Abnormal left ventricular relaxation in hypertensive patients

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Summary

1. The maximum rates of left ventricular ejection and filling were derived (Fourier analysis) from the left ventricular volume curve (technetium–human serum albumin gated blood pool studies) in 12 normotensive subjects and 15 hypertensive patients of matched age groups.

2. Average values of cardiac output, ejection fraction, heart rate and left ventricular ejection rate were not significantly different in the two groups.

3. Hypertensive patients had a slower rate of left ventricular filling ($P < 0.05$), suggesting diminished left ventricular compliance in hypertension.

Key words: ejection fraction, filling rate, hypertension, radionuclide.

Introduction

In contrast with the many investigations related to cardiac systole (Braunwald, Ross & Sonnenblick, 1976), the relaxation and filling of the heart have been little studied (Grossman & McLaurin, 1976). In response to the increased pressure load, the performance of the myocardium has been variously described as normal, increased or reduced (Burton, 1957; Downing & Sonnenblick, 1964; Wilcken, Charlier, Hoffman & Guz, 1964; Sagawa, 1967). However, filling and relaxation rates of the left ventricle in hypertension have not yet been investigated in any detail. The development of radionuclide techniques has allowed the inscription of ventricular volume curves in man by minimally invasive means (Pitt & Strauss, 1977). A single descriptive study of a heterogeneous group of patients suggested that the velocity of left ventricular filling appeared to be reduced among hypertensive patients (Qureshi, Wagner, Alderson, Housholder, Douglas, Lotter, Nickoloff, Tanabe & Knowles, 1978). The present study was therefore designed to determine left ventricular ejection and filling rates in hypertensive patients.

Materials and methods

Twelve normotensive subjects with no clinical or electrocardiographic evidence of heart disease volunteered for the study. A group of 15 untreated patients with essential hypertension was investigated concurrently. Age range was the same for both groups (20–66 years). All gave their informed consent. The doses of radionuclides used were approved by the Radioisotope Safety Committee and the Institutional Review Committee.

Left ventricular volume curves were obtained from gated blood pool studies (Pitt & Strauss, 1977) after intravenous injection of 12 mCi of technetium–human serum albumin. All studies were performed in the morning with subject at rest in the supine position. Cardiac output was obtained from the same radionuclide during its first-pass flow (Fouad, Tarazi, MacIntyre & Durant, 1979). Simultaneously, blood pressure and heart rate were recorded and derived data calculated (Tarazi, Ibrahim, Dustan & Ferrario, 1974).

Analysis of left ventricular volume curves: left ventricular (LV) ejection fraction was calculated as (LV end-diastolic counts – LV end-systolic counts) LV end-diastolic counts.

Rates of ejection and filling: Fourier analysis (Geffers, Adam, Bitter, Sigel & Kampmann, 1978) was applied to fit a curve to the data points (16 in our system) by the method of least squares; the time derivative of the curve was computed by...
using the Fourier transform technique as a global estimate of the tangent to the curve at each data point. Since this curve represents the radioactivity counts as a mathematical function of time, the derivatives are expressed in c.p.s. The negative derivatives correspond to the decrease in counts or ejection phase (-dv/dt) and the positive derivatives correspond to the increase in counts or filling phase (+dv/dt). In this analysis we looked at the largest negative and maximum positive derivatives. These derivatives were sealed by the maximum absolute counts equivalent to the end-diastolic counts to compensate for variation in injected dose and efficiency of the acquisition system. In this way it was possible to compare data from different patients. The units of these new variables are therefore expressed in units of fractional change per second or Hertz and are proportional to the change in volume per unit time (dv/dt).

Results

The two groups of subjects did not differ significantly with respect to cardiac output, ejection fraction of heart rate [3.05 ± 0.18 vs 3.01 ± 0.19 litres min⁻¹ m⁻², 0.52 ± 0.01 vs 0.55 ± 0.02 or 62 ± 2.50 vs 65 ± 3.18 beats/min, for normotensive and hypertensive subjects respectively; P: not significant (N.S.) for all]. The velocity of ventricular ejection (maximum -dv/dt) was not significantly different in normotensive and hypertensive subjects (2.27 ± 0.98 vs 2.48 ± 0.16; P: N.S.); its correlation with the ejection fraction was not significant in either group (r = 0.39, P N.S. in normotensive subjects and r = 0.12, P N.S. in hypertensive patients).

In contrast with these similarities between normotensive and hypertensive subjects, the two groups differed significantly in respect to the maximum rate of left ventricular filling (maximum +dv/dt). The filling rate was significantly slower in hypertensive patients than in normotensive subjects (Fig. 1); the two groups could be distinctly separated by linear discriminant analysis (Lachenbruch, 1975). Also, the slopes of the regression equations relating maximum +dv/dt to maximum -dv/dt, in either group, were significantly different (P < 0.05). It is to be noted that data for four of the hypertensive patients fell in a grey zone; study of their haemodynamic data showed that they differed from other hypertensive patients in the group by a higher cardiac index (> 3.6 litres min⁻¹ m⁻²) and shorter mean transit time (< 7 s) indicative of hyperkinetic circulations. Therefore they were considered separately in the analysis of slopes. In both groups, the maximum +dv/dt did not correlate with heart rate, stroke volume or ejection fraction. As regards blood pressure, the alteration in ventricular filling did not correlate with either mean arterial pressure or systolic blood pressure within the hypertensive and the normotensive groups. For all subjects considered as a group, there was a significant negative correlation between mean arterial pressure and maximum filling rate (r = -0.622, P < 0.001) after exclusion of the four hyperkinetic hypertensive patients (their inclusion lowered the r value to -0.328, P > 0.05).

Discussion

Our results suggest that patients with hypertension frequently show a reduced rate of left ventricular filling even in the absence of other signs of cardiac involvement. Only two of our 15 patients had electrocardiographic evidence of left ventricular hypertrophy; the average cardiac output, heart rate and ejection fraction were not significantly different between the normotensive and hypertensive patients although the maximum +dv/dt was significantly reduced in the latter.

The left ventricle has frequently been assumed to become less compliant than normal in
increased muscle mass and/or increased content of interstitial and connective tissue in the left ventricular wall. Most studies of left ventricular compliance, however, were obtained from patients with either aortic stenosis or cardiomyopathy (Sutton, Tajik, Gibson, Brown, Seward & Giuliani, 1977; Sanderson, Traill, Sutton, Brown, Gibson & Goodwin, 1978; Grossman et al., 1979; Nesje & Enge, 1979). Very few data were reported from hypertensive patients. Our results confirm initial impressions of reduced compliance, inasmuch as the reduction in maximum filling rate of the ventricle can be related to a reduced yielding of the left ventricle to the inrushing blood from the left atrium. Further, our results are also in agreement with other studies showing that left atrial hypertrophy can occur very early in hypertension and constitute the sole sign of cardiac involvement (Tarazi, Miller, Frohlich & Dusant, 1966). This atrial abnormality was interpreted as reflecting reduced compliance of the left ventricle (Gibson, Madry, Grossman, McLaurin & Craig, 1974). Somewhat unexpected, however, was the finding that this reduction in rate of left ventricular filling could be the earliest demonstrable disturbance in cardiac function. More precise estimates of left ventricular wall thickness by echocardiography are needed to correlate left ventricular wall thickness with changes in ejection and filling velocity since the echocardiogram is more sensitive than electrocardiographic studies in determining the structural conditions of the left ventricular wall.

The factors associated with the reduced rate of filling could not be determined from this study; neither heart rate nor stroke volume nor ejection fraction correlated with the rate of ejection or filling of the heart. Parmley & Sonnenblick (1969) have reported a reduced relaxation rate of isolated papillary muscles in response to isoprenaline stimulation. Recent studies have confirmed this abnormality in the hypertrophied hearts of spontaneously hypertensive rats (Saragoca & Tarazi, 1980). There was, however, no particular evidence of sympathetic hyperactivity in our group of patients. Further, in the absence of direct measurements of left ventricular diastolic pressure, it is difficult to speculate on alterations in ventricular compliance. Nevertheless, our studies point to a long neglected yet potentially important pathophysiological disturbance of cardiac relaxation in hypertension, which may play an important role in the mosaic of factors determining its evolution. Thoren (1979) has reported significant alterations in atrial and ventricular reflexes secondary to a reduction of left ventricular compliance in hypertensive animals.

We did not find a significant correlation between mean arterial pressure (or systolic blood pressure) and +dP/dt either among normotensive subjects or among the 15 hypertensive patients. Studies of larger groups, particularly in response to blood pressure variations, are obviously needed to differentiate functional and structural components in the reduced rate of left ventricular filling.

Acknowledgments
We thank Mr Bruno Sufka for computer programming, Carmen Napoli, Steve Saverna and Mary Kay Kruchan for technical assistance, and Aldona Raulinaitis and Susan Bir for secretarial assistance. Statistical analysis was accomplished by using PROPHET, a national computer resource supported by the Biotechnology Resources Program, Division of Research Resources, National Institutes of Health. The studies were supported in part by a grant from the National Heart, Lung and Blood Institute (HL-6835).

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