Ejection Flow Dynamics Assessed by Ventricular Impulse and Elastance in the Human Hypertensive Heart

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Left ventricular elastance is the intrinsic mechanical property of the chambers that generates pressure for a given volume, but the dynamics of the ejection flow are characterized by the ventricular impulse in early systole. The purpose of this study was to characterize the ejection dynamics in the human hypertensive heart according to the concept of ventricular impulse and elastance. Nineteen hypertensive patients without left ventricular hypertrophy (HT-I), 42 hypertensive patients with left ventricular hypertrophy (HT-II), and 43 normotensive subjects (NT) were studied by pulsed Doppler echocardiography. The maximum ejection force ($F_{\max}$; kdyne) and the end-systolic wall stress/end-systolic volume index (ESWS/ESVI; kdyne/cm²/ml/m²) were examined as indexes of maximal impulse and elastance, respectively. $F_{\max}$ was calculated on the basis of the unsteady Bernoulli equation. With regard to impulse and elastance in NT, $F_{\max}$ was 43.7 ± 6.1 and ESWS/ESVI was 2.26 ± 0.78 . In the hypertensive groups, HT-I showed normal $F_{\max}$ (46.0 ± 5.5) with a significantly higher ESWS/ESVI (3.52 ± 1.12 , $p < 0.01$ vs. NT), and HT-II showed a significantly lower $F_{\max}$ (34.4 ± 7.2 , $p < 0.01$ vs. NT) with normal ESWS/ESVI (2.65 ± 1.38). There was a significant inverse correlation between $F_{\max}$ and left ventricular mass index ($r = -0.45$, $p < 0.001$). This study shows for the first time the dissociation of maximum impulse and maximum elastance in the human hypertensive heart. The characteristics of elastance are well preserved, but those of the impulse are not preserved in the hypertensive hypertrophied heart. Further more, this dissociation is observed from the undetected hypertrophic state in the human hypertensive heart. (*Hypertens Res* 1994; 17: 123-131)

Key Words: hypertension, hypertrophy, Doppler flow dynamics, impulse, elastance

Both clinical (1-9) and experimental studies (10-18) of systolic functions in the pressure-dependent hypertrophied heart have yielded conflicting results. This controversy could be due to species differences, differences in the severity of myocardial hypertrophy, or differences in the variables measured in each study. Recently, using Doppler echocardiography, Isaaz and Pasipoularides (19) devised a noninvasive method to measure the left ventricular impulse that generates intraventricular pressure gradients (impulse gradients) and ejection flows. The new method seems to provide an improved insight into the significance of cardiac function in the hypertensive heart. The dynamics of ejection flow are characterized as a sudden imparting of momentum to the blood by the left ventricular impulse in early systole (20-22). In contrast, the maximal left ventricular elastance ($E_{\max}$), obtained from the end-systolic pressure-volume relationship, represents well the ventricular basal contractile state (21-30) and is widely used as a sensitive indicator of left ventricular contractile function in various heart diseases.

With the advent of Doppler echocardiography, real-time flow dynamics in the heart can be studied (19, 31, 32). However, to our knowledge, there have been no reports of studies done to assess cardiac functions from analysis of Doppler flow at the aortic annulus level in the human hypertensive heart. We have reported preliminary results regarding the ventricular impulse in the human hypertensive heart (33). In the present study, we used both quantitative M-mode and Doppler echocardiography to study patients with essential hypertension and normotensive control subjects. In particular, we measured the ventricular impulse and $E_{\max}$ to elucidate ejection flow dynamics in the hypertensive hypertrophied heart.

Methods

Patient Population

Sixty-one patients with uncomplicated essential hypertension (HT) (44 men and 17 women), aged 26 to 68 years (50.3 ± 10.1 years, mean $\pm$ SD) participated in this study. Forty-three normotensive

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Table 1. Baseline Clinical Characteristics of Normotensive and Hypertensive Groups

Variable	Normotensive group (NT) (n=43)	Hypertensive groups	
		HT-I (n=19)	HT-II (n=42)
Sex (M/F)	31 / 12	12 / 7	32 / 10
Age (year)	50 ± 11	51 ± 8	50 ± 11
BSA (m ²)	1.62 ± 0.15	1.59 ± 0.15	1.65 ± 0.13
SBP (mmHg)	116 ± 12	157 ± 11 [#]	160 ± 12 [#]
DBP (mmHg)	72 ± 10	92 ± 8 [#]	95 ± 8 [#]
MBP (mmHg)	87 ± 10	113 ± 8 [#]	117 ± 8 [#]
HR (beats/min)	66 ± 10	69 ± 12	65 ± 11

Values are mean ± SD. HT-I, hypertensive group without concentric cardiac hypertrophy; HT-II, hypertensive group with concentric cardiac hypertrophy. [#]*p* < 0.01 vs. NT. BSA, body surface area; SBP, systolic blood pressure; DBP, diastolic blood pressure, MBP, mean blood pressure; HR, heart rate.

subjects (31 men and 12 women), aged 30 to 66 years (50.0 ± 11.2 years) (NT), who were matched for age, sex, and body surface area were selected as controls (Table 1). Hypertension was diagnosed when the diastolic blood pressure was consistently > 90 mmHg in the outpatient clinic on at least three visits over one to two months. After admission, secondary types of hypertension were excluded by routine examinations. Patients with cardiac valvular disease, diabetes mellitus, or pulmonary disease were excluded. None had a history of chest pain or any signs or symptoms suggesting congestive heart failure. Hypertensive patients were divided into two groups: HT-I (*n* = 19) was the untreated hypertensive group without concentric cardiac hypertrophy, and HT-II (*n* = 42) was the untreated hypertensive group, which showed concentric hypertrophy of the heart. Concentric hypertrophy of the heart was defined as elevated relative wall thickness with an increased left ventricular mass index (estimated as more than 2 SD greater than the mean value in NT) (34).

Echocardiography and Doppler Flow Variables

M-mode, two-dimensional and pulsed Doppler echocardiographic examinations were done with an Aloka SSD870 imaging system (Tokyo, Japan) by standard techniques in all subjects (32). Left ventricular internal dimensions, and septal and posterior wall thickness were measured at end-diastole and end-systole, according to the recommendations of the American Society of Echocardiography (35), and used for measurement of all variables except left ventricular mass. Left ventricular mass was calculated according to the Penn convention (36, 37). Relative wall thickness was measured at end-diastole as the ratio of 2 × posterior wall thickness/internal dimension (38). Left ventricular end-diastolic volume was estimated with Teichholz's formula (39). To record the velocity at the annulus level, the sample volume was placed into the aortic leaflets and gradually moved backward until the first clear ventricular outflow velocity was obtained. As shown in Fig. 1, pulsed Doppler echocardiographic analysis was done with a computer graphic analysis

system (model CARDIO 500, Kontron Elektronik, Munich, Germany), and peak velocity was measured. From the time-velocity derivative curve, peak acceleration, ejection time, and time intervals from the onset of upstroke of the flow velocity to the peak acceleration and to the peak velocity were obtained.

Stroke volume was calculated by multiplying the total flow velocity integral by the aortic valve area. Stroke work index, which is clinically the product of mean blood pressure and stroke volume index, was obtained as an index of left ventricular external work by the following equation:

Stroke work index (gm/m²) = 0.0136 × mean blood pressure × stroke volume index, where stroke volume index = stroke volume/body surface area, mean blood pressure = diastolic blood pressure + (systolic blood pressure − diastolic blood pressure)/3.

Intraobserver and interobserver correlations of duplicate measurements of peak velocity were *r* = 0.98 (*n* = 35, *p* < 0.001) and *r* = 0.92 (*n* = 35, *p* < 0.001), respectively. Intraobserver and interobserver correlations of duplicate measurements of peak acceleration were *r* = 0.97 (*n* = 35, *p* < 0.001) and *r* = 0.87 (*n* = 35, *p* < 0.001), respectively.

Preload and Afterload Indexes of the Left Ventricle

Left ventricular end-diastolic volume was used as an index of preload of the left ventricle. End-systolic meridional wall stress (ESWS) is reported to be the best index of afterload of the left ventricle (5, 7). ESWS was calculated on the basis of principles derived by Grossman *et al.* (40) and verified by Wilson *et al.* (41), with M-mode echocardiographic determination of left ventricular diameter and wall thickness, and cuff blood pressure obtained with a random-zero sphygmomanometer. In addition, peak systolic meridional wall stress (PSWS) was also computed with the standard formula (41).

Maximum Impulse Index

The impulsive mode of generator, which generates intraventricular pressure gradients and flows, is governed by the unsteady Bernoulli equation (21, 22).

The impulse gradients (P), which are early intraventricular and transvalvular gradients, consist of convective (C) and local (L) acceleration components ($P = C + L = A \times Q^2 + B \times dQ/dt$, where Q is flow rate, dQ/dt is rate of change of flow rate, and A and B are variables related to the geometry of the outflow tract and the ventricle) (22). According to Isaaz and Pasipoularides (19), the ejection force (F), which generates impulse gradients, is calculated by the following equation:

$$F = \rho \times S \times v^2 + d/dt (\rho \times V \times k \times v), \quad (i)$$

where ρ is blood density (1.06 g/cm³), S is cross-sectional area of the aortic annulus, and v and V are instantaneous outflow velocity and chamber volume. The factor k is the scaling factor, which is dimensionless and remains approximately constant during ejection.

Equation (i) becomes:

$$F = \rho \times S \times v^2 + \rho \times k \{ dV/dt \times v + V \times dv/dt \} \quad (ii)$$

Because the term (dV/dt) means ejection volume per unit time, it is possible to rewrite the term ($-S \times v$).

$$(iii)$$

So, the term (V) can be obtained from

$$V = LVEDV - \int v dt, \quad (iv)$$

where $LVEDV$ is left ventricular end-diastolic volume. With substitution of equation (iii) and (iv) for dV/dt and V , equation (ii) then becomes:

$$F = \rho \times S \times v^2 + \rho \times k \times [-Sv^2 + dv/dt (LVEDV - \int v dt)] \\ = (1-k) \times \rho \times S \times v^2 + k \times \rho \times (LVEDV - \int v dt) \times dv/dt. \quad (v)$$

Pasipoularides (22) suggested that the ratio of aortic annulus cross section to inner wall surface area is a major geometric determinant of intraventricular ejection gradient. Therefore, it is necessary to correct this ventriculoannular disproportion gradient by the factor k . Isaaz *et al.* (19) simplified factor k as $d^2/4R^2$ by solving the Laplace equation in the interior of the ventricle with Legendre polynomials and trigonometric identities, where d is the aortic ring diameter and R is the radius of a sphere having the same volume as the ventricle. The peak value of F (F_{max}) is attained very early in ejection, and corresponds to the time of peak acceleration (19). Accordingly, F_{max} is calculated from equation (v) as follows:

$$F_{max} = (1-k) \times \rho \times S \times va^2 + k \times \rho \times \{ LVEDV - S \times \int_0^{ta} v(t) dt \} \times dv/dt_{max},$$

where va is v at the time of peak acceleration, ta is the time of peak acceleration, dv/dt_{max} is the peak acceleration, and S is calculated as $\pi d^2/4$.

Maximum Elastance Index

The left ventricle has a time-varying elastance that is represented by the slope of the pressure-volume relationship curve during systole. It has been well appreciated that E_{max} is independent of wide variations in preload and afterload in a given inotropic state and is strongly correlated with basal contractility and inotropic state (23–27, 30). McKay *et al.* (29) have reported a good correlation between the true E_{max} calculated with the time-varying elastance model by Suga and Sagawa and the modified E_{max} obtained by single-point pressure-volume ratios.

However, wall thickness and chamber radius differ considerably in different diseases and stages of disease. Therefore, in this study, to correct for the variability in wall thickness and chamber radius, ESWS/ESVI was used as an index of maximum left ventricular elastance (7, 9, 28). ESVI was calculated from the formula: $ESVI \text{ (ml/m}^2\text{)} = \text{left ventricular end-diastolic volume index} - \text{stroke volume index}$.

Statistical Analysis

All data are expressed as mean value $\pm$ SD. Comparisons between two groups were performed by unpaired *t*-test, and differences among three groups were tested by one-way analysis of variance, followed by Duncan's test. Correlations between variables were assessed with univariate linear regression analysis and Pearson's correlation coefficient. Differences associated with *p* values less than 0.05 were considered to be statistically significant.

Results

Echocardiographic Characteristics of Normotensive and Hypertensive Groups

Echocardiographic measurements are shown in Table 2. Both the interventricular septal wall and the posterior wall in HT-II were significantly thicker than those in NT and HT-I. No differences were observed among the three groups with regard to left ventricular end-diastolic or end-systolic diameters, or left ventricular end-diastolic volume index. Left ventricular mass index in HT-I was similar to that in NT, while left ventricular mass index in HT-II was significantly greater than that in NT. ESWS was significantly greater in HT-I than in NT, and that in HT-II was not significantly different from NT. PSWS was significantly greater in HT-I than in NT and HT-II. Stroke volume index was not statistically different among the three groups, but stroke work index was significantly higher in HT-I and HT-II than in NT.

Doppler Flow Variables in Normotensive and Hypertensive Groups

Doppler flow variables are shown in Table 3. Both peak velocity and peak acceleration were significantly lower in HT-II than in NT and HT-I, and there were no differences between the latter two. The time interval from the onset of the flow upstroke to the peak acceleration and to the peak velocity were significantly longer in HT-II than in NT and HT-I. Ejection time was not significantly different among the three groups. As shown in Fig. 2, there was a significant inverse correlation between peak acceleration and left ventricular mass index ($r = -0.54$, $p < 0.001$).

Maximum Impulse and Elastance Index

Figure 3 shows ESWS/ESVI (upper panel) and F_{max} (lower panel) in NT, HT-I, and HT-II. ESWS/ESVI was significantly higher in HT-I (3.52 ± 1.12 kdyne/cm²/ml/m²) than in NT (2.26 ± 0.78 kdyne/cm²/ml/m²) and HT-II (2.65 ± 1.38 kdyne/cm²/ml/m²), but that in HT-II was not significantly different from

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Variable	Normotensive group (NT) (n=43)	Hypertensive groups	
		HT-I (n=19)	HT-II (n=42)
Sa (cm ²)	4.20 ± 0.60	4.47 ± 0.52	4.45 ± 0.49
IVST (cm)	0.73 ± 0.08	0.78 ± 0.09	1.05 ± 0.17 #¶
PWTd (cm)	0.78 ± 0.09	0.82 ± 0.06	1.12 ± 0.13 #¶

Fig. 5. Representative Doppler flow waveforms obtained from a normal subject (top), a patient in HT-I (middle) and a patient in HT-II (bottom). High ESWS/ESVI with normal F_{max} in HT-I and normal ESWS/ESVI with low F_{max} in HT-II are observed.

Fig. 6. Relationship between F_{max} and PSWS. There is a significant positive correlation between the two variables, especially in the hypertensive groups ($r=0.58$, $p<0.001$): $Y = 17.6 + 1.24 \times 10^{-1}X$. Open circles (○) are NT, closed circles (●) are HT-I and closed triangles (▲) are HT-II.

portion was also a geometric determinant of intraventricular ejection gradient, especially in the enlarged ventricle. In our study, Issaz's equation (19), which is derived from the unsteady Bernoulli equation and corrects the ventriculoannular disproportion gradient with the factor k , was used to compute an index of the impulse. Our data analyzer, CARDIO 500, is different from Issaz's computer, but a normal value of F_{max} in our study is almost the same as that in Issaz's study.

With regard to the hypertensive heart, F_{max} in HT-I was normal, but that in HT-II was lower than that in the normotensive group. These findings imply that the hypertensive non-hypertrophied heart maintains a normal ventricular impulse at rest, but the hypertensive hypertrophied heart cannot maintain a normal ventricular impulse even at rest. As shown in Fig. 4, F_{max} was significantly and inversely correlated with the left ventricular mass index. This result indicates that the ventricular impulse in the hypertensive heart gradually decreases in parallel with left ventricular hypertrophy. As in the report by Issaz *et al.* (19), a strong positive correlation between F_{max} and peak acceleration was observed in the present study ($r=0.824$, $p<0.0001$). Issaz also suggested that peak acceleration was positively influenced by myocardial contractility and left ventricular end-diastolic volume, and negatively influenced by early ejection afterload (19). F_{max} is attained very early in ejection, so the left ventricular volume and wall thickness are close to their end-

intraventricular ejection pressure gradient. They

Fig. 1. Measurements of ejection flow waveform by pulsed Doppler echocardiography.

Fig. 2. Relationship between peak acceleration and left ventricular mass index. There is a significant inverse correlation between the two variables ($r = -0.54$, $p < 0.001$): $Y = 2,660.3 - 7.68X$. Open circles (○) are NT, closed circles (●) are HT-I and closed triangles (▲) are HT-II.

of preserved ventricular elastance. In other words, the concentric hypertrophied heart can generate a high pressure for a given volume, but it cannot generate a normal acceleration of intraventricular blood. In contrast, the non-hypertrophied heart in hypertensive patients had supernormal elastance

Fig. 3. Top panel: ESWS/ESVI in the three groups. Significantly higher ESWS/ESVI in HT-I and normal ESWS/ESVI in HT-II are observed. Bottom panel: F_{max} in the three groups. Normal F_{max} in HT-I and significantly lower F_{max} in HT-II are observed. * $p < 0.01$ vs. NT.

Fig. 4. Relationship between F_{max} and left ventricular mass index. There is a significant inverse correlation between the two variables ($r = -0.45$, $p < 0.001$): $Y = 54.0 - 1.3 \times 10^{-1}X$. Open circles (○) are NT, closed circles (●) are HT-I and closed triangles (▲) are HT-II.

and could generate a normal impulse.

Impulse of the Hypertensive Heart

Rushmer (20) reported that left ventricular ejection is characterized by a sudden imparting of momentum to blood, in the form of high velocity in early systole, and he termed the ventricle the impulse generator. Pasipoularides *et al.* (21) showed that the ventricular impulse was generated by contraction of the left ventricular walls and was manifested as an

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intraventricular ejection pressure gradient. They termed this pressure gradient the impulse gradient. It embodies local acceleration and convective acceleration components on the basis of the unsteady Bernoulli equation. In their study, the impulse gradient consisted mainly of local acceleration components, which depended greatly on acceleration rather than on velocity. Furthermore, Pasipoularides (22) showed that the ventriculoannular dispro-

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ic wall stress. In addition, there was no significant relationship between $F_{\max}$ and LVEDV or ESWS, and the myocardial contractility estimated by ESWS/ESVI in HT-II remained normal. Therefore, we cannot explain exactly why peak acceleration and $F_{\max}$ in HT-II were suppressed. To elucidate this mechanism, further studies are needed.

Analysis of early ventricular ejection dynamics by Doppler echocardiography was done to assess left ventricular performance. To our knowledge, the present study is the first application of left ventricular Doppler ejection variables in patients with hypertension. Peak acceleration values in NT were attained within about 28 msec from the onset of the upstroke of flow velocity. This result is in accord with the finding of Pasipoularides *et al.* (21), which was about 25 msec. Doppler left ventricular ejection variables in HT-I were normal, but those in HT-II were low. It is known that inotropic stimulation augments the ventricular impulse and shortens the time from the onset to the peak of the impulse (20, 21). Therefore, the difference in ejection variables between HT-I and HT-II may reflect a difference in inotropic state. In addition, stroke volume index in HT-II was not significantly different from that in NT. This finding indicates that cardiac function in early systole is more sensitive to the cardiac condition of hypertensive patients than that in pansystole. Johnson *et al.* (42) have reported that despite the presence of a normal ventriculogram, patients with coronary artery stenosis have a depressed mean normalized systolic ejection rate during the first third of systole. The present findings and those reported by Johnson *et al.* indicate that variables measured early in ejection should be used to evaluate the cardiac condition in various cardiac diseases.

Elastance of the Hypertensive Heart

The elastic properties of the heart can be expressed as the stress/strain ratio, which expresses the ability of the heart to return to its original shape and dimensions after deformation. In our study, ESWS/ESVI was used as an indirect index of myocardial contractility, and was independent of variations in the left ventricular end-diastolic volume index and ESWS. There are only a few reports on myocardial contractility in patients with hypertension in which the stress/strain relationship was used (1, 6-9). In the present study, ESWS/ESVI was high in HT-I and normal in HT-II. These results are in agreement with previous studies (4-9), which show that hypertensive hearts without hypertrophy are in an increased inotropic state and hypertensive hearts with concentric hypertrophy remain in a normal inotropic state. Takahashi *et al.* (1) reported that in advanced left ventricular hypertrophy, in which left ventricular posterior wall thickness was more than 1.3 cm, myocardial contractility was low. However, in their study, myocardial contractility remained normal in patients whose left ventricular posterior wall thickness was between 1.0 cm and 1.2 cm, almost equal to that of HT-II in the present study. Thus, myocardial contractility may be preserved in hypertensive patients such as

those in the present study. In more advanced left ventricular hypertrophy, myocardial contractility may be low. According to previous clinical and experimental studies (5, 16), increased sympathetic tone could play a key role in the increased inotropic state of the hypertensive non-hypertrophied heart, but the exact reason for the increased inotropic state in hypertensive patients without cardiac hypertrophy remains to be determined.

Characteristics of Pump Function in the Hypertensive Heart

In the present study, stroke volume index and stroke work index of the hypertensive heart were normal or high. These results agree with those of previous human studies (2-8), which showed preservation of cardiac performance in the hypertensive heart. However, in the present study maximum impulse and maximum elastance were dissociated in the hypertensive heart.

Capasso *et al.* (13) examined isometric and isotonic contractions of papillary muscles from hypertensive hypertrophied rat hearts, and confirmed the dissociation of two commonly used measures of contractility, peak force development and velocity of shortening. Their study suggested that the hypertrophic myocardium might maintain ventricular performance in terms of force development while speed of shortening decreases. Considering their study, we think that there is a dissociation of the change of impulsive state and elastic state associated with hypertensive hypertrophy, and this dissociation begins while ventricular hypertrophy in the hypertensive heart in humans is still undetectable. The mechanism of the dissociation between the impulsive state and the elastic state has not been clarified. Further work is needed to clarify the mechanism of the link between the pressure overload state and the dissociation of impulse and elastance.

Conclusion

This study showed for the first time the dissociation of impulsive and elastic states in the hypertensive hypertrophic process in humans. The characteristics of elastance are well preserved, but those of the impulse are not preserved in the hypertensive hypertrophic heart. In addition, this dissociation starts during undetected hypertrophy in the hypertensive heart in humans.

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