Diastolic Dysfunction Beyond Distensibility
Adverse Effects of Ventricular Dilatation

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In order for the left ventricle (LV) to function as an effective pump, it must not only be able to empty but also to fill without requiring an elevated left atrial pressure. Furthermore, the stroke volume must be able to increase in response to stress, such as exercise, without much increase in left atrial pressure. Thus, LV diastolic function is an important determinant of cardiac performance.

Diastolic function has conventionally been assessed on the basis of the LV end-diastolic pressure-volume relation (Figure 1). A shift of this curve upward and to the left (curve A, Figure 1) has been considered to be the hallmark of diastolic dysfunction. In this situation, each LV end-diastolic volume is associated with a higher end-diastolic pressure, and therefore, the ventricle is less distensible.

In contrast, in dilated cardiomyopathy, the LV end-diastolic pressure-volume relation is shifted substantially to the right (curve B, Figure 1). In this situation, each volume is associated with a lower pressure; thus, the ventricle is more distensible. This has been interpreted as indicating there is enhanced diastolic function. However, patients with dilated cardiomyopathy have abnormal LV filling dynamics, elevated left atrial pressure, and an inability to increase stroke volume without further elevation of left atrial pressure. The severity of heart failure and prognosis are related to the severity of the filling abnormalities regardless of ejection fraction.

Why are measures of LV diastolic function so abnormal in a dilated ventricle with enhanced distensibility? Is this merely a manifestation of overfilling of the LV that has displaced the ventricle and makes it more distensible? This has been interpreted as indicating there is enhanced diastolic function. However, patients with dilated cardiomyopathy have abnormal LV filling dynamics, elevated left atrial pressure, and an inability to increase stroke volume without further elevation of left atrial pressure. The severity of heart failure and prognosis are related to the severity of the filling abnormalities regardless of ejection fraction.

The rate of early LV filling is determined by the pressure gradient from the left atrium to the LV apex. Although peak filling occurs after the peak pressure gradient, the 2 are closely related. The lower the early diastolic LV pressures, the greater the gradient for filling, which allows the heart to function at low left atrial pressures. Furthermore, the ability to decrease LV early diastolic pressures in response to stress allows an increase in LV stroke volume without much increase in left atrial pressure. This ability to increase LV filling without an increase in left atrial pressure is reduced or absent in heart failure.

After the filling of the LV begins, the pressure gradient from the left atrium to the LV apex decreases and then transiently reverses. The reversed mitral valve pressure gradient decelerates and then stops the rapid flow of blood into the LV early in diastole. The time for flow deceleration is determined predominantly by LV chamber stiffness and provides a noninvasive measure of stiffness.

During the midportion of diastole (diastasis), the pressure in the left atrium and LV equilibrates, and mitral flow nearly ceases. Late in diastole, atrial contraction produces a second left atrium-to-LV pressure gradient that again propels blood into the LV. After atrial systole, as the left atrium relaxes, its pressure decreases below LV pressure, which causes the mitral valve to begin closing. The onset of ventricular systole produces a rapid increase in LV pressure that seals the mitral valve and ends diastole. Under normal circumstances, more than two thirds of the stroke volume enters the LV during early diastole.
Although early diastolic LV filling can be evaluated from the mitral valve inflow velocity assessed by Doppler echocardiography, these measurements are influenced not only by LV diastolic properties but also by left atrial pressure. In contrast, tissue Doppler measurement of mitral annular velocity and color M-mode measurement of the velocity of propagation of mitral inflow to the apex are much less load sensitive. Because the position of the apex of the LV remains relatively constant during diastole, the rate of expansion of the ventricle in the long axis can be assessed by the velocity of the mitral annulus away from the apex. Peak early diastolic mitral annular velocity provides a relatively load-insensitive measure of LV relaxation.\(^{15,16}\)

Color M-mode imaging performed from the apex provides a temporal and spatial map of the velocities of blood flow in early diastole along the long axis of the LV. Thomas and colleagues\(^{17,18}\) first recognized that because blood flow is imaged along a streamline, the Euler equation applies. This is a differential equation that relates the rate of change of pressure over distance to the rates of change of velocity with respect to time and distance. Thus, integration of the Euler equation using the velocity, distance, and time information contained in the color M-mode provides a noninvasive measurement of the diastolic intraventricular pressure gradient generated between the base and the apex during early diastole. The accuracy of this calculation has been demonstrated in normal animals\(^{3,17}\) and in patients with hypertrophic cardiomyopathy.\(^{10}\) Rovner et al\(^ {11}\) used this technique to demonstrate that the early diastolic base-to-apex pressure gradient is reduced in patients with hypertrophic cardiomyopathy and is improved by septal ablation.

Yotti et al\(^ {3}\) have now used this technique to noninvasively determine the early diastolic intraventricular pressure gradients in healthy subjects and in patients with dilated cardiomyopathies. In healthy subjects, they observed a progressive early diastolic pressure gradient from the base to the apex. The peak total gradient was \(2.5 \pm 0.8\) mm Hg. This pressure gradient, which accelerates blood to the apex, is reduced by \(\approx 50\%\) in patients with dilated cardiomyopathies. Furthermore, they found that dobutamine increased the gradient in healthy individuals, but the response was impaired in dilated cardiomyopathy.

Is it necessary to solve the differential Euler equation and calculate the intraventricular pressure gradient to recognize impaired diastolic suction? The reduced and delayed mitral annular velocity and the diminished velocity of flow propagation seen on color M-mode convey the same information.\(^ {15}\) Although calculation of the intraventricular pressure gradient is an important research tool, further study is needed to understand whether the intraventricular pressure gradient provides additional clinically important information.

Yotti et al\(^ {3}\) extended their study by using the Euler equation to investigate the mechanisms of the reduced diastolic pressure gradient in dilated cardiomyopathy. The Euler equation relates the pressure gradient to inertial acceleration and convective deceleration. Inertial acceleration is the change in velocity with respect to time, whereas convective deceleration is proportional to the reduction in velocity with respect to distance.\(^ {15}\) Convective deceleration would be expected to be increased in dilated ventricles because of divergence of the blood flow away from the longitudinal axis of the ventricle, forming vortices (Figure 2).\(^ {19,20}\) Such an increase in convective deceleration would decrease the intraventricular pressure gradient.

In fact, Yotti et al\(^ {3}\) found that the intraventricular diastolic pressure gradient was reduced in dilated cardiomyopathy because of both impaired inertial acceleration and enhanced convective deceleration. The reduced inertial acceleration presumably was the result of impaired elastic recoil. The amount of convective deceleration was proportional to the ventricular-annular disproportion; the more dilated the ventricle, the greater the convective deceleration. These findings are consistent with the theoretical considerations of Pasipoularides et al\(^ {19,20}\) and their observations in the right ventricle. The increased convective deceleration in dilated cardiomyopathy is also consistent with the observation that the velocity of longitudinal expansion, measured by tissue Doppler, is not only reduced but delayed in.
experimental animals and patients with substantial ventricular dysfunction.\textsuperscript{15,16} Thus, the dilated, hypocontractile ventricle produces a lower intraventricular pressure gradient in early diastole as the result of both reduced elastic recoil and increased convective deceleration. The increased convective deceleration in a dilated ventricle may also diminish the ability of the LV to augment the filling in response to stress.

In conclusion, the study by Yotti et al\textsuperscript{3} suggests that ventricular dilatation itself impairs diastolic filling by enhancing convective deceleration. This reduces the ability of the ventricle to generate a diastolic intraventricular pressure gradient. Thus, adverse ventricular remodeling impairs not only LV systolic function but also LV diastolic filling. In patients with dilated cardiomyopathies, left atrial pressure is elevated, and LV filling is impaired because of slowed relaxation, reduced elastic recoil, displacement onto a stiff portion of the LV end-diastolic pressure-volume relation, and impairment of filling from the ventricular dilatation itself. Thus, despite the enhanced passive distensibility, the dilated LV has substantial diastolic dysfunction.

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Disclosure
Dr. Little is a consultant to CorAssist Cardiovascular, Ltd., which is developing a device to increase ventricular recoil.

References

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