

**Editorial Comment**

Noninvasive Analysis of Ventricular Diastolic Performance: In Quest of a Clinical Tool*

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Since Hammermeister and Warbasse (1) reported a reduction in the rate of early diastolic left ventricular volume expansion in certain cardiac disease states, clinicians have attempted to replicate this work using noninvasive imaging methodologies. This field has been fueled by the recent publication of reports (2-5) documenting a high incidence and sometimes severe degree of congestive heart failure due to diastolic ventricular dysfunction.

**Noninvasive evaluation of ventricular diastolic function.**

Many clinical studies of diastolic performance have attempted to evaluate ventricular relaxation as reflected by peak rates of left ventricular filling. An early example of this (6,7) was the measurement of left ventricular radial lengthening and septal and posterior wall thinning using computer digitization of the M-mode echocardiogram. The left atrial emptying index, a simple M-mode observation of posterior aortic root motion (8), was the first noninvasive variable to describe ventricular filling abnormalities in diastolic congestive heart failure (2). Radionuclide ventriculography (9,10) and, more recently, transmittal pulsed Doppler ultrasound (11) have been used to portray left ventricular filling in volumetric terms.

The various noninvasive imaging techniques all possess particular advantages and limitations. For example, whereas digitized M-mode echocardiography is the only modality capable of determining wall thinning rates, it suffers from an intrinsically regional view of the heart that makes it inappropriate for evaluation of segmental coronary artery disease. Radionuclide ventriculography, while providing superior assessment of global ventricular function, does not possess the temporal resolution of Doppler and M-mode techniques.

**Clinical validation of available techniques.**

Clinical validation of these methodologies has enjoyed mixed success and has been based largely on correlative studies. In one of the few hemodynamic analyses, Magorien et al. (12) found a weak but significant correlation between an invasive index of ventricular relaxation, the peak rate of ventricular pressure decay (-dP/dT), and radionuclide peak ventricular filling rate. Validation of digitized M-mode and pulsed Doppler echocardiographic with contrast ventriculographic filling rates has also been performed (13,14). Unfortunately, the comparison of noninvasive imaging techniques with each other has been less impressive particularly in regard to peak filling rate (15-18). This is not surprising when one considers the disparity in normalization indexes, sampling rates and interstudy performance delays involved in some of these studies. In addition, attempts to correlate dissimilar filling variables may also have contributed to the sometimes disappointing results. This latter point is supported by the fact that the techniques compare favorably when identical variables such as degree of fractional filling during early diastole, atrial systole or the ratio of early to late diastolic filling are measured (15).

Another significant issue that needs to be addressed is the choice of filling rate normalization variables in diastolic function assessment. In particular, the effects of age, heart rate, ventricular preload and afterload should be accounted for in any serious investigation of ventricular filling. Whereas a volumetric reference standard of filling rate normalization has never been established, most previous reports (6,8-10) have utilized indexes of end-diastolic or instantaneous volume for this purpose. Hammermeister and Warbasse (1) observed strong correlations between peak filling rate and both ventricular stroke volume and end-diastolic volume in normal subjects, suggesting that either of these values may provide for adequate volumetric normalization. However, the other covariates, such as age, heart rate and so forth, need to be accounted for as well.

**Doppler-derived variables of filling rate and stroke volume.**

In this issue of the Journal, Bowman et al. (19) present an innovative Doppler-based approach to determine normalized peak filling rate. By assuming that the annular cross-sectional area is the same during early peak velocity and throughout diastole, the peak filling rate normalized to integrated mitral inflow velocity can be derived without actually determining the mitral annular area. Because the shape as well as the annular area may change during diastole (20), this approach has an inherent, though presumably
small, error as the authors have noted. This new variable is compared with the peak filling rate normalized to stroke counts as determined by scintigraphy. Whereas these two methods are usually related they may not always be strictly comparable, as in aortic regurgitation, for example, where stroke count determination will overestimate effective forward stroke volume. Therefore, the validity of this comparison is open to question in certain situations.

A major advantage of this new method is its elimination of the Doppler technique’s dependence on two-dimensional echocardiography for determination of mitral annular area and diastolic ventricular dimension (the latter for volumetric normalization). In addition, unlike the ratio of peak early velocity to peak atrial velocity that varied with sample volume location, the peak filling rate normalized to integrated mitral inflow velocity was not influenced by the position of the sample volume. Finally, the authors (19) have, for the first time, provided convincing evidence that the Doppler and radionuclide techniques correlate well in measuring the peak ventricular filling rate. This is relevant because pulsed Doppler echocardiography is easier to perform and analyze and is generally more available to the practicing cardiologist than is its radionuclide counterpart.

Despite the impressive intermethod correlation detailed in this report (19), several extremely important caveats must be heeded. First, because the authors failed to demonstrate a significant correlation between the two methods of radionuclide normalization (diastolic counts versus stroke counts), it cannot be assumed that prior studies relying on the former method can provide clinical validation of the latter. In addition, ventricular diastolic function is a complex process that cannot be adequately characterized by a single measurement. Assessment of peak filling rate in isolation fails to address the isovolumic relaxation and atrial systolic phases of diastole that may have clinical relevance. Also, peak filling rate may sometimes be independent of another significant component of diastolic performance: ventricular compliance or its reciprocal, chamber stiffness. With the present state of the art methods, evaluation of these variables requires cardiac catheterization for the generation of pressure-volume curves. Although there may be a relation between ventricular relaxation and compliance, the terms are hardly synonymous.

Ventricular filling rate to assess ventricular relaxation. Ishida et al. (21) have recently recognized a potential fundamental flaw affecting many of the current approaches to ventricular filling analysis by demonstrating a direct relation between peak filling rate and transmural pressure gradient. Thus the peak filling rate is established not only by the rate of left ventricular relaxation but also by atrial pressure. Atrial pressure is dependent on atrial and pulmonary venous compliance and atrial volume (22). Therefore, although it is tempting to use filling rates to assess ventricular relaxation, what is actually measured may relate more to changes in atrial rather than ventricular function. This is of particular concern when using changes in peak filling rates to assess the efficacy of drug interventions in the setting of diastolic dysfunction. For example, administration of a calcium channel blocking agent might result in an increased peak rate of left ventricular filling, which might be due to enhancement of ventricular relaxation, but could also result from atrial systolic poisoning. If the latter occurred, resultant high residual atrial and pulmonary venous volumes could lead to increased atrial pressure with consequent elevation of peak filling rate.

Conclusions. It is clear then that, despite current interest in the noninvasive analysis of left ventricular filling, further investigation is required before the imaging variables discussed here can be accepted on a clinical basis. Although noninvasive imaging methodologies such as pulsed Doppler echocardiography are relatively easy to perform and are widely available, their use in the evaluation of diastolic function should, at present, be limited to the area of clinical investigation. Premature acceptance of these techniques before their rigorous evaluation and validation may only serve to damage the credibility of potentially useful, future clinical tools.

References


