EDITORIAL COMMENT

Hypertrophic Cardiomyopathy and Diastolic Dysfunction*

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Hypertrophic cardiomyopathy (HCM) is a disease state with characteristic pathologic changes most likely to result in abnormalities of diastolic function. Indeed, HCM may well be considered a “poster child” for diastolic dysfunction, because pronounced ventricular hypertrophy is associated with a reduced left ventricular (LV) cavity. The pressure-volume relationship would almost certainly be shifted, resulting in a steeper rise in pressure for a given increase in filling volume. The symptoms in nonobstructive HCM cases are generally attributed to abnormal diastolic function. It has proved far more difficult to measure diastolic function than to conceptualize it.

Normal diastolic function may be defined in terms of pressure-volume relationship, such that physiologic variations in filling are not associated with elevated end-diastolic or filling pressures. Although it is technically possible to continuously measure high-fidelity pressures and intracavitary volumes using specialized invasive approaches, their use is limited to investigational studies in few laboratories. Hence, noninvasive measures of diastolic function are necessary for applications in mainstream clinical settings.

Ventricular diastole as defined by Wiggers is composed of isovolumic relaxation phase, rapid filling phase, diastasis, and atrial systolic filling period. These time periods are based on timing of rates and mechanisms of ventricular filling. These are influenced by complex muscle mechanics that include active myofiber relaxation (or lengthening), elastic recoil, atrial filling pressures at moment of atrioventricular valve opening (i.e., atrial “V” wave), myocardial stiffness, and force and timing of atrial contraction. Thus, conventional spectral Doppler parameters of diastolic filling function based on mitral valve inflow velocity patterns, described in terms of “impaired relaxation pattern,” “pseudo normal filling pattern,” and “restrictive pattern” are too simplistic and subject to a number of physiologic or functional influences. For example, impaired relaxation pattern of mitral inflow observed in association with increased myocardial stiffness, such as hypertrophy or infiltration or replacement fibrosis, is also influenced by rate of active relaxation and by magnitude of atrial pressure (i.e., atrial pressure-volume relationship). The so-called restrictive pattern is indicative of high left atrial (LA) pressures and should be better designated as “high filling pressure pattern.” The pulmonary venous flow pattern has been used as a rough gauge of LA pressure. These noninvasive estimates of LA pressures are shown to be accurate only in presence of depressed LV systolic function. Nishimura et al. (1) have reported that mitral flow velocity curves cannot be used reliably to reflect filling pressures in patients with HCM. Furthermore, attempts to correlate exercise capacity with Doppler indices of diastolic function have not been successful (2–5). Tissue Doppler imaging (TDI) of mitral annulus motion with the transducer placed at the apex has also been proposed as a load-independent parameter of diastolic function. In clinical practice, the velocity of annular motion in one dimension obtained from the apex, although useful, is not consistently reliable.

In this issue of the Journal, Kato et al. (6) report an approach to directly measure myocardial velocity gradient (MVG), defined as the difference in myocardial velocity between the endocardium and the epicardium divided by wall thickness. This measure of diastolic thinning was first reported by Fleming et al. (7) in 1994 as being somewhat insensitive to preload or atrial filling pressures. The present report compares hemodynamic parameters obtained with high-fidelity pressure recordings, traditional Doppler parameters of filling, and peak negative MVG in 36 patients with nonobstructive HCM with 26 age-matched controls studied for atypical chest pain and found to be free from disease (i.e., normal subjects). The peak negative MVG coincided with the initial phase of early filling, was significantly reduced in HCM, and was inversely correlated with LV end-diastolic pressure, pulmonary artery wedge pressure, and tau. The authors conclude that peak negative MVG is a novel indicator of auxotonic relaxation, which follows isovolumic relaxation, with filling occurring at variable ventricular pressures. They suggest that this index should prove useful in predicting diastolic dysfunction characterized by increased stiffness and prolonged active relaxation.

There are a few concerns with these conclusions. The initial phase of filling is influenced by active relaxation, elastic recoil, myocardial stiffness, and LA pressure at the time of mitral valve opening (i.e., preload). Because the peak negative MVG correlated with preload (i.e., pulmonary artery wedge pressure), it is unlikely to be independent of preload. Furthermore, because active relaxation and myocardial stiffness are subject to variable influences, peak negative MVG cannot be viewed as a “pure” measure of diastolic function. Active relaxation may be influenced by heart rate, catecholamines, and autonomic influences in addition to underlying hypertrophy or ischemia. Thus, it is unlikely that this measure would provide a purer or more accurate assessment of diastolic dysfunction in HCM. Further studies are needed to test if alterations in preload,
heart rate, or catecholamines affect this measure. It appears that a search for a reliable and “pure” noninvasive index of LV diastolic function as exemplified by a steep pressure-volume relationship must continue. In the meanwhile, peak negative MVG may serve as a parameter in the clinical study of diastole, in addition to mitral inflow velocities, pulmonary venous flow velocities, and TDI of the mitral annulus.

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