Assessment of Diastolic Hemodynamics by Analyzing Left Ventricular Filling Flow Propagation Velocity in Patients with Hypertensive Left Ventricular Hypertrophy

Shinichi Tokuoka, Sachihiko Nobuoka, Junzo Nagashima, and Fumihiko Miyake

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Abstract

Objectives: The purpose of this study was to assess the left ventricular (LV) filling flow propagation both in early and late diastolic phases using the color M-mode Doppler technique, and to assess relation of diastolic hemodynamics to cardiac alterations in patients with hypertensive LV hypertrophy.

Methods: Subjects included 45 consecutive patients with hypertensive LV hypertrophy (HT group) and thirty-one subjects with no evidence of heart disease (Control group).

Echocardiographic and pulsed Doppler examinations were performed, and the data was analyzed to determine the LV mass index (LVMI), relative wall thickness (RWT), and the maximal early (E) and late (A) transmitral Doppler velocities. A color M-mode Doppler image of the LV filling flow was recorded and the flow propagation velocity was measured during early (FPV-E) and late (FPV-A) LV filling phases. Then, 1) FPV-E/E, FPV-A/A and the ratio of FPV-A/A to FPV-E/E (the FPV ratio) were compared between the two groups, 2) correlation between FPV-E/E or FPV-A/A and LVMI or RWT was assessed in the HT group.

Results: 1) FPV-E/E and FPV-A/A were significantly lower in the HT group than in the Control group, and the FPV ratio was significantly higher in the HT group than in the Control group. 2) There was a significant negative correlation between FPV-E/E and LVMI, and there was a significant negative correlation between FPV-A/A and RWT in the HT group.

Conclusions: In patients with hypertensive LV hypertrophy, diastolic function was considered to be impaired both in early and late diastolic phases, and this impairment was considered more severe in the early diastolic phase than in the late diastolic phase. It was considered that LV diastolic dysfunction was more severe in patients with hypertensive LV hypertrophy in cases having a higher RWT and larger LVMI.

Key words
hypertensive left ventricular hypertrophy, diastolic function, flow propagation, color M-mode Doppler method
INTRODUCTION

Impairment of the left ventricular (LV) diastolic function occurs in the early stage of hypertension and is considered to be an important factor contributing to hypertensive heart failure\(^1\)\(^2\). In view of the importance of LV hypertrophy and associated myocardial fibrosis in the development of diastolic dysfunction\(^3\)\(^4\), it is meaningful to assess how LV diastolic hemodynamics are related to cardiac alterations and geometric remodeling in patients with hypertension.

The assessment of the blood flow propagation of the LV filling phase by using a color M-mode Doppler technique has recently attracted attention as a new non-invasive method for assessing LV diastolic function. Several reports\(^5\)\(^\sim\)\(^7\) have emphasized the advantages of the LV filling flow propagation for conventional non-invasive parameters obtained by pulsed Doppler examination. However, the LV filling flow propagation in patients with hypertension has not been well examined, and assessment of the flow propagation in the late diastolic phase has not been studied.

The purpose of this study was to assess the LV filling flow propagation both in early and late diastolic phases using the color M-mode Doppler technique, and to assess how LV diastolic hemodynamics are related to cardiac alterations in patients with hypertensive LV hypertrophy.

METHODS

Subjects

We studied 45 consecutive patients with hypertensive LV hypertrophy (HT group) who underwent routine echocardiographic examinations in addition to conventional pulsed Doppler and color M-mode Doppler examinations. The presence of LV hypertrophy was established when the LV mass index (LVMI) obtained from echocardiography was >111 g/m\(^2\) for men and >106 g/m\(^2\) for women\(^8\). All subjects had normal sinus rhythm. No patient had evidence of valvular disease or myocardial infarction determined clinically, by Doppler imaging, or by electrocardiography. Thirty-one patients with no evidence of heart disease served as control subjects (Control group) (Table 1).

Table 1 Clinical characteristics of the study subjects

<table>
<thead>
<tr>
<th></th>
<th>HT Group</th>
<th>Control Group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>45</td>
<td>31</td>
<td></td>
</tr>
<tr>
<td>Age (yr.)</td>
<td>64.8 ± 12.9</td>
<td>63.0 ± 9.8</td>
<td>NS</td>
</tr>
<tr>
<td>Male/Female</td>
<td>20/25</td>
<td>19/12</td>
<td></td>
</tr>
<tr>
<td>BSA (m(^2))</td>
<td>1.65 ± 0.19</td>
<td>1.67 ± 0.16</td>
<td>NS</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>150.2 ± 13.5</td>
<td>128.5 ± 9.4</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>85.9 ± 10.2</td>
<td>79.5 ± 9.0</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>MBP (mmHg)</td>
<td>107.2 ± 10.2</td>
<td>95.9 ± 7.2</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>HR (beats/min)</td>
<td>69.4 ± 8.2</td>
<td>68.7 ± 8.1</td>
<td>NS</td>
</tr>
</tbody>
</table>

Abbreviations: BSA=body surface area, SBP=systolic blood pressure, DBP=diastolic blood pressure, MBP=mean blood pressure, HR=heart rate

Echocardiographic study

Echocardiograms were obtained using a TOSHIBA SSH-160A equipped with a 2.5-MHz transducer. A two-dimensional targeted M-mode echocardiogram was recorded in each patient with simultaneous recording of a II-lead electrocardiogram and phonocardiogram. All examinations were performed in the 30° left-lateral decubital position. On the M-mode LV echocardiogram, LV end-diastolic dimension (LVDd), LV end-systolic dimension (LVDs), diastolic wall thickness of interventricular septum (IVSTh), and posterior wall thickness (PWTh) were measured. The LV internal dimension and diastolic septal and posterior wall thickness were measured at the peak of R wave of the electrocardiogram. The percentage of fractional fiber shortening (FS) (%) was calculated as \([\text{LVDd}–\text{LVDs}/\text{LVDd}] \times 100\). Relative wall thickness (RWT) was calculated as \(2 \times \text{PWTh}/\text{LVDd}\). LV mass (LVM) was calculated using the following formula validated by Devereux and Reichek\(^9\):

\[
\text{LVM (g)} = 1.04 \times \left(\frac{(\text{LVDd} + \text{IVSTh} + \text{PWTh})^3}{\text{LVDd}^3}\right) – 13.6
\]

LVMI (g/m\(^2\)) was obtained by dividing LVM by the body surface area.

Doppler study

Pulsed Doppler imaging was performed with reference to a two-dimensional echocardiographic image from an apical two-chamber view in each patient. The pulsed Doppler sample was placed at the mitral leaflet tips to obtain maximal transmural
flow velocities during the LV filling phase, and the maximal early (E) and late (A) diastolic transmitral velocities were measured. Color M-mode Doppler images of the LV filling flow were recorded in the early and late diastolic phases, and flow propagation velocities in the early (FPV-E) and late (FPV-A) diastolic phases were measured as the slopes of the flow wave fronts during the early and late LV filling, respectively.

The ultrasound beam was interrogated from the apex of the heart towards the center of the mitral orifice as parallel to the LV filling flow as possible. Measurements were obtained from an average of three consecutive cardiac cycles.

Since the color Doppler flow signal may also change due to relation in the angle between the ultrasonic beam and flow, we calculated the following three ratios: FPV-E divided by E (FPV-E/E), FPV-A divided by A (FPV-A/A), and FPV-A/A divided by FPV-E/E (FPV ratio).

Then, we 1) compared FS, the ratio of A to E (A/E), FPV-E/E, FPV-A/A and the FPV ratio between the HT and Control groups; 2) assessed the correlation of LVMI with FPV-E/E or FPV-A/A in the HT group; 3) and assessed the correlation of LVMI with FPV-E/E or FPV-A/A in the HT group.

### Table 2 Comparison of echocardiographic and Doppler parameters between the two groups

<table>
<thead>
<tr>
<th></th>
<th>HT Group (n=45)</th>
<th>Control Group (n=31)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVDd (mm)</td>
<td>46.9 ± 4.8</td>
<td>42.7 ± 4.1</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>FS (%)</td>
<td>40.7 ± 9.5</td>
<td>38.3 ± 5.0</td>
<td>NS</td>
</tr>
<tr>
<td>A (cm/sec)</td>
<td>0.74 ± 0.20</td>
<td>0.73 ± 0.14</td>
<td>NS</td>
</tr>
<tr>
<td>E (cm/sec)</td>
<td>0.61 ± 0.21</td>
<td>0.67 ± 0.18</td>
<td>NS</td>
</tr>
<tr>
<td>A/E</td>
<td>1.16 ± 0.32</td>
<td>1.32 ± 0.45</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Abbreviations: LVDd=left ventricular end-diastolic dimension, FS=fractional shortening, A=maximal late diastolic transmitral flow velocity, E=maximal early diastolic transmitral flow velocity, A/E=the ratio of the maximal late (A) to the early (E) diastolic transmitral flow velocities

### Statistical analysis

Values were expressed as means ± SD, and comparisons were assessed by the Student’s paired t-test. Differences were considered significant at p values of <0.05. Simple regression analysis was employed to test correlations.

### RESULTS

#### Comparison of echocardiographic and Doppler parameters between the two groups

1) LVDd was significantly larger in the HT group than in the Control group (p<0.01).

2) There was no significant difference in FS, used as the parameters of LV systolic function, between the two groups. A/E, which was conventional Doppler derived index of LV diastolic function was significantly higher in the HT group than in the Control group (p<0.01) (Table 2).

3) FPV-E/E and FPV-A/A were significantly lower in the HT group than in the Control group (p<0.01, p<0.01, respectively) (Fig. 2).

4) The FPV ratio was significantly higher in the HT group than in the Control group, demonstrating impairment of diastolic function is more severe in the early diastolic phase than in the late diastolic phase (p<0.01) (Fig. 3).

#### Flow propagation velocity in the HT group

1) FPV-E/E was lower in cases having larger LVMI, and there was a significant negative correlation between FPV-E/E and LVMI (r=-0.427, p<0.001) (Fig. 4). There was no significant cor-
relation between FPV-E/E and RWT ($r = -0.168$).

2) FPV-A/A was lower in cases having RWT and there was a significant negative correlation between FPV-A/A and RWT ($r = -0.411$, $p < 0.001$) (Fig. 5). There was no significant correlation between FPV-A/A and LVMI ($r = -0.137$).

**DISCUSSION**

**LV flow propagation and the color M-mode Doppler technique**

In the LV diastolic phase, the inflow of blood from the left atrium to the left ventricle results in a propagation of the blood flow from the mitral orifice.
toward the apex. Assessment of the LV blood flow propagation in the LV filling phase using color M-mode Doppler imaging has recently attracted attention as a new non-invasive method for assessing LV diastolic function.

Pulsed Doppler measurement of the transmitral flow velocity pattern has been widely used to assess the LV diastolic function\(^{10,11}\). However, as previously discussed, the transmitral flow velocity pattern is influenced by many factors other than primary diastolic function indices, including left atrial pressure, age, and heart rate\(^{12,13}\). Indeed, patients who have diastolic dysfunction and markedly elevated pulmonary venous pressure can also have a normal pattern of transmitral flow velocity\(^{14}\).

Regarding the difference between the pulsed Doppler transmitral flow velocity pattern and the flow propagation velocity, the pulsed Doppler technique displays the velocity spectrum at a single location, whereas the color M-mode Doppler technique displays the spatiotemporal distribution of the velocity. Several published studies\(^5-7\) on the LV flow propagation velocity using the color M-mode Doppler technique emphasized its usefulness for assessing diastolic dysfunction. Brun \textit{et al.}\(^5\) demonstrated that the velocity of flow propagation during early filling reduced in patients with LV hypertrophy and seemed to be highly dependent on the LV relaxation rate. Based on their findings, they suggested that flow propagation velocity could be an important tool in studying diastolic function. In addition, Takatsuji \textit{et al.}\(^6\) demonstrated that FPV was free of pseudonormalized transmittial flow velocity pattern, and Nagueh \textit{et al.}\(^7\) reported that the flow propagation velocity was useful as a noninvasive parameter of LV diastolic function in patients with atrial fibrillation. Furthermore, several reports\(^6,15-17\) demonstrated that the ratio of

![Fig. 5 Correlation between FPV-A/A and RWT.](image)

There was a significant negative correlation between FPV-A/A and RWT ($r=-0.411$, $p<0.001$).
FPV-E to E was appropriate for evaluating LV diastolic function by the preload effect on the early transmural flow velocity.

**LV diastolic function in patients with hypertension**

Congestive heart failure is a common and often lethal complication of systemic hypertension, and evaluation of LV function is important for the management of hypertensive heart disease. For these reasons, LV function has been thoroughly examined in patients with hypertension. Phillips et al. reported that the early detection and prevention of cardiac dysfunction is an important goal in the management of hypertensive patients.

According to previous evaluations of hypertensive subjects, their systolic function is similar to normal subjects, and their LV diastolic abnormalities tend to precede systolic dysfunction. In the present study, there was no significant difference in FS between the two groups, whereas the pulsed-Doppler-derived index A/E was significantly higher in the HT group than in the Control group. These findings are in agreement with the observations of several previous studies. Papademetriou et al. demonstrated that indexes of systolic LV function were similar in patients with mild hypertension and normal persons, whereas indexes of diastolic function were abnormal in patients with mild hypertension. Based on this finding, they concluded that subtle abnormalities of diastolic LV function may be present in patients with mild hypertension when LV systolic function remains normal. Soufer et al. found that slowing of the maximal LV filling rate was common in hypertensive patients, even before signs of decreased systolic performance. While these studies have drawn recent attention to the evaluation of diastolic LV function in patients with hypertensive LV hypertrophy, there have been no thorough investigations of the LV filling flow propagation in patients with hypertension or the flow propagation velocity in the late diastolic phase. Accordingly, we considered that the flow propagation velocity obtained by the color M-mode Doppler technique should be assessed as a parameter of diastolic function in patients with hypertension.

**LV flow propagation in patients with hypertensive LV hypertrophy**

The main findings of the present study are that; 1) FPV-E/E and FPV-A/A, were significantly lower in the HT group than in the control group; 2) the FPV ratio was significantly higher in the HT group than in the control group; 3) there was a significant negative correlation between FPV-E/E and LVMI; and 4) there was a significant negative correlation between FPV-A/A and RWT.

A delay in LV blood flow propagation in patients with dilated cardiomyopathy was first described by Jacobs et al. Several recent studies have shown a decrease in the flow propagation velocity in the early diastolic phase in patients with diastolic dysfunction.

Two mechanisms have been proposed as determinants of the flow propagation velocity. One is the presence of intraventricular pressure gradient, and the other is the formation of vortexes. In the early diastolic phase, rapid LV relaxation generates a dynamic pressure gradient in the left ventricle. This pressure gradient generates the driving force to pump the blood deep into the left ventricle, resulting in a propagation of blood flow from the mitral orifice towards the apex. In states of diastolic dysfunction such as myocardial ischemia, impairment of rapid filling leads to a decrease in intraventricular pressure gradient, thereby decreasing the flow propagation velocity. Courtois et al. showed that early diastolic intraventricular pressure gradient decreased after coronary artery occlusion in dogs. Flow propagation velocity is also determined by an intraventricular vortex formation. Garcia et al. observed that vorticity is generated by shear stress between inflowing blood and the stationary blood already in the ventricle. Since the shear stress correlates with the area in which inflowing blood contacts the stationary blood already in the ventricle, vortex formation could increase the incidence of dilated ventricles. Therefore, vortex formation increases the size of the smaller mitral orifices and dilated ventricles, thereby resulting in a slower FPV. In summary, it is suggested that abnormal relaxation and a higher relative mitral orifice size leads to a slower FPV.
In view of the importance of LV hypertrophy and associated myocardial fibrosis in the development of diastolic dysfunction, we considered that it was meaningful to assess the relation between diastolic hemodynamics and cardiac alterations or geometric remodeling in patients with hypertension. In the present study, we used LVDd, LVMI, and RWT as the parameters of cardiac alterations and geometric remodeling, and we assessed the relation between ventricular LV filling flow propagation and these parameters in patients with hypertensive LV hypertrophy.

In the present study, FPV-E/E were significantly lower in the HT group than in the control group. This result indicates diastolic dysfunction in the early diastolic phase in patients with hypertensive LV hypertrophy. This result also suggests that the slower FPV-E in patients with hypertensive LV hypertrophy could be related to an increase of LVDd. In addition, there was a significant negative correlation between FPV-E/E and LVMI. It is suggested that FPV-E/E could be a useful parameter for evaluating LV diastolic dysfunction associated with LV hypertrophy in patients with hypertensive LV hypertrophy.

In the present study, FPV-A/A was significantly lower in the HT group than in the control group. Several studies\(^1\)\(^2\)\(^6\)\(^26\)\(^27\) have shown an increase of A in patients with hypertensive LV hypertrophy, suggesting atrial hypercontractility due to compensation of early diastolic dysfunction. Our result seems to contradict the results of the these recent reports. However, Thomas et al.\(^23\) found that the peak velocity of early diastolic phase reached its maximum value closer to the apex, whereas the highest peak velocity of late diastolic phase occurred near the mitral leaflet tips. We speculated that the peak flow velocity in the late diastolic phase at the mitral orifice was higher in patients with hypertensive LV hypertrophy, whereas the flow propagation velocity in the late diastolic phase was decreased. Thus, patients with hypertensive LV hypertrophy seem to have impaired LV function in the late diastolic phase. Moreover, since the FPV ratio was significantly lower in the HT group, diastolic function seemed to be impaired in both the early and late diastolic phases in patients with hypertensive LV hypertrophy, especially in the early diastolic phase.

There was a significant negative correlation between FPV-A/A and RWT in the present study, whereas there was no correlation between FPV-A/A and LVMI. Phillips et al.\(^18\) reported that abnormality of the peak velocity of late filling phase in patients with hypertension may be independent of LV hypertrophy. However, flow propagation velocity has never been examined in patients with hypertension. Our results suggest that the impairment of diastolic function in the late diastolic phase was related not to the extent of LV hypertrophy, but to the geometric remodeling of LV hypertrophy. Further, among patients with hypertensive LV hypertrophy, the LV diastolic dysfunction was more severe in cases having a higher RWT and larger LVMI.

**CONCLUSION**

In patients with hypertensive LV hypertrophy, diastolic function is considered to be impaired both in early and late diastolic phases, this impairment considered is more severe in the early diastolic phase than in the late diastolic phase. It was considered that the LV diastolic dysfunction was more severe in patients with hypertensive LV hypertrophy in cases having a higher RWT and larger LVMI.

**References**


抄 録

左室内血流伝播速度の解析による高血圧性心肥大例の
拡張期血行動態の検討

【目的】本研究は、カラー M モード Doppler 法を用いて、高血圧性心肥大例の左室内血流伝播
速度を解析し、高血圧性心肥大例の拡張期血行動態と心臓形態との関連を検討することを目的と
した。

【方法】対象は高血圧性心肥大（HT 群）45 例、健康者 31 例を対照（コントロール群）とし
て用いた。

心エコー・超音波 Doppler 法により、左室心筋重量係数（LVMi）、相対的左室壁厚、（RWT）、
および拡張期最大左室流入血流速度（E）および拡張期後期（心房収縮期）同速度（A）を測定し
た。カラー M モード Doppler 法を用いて拡張期左室流入血流を記録し、拡張期後期左室流入血流伝
播速度（FPV-E）、拡張期後期（心房収縮期）同播速度（FPV-A）を記録した。次いで 1）FPV-
E/E, FPV-A/A, およびその比（FPV-A/FPV-E: FPV 比）を HT 群とコントロール群とで比較し
た。2）HT 群において、FPV-E/E, FPV-A/A と LVMi, RWT とのそれぞれの相関を検討した。

【結果】1）FPV-E/E, FPV-A/A はコントロール群に比し、HT 群でいずれも有意に低値を示し、FPV
比は HT 群で有意に高値を示した。2）FPV-E/E と LVMi との間に有意な負の相関がみられ、
FPV-A/A と RWT との間に有意な負の相関がみられた。

【結論】高血圧性心肥大例の左室拡張機能は、拡張早期、拡張後期のいずれにおいても低下し
ており、その程度は拡張早期に強いと考えられた。また高血圧性心肥大例では、左室心筋重量係
数が大きく、かつ相対的左室壁厚が厚いものほど左室拡張機能障害の程度が強いと考えられた。
（聖マリアンナ医大誌, 29, 241-249, 2001）

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