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Editorial Comment

"Diastology": Beyond E and A*

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In the past two decades, Doppler echocardiography has emerged as a noninvasive alternative to cardiac catheterization for evaluation of hemodynamic variables (1). Stenotic valve gradients and areas, regurgitant pressure gradients and volumetric flow rates are now able to be accurately and reproducibly obtained by most echocardiographic laboratories. A well performed Doppler examination will provide more accurate data than conventional cardiac catheterization in specific clinical situations (2). Thus, two-dimensional and Doppler echocardiography can obviate the need for invasive cardiac catheterization for many patients with cardiac disease, provided that the results obtained from this noninvasive modality correlate with the clinical impression.

Doppler assessment of diastolic filling. It has been the noninvasive assessment of left ventricular diastolic function that requires further investigation. Diastolic function of the left ventricle plays a major role in producing the signs and symptoms of heart failure in diseases of the myocardium, the end result of which is elevation of left ventricular pressure per unit volume of blood entering the left ventricle (3–6). This elevated filling pressure increases left atrial pressure, which is reflected back to the pulmonary circulation and causes symptoms of shortness of breath and signs of pulmonary congestion. Because of the complexity of the multiple interrelated events that comprise diastolic filling of the heart, assessment of left ventricular diastolic function in the past was limited to the catheterization laboratory, where complex measurements of pressure–volume relations and rates of decrease in pressure from high fidelity pressure curves were used (7,8).

It has been speculated that Doppler echocardiography could be used to assess diastolic filling and function of the left ventricle noninvasively (9,10). Kitabatake et al. (11) in 1982 described the different flow velocity curves that occur in different disease states from Doppler interrogation of transmitral flow. Multiple investigations in both animals and humans followed and provided insight into interpretation of these flow velocity patterns (12–16). The mitral flow velocity curves can be viewed as determined by the relative driving pressure across the mitral valve from the left atrium to the left ventricle (12,13). There is an initial rapid acceleration of flow as left ventricular pressure drops rapidly below left atrial pressure during ventricular relaxation (measured as the E wave velocity). As the left ventricle fills in early diastole, there is a rise in pressure that exceeds left atrial pressure, causing a deceleration of flow. The rate of deceleration of flow is measured as the mitral deceleration time and is dependent mainly upon the effective operating compliance of the left ventricle (17). During mid-diastole there is equilibration of left ventricular and left atrial pressures, with a low velocity of forward flow as a result of inertial forces. Finally, at atrial contraction there is a reacceleration of transmitral flow as left atrial pressure rises above left ventricular pressure (measured as the A wave velocity). These flow velocity curves are dependent on multiple intrinsic factors that include the rate of left ventricular relaxation and elastic recoil (diastolic suction), left atrial and left ventricular compliance, left atrial pressure as well as varying patient conditions, such as load, age and heart rate (12–21).

Clinical applications. The question has emerged as to whether mitral flow velocity curves can be used in clinical practice to assess left ventricular diastolic function, left ventricular filling pressures and prognosis in patients with cardiac disease. Left ventricular filling patterns change with age (22), and it has been hypothesized (23) and shown in experimental models of heart failure (17) that there is also a progression of abnormal patterns that occur over time with diseases of the myocardium. In the early stage of dysfunction, impaired (delayed) relaxation of the left ventricle dominates, which decreases early diastolic filling although filling pressures remain normal in the rest state. This is reflected by a decrease in the initial E wave velocity, prolongation of deceleration time and increased proportion of filling due to atrial contraction. With disease progression, left atrial pressure rises, which increases the driving pressure across the mitral valve. This is accompanied by a gradual increase in E wave velocity and a decrease in effective operating compliance of the left ventricle, which shortens the mitral deceleration time, either due to abnormalities of myocardial stiffness or a higher preload. With advanced stages of disease, there will be even higher pressures, a higher E/A ratio and a very abbreviated mitral deceleration time.

This concept of a progression of the mitral flow velocity curves with worsening disease can be used for clinical application in certain patient groups. In patients with known left ventricular systolic dysfunction, mitral deceleration time shortens as left atrial and left ventricular filling pressures increase (24–26). Of great interest has been the finding that the prognosis of patients with either dilated or infiltrative cardiomyopathy is predicted by a short mitral deceleration time (27–30), with <140 ms indicating a poor prognosis, independent of the degree of systolic dysfunction.

Current limitations. Although it has been shown that these clinical applications of mitral flow velocity are useful in patients with systolic dysfunction, it becomes more difficult to determine the presence and severity of abnormalities of dia-

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stolic filling from the mitral flow velocity curves in patients with a normal left ventricular ejection fraction. For instance, normal subjects with rapid ventricular relaxation and vigorous diastolic suction may have a mitral flow velocity curve that has the same appearance as a patient with diastolic dysfunction caused by a combination of abnormal relaxation (which in itself would decrease E wave velocity and lengthen deceleration time) and high left atrial pressure (which will increase the E wave velocity and shorten deceleration time) (15,23,31). Unless reliable ways to differentiate these normal and "pseudonormal" filling patterns are found, the use of mitral flow velocity curves alone to assess diastolic function in patients with normal or near-normal left ventricular systolic function will be limited. It is exactly this group of patients in whom assessment of diastolic function is most important because over one-third of elderly patients who present with symptoms of heart failure have "isolated" left ventricular diastolic dysfunction. Recent investigation in the field of "diastology" has focused on this problem, and a number of new innovative methods for identifying abnormal physiologic or hemodynamic variables have been described. For instance, analysis of the difference between the duration of flow at atrial contraction in mitral and pulmonary venous flow velocities has been shown to identify patients with increased left ventricular end-diastolic pressure (32,33). The rate of fall of a mitral regurgitation velocity curve may provide a direct measurement of the rate of ventricular relaxation (34), whereas changes in mitral flow velocity after altered loading conditions may provide further insight into interpretation of left ventricular filling patterns. Doppler tissue imaging has also been proposed as a new method by which the rate of myocardial relaxation can be directly visualized.

Color M-mode: flow propagation. In this issue of the Journal, Takatsuji et al. (35) investigate the concept of measuring the rate of left ventricular early diastolic flow propagation to separate normal from pseudonormal mitral flow velocity patterns. Color M-mode is ideal for the study of mitral inflow propagation because of its high sampling rate and ability to measure flow velocities in both a temporal and spatial distribution. This new use of color M-mode technique was first described by Brun et al. (36), who reported that the velocity of mitral inflow propagation was lower in patients with heart disease than in normal subjects, that flow propagation was highly dependent on the rate of left ventricular relaxation and that this decrease in flow propagation was seen in various cardiac disease forms with or without ventricular enlargement. Importantly, their study included patients with impaired left ventricular relaxation, elevated filling pressures and normal mitral E/A wave velocity ratios, a group which undoubtedly had pseudonormal mitral flow velocity patterns. These results were later confirmed by Stugaard et al. (37) in patients undergoing balloon angioplasty. During coronary ischemia the timing of peak mitral inflow velocity was progressively delayed from the mitral valve to the left ventricular apex, with the delay again being highly correlated with changes in the rate of left ventricular relaxation. The results of Takatsuji et al. (35) provide further evidence that color M-mode flow propagation can detect the delayed relaxation present in patients with pseudonormal mitral flow velocities and that this method can distinguish these patients from subjects with normal left ventricular relaxation and filling.

The certainty that mitral inflow propagation directly reflects the rate of left ventricular relaxation appears secure because the combined results of the aforementioned three studies include patients with various cardiac diseases, normal and enlarged ventricles, normal and increased filling pressures and various mitral filling patterns. Furthermore, the methods used for measuring the rate of flow propagation were somewhat different in each study, yet similar results were found. In retrospect, the hysteresis between mitral flow velocity patterns and mitral flow propagation is not surprising because pulsed wave Doppler shows the left ventricular filling pattern at a single location only, whereas the color M-mode technique has the ability to visualize the propagation of flow along the entire length of the ventricle throughout diastole.

The technique proposed by Takatsuji et al. (35) of measuring the rate of flow propagation by shifting the color baseline to identify the point at which mitral inflow velocity decreases to 70% of its peak value appears to be a simple and reproducible method that could be easily performed by most echocardiographic laboratories. However, as with mitral and pulmonary venous flow velocity curves themselves, further study will be necessary to determine the full clinical utility and limitations of this new technique. Many inviting opportunities for immediate research are apparent. For instance, what is the best method of measuring the velocity of flow propagation, and what are the basic mechanisms in regional left ventricular pressure differences that correlate with these results?

At the current time, clinically useful information about diastolic filling of the heart can be elicited from two-dimensional echocardiography (33), mitral and pulmonary venous flow velocities (23,32) and respiratory changes in right- and left-sided flow (38,39). However, there still remains much to be learned about the noninvasive assessment of left ventricular diastolic function. With new methods such as those proposed by Brun et al. (36), Stugaard et al. (37) and Takatsuji et al. (35), the goal of practical Doppler echocardiographic methods to noninvasively assess left ventricular diastolic function and filling pressures continues to draw nearer.

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