Evaluation of Left Ventricular Diastolic Hemodynamics from the Left Ventricular Inflow and Pulmonary Venous Flow Velocities in Hypertrophic Cardiomyopathy

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SUMMARY

We evaluated the characteristics of left ventricular diastolic hemodynamics in hypertrophic cardiomyopathy (HCM) by measuring left ventricular inflow (LVIF) and pulmonary venous flow (PVF) velocities in 62 patients with asymmetric septal hypertrophy and 34 normal controls. The patients were divided into four groups according to the LVIF pattern and left ventricular end-diastolic pressure (LVEDP): 1) the pseudonormalization group; 13 patients with the ratio of peak atrial systolic (A) to early diastolic (E) LVIF velocity (A/E ≤ 1 and LVEDP ≥ 15 mm Hg, 2) the normal pattern group; 10 patients with the A/E ≤ 1 and LVEDP < 15 mm Hg, 3) the relaxation failure group; 25 patients with the A/E > 1, and 4) the mid-diastolic wave group; 14 patients with a mid-diastolic wave. The peak early diastolic LVIF velocities in the pseudonormalization, relaxation failure, and mid-diastolic wave groups were significantly smaller than in the control group. The deceleration time from the peak of the E wave and the isovolumic relaxation time were significantly prolonged in the relaxation failure and mid-diastolic wave groups. The peak diastolic PVF velocity in the relaxation failure and mid-diastolic wave groups were significantly decreased, and was significantly increased in the pseudonormalization group. The peak atrial systolic PVF velocity was significantly increased in all patients with HCM, particularly in the pseudonormalization group. LVEDP was the highest in the pseudonormalization group, followed by the mid-diastolic wave, relaxation failure and normal pattern groups, in that order. In conclusion, combined analysis of the LVIF and PVF provides useful information regarding various abnormalities of left ven-
tricular diastolic hemodynamics in patients with HCM. (Jpn Heart J 36: 617–627, 1995)

Key words: Hypertrophic cardiomyopathy  Left ventricular diastolic hemodynamics  Left ventricular inflow velocity  Pulmonary venous flow velocity

HYPERTROPHIC cardiomyopathy (HCM) causes abnormalities of left ventricular diastolic function with hypertrophy of the ventricular myocardium and associated abnormal relaxation and filling of the left ventricle.\textsuperscript{1} The distribution of left ventricular hypertrophy in HCM is not uniform, and the diastolic dysfunction is reported to vary with the magnitude of the hypertrophy and other characteristics of the myocardium.\textsuperscript{2}

Recently, the left ventricular inflow velocity (LVIF) recorded by pulsed Doppler echocardiography has been used to evaluate left ventricular diastolic function.\textsuperscript{3-9} Since the information obtained by this method is relatively unaffected by the morphology of the left ventricle, it is useful for pathophysiologic studies of HCM.

In this study, we evaluated variations in left ventricular diastolic dysfunction in patients with HCM by analyzing LVIF and pulmonary venous flow velocity (PVF) recorded by transesophageal echocardiography.

METHODS

We examined 62 patients with asymmetric septal hypertrophy (ASH) (mean age 46 ± 12 years) in whom the end-diastolic interventricular septal thickness and the left ventricular posterior wall thickness were 15 mm or greater and 11 mm or smaller, respectively, and in whom the ratio between the two wall thicknesses was 1.3 or greater. Thirty-four healthy subjects (mean age 44 ± 11 years) without cardiac disorders were used as normal controls. Transesophageal echocardiography was performed in all subjects. The peak atrial systolic (A) and early diastolic (E) velocities and their ratio (A/E), the isovolumic relaxation time (IRT) between the aortic component of the second heart sound on phonocardiogram and the onset of the early diastolic wave, and the deceleration time from the peak of the early diastolic wave (E-DT) were measured from the LVIF (Figure 1, LVIF). The peak second systolic (PVS\textsubscript{2}), peak diastolic (PVD) and peak atrial systolic (PVA) PVF velocities, and the amplitude of the interatrial septal motion during atrial contraction (IAS-A) also were determined (Figure 1, PVF and IAS). Cardiac catheterization was performed in all subjects, and the left ventricular end-diastolic pressure (LVEDP) was measured. Patients with moderate-to-severe mitral regurgitation were excluded from this study.
Figure 1. Method of determining the various parameters of pulmonary venous flow (PVF) and left ventricular inflow (LVIF) velocities, and interatrial septal (IAS) motion recorded by transesophageal echocardiogram. PVS$_2$ = peak second systolic PVF velocity; PVD = peak diastolic PVF velocity; PVA = peak atrial systolic PVF velocity; E = peak early diastolic LVIF velocity; A = peak atrial systolic LVIF velocity; IRT = time interval between the aortic component of the second heart sound and the onset of the early diastolic wave of LVIF; E-DT = deceleration time from the peak of the early diastolic wave of LVIF; IIA = aortic component of the second heart sound; IAS-A = amplitude of the IAS motion during atrial contraction; LA = left atrium; RA = right atrium.

M-mode and pulsed Doppler echocardiograms were recorded with a Toshiba SSH-65A (Toshiba Corp., Tokyo, Japan) and an Aloka SSD-870 (Aloka Co., Ltd., Tokyo, Japan) ultrasound diagnostic system using a 2.5-MHz transthoracic probe and a 5-MHz transesophageal probe, respectively, on a strip chart at a paper speed of 5 cm/sec. Each subject was premedicated with 1% lidocaine spray applied to the posterior pharynx for the transesophageal echocardiographic examination. Food intake was withheld for at least 5 hours prior to the procedure.

All values are expressed as the mean ± standard deviation. Differences between groups were examined by unpaired Student-Newman Keuls test and were regarded as significant when the p value was < 0.05.

Results

Study population: The patients were divided into the following four groups according to the LVIF and LVEDP: 13 patients in whom the A/E of the LVIF was one or less and the LVEDP was 15 mm Hg or greater (pseudonormalization group), 10 patients in whom the A/E was one or less and the LVEDP was less than 15 mm Hg (normal pattern group), 25 patients in whom the A/E was greater than one (relaxation failure group), and 14 patients in whom mid-diastolic waves were observed (mid-diastolic wave group). No significant difference
was observed in interventricular septal thickness (24.3 ± 2.6 mm in the pseudonormalization group, 25.5 ± 4.4 mm in the relaxation failure group, 22.1 ± 3.5 mm in the mid-diastolic wave group and 23.0 ± 8.2 mm in the normal pattern group) or posterior wall thickness (9.5 ± 1.3 mm in the pseudonormalization group, 10.6 ± 2.2 mm in the relaxation failure group, 9.1 ± 2.7 mm in the mid-diastolic wave group and 8.9 ± 6.3 mm in the normal pattern group) among the four HCM groups.

**Case presentation:** In the pseudonormalization group (Figure 2, upper), the peak early diastolic and atrial systolic LVIF velocities were decreased compared with those of normal controls, but their ratio (A/E) was less than one, and the deceleration time from the peak of the early diastolic wave of the LVIF was normal. However, the peak atrial systolic PVF velocity showed a marked increase. In the normal pattern group (Figure 2, lower), the peak early diastolic and atrial systolic LVIF velocities were normal, and the peak atrial systolic PVF velocity was slightly increased, but the peak diastolic PVF velocity was normal.

![Figure 2](image-url) Representative LVIF and PVF patterns in the pseudonormalization group and normal pattern group of patients with hypertrophic cardiomyopathy. Differentiation of the pseudonormalization group (upper) from the normal pattern group (lower) is difficult by LVIF alone, because of the "normalized" patterns in both groups. However, the peak atrial systolic PVF velocity is markedly increased in the pseudonormalization group compared to the normal pattern group. PVS1 = peak first systolic PVF velocity. Other abbreviations are the same as in Figure 1.
Figure 3. Representative LVIF and PVF patterns in the relaxation failure group and the mid-diastolic wave group. In the relaxation failure group (upper), the A/E of the LVIF is greater than one, and the PVA is increased despite the decrease in the PVD. A mid-diastolic wave (MD) can be observed in both the LVIF and PVF patterns in the mid-diastolic wave group (lower). Abbreviations are the same as in Figure 1.

In the relaxation failure group (Figure 3, upper), the peak early diastolic LVIF velocity was decreased, the peak atrial systolic LVIF velocity showed a compensatory increase, and their ratio (A/E) was greater than one. The isovolumic relaxation time and the deceleration time from the peak of the early diastolic wave of the LVIF were prolonged, the peak atrial systolic PVF velocity was increased, and the peak diastolic PVF velocity was decreased. In the mid-diastolic wave group (Figure 3, lower), the isovolumic relaxation time was prolonged, but the peak early diastolic LVIF and peak diastolic PVF velocities were slightly decreased, and the peak atrial systolic PVF velocity was increased. A distinct forward wave was seen in PVF of this group after the diastolic wave (PVD), and this wave coincided in timing with the mid-diastolic wave of the LVIF.

Comparisons of LVIF parameters among HCM and control groups (Table I): The peak early diastolic (E) velocity was significantly smaller in the pseudonormalization group, mid-diastolic wave group and relaxation failure group than in the control group (p < 0.05, p < 0.01 and p < 0.01, respectively), and the decreases in the latter two groups were especially notable. The peak atrial systolic (A) velocity, on the other hand, was significantly greater in the relaxation failure group than in the control group, pseudonormalization group
and mid-diastolic wave group (p < 0.01 for all), and was significantly smaller in the pseudonormalization group than in the control group (p < 0.05). Consequently, the A/E was significantly greater in the relaxation failure group than in the control group and the other HCM groups (p < 0.01 for all).

In the mid-diastolic wave group and relaxation failure group, the deceleration time (E-DT) from the peak of the early diastolic wave and the isovolumic relaxation time (IRT) were significantly prolonged compared with the control group (p < 0.01 for all), but no significant difference was observed between the pseudonormalization group and the control group. In the normal pattern group, E-DT was not significantly different, but IRT was significantly prolonged compared with the control group (p < 0.01).

**Comparisons of PVF parameters among the HCM and control groups (Table II):** The peak second systolic (PVS2) velocity showed no significant difference between any of the HCM groups and the control group. The peak diastolic (PVD) velocity was significantly smaller in the mid-diastolic wave group and the relaxation failure group than in the control group (p < 0.01 for both). The PVD was significantly greater in the pseudonormalization group than in the mid-diastolic wave group and relaxation failure group (p < 0.01 for both), but no
significant difference was observed between the control group and the pseudonormalization group or the normal pattern group.

The peak atrial systolic (PVA) velocity was significantly greater in all the HCM groups than in the control group ($p < 0.01$ for all). It was markedly greater in the pseudonormalization group than in the mid-diastolic wave group, relaxation failure group and normal pattern group ($p < 0.01$ for all).

**Comparisons of IAS-A and LVEDP among the HCM and control groups (Table III):** The IAS-A was slightly greater in all the HCM groups than in the control group, but there were no significant differences among the groups.

The LVEDP was greatest in the pseudonormalization group, followed by the mid-diastolic wave group, relaxation failure group and normal pattern group, in this order. It was significantly greater in the pseudonormalization group than in the relaxation failure group and normal pattern group ($p < 0.01$ for all).

**DISCUSSION**

The primary pathophysiologic feature of hypertrophic cardiomyopathy (HCM) is a decrease in the extensibility of the ventricular wall due to myocardial hypertrophy, i.e. an impairment of relaxation with subsequent deterioration of left ventricular filling. The distribution of left ventricular hypertrophy varies among different sections of the myocardium in each patient, and the diastolic behavior is reported to vary with the site and degree of wall thickening. However, Koide et al. have reported the presence of HCM with no remarkable left ventricular hypertrophy, and Spirito et al. and Bonow et al. have found that the severity of left ventricular diastolic dysfunction is not necessarily associated with the site or the degree of left ventricular wall thickening, but that it primarily depends on the severity of myocardial fiber disarray or fibrosis.

Recently, evaluation of the left ventricular inflow (LVIF) velocity by pulsed Doppler echocardiography has been used to assess the left ventricular diastolic property, as this method is relatively free from the effects of left ventricular...
morphology and wall motion abnormalities. A decrease in the peak early diastolic (E) velocity, prolongation of the deceleration time from the peak of the early diastolic wave, a compensatory increase in the peak atrial systolic (A) velocity, and a consequent increase in A/E are common findings in HCM patients, as seen in the relaxation failure group in this study. A slow and linear decrease in velocity from the peak of the early diastolic wave is considered to reflect most accurately impairment of left ventricular relaxation and abnormal left ventricular filling from early to mid-diastole. There have not been many reports on the characteristics of pulmonary venous flow (PVF) velocity in HCM patients, but Ogawa et al\textsuperscript{14} have reported that the PVF in HCM patients is characterized by a decreased peak diastolic (PVD) velocity, and that this peak velocity is closely related to the peak early diastolic LVIF velocity.

However, it is difficult to conceptualize a pattern of left ventricular inflow in all HCM patients. In fact, in the present study, the LVIF showed various patterns according to hemodynamic differences among patients, even in patients with a similar distribution of hypertrophy, namely asymmetric septal hypertrophy. In the pseudonormalization group, both the peak early diastolic and atrial systolic LVIF velocities were decreased, but the deceleration time from the peak of the early diastolic wave was normal or was shortened, so that the shape of the LVIF in this group was apparently similar to that of the control group. However, the pseudonormalization group showed a significant increase in peak atrial systolic PVF velocity and the highest LVEDP among all the HCM groups. Waller et al\textsuperscript{15} have reported that the left ventricular pressure curve shows a dip and plateau pattern in some patients with hypertrophic nonobstructive cardiomyopathy, and Oki et al\textsuperscript{3} and Okushi et al\textsuperscript{16} have found that the deceleration time from the peak of the early diastolic wave of the LVIF is normal or shortened in some patients with HCM. Therefore, a group of patients with HCM exhibit a hemodynamic profile resembling that of restrictive cardiomyopathy.

In such cases, the relaxation ability and compliance of the left ventricle are markedly decreased due to progression of extensive degeneration and fibrosis of the myocardium. Moreover, LVEDP is increased markedly, and the pressure gradient between the left atrium and ventricle is reversed in early diastole, causing early termination of the rapid filling.\textsuperscript{17} On the other hand, the inflow of pulmonary venous blood into the left atrium during atrial contraction is prevented by the increased left atrial pressure, and regurgitation into the low-pressure pulmonary vein is augmented with a consequent increase of peak atrial systolic PVF velocity.\textsuperscript{18} This induces afterload mismatch of the left atrium and suggests the possibility of congestive heart failure due to marked left ventricular diastolic dysfunction despite normal contractility of the left ventricle.\textsuperscript{19}

The isovolumic relaxation time was prolonged in the mid-diastolic wave
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A group of this study, and peak diastolic PVF velocity was slightly decreased, but the peak atrial systolic PVF velocity was increased, compared with the control group. Given the degree of the increase in the LVEDP, it appears a proper conclusion might be that left ventricular diastolic dysfunction in the mid-diastolic wave group was more severe than that in the relaxation failure group or the normal pattern group. Keren et al. and Nishimura et al. have speculated that mid-diastolic waves are produced as blood flows from the pulmonary vein into the left atrium during the rapid decline in early diastolic LVIF, increasing the pressure gradient between the left atrium and ventricle, and consequently reopening the mitral valve. Lorell et al. and Courtois et al., on the other hand, have confirmed a sustained depression of the left ventricular pressure curve in mid-diastole. Therefore, this group is thought to have peculiar hemodynamic abnormalities that differ from those of the other HCM groups.

The isovolumic relaxation time showed a slight prolongation in the normal pattern group, but the LVEDP was not markedly increased, and the LVIF and PVF appeared nearly normal. Therefore, differentiation of this group from the control group was difficult by examination of the LVIF pattern alone. Spirito et al. have emphasized that the magnitude of left ventricular hypertrophy in HCM is not necessarily associated with the degree of left ventricular filling impairment. Sanderson et al. also have reported some cases of HCM showing satisfactory left ventricular filling despite the existence of left ventricular hypertrophy. Left ventricular diastolic dysfunction in this group is considered to be mildest among HCM patients, and differentiation of this group from the pseudonormalization group is difficult by examination of LVIF alone. More comprehensive examinations, including PVF, are needed for accurate discrimination between these two groups.

Left ventricular diastolic filling is a complex phenomenon determined by multiple factors, including left ventricular relaxation, intrinsic myocardial muscle properties and loading conditions of the left ventricle. While Doppler measurements of left ventricular inflow velocity provide an assessment of left ventricular diastolic performance, this technique does not permit an independent estimate of these different determinants of diastolic function.

In conclusion, the LVIF shows various patterns in HCM, even in patients with a similar distribution of left ventricular hypertrophy. A comprehensive evaluation, including examination of the PVF, is needed to assess the severity of left ventricular diastolic dysfunction in patients with HCM.
REFERENCES


