricular systolic and diastolic function at rest and during exercise in 23 hypertensive patients

Measurement	Rest	Exercise
Ejection fraction	-0.26 (3.23)	+1.05 (6.38)
Peak filling rate	-0.09 (0.34)	+0.16 (0.61)
Time to peak filling rate	+0.02* (0.03)	0.00 (0.02)
One third filling fraction	-0.01 (0.06)	0.00 (0.14)

* $p < 0.05$.

(0.1) and 0.9 (0.1) end diastolic volumes per second; first third filling fraction 0.29 (0.03) and 0.37 (0.05) ($p = \text{NS}$).¹⁷

The blood pressure of the hypertensive subjects was recorded with a Hawksley random zero sphygmomanometer after they had rested quietly for 15 minutes; the systolic blood pressure was also recorded during the exercise tests using an aneroid sphygmomanometer.

The electrocardiograms were analysed by an observer who was unaware of the other results. The criteria of Romhilt and Estes were used to diagnose left ventricular hypertrophy.¹⁸ Ischaemia was diagnosed from the exercise test if the subjects developed planar or downsloping ST segment depression of 1.5 mm or more below the resting level 60 ms after the J point.

Results within groups were compared by Student's paired t test, and between groups by Student's unpaired t test (both two tailed). Individual variables were compared by linear correlation analysis.

Results

There were 27 healthy volunteers (11 men and 16

Caruana, Al-Khawaja, Lahiri, Lewis, Rafter

women) with a mean age of 49 years (range 40–74 years). There were 29 hypertensive patients (24 men and 5 women, mean age of 53 years (range 39–76 years)). The age difference was not statistically significant.

Table 1 shows the mean interobserver differences in the diastolic function measurements from 23 hypertensive patients, together with the statistical significance of these differences. The time to peak filling rate showed a mean (SD) interobserver difference of 20 (30) ms ($p < 0.05$).

The resting ejection fraction measurements of the control and the hypertensive groups were compared. The mean (SD) resting ejection fraction of the hypertensives of 59.9 (9.4)% was not significantly different from the value of 58.7 (8.4)% in the controls (tables 2 and 3). The ejection fraction was below the normal range in one hypertensive patient, who had a normal rest and exercise electrocardiogram and normal wall motion (table 4).

In fig 1 the peak filling rate of the two groups is compared. The mean (SD) value for the controls (2.57 (0.42) end diastolic volumes per second) was not statistically different from that of the hypertensive patients (2.56 (0.78)) (tables 2 and 3).

Figure 2 compares the time to peak filling rate in the two groups. The mean (SD) times to peak filling in the controls (164 (45) ms) and hypertensive patients (186 (51) ms) were not significantly different (tables 2 and 3).

Figure 3 shows the first one third filling fraction in the two groups. The mean (SD) first one third filling fraction in the hypertensive group (0.27 (0.14)) was significantly lower than in the control group (0.45 (0.26)) ($p < 0.001$, table 3).

The group with hypertension was subdivided into

Table 2 Radionuclide measurements (mean (SD)) of left ventricular systolic and diastolic function at rest and during exercise in 27 controls and 29 hypertensive patients and subgroups of 12 hypertensive patients with abnormal electrocardiograms and 17 hypertensive patients with normal electrocardiograms

	Controls		Patients with hypertension					
			All		Abnormal ECG		Normal ECG	
	Rest	Exercise	Rest	Exercise	Rest	Exercise	Rest	Exercise
No	27	24	29	27	12	10	17	16
Age (years)		48.8 (7.6)		53.1 (9.3)		54.1 (10.9)		52.1 (8.3)
Ejection fraction (%)	58.7 (8.4)	62.5 (9.1)	59.5 (9.4)	61.4 (8.3)	61.6 (11.2)	60.1 (8.9)	58 (7.8)	62.3 (8)
Peak filling rate (EDV/s)	2.57 (0.42)	5.77 (1.39)	2.56 (0.78)	5.28 (1.41)	2.45 (0.78)	5.87 (1.74)	2.64 (0.79)	4.92 (1.07)
Time to peak filling (ms)	164 (45)	116 (30)	186 (51)	109 (34)	213 (56)	101 (34)	168 (38)	114 (34)
First one third filling fraction	0.447 (0.160)	0.404 (0.167)	0.266 (0.139)	0.479 (0.225)	0.243 (0.092)	0.518 (0.232)	0.282 (0.164)	0.445 (0.244)
Heart rate (beats/min)	69.1 (9.9)	139.3 (22.3)	78.3 (14.8)	130.9 (19.7)	76.4 (13.3)	134.1 (22.5)	79.7 (16.0)	128.6 (17.9)

ECG, electrocardiogram; EDV, end diastolic volume.

Table 3 Statistical significance of comparisons of groups in table 2 by unpaired *t* tests

	Controls vs total hypersensitive groups		Controls vs hypersensitive patients with abnormal ECG		Controls vs hypersensitive patients with normal ECG		Hypersensitive patients with normal ECG vs those with abnormal ECG	
	Rest	Exercise	Rest	Exercise	Rest	Exercise	Rest	Exercise
Ejection fraction	NS	NS	NS	NS	NS	NS	NS	NS
Peak filling rate	NS	NS	NS	NS	NS	<0.05	NS	NS
Time to peak filling rate	NS	NS	<0.01	NS	NS	NS	<0.02	NS
One third filling fraction	<0.001	NS	<0.001	NS	<0.002	NS	NS	NS
Heart rate	<0.01	NS	NS	NS	<0.01	NS	NS	NS

None of the age differences between any of the groups was significant.

those patients with a normal electrocardiogram and those showing a definite abnormality of either the rest or the exercise electrocardiogram. Table 4 lists these individual electrocardiographic abnormalities together with the abnormalities of radionuclide measurements (defined as any value outside the normal range). Twelve patients had abnormalities of the electrocardiogram: three (25%) had resting ST segment depression, eight (67%) developed ST depression of ≥ 1.0 mm during exercise, and six (50%) had evidence of left ventricular hypertrophy (see open circles in figs 1-3).

Wall motion abnormalities were evident during radionuclide angiography in five patients; four of these also had an abnormal electrocardiogram (table 4).

Ten patients with hypertension had first one third

filling fractions that were below the lower limit measured in the controls; six of these ten patients had a normal electrocardiogram. This measurement was low in the patient with a depressed ejection fraction. The peak filling rate was depressed in five patients: two with a normal electrocardiogram and three with an abnormal electrocardiogram. Two of these three also had abnormal wall motion and ST segment depression on exercise. The time to peak filling rate was prolonged in only one patient, who also had an abnormal rest and exercise electrocardiogram, abnormal wall motion, and depression of the peak filling rate. There was no overlap between the subjects with depression of the peak filling rate and those with a low first one third filling fraction.

Of the six patients with voltage criteria of left ventricular hypertrophy, two had an abnormal peak

Table 4 Electrocardiographic abnormalities, wall motion, systolic and diastolic function abnormalities in 20 patients with hypertension

Patient No	Resting electrocardiogram	Exercise ST depression (mm)	Peak filling rate (EDV/s)	Time to peak filling (ms)	First one third filling fraction	Ejection fraction (%)	Wall motion
3	T-wave inversion LVH						
5							
7		2.5	1.6		0.13	39	
8			1.5				A
9					0.16		
11	T-wave inversion LVH, left axis deviation						A
12	Left axis deviation	3					
17	T-wave flattening				0.15		
18		1.5					
19	LVH and strain	1.5	1.5	330			A
20					0.18		
21	LVH and strain	2	1.0				
22					0.15		A
23					0.17		
24			1.5				
25	Loss of septal R wave	2.5 (pain)			0.15		
27	LVH	3			0.15		A
29		2 (pain)					
30	LVH and strain				0.15		
31					0.18		

LVH, left ventricular hypertrophy; A, abnormal.

Fig 1 Comparison of individual peak filling rates (end diastolic volumes per second (EDV/s)) in controls and patients with hypertension with mean (1SD) value shown alongside. ● = Normal rest and exercise electrocardiogram; ○ = abnormal rest and exercise electrocardiogram.

filling rate and another two had depression of the first one third filling fraction. Of the five patients with wall motion abnormalities, two had a low peak filling rate and a further two had a low one third filling fraction.

Table 2 lists the mean (SD) of the diastolic measurements of both the subgroups of patients with and without electrocardiographic abnormality, and table 3 shows the results of the comparison with the normal group by unpaired *t* tests.

The one third filling fraction (0.28 (0.16)) was significantly lower in the subgroup of hypertensive patients with a normal electrocardiogram than in the normal group (0.45 (0.16)) ($p < 0.002$). In this subgroup the other two diastolic measurements did not differ significantly from the values in the normal group (tables 2 and 3).

The mean (SD) one third filling fraction in the hypertensive subgroup with electrocardiographic abnormalities was even lower (0.24 (0.09)), and the difference from normal was highly significant ($p < 0.001$). The time to peak filling rate (213 (56) ms) was

also significantly longer than in the control group (164 (45) ms) ($p < 0.01$). The peak filling rate of 2.45 (0.78) end diastolic volumes per second was lower than the value of 2.57 (0.42) end diastolic volumes per second in the control group but not significantly.

Because of the different sex ratio between the control group and the patients, we examined the normal subjects for any sex difference between radionuclide measurements. The values of ejection fraction, peak filling rate, and time to peak filling were almost identical in both sexes but the mean first one third filling fraction was 0.376 (0.113) in the 16 women and 0.549 (0.166) in the 11 men. This difference, which was significant ($p < 0.005$) was not related to differences in age, heart rate, or blood pressure between the two sexes.

To explore how the diastolic filling characteristics were influenced by blood pressure and heart rate, each measurement was plotted with the corresponding systolic blood pressure and heart rate measurement. Peak filling rate was strongly correlated with heart rate in the hypertensive patients ($r = 0.60$, $p < 0.001$) but not in the control group. The first one third filling fraction was weakly, negatively cor-

Fig 2 Time to peak filling in the controls and in patients with hypertension. Mean (1SD) values are also shown. ● = Normal rest and exercise electrocardiogram; ○ = abnormal rest and exercise electrocardiogram.

Fig 3 Comparison of individual first one third filling fractions in controls and patients with essential hypertension. Group mean value (1SD) is shown alongside. ● = Normal rest and exercise electrocardiogram; ○ = abnormal rest and exercise electrocardiogram.

related with heart rate in the hypertensive patients ($r = -0.38$, $p < 0.05$) but not in the controls. The time to peak filling rate in the patients with hypertension correlated with systolic blood pressure ($r = 0.52$, $p < 0.005$) but not with heart rate.

At peak exercise the mean (SD) heart rate in the controls was 139.3 (22.3) beats/min and in the hypertensive patients it was 130.9 (19.7) beats/min. This difference was not statistically significant, and there was no significant difference between the exercise time, the peak filling rate, time to peak filling rate, or first one third filling fraction between the two groups at peak exercise. The exercise peak filling rate of the hypertensive patients with a normal electrocardiogram was significantly lower than in the normal group ($p < 0.05$).

Finally, the value of the measurements of exercise diastolic function was examined by dividing those hypertensive patients with normal rest and exercise electrocardiograms according to their ejection fraction response during exercise. Sixteen of these patients had satisfactory exercise studies. In eleven (69%) the ejection fraction during exercise was

greater than at rest. In five patients (31%) the ejection fraction fell or remained unchanged at peak exercise. There were no significant differences between any of the measures of diastolic function of these two groups.

Discussion

The results of this study and others suggest that of three diastolic function measurements the first one third filling fraction is the most discriminatory variable for hypertensive patients, both with or without electrocardiographic evidence of ischaemia. There were, however, some noteworthy differences between our study and another study. In the present study, 37% of the patients had a one third filling fraction outside the normal range, compared with 81% of the previously reported patients.¹⁵ The ages of the patients in both studies were comparable, but in the previous study the control subjects were not age matched with the patients and the control group consisted of only 11 healthy men. We found a highly significant difference in the mean one third filling fraction of the 11 male controls and the 16 female controls. This difference could not be accounted for by any age, blood pressure, or heart rate difference. The mean one third filling fraction in these 11 men was 0.55 and Inouye *et al* found a comparable value (0.60) in 11 male controls.¹⁵ Although no sex difference has been found in radionuclide systolic function,¹⁹ it seems that there may be an important sex difference in first one third filling fraction which, to our knowledge, has not been reported previously. This does not weaken the finding that the one third filling fraction, alone of the three diastolic function measurements tested, was abnormally reduced in the hypertensive subgroup with a normal electrocardiogram and normal exercise radionuclide angiography. Balancing the sex distribution of the controls and patients, either by increasing the proportion of men among the controls or by increasing the proportion of women among the patients, would in both instances have tended to exaggerate the difference between the two groups.

The value of the time to peak filling corresponded well with previous reports.^{15 20} Although this measurement was not significantly longer in the whole hypertensive group than in the controls, it was significantly longer in the hypertensive subgroup with an abnormal electrocardiogram. Similar prolongation of the time to peak filling has been reported in patients with coronary artery disease,^{21 22} so there is a problem of interpreting such findings in patients with hypertension. In an attempt to resolve this we considered the patients with any electrocardiographic or wall motion abnormality as a separate

subgroup. There were 12 such patients, 10 (83%) of whom had evidence of myocardial ischaemia as ST segment depression or localised wall motion abnormality. Six had additional evidence of left ventricular hypertrophy on voltage criteria. When this subset of patients with electrocardiographic abnormalities was excluded, the time to peak filling in the remaining hypertensive patients was almost identical to that of the controls. ST segment depression developing during exercise testing in patients with left ventricular hypertrophy does not necessarily indicate obstructive coronary artery disease.^{23 24} Presumably "ischaemic" electrocardiographic changes in hypertensive patients with angiographically normal coronary arteries indicate an imbalance between blood supply and demand of the ventricle. Even in the absence of left ventricular hypertrophy, raised systolic blood pressure alone may increase the myocardial oxygen requirement and impair left ventricular coronary reserve.²⁵

The statistically significant mean difference between the two observers indicated poor inter-observer reproducibility of the time to peak filling. Lack of reproducibility of the same measurement was also found when the nuclear stethoscope was used repeatedly to assess left ventricular function in heart failure.²⁶ This poor reproducibility was partly explained by difficulty in accurately identifying the end systolic point—this may also have been important in our study, since the hypertensive patients with depressed early diastolic filling tended to have a "flattened" time-activity curve adjacent to the end systolic point. The ejection fraction, filling fraction, and peak filling rate would have been affected less by inaccuracies of end systolic point definition because these measurements were not made exclusively from the time axis of the time-activity curve and whenever a time measurement was used it appeared in the denominator. Other workers have also described wide variations in the measurement of time to peak filling made on two separate occasions.²⁷

When others compared radionuclide time to peak filling with the contrast angiography measurement they found a poor agreement.²⁷ Part of this discrepancy may have been caused by heart rate differences, as the time to peak filling has been reported to be heart rate dependent.^{14 15} We found no such association in our study; the measurement was more closely related to systolic blood pressure. Moreover, even when heart rate was fixed by atrial pacing and time to peak filling was compared with a number of haemodynamic variables obtained during cardiac catheterisation, no significant associations were found.²⁸ For these reasons, the usefulness of this measurement as an early indicator of hypertensive

heart disease is open to serious doubt, although the measurement may be a marker for coexistent coronary artery disease. But even this use of the measurement has been questioned.²²

Our filling rate values corresponded with previously reported figures in hypertension.^{14 15} The mean peak filling rate of the hypertensive patients was almost identical to that of the controls. When the subgroup of patients with an abnormal electrocardiogram (who had a mean depressed peak filling rate) was removed, the mean peak filling rate of the remaining hypertensive patients was actually slightly higher than that of the controls. None of these differences was statistically significant. Depression of the peak filling rate has been reported to be an indicator of obstructive coronary artery disease.^{21 22 29} On the evidence of the present study, this measurement seemed to contribute little to the early identification of hypertensive heart disease as it was within the normal range in nine (75%) of the patients with an abnormal electrocardiogram.

During exercise the peak filling rate was reduced in the hypertensive patients with a normal electrocardiogram; this difference was just statistically significant ($p < 0.05$) when compared with the controls. The corresponding measurement in the hypertensive group with an abnormal electrocardiogram, however, was not significantly different from normal, even though two thirds of these patients developed electrocardiographic evidence of ischaemia during exercise. This observation is therefore unlikely to be of any clinical importance; this difference with a low level of statistical significance may well have arisen as a consequence of multiple significance testing. All the remaining diastolic function tests failed to discriminate between controls and hypertensive patients at peak exercise. Furthermore, there were no differences between the diastolic measurements when the hypertensive patients with a normal electrocardiogram were subdivided and compared according to the response of their ejection fraction to exercise.

The reason why there was a correlation between some resting diastolic measurements and heart rate and blood pressure in the hypertensive patients but not in the controls may have been because the ranges of diastolic function, heart rate, and blood pressure were wider in the hypertensive group. For example, the heart rate range in the controls was 50–92 beats/min, while in the hypertensives it was 48–130 beats/min. The range of peak filling rate in the hypertensives was 1.5–4.2 end diastolic volumes per second, compared with a range of 1.7–3.2 end diastolic volumes per second among the controls, and the range of time to peak filling rate was 80–330 ms in the hypertensive patients and 110–280 ms in the

Radionuclide diastolic function in hypertension

normal group. These wider ranges of measurements would have increased the likelihood of any correlations between measurements reaching statistical significance.

In conclusion, the results of this study confirm previous observations that the first one third filling fraction is abnormally low in patients with hypertension, even after the exclusion of those with electrocardiographic evidence of ischaemia or left ventricular hypertrophy. The time to peak filling rate was prolonged in the hypertensive group but this abnormality was confined to those with electrocardiographic abnormalities and may have been caused by coexisting ischaemia. Although the mean peak filling rate was reduced in the hypertensive group with electrocardiographic abnormalities the measurement appeared to be less useful than the electrocardiogram for identifying individuals with cardiac abnormalities since many patients with an abnormal electrocardiogram had normal filling rates despite definite evidence of left ventricular hypertrophy in half of them. The wide normal range of all the diastolic measurements was another indication that they would be of limited use for identifying cardiac abnormalities in individual patients. The effect of treatment on the mean first one third filling fraction in a group of hypertensive patients merits further study.³⁰ Of the three radionuclide diastolic measurements, only the first one third filling fraction was appreciably different in male and female controls. This new observation requires further investigation with careful control of factors that might affect the measurement, such as the degree of cardiovascular fitness and smoking habits.

We thank Mr D Hinge for his help in performing the radionuclide angiography during the study.

References

- 1 Kannel WB. Role of blood pressure in cardiovascular morbidity and mortality. *Prog Cardiovasc Dis* 1974; 17:5-24.
- 2 Kannel W, Gordon T, Schwartz M. Systolic versus diastolic blood pressure and risk of coronary heart disease: the Framingham Study. *Am J Cardiol* 1971;27:335-46.
- 3 Hugenholtz PG, Kaplan E, Hull E. Determination of left ventricular wall thickness by angiocardiology. *Am Heart J* 1969;78:513-22.
- 4 Dodge HT, Frimer M, Stewart DK. Functional evaluation of the hypertrophied heart in man. *Circ Res* 1974;34/35 (suppl 2):122-7.
- 5 Savage D, Drayer J, Henry W, et al. Echocardiographic assessment of cardiac anatomy and function in hypertensive subjects. *Circulation* 1979;59:623-32.
- 6 Feigenbaum H, Popp RL, Chip JN, Haine CL. Left ventricular wall thickness measured by ultrasound. *Arch Intern Med* 1968;121:391-5.
- 7 Feigenbaum H, Popp RL, Wolfe SB, et al. Ultrasound measurements of the left ventricle: a correlative study with angiocardiology. *Arch Intern Med* 1972;129:461-7.
- 8 Guazzi M, Fiorentini C, Olivari M, Polese A. Cardiac load and function in hypertension. *Am J Cardiol* 1979;44:1007-12.
- 9 Karliner JS, Williams D, Gorwit J, Crawford MH, O'Rourke RA. Left ventricular performance in patients with left ventricular hypertrophy caused by systemic arterial hypertension. *Br Heart J* 1977; 39:1239-45.
- 10 Gibson DG, Traill TA, Hall RJC, Brown DJ. Echocardiographic features of secondary left ventricular hypertrophy. *Br Heart J* 1979;41:54-9.
- 11 Logan A, Gilbert B, Haynes R, Milne B, Flanagan P. Early effects of mild hypertension on the heart; a longitudinal study. *Hypertension* 1981;3 (suppl II): 187-90.
- 12 Strauer BE. Ventricular function and coronary haemodynamics in hypertensive heart disease. *Am J Cardiol* 1979;44:999-1006.
- 13 Nishimura H, Kubo S, Nishioka A, Imamura K, Kauramura K, Hasegawa M. Left ventricular diastolic function of spontaneously hypertensive rats and its relationship to structural components of the left ventricle. *Clin Sci* 1985;69:571-80.
- 14 Smith V-E, Schulman P, Karimeddini M, White W, Meeran M, Katz A. Rapid ventricular filling fraction in left ventricular hypertrophy: II pathologic hypertrophy. *J Am Coll Cardiol* 1985;5:869-74.
- 15 Inouye I, Massie B, Loge D, et al. Abnormal left ventricular filling: an early finding in mild to moderate systemic hypertension. *Am J Cardiol* 1984;53:120-6.
- 16 Hains ADB, Al-Khawaja I, Hinge DA, Lahiri A, Raftery EB. Radionuclide left ventricular ejection fraction: a comparison of three methods. *Br Heart J* 1987;57:242-6.
- 17 Lahiri A, Rodrigues EA, Al-Khawaja I, Raftery EB. Effects of a new vasodilating beta-blocking drug, carvedilol, on left ventricular function in stable angina pectoris. *Am J Cardiol* 1987;59:769-74.
- 18 Romhilt DW, Estes EH. A point score system for the ECG diagnosis of left ventricular hypertrophy. *Am Heart J* 1968;75:752-8.
- 19 Hakki AH, Iskandrian AS. Effect of gender on left ventricular function during exercise in patients with coronary artery disease. *Am Heart J* 1986;111:543-6.
- 20 Magorien D, Shaffer P, Bush C, et al. Assessment of left ventricular pressure-volume relationships using gated radionuclide angiography, echocardiography, and micromanometer pressure recordings. *Circulation* 1983;67:844-53.
- 21 Bonow R, Bacharach S, Green M, et al. Impaired left ventricular diastolic filling in patients with coronary artery disease: assessment with radionuclide angiography. *Circulation* 1981;64:315-23.
- 22 Mancini G, Slutsky R, Norris S, Bhargava V, Ashburn W, Higgins C. Radionuclide analysis of peak filling

- rate, filling fraction and time to peak filling rate. Response to supine bicycle exercise in normal subjects and patients with coronary disease. *Am J Cardiol* 1983;51:43–51.
- 23 Fortuin NJ, Weiss JL. Exercise stress testing. *Circulation* 1977;56:699–712.
 - 24 Harris C, Aronow W, Parker D, Kaplan M. Treadmill stress testing in left ventricular hypertrophy. *Chest* 1973;63:353–7.
 - 25 Strauer BE. Myocardial oxygen consumption in chronic heart disease; role of wall stress, hypertrophy and coronary reserve. *Am J Cardiol* 1979;44:730–40.
 - 26 Caruana M, Jones R, Lahiri A, *et al.* The nuclear stethoscope: a comprehensive clinical validation. *Nucl Med Commun* 1986;7:717–28.
 - 27 Sugrue D, Dickie S, Newman H, Myers M, Lavender J, McKenna W. Comparison of equilibrium radionuclide and contrast angiographic measurements of left ventricular peak ejection and filling rates and their time intervals. *Nucl Med Commun* 1984;5:619–25.
 - 28 Magorien D, Shaffer P, Bush C, *et al.* Haemodynamic correlates for timing intervals, ejection rate and filling rate derived from the radionuclide angiographic volume curve. *Am J Cardiol* 1984;53:567–71.
 - 29 Reduto L, Wickemeyer W, Young J, *et al.* Left ventricular diastolic performance at rest and during exercise in patients with coronary artery disease. *Circulation* 1981;63:1228–37.
 - 30 Inouye I, Massie B, Loge D, Simpson P, Tubau J. Failure of anti-hypertensive therapy with diuretic, beta-blocking and calcium channel blocking drugs to consistently reverse left ventricular diastolic filling abnormalities. *Am J Cardiol* 1984;53:1583–7.

Caruana, Al-Khawaja, Lahiri, Lewis, Raftery