Chapter 2

Color M-mode Doppler Echocardiographic Evaluation of Left Ventricular Diastolic Function

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Introduction

Different diagnostic techniques have been used to assess left ventricular diastolic function in patients with cardiac diseases. Among the invasive parameters, the time constant of early diastolic left ventricular pressure decay (Tau) is measured from the left ventricular pressure curve recorded using a high-fidelity tip manometer, and is an established index of left ventricular relaxation which is not influenced by heart rate, systolic pressure or preload[1-3]. Several noninvasive approaches have also been employed to detect diastolic dysfunction. Diastolic left ventricular volume change reflects left ventricular diastolic function and can be directly or indirectly assessed using radionuclide ventriculography[4], M-mode echocardiography[5] and pulsed-Doppler technique[6-8]. However, these parameters have a serious fault that they may pseudonormalize when the left atrial pressure rises due to congestive heart failure[9]. A color M-mode Doppler index, flow propagation velocity, is a newer noninvasive parameter of left ventricular diastolic function. Recent reports have shown that this index does not pseudonormalize and can sensitively and accurately detect the diastolic impairment in patients with different types of cardiac diseases[10-16]. We briefly review the aims and methods of the noninvasive assessment of left ventricular diastolic function, and focus on the clinical usefulness of the color M-mode index, flow propagation velocity.

Left ventricular diastolic dysfunction and congestive heart failure

Echeverria et al[17] reported in 1983 that the prevalence of patients with normal left ventricular systolic function was as high as 40% among 50 consecutive patients who were referred to their echocardiographic laboratory for the evaluation of congestive heart failure. Other investigators have also reported the high prevalence of acute or chronic heart failure with normal systolic function, which ranged from 13 to 42%[18]. In these patients with normal systolic function, congestive heart failure is supposed to be caused by left ventricular diastolic dysfunction. Previous studies have reported high incidence of such a type of heart failure in patients with hypertrophic cardiomyopathy, hypertensive heart disease and ischemic heart disease. In addition, it is also generally considered that patients with systolic dysfunction caused by dilated cardiomyopathy, myocardial infarction or other cardiac disorders never occurs in the absence of concomitant diastolic dysfunction, which enhances the decompensation. However, it is difficult to directly confirm the presence of diastolic dysfunction in patients with heart failure because the noninvasive determination of diastolic abnormality is not clear-cut.

Pulsed Doppler analysis of transmitral flow velocity pattern

In 1982, Kitabatake et al. demonstrated that the transmitral flow velocity pattern obtained by pulsed Doppler technique reflects the left ventricular volume curve obtained by cine ventriculography, and that the Doppler measurement could allow us to estimate left ventricular diastolic function[6] (Figure 1). They also indicated that the ratio of early diastolic wave amplitude to late diastolic one and the deceleration rate of early diastolic flow velocity were decreased in various cardiac disorders, such as hypertension, hypertrophic cardiomyopathy and myocardial infarction compared with healthy subjects. Following this paper, many investigators have examined the feasibility and validity of the Doppler measurement to assess the left ventricular diastolic function in various heart diseases. After that, this technique has become the most popular noninvasive method to assess diastolic function[7), 8)].

However, in 1988, Appleton et al.[9] reported that an increase in left atrial pressure can pseudonormalize an abnormal mitral flow velocity pattern and mask left ventricular diastolic dysfunction. Now, we have sufficient evidences that pseudonormalization is observed in any indexes derived from transmitral flow velocity pattern, such as E velocity, E/A ratio, deceleration rate of E wave and

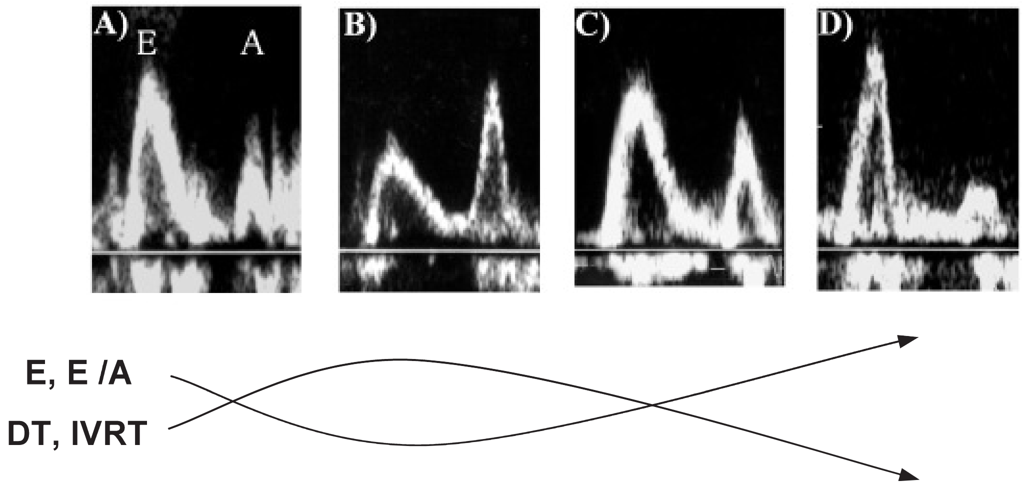


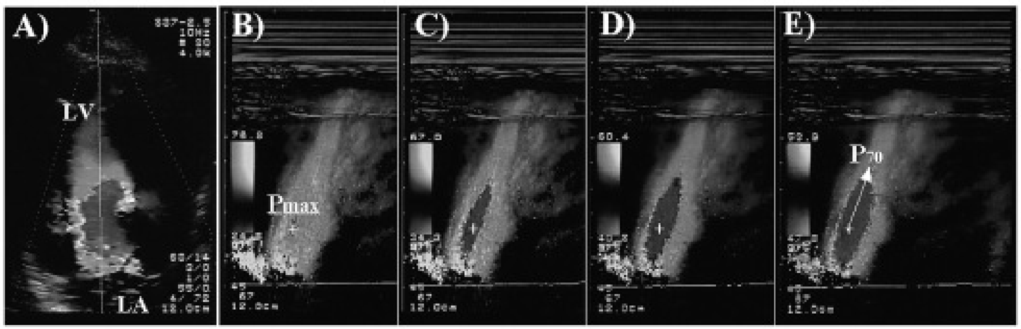
Figure 1 Changes in transmitral flow velocity pattern by the elevation of left atrial pressure.
In normal transmitral flow velocity pattern (panel A), early diastolic velocity (E) is greater than late diastolic velocity (A), while E velocity decreases and A velocity increases in patients with left ventricular diastolic dysfunction (panel B). An increase in left atrial pressure due to diastolic dysfunction and/or systolic dysfunction causes pseudonormalization of the flow pattern (panel C), and further elevation of left atrial pressure may lead to the restrictive transmitral flow pattern with very high E velocity and very low A velocity (panel D).

isovolumic relaxation time (Figure 1). This is the most profound fault of these indexes for assessing left ventricular diastolic function in patients with congestive heart failure.

Color M-mode Doppler measurement of flow propagation velocity

In 1996, we proposed a new index to assess left ventricular diastolic function using color M-mode Doppler echocardiography and base-line shift technique[10]. This index, flow propagation velocity (FPV), represents an average velocity of early diastolic left ventricular filling flow from mitral orifice to mid-ventricle. Although there were a little difference in the measuring method, we and other investigators have found several advantages of color M-mode diastolic indexes over the conventional pulsed-Doppler indexes[11-16]. In this text, we describe our method to measure FPV and summarize the clinical usefulness for the evaluation of left ventricular diastolic function in various cardiac diseases.

We used apical approach to obtain a color M-mode Doppler image of left ventricular filling flow in early diastole, which represents distribution of the filling flow velocity along the ultrasound beam in the vertical axis and time in the horizontal axis (Color Fig. 9). By changing the aliasing area, we determined the location of maximal velocity at the mitral orifice in early diastole as a small blue dot. Then, by lowering of the aliasing velocity, the blood area with the velocity faster than 70% of the maximal velocity was visualized and the nearest point to the apex of the aliasing area was determined. The upward slope between these two



Color Fig 9 Our method to measure flow propagation velocity using color M-mode Doppler and color baseline-shift technique.
A color M-mode Doppler image of left ventricular filling flow was recorded by putting M-mode cursor along of the filling flow on the apical long-axis color Doppler image (panel A). Changing the aliasing area, we located the maximal velocity point around the mitral orifice in early diastole (Lmax, panel B). Then, the aliasing area was extended by reducing aliasing velocity (panel C and D). In the color M-mode image with the aliasing velocity decreased to 70% of the maximal velocity, the point nearest to the transducer in the aliasing area (L70, panel E) was determined. Flow propagation velocity (FPV) was measured as the upward slope of the line between these two points. LA; left atrium, LV; left ventricle.

points was measured and defined as FPV.

FPV in patients with left ventricular systolic dysfunction

Patients with left ventricular systolic dysfunction, such as dilated cardiomyopathy and myocardial infarction, is considered to have diastolic dysfunction, but the conventional pulsed-Doppler approaches have often failed to detect the diastolic abnormality because of pseudonormalization in the transmitral flow pattern. Therefore, we studied the usefulness of FPV in patients with left ventricular systolic dysfunction including those having severely depressed systolic function with pseudonormalized transmitral flow pattern[10]. The subjects consisted of 12 with chest pain syndrome, 8 with angina pectoris, 23 with old myocardial infarction and 16 with dilated cardiomyopathy. Left ventricular ejection fraction (EF) was measured by the biplane disk summation method using two-dimensional echocardiography. E, A, E/A ratio and deceleration time of E velocity (DT) and isovolumic relaxation time (IRT) were measured using the conventional Doppler techniques, and the measurements of FPV and the ratio of FPV to E velocity (FPV/E) were done using color M-mode Doppler echocardiography. The subjects were divided into 3 groups according to E/A ratio and ejection fraction (EF); control group without systolic dysfunction consisted of 20 patients with EF>=60%, diastolic dysfunction group consisted of 21 patients with EF<60% and E/A<1, and pseudonormalization group consisted of 18 patients with EF<60% and E/A>=1. E/A was lower in diastolic dysfunction group than in the control group, but no difference was seen between the pseudonormalization and control group, whereas FPV clearly distinguished the pseudonormalization group from the control group (Figure 2). FPV each in the diastolic dysfunction group and pseudonormalization group was distinctly decreased compared to the control group (33.8+/−13.8 and 30.0+/−8.6 vs. 74.3+/−17.4 cm/s, p<0.001, respectively). Although E/A, DT and IRT showed no correlation with Tau, FPV and FPV/E exhibited good correlation with Tau (r=0.82, p<0.001 and r=0.74, p<0.001, respectively, Table 1). These results indicate that the color M-mode indexes do not pseudonormalize and thus might be useful to evaluate left ventricular diastolic dysfunction in patients with dilated cardiomyopathy and myocardial infarction.

FPV in patients with hypertrophic cardiomyopathy

Based on several previous studies showing that Tau is prolonged in hypertrophic cardiomyopathy (HCM), it has been believed that diastolic abnormality is one of the most important pathological features of this disease[1,2,19]. However, the conventional noninvasive parameters have failed to reflect Tau in HCM patients. Therefore, we studied the usefulness of FPV for the detection of left ventricular diastolic abnormality in 23 patients with HCM and 26 patients with chest pain syndrome[16]. Correlation and regression analysis among all the subjects showed that each of FPV and FPV/E well correlated with Tau (r=−0.76, p<0.001 and

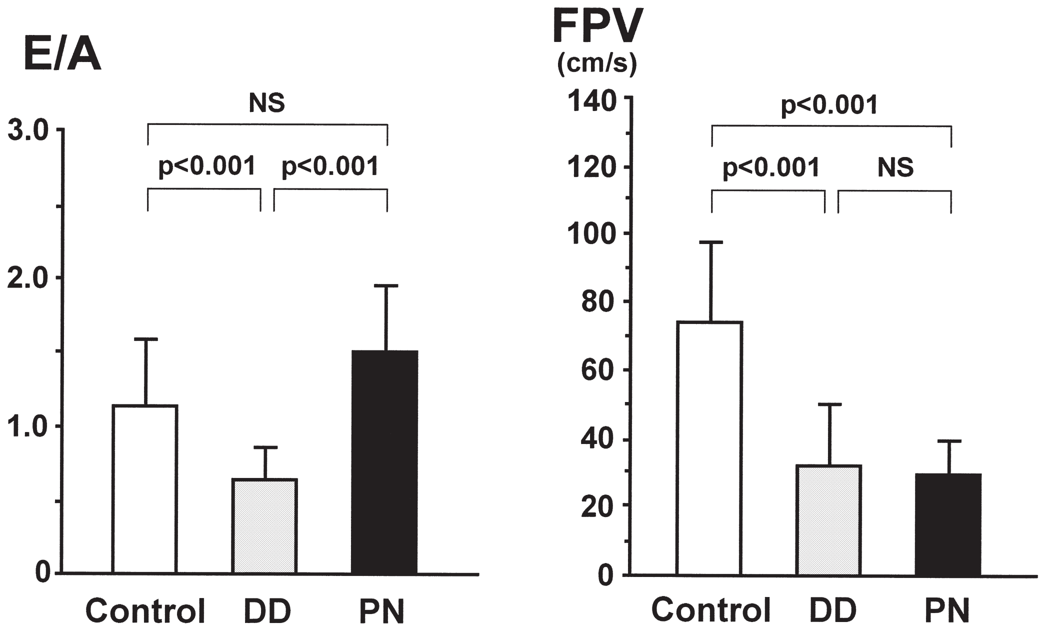


Figure 2 Comparison of E/A and flow propagation velocity among the control, diastolic dysfunction (DD) and pseudonormalization (PN) groups.
The values of E/A (left panel) and flow propagation velocity (right panel) were compared among the 3 groups. E/A was significantly lower in DD group than in the control group, but no significant difference was seen between PN and control group, whereas FPV in PN group was distinctly lower than that of control group. The mean and SD values were shown.

Table 1 Correlations of Doppler indexes to the time constant of Left ventricular early diastolic pressure decay in 20 control subjects and 39 patients with left ventricular systolic dysfunction

Indexes	Correlation coefficient	P value
E/A	0.01	NS
DT	0.18	NS
IRT	0.24	NS
FPV	−0.81	<0.0001
FPV/E	−0.74	<0.0001

$r = -0.73$, $p < 0.001$) in contrast to no significant correlations between each of the pulsed Doppler parameters and Tau (Table 2).

There have been reported a few other methods to measure the propagation speed of early diastolic left ventricular filling flow in addition to our own method. The most popular one is reported by Brun and his colleagues[11)], who measured the slope of wave front of the filling flow (WFV). In the measurements of patients with left ventricular systolic dysfunction, the value of WFV is not so different from FPV. However, we often observe an additional high velocity area at the level of

Table 2 Correlations of Doppler indexes to the time constant of Left ventricular early diastolic pressure decay in 26 control subjects and 20 patients with hypertrophic cardiomyopathy

Indexes	Correlation coefficient	P value
E/A	0.20	NS
DT	0.26	NS
IRT	0.24	NS
FPV	−0.76	<0.001
FPV/E	−0.73	<0.001

the mid-ventricle in patients with HCM. In such cases, careful interpretation should be made, because the value of WFV is quite different from that of FPV. In our study, WFV in HCM group was not significantly different from that in the control group, while FPV in HCM was significantly decreased compared with that in the control (Figure 3).

FPV in patients with hypertension

We also applied our method to patients with hypertension with or without signs of left ventricular hypertrophy. Study population consisted of 24 normal subjects, 24 hypertensive patients with left ventricular mass index less than 120g/m^2 (HT group), and 13 hypertensive patients with left ventricular mass index greater than 120g/m^2 (HT-LVH group). FPV was significantly lower in HT group (36±13cm/s, $p<0.0001$) as well as in HT-LVH group (34±7cm/s, $p<0.0001$) compared with normal group (73±20cm/s) (Figure 4). These results suggested that the existence of left ventricular diastolic dysfunction even in the hypertensive patients without left ventricular hypertrophy.

Prognostic significance in patients with systolic dysfunction

To determine whether the evaluation of left ventricular diastolic function by FPV is useful to predict prognosis of patients with left ventricular systolic dysfunction, a total of consecutive 126 subjects with left ventricular systolic dysfunction (84 with previous myocardial infarction and 41 with dilated cardiomyopathy) underwent Doppler echocardiographic evaluation. The measurements included E and A velocities, E/A ratio, deceleration time of E velocity and isovolumic relaxation time obtained using conventional echo-Doppler techniques and FPV and FPV/E determined using color M-mode Doppler. During the mean follow-up period of 30+/−26 months, 26 patients had cardiovascular events (death in 4, congestive heart failure in 13, ventricular tachycardia in 6, and cerebral infarction in 3). Among the noninvasive diastolic parameters, FPV/E was the single best predictor of cardiovascular events by Cox proportional hazard model analysis. When the patients were divided into subgroups according to the FPV value of 0.60, each of the survival rate and event-free rate in subgroup with FPV>=0.60 was better than that in

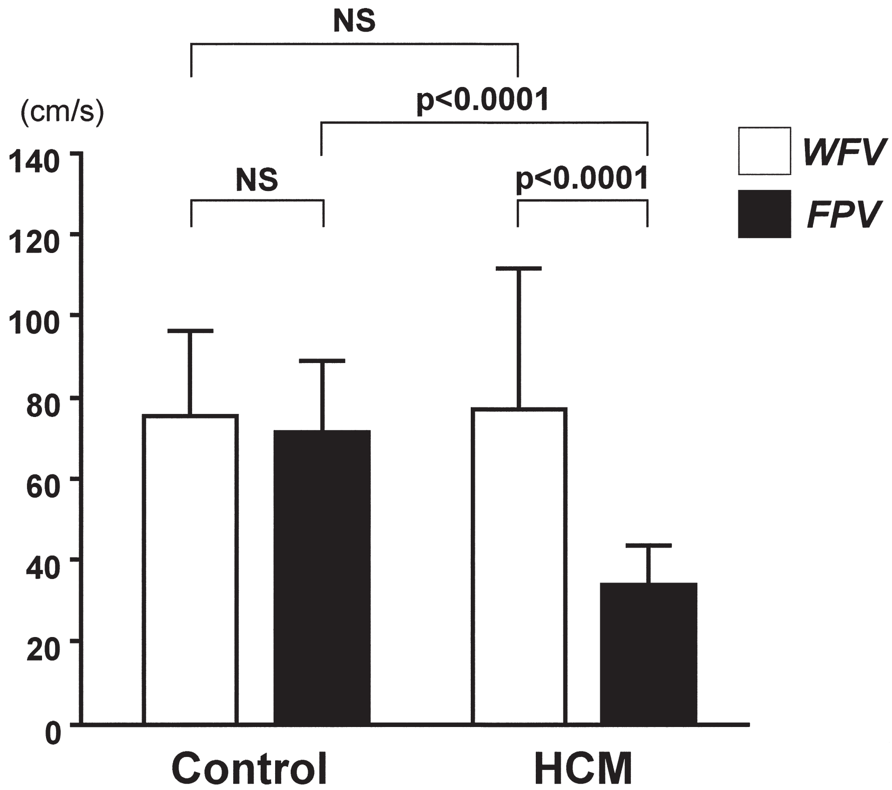


Figure 3 Comparison of two methods to measure flow propagation velocity in patients with hypertrophic cardiomyopathy.
Flow propagation velocity was measured using two different methods; that is, our method using color baseline-shift technique (FPV) and that measuring wave front of the filling flow reported by Brun et al (WFV). The value of WFV was significantly greater than that of FPV in HCM group and was similar to WFV in the control group. The mean and SD values were shown.

subgroup with FPV < 0.60 (Figure 5). Thus, the evaluation of diastolic function using color M-mode Doppler derived FPV/E contributes to predicting clinical outcome of patients with left ventricular systolic dysfunction.

Prognostic significance in patients with hypertrophic cardiomyopathy

The effect of left ventricular diastolic function on the clinical course of patients with HCM is still unclear. Because FPV has been shown to well reflect diastolic function in patients with HCM, it can be a good predictor of long-term clinical outcome of HCM patients. To determine whether FPV is actually related to the clinical course of HCM, 43 patients with HCM were studied. Echo-Doppler measurements included left ventricular end-diastolic dimension, interventricular septum thickness, left ventricular posterior wall thickness, percent fractional shortening, left atrial dimension, E, A, E/A, DT, IRT, FPV and FPV/E. During the

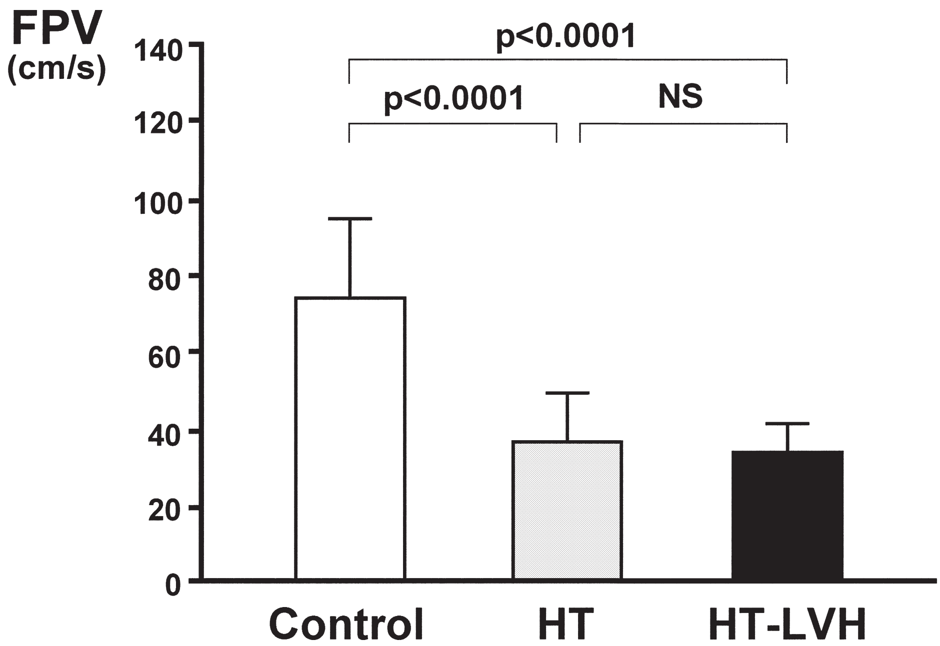


Figure 4 Flow propagation velocity in patients with hypertension with or without left ventricular hypertrophy.
Compared with the control group, flow propagation velocity (FPV) was significantly reduced both in the group of patients with hypertension but without hypertrophy (HT group) and in the group with hypertension and hypertrophy (HT-LVH group). The mean and SD values were shown.

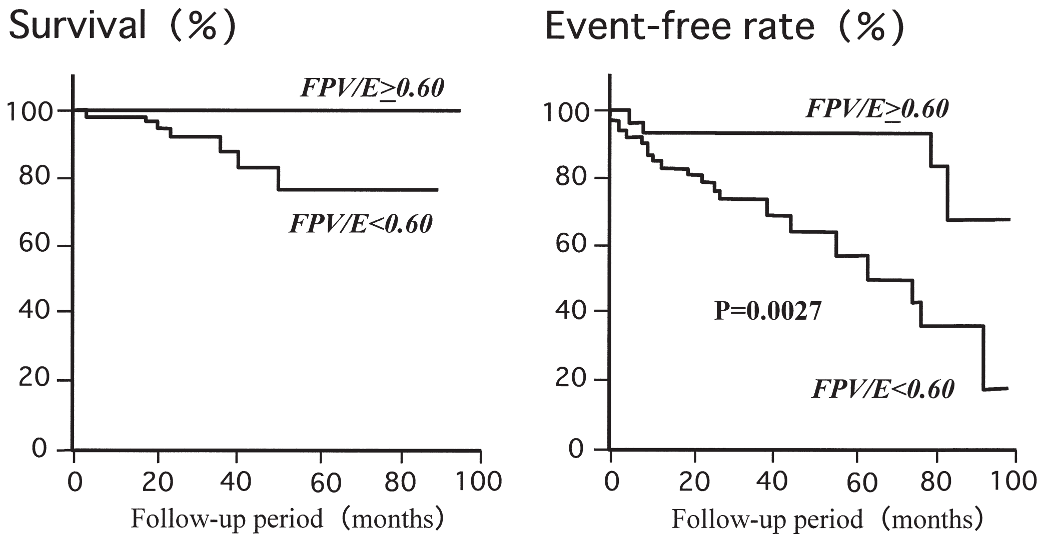


Figure 5 Kaplan-Meier Curves comparing the survival rate and event-free rate between patients with FPV/E>=0.60 and those with FPV/E<0.60.

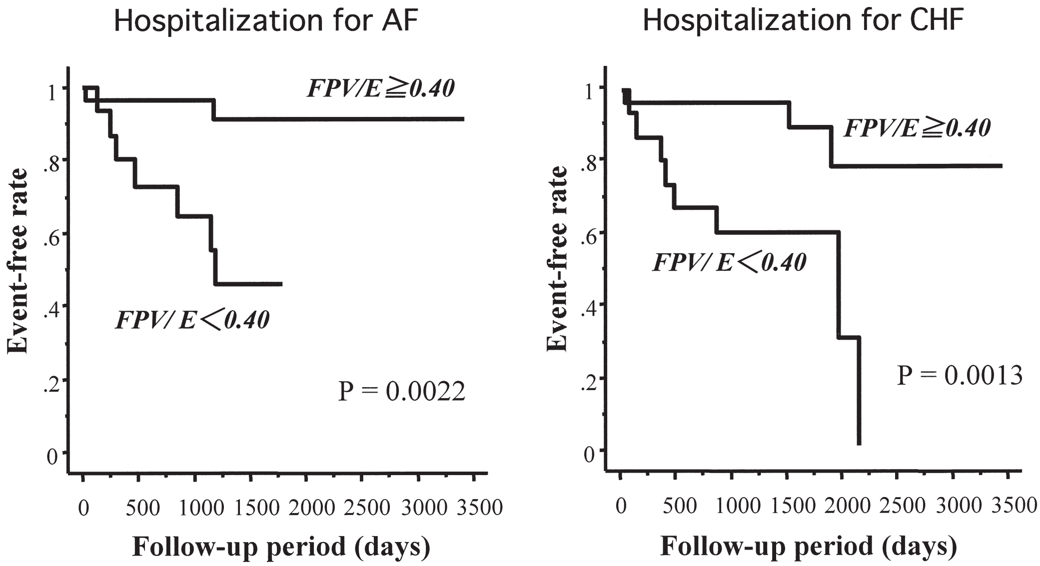


Figure 6 Kaplan-Meier Curves comparing the event-free rate for hospitalization for atrial fibrillation (AF) and that for congestive heart failure (CHF) between patients with FPV/E>=0.40 and those with FPV/E<0.40.

mean follow-up period was 42±23 months, 9 of the 43 patients (21%) were hospitalized for atrial fibrillation, 7 (16%) did for ventricular tachycardia and 11 (26%) did for congestive heart failure. The other cardiac events occurred in 6 patients (14%) including 2 patients with embolism, 3 with the other arrhythmias and 1 with sudden death. In total, cardiac events were seen in 19 patients (44%). The Cox proportional hazard model analysis indicated that FPV/E was an independent predictors for hospitalization due to atrial fibrillation (x^2=7,16, p=0.047), hospitalization due to congestive heart failure (x^2=12.76, p=0.008) and total cardiac events (x^2=4.47, p=0.034). Both hospitalization for atrial fibrillation and that for congestive heart failure were more frequent in patients with severely depressed FPV/E (<0.40) compared with those without (Figure 6). Hospitalization for congestive heart failure was associated with that for atrial fibrillation in 7 of 11 patients (64%). These findings suggest that diastolic dysfunction indicated by reduced FPV/E can be a strong predictor of cardiac events in patients with HCM. Diastolic dysfunction may be a principal cause of AF that frequently leads to more serious cardiac events such as congestive heart failure.

Conclusions

The flow propagation velocity, FPV and FPV/E, measured using color M-mode Doppler technique is a useful noninvasive index of left ventricular diastolic function. They sensitively and accurately detect the diastolic impairment in many clinical settings such as dilated cardiomyopathy, myocardial infarction, hypertrophic cardiomyopathy and hypertension. Moreover, FPV/E is useful to predict the clinical course of patients with left ventricular systolic dysfunction and of those with hypertrophic cardiomyopathy. Wider use of these color M-mode diastolic indexes may lead to the better understanding of patients with diastolic heart failure.

Summary

Transmitral flow velocity pattern obtained by pulsed Doppler technique reflects left ventricular (LV) diastolic function, but an increase in left atrial pressure pseudonormalizes the flow pattern and mask diastolic dysfunction. Flow propagation velocity (FPV) measured using color M-mode Doppler and baseline-shift technique represents an average velocity of early diastolic LV filling flow from mitral orifice to mid-ventricle. In patients with ischemic heart disease and dilated cardiomyopathy including those with pseudonormalized transmitral flow pattern, FPV had good correlation with the time constant of early diastolic LV pressure decay (Tau), indicating that FPV is a useful noninvasive parameter of diastolic function which does not pseudonormalize. Unlike the conventional Doppler parameters, FPV well correlated with Tau in patients with hypertrophic cardiomyopathy, and was distinctly decreased even in the hypertensive patients without LV hypertrophy. Moreover, FPV/E is useful to predict the clinical course of patients with left ventricular systolic dysfunction and those with hypertrophic cardiomyopathy. Thus, color M-mode Doppler echocardiography provides useful and reliable parameters for the noninvasive evaluation of left ventricular diastolic function in patients with various cardiac diseases.

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