Quantitation of mitral annular oscillations and longitudinal “ringing” of the left ventricle: a new window into longitudinal diastolic function

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Riordan, Matt M., and Sándor J. Kovács. Quantitation of mitral annular oscillations and longitudinal “ringing” of the left ventricle: a new window into longitudinal diastolic function. J Appl Physiol 100: 112–119, 2006. First published September 8, 2005; doi:10.1152/japplphysiol.00844.2005.—For diastolic function (DF) quantification, transmitral flow velocity has been characterized in terms of the geometric features of a triangle (heights, widths, areas, durations) approximating the E-wave contour, whereas mitral annular velocity has only been characterized by E’-wave peak amplitude. The fact that E-waves convey global DF information, whereas annular E’-waves provide longitudinal DF information, has not been fully characterized, nor has the physiological legitimacy of combining fluid motion (E)- and tissue motion (E’)-derived measurements into routinely used indexes (E/E’) been fully elucidated. To place these Doppler echo measurements on a firmer causal, physiological, and clinical basis, we examined features of the E’-wave (and annular motion in general), including timing, amplitude, duration, and contour (shape), in kinematic terms. We derive longitudinal rather than global indexes of stiffness and relaxation of the left ventricle and explain the observed difference between E- and E’-wave durations. On the basis of the close agreement between model prediction and E’-wave contour for subjects having normal physiology, we propose damped harmonic oscillation as the proper paradigm in which to view and analyze the motion of the mitral annulus during early filling. Novel, longitudinal indexes of left ventricular stiffness, relaxation, viscosity, and stored (end-systolic) elastic strain can be determined from the E’-wave (and any subsequent waves) by modeling annular motion during early filling as damped harmonic oscillation. A subgroup exploratory analysis conducted in diabetic subjects (n = 9) and nondiabetic controls (n = 12) indicates that longitudinal DF indexes differentiate between these groups on the basis of longitudinal damping (P < 0.025) and longitudinal stored elastic strain (P < 0.005).

Doppler tissue imaging; mitral annulus; echocardiography; E’-wave; diabetes

Diastolic heart failure, in contrast to systolic heart failure, commonly refers to heart failure with a preserved ejection fraction (38, 51). Because of its prevalence, this form of heart failure is becoming increasingly recognized (37) and was the diagnosis in up to 49% of heart failure admissions (9). Diagnosis of diastolic dysfunction and diastolic heart failure is largely empiric and employs a myriad of imaging-based indexes, relies on subjective clinical signs and symptoms of heart failure in the setting of a normal left ventricular (LV) ejection fraction (LVEF), and lacks both a firm conceptual/physiological basis from which imaging-based indexes have been derived and in vivo validation. The clinical and physiological picture is further complicated by the onslaught of phenomenological, imaging-based (echo, MRI) longitudinal and azimuthal indexes (annular displacement and velocity, strain, strain rate, torsion, etc.) of LV diastolic function, whose relation to global diastolic function indexes and the physiological “big picture” has not been established (44).

Current state of diastolic function analysis. Noninvasive diastolic function assessment is commonly achieved by two-dimensional pulsed Doppler echocardiography (3, 33). Diastolic function is commonly evaluated via transmitral flow and/or motion of the mitral annulus with or without consideration of the pulmonary vein flow pattern. Selected geometric features of the E- and A-wave [i.e., ratio of peak E-wave to peak A-wave velocity (E/A), deceleration time (DT), etc.] have been correlated with the presence of dysfunction (2); however, their utility in characterizing intrinsic properties of the LV such as relaxation and stiffness is limited, and they neglect the information contained in the entire curvilinear shape of the E-wave contour (19). Furthermore, E/A and similar indexes are load dependent (3).

Doppler tissue imaging (DTI) has more recently been used to aid in diastolic function evaluation (41, 42). With the sample volume positioned at the (septal or lateral) mitral annulus, continuous annular velocity (E’) can be measured. Because the apical epicardium remains fixed relative to sternal structures, E’ is a direct measurement of the rate of change of LV dimension in the longitudinal direction (i.e., E’ = dLv/dt, where Lv denotes the long-axis dimension of the chamber and t is time). During early rapid filling, the E’-wave is inscribed, and during atrial filling, the A’-wave is inscribed. Myocardial (tissue) motion is less load dependent than transmitral (fluid) flow (15, 31, 32). Currently, the only DTI feature measured is the peak amplitude of the E’-wave, and the only DTI-associated index with widespread use is E/E’, even though the peaks of E- and E’-waves are not simultaneous (26). Commonly measured aspects of the E-wave such as acceleration time (AT), DT, E-wave duration, and velocity-time integral (VTI), and the physiological information they convey have not been integrated into analysis of the E’-wave specifically or annular motion in general.

Because all ventricles initiate filling by mechanical suction, the ability to mathematically predict E-wave contours from a kinematic model is one way to state the diastolic function problem (25). This approach, termed the parameterized dia-

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stolic filling (PDF) formalism, provides global indexes of diastolic function by using the clinical E-wave contour as input and computes the (unique) spring constant (\( k \)), initial spring displacement (\( x_0 \)), and damping constant (\( c \)) of an equivalent simple harmonic oscillator (SHO). The physiological analogs of \( x_0, c, \) and \( k \) are the VTI of the E-wave, chamber viscosity and relaxation, and chamber stiffness, respectively (23). The model has been extensively validated and applied in numerous clinical scenarios characterized by hypertension (24), diabetes (11, 40), and heart failure (30, 39), as well as peak transmitral (atrioventricular) pressure gradient characterization (5).

By utilizing idealized ventricular geometry and the “constant volume attribute” (8) of the four-chambered (and two-chambered) heart to relate fluid (E-wave) to tissue motion (E’-wave), the empirically observed linear correlation between E/E’ and left ventricular end-diastolic pressure (LVEDP) has been causally elucidated (26). However, no other prior attempts have been made to mathematically predict the contour and other properties of the E’-wave either in physiological or kinematic terms.

The kinematics of longitudinal motion of the mitral annulus can be appreciated by considering an idealized geometry of simultaneous radial and longitudinal expansion. During transmitral flow, the LV wall thins and the endocardium moves toward the epicardium [shown by cine-MRI short-axis slices to be relatively fixed (4)]. Because of the incompressibility of the LV wall and the (within ~5%) constant-volume attribute of the normal four-chambered heart [i.e., reciprocating atrial and ventricular volumes during systole and diastole (8)], the radial motion (wall thinning) must be accompanied by simultaneous longitudinal mitral annular motion toward the LA (the epicardial apex remains fixed relative to sternal structures) (26). For simplicity and ease of visualization, the geometric and volumetric aspects of mitral annular motion and transmitral flow during early rapid filling can be modeled in terms of a right circular cylinder having fixed height and fixed outer (epicardial) dimension. It is subdivided into atrial and ventricular segments having radius \( r \) and lengths \( L_A \) and \( L_V \), respectively (Fig. 1). On the basis of this geometric approximation, LV volume is described by the following expression:

\[
V = \pi r^2 L_v
\]

Because LV tissue volume is conserved, the time rate of change of LV chamber (blood) volume can therefore be expressed as the combination of the radial and longitudinal rates of change in epicardial chamber dimensions:

\[
\frac{dV}{dt} = 2\pi r L_v \left( \frac{dr}{dt} \right) + \pi r^2 \frac{dL_v}{dt}
\]

The first term accounts for the rate of epicardial displacement in the radial (short-axis) dimension, which, because the epicardial dimension is essentially constant throughout filling (26) in normal subjects, is deemed negligible compared with the longitudinal rate. A recent cardiac MRI study (48) has shown that the ~5% decrease in the volume enclosed by the pericardium during mechanical systole is primarily due to a decrease in the radial dimension of the pericardial/epicardial contour of the LV (the “crescent effect”) and is recovered during the E-wave (and pulmonary vein D-wave volume) primarily through radial displacement of the epicardial surface. Consequently, expansion of the LV in the longitudinal (long-axis) dimension with concomitant wall thinning is the dominant kinematic degree of freedom during filling in the normal heart. The second term on the right side incorporates the longitudinal velocity of the mitral annulus, \( dL_v/dt \), which is routinely measured by DTI as E’. Because the sum of left atrial and LV volumes is (nearly) constant throughout the cardiac cycle (7), the relation of the E’-wave to the E-wave (see Fig. 1) can be expressed as:

\[
E' = E \cdot \frac{[MVA/(A - MVA)]}{V/dt}
\]

where MVA denotes the effective mitral valve area, \( (A - MVA) \) represents the effective cross-sectional area of the mitral annulus, and \( E' \) and \( E \) denote the instantaneous mitral annular and transmitral flow velocities, respectively, as functions of time (for simplicity, septal and lateral annular velocities are approximated as equal and any azimuthal variations are deemed small) (26). Hence, as Eq. 3 indicates, the legitimacy of E/E’ as an index of diastolic function is a direct consequence of the (near) constant-volume property of the two-chambered heart and the fact that tissue and blood are incompressible (8, 26).

Because E-wave contours are predicted by the kinematics of SHO motion to good accuracy, and because the two-chambered heart is a constant volume pump to very good approximation, we hypothesized that the E’-wave contour must similarly obey the kinematics of SHO motion. We therefore analyzed mitral annular E’-waves in accordance with the kinematic rule of damped harmonic oscillation and determined longitudinal indexes of chamber stiffness and viscosity/relaxation. Because annular motion is not constrained by a rectifier, requiring motion in one direction only (in contrast to transmitral blood flow, which is rectified by closing of the mitral valve after the E-wave, during diastasis), it may oscillate about a baseline until it is damped out. Annular motion also permits
testing of the model-predicted phenomenon of diastolic “ringing” of the chamber in the longitudinal direction and assessment of its physiological significance. To determine utility of longitudinal diastolic function indexes for phenotypic characterization of (preclinical) diabetic cardiomyopathy in subjects with normal LVEF, we analyzed E’-waves in diabetic and nondiabetic controls and carried out a subgroup exploratory analysis by comparing longitudinal diastolic function index values between the groups.

METHODS

Patient selection. A sample of 21 subjects, 12 nondiabetic and 9 diabetic, was selected from an existing database (27) of simultaneous high-fidelity (Millar) ventricular pressure, Doppler echocardiographic recordings of transmitral flow, and DTI recordings of the lateral mitral annulus. Subjects’ ages ranged from 35 to 75 yr (61.5 ± 10.6 yr). The groups did not differ significantly with respect to age, height, weight, race, gender, heart rate, or LVEF. Inclusion criteria were LVEDP < 18 mmHg. LVEF ≥ 55%, 1 < E/A < 2, normotensive, normal sinus rhythm, clearly discernible E-waves and annular velocities/oscillations, and normal valvular function. Subjects having comorbidities including, but not limited to, previous myocardial infarction, wall-motion abnormalities on ventriculography, active ischemia, cardiomyopathy, congestive heart failure, or renal insufficiency were excluded. The controls were chosen with the intent to match as closely as possible the demographics of the diabetic group, including race, sex, age, height, weight, and history of smoking. It is also notable that all nondiabetic subjects had normal D Ts (≤220 ms) (31) and normal time constants of isovolumic relaxation (<50 ms). Ecllusive cardiac catheterization was performed in all subjects at the request of their referring physician on the basis of suspected coronary artery disease (CAD), and a comparable percentage of subjects in the diabetic (33%) and normal group (25%) had presence of angiographically diagnosed CAD. All subjects gave informed consent in accordance with a protocol approved by the Washington University Medical Center Human Studies committee before data acquisition.

Data acquisition. The methodology has been previously described (27). Briefly, immediately before cardiac catheterization, a full two-dimensional/Doppler examination is performed in the catheterization laboratory. Transmitral flow velocity acquisition was performed simultaneously with LV pressure recording as previously described (27). From the known relation between spring constant and period of oscillation, longitudinal stiffness can be derived from E’-wave duration (E’_wave) as k’ = π/E’_wave^2. This requires neither a sinusoidal E’-wave contour nor the presence of an E’-wave. If the E’-wave exists, longitudinal relaxation (damping) can be determined from the equation c’ = –2[ln(E’_peak/E’_peak)]/(τ_0 – τ_0) by fitting a decaying exponential from the peak of the E’-wave to the peak of the E’-wave. Alternatively, if the E’-wave is absent, c’ may be approximated by considering the E’-wave as a critically damped sine wave. As a result, c’ may be determined from k’ by the equation c’ = 2k’/4k’. The critically damped assumption is preferable to an overdamped assumption in these cases because it determines the value of c’ in terms of k’ as a specific number, whereas the overdamped assumption only provides a lower limit on possible values for c’. Although we recognize that this assumption has limitations, the E’-waves we observed that were not followed by an E’-wave did not appear to be more than slightly overdamped, if at all, giving us confidence that the critically damped approximation is reasonable. Accordingly, the presence of the E’-wave and subsequent oscillations that can be well fit by damped sinusoids is not essential for the derivation of indexes of longitudinal relaxation and stiffness.

RESULTS

We note that the subgroup exploratory analysis of diabetic subjects and nondiabetic controls was conducted after the
methodological approach to analyzing longitudinal diastolic function and characterizing “longitudinal ringing” of the ventricle had been developed. Assessment of the clinical utility of longitudinal indexes of diastolic function in these groups was a logical next step considering that differences in global parameters have been previously reported in diabetic subjects vs. nondiabetic controls (humans and animals) by applying the PDF formalism to the Doppler E-wave (11, 40). As such, the group of diabetic subjects and nondiabetic controls discussed in this study represent the only groups in which we assessed longitudinal diastolic function.

The values of all DTI measurements, parameters, and indexes analyzed for both groups are shown in Table 1. Although neither E’- or E”-wave peak amplitude nor E’/E” ratio was significantly different between the diabetic and control subjects, the longitudinal damping parameter c’ obtained by analysis of the E’- and E”-waves was significantly greater in the diabetic group (P < 0.025). Interestingly, the separation in time between the E’- and E”-waves peaks (tE’− tE”), a component of the expression for longitudinal damping, was significantly less in the diabetic group (P < 0.024). The parameter x′₀ (P = 0.005) and index 1/2k’x′₀² (P = 0.025) were also significantly less in the diabetic subjects. The values of k’, k’x′₀, and β’ were not significantly different between groups, although k’ was close to significance (P = 0.10). Intraobserver variation was assessed by twice fitting five representative E’-waves of varying shapes from both the normal and diabetic group. The coefficients of variation (6) for c’, k’, x′₀, and tE’− tE”, from these 10 fits were determined to be 2.5, 5.1, 6.5, and 1.5%, respectively. The maximum variations in c’, k’, x′₀, and tE’− tE” for these fits were 5.3, 7.8, 11.3, and 4.3%, respectively.

**DISCUSSION**

Cardiac anatomy and physiology. The potential clinical importance of the echocardiographic assessment of mitral annulus motion was first suggested by Zaky et al. (50), who also noted that the annular motion often exhibits a reversal in the chamber wall causes the layers of the LV wall to untwist and the chamber to expand in the longitudinal direction, manifesting as motion of the mitral annulus (the apex remains essentially fixed in space). End-systolic strain energy stored in the left atrial wall and in the LV (titin, extracellular matrix) causes apical displacement of the roots of the great vessels, etc. Because transmural flow can be modeled in analogy to the kinematics of a recoiling spring (4, 23), whose motion is coupled to the motion of the annulus according to the approximate constant volume property of the left atrium and LV as described by Eq. 3, it is reasonable to model the annular velocity contour as an oscillator. Both annular motion and transmural flow may therefore be described as either underdamped or overdamped oscillations; however, transmural flow is rectified by the closing (coaptation) of the mitral valve (as seen on M-mode images during diastasis), whereas annular motion is not rectified. Examination of DTI displays (for certain patients) often reveals continued oscillation (i.e., ringing of the lateral mitral annulus during early filling); that is, there are one or more oscillations of the annulus relative to the baseline following (and continuous with) the E’-wave, as previously noted (19). These oscillations (which we denote as E’-wave, E”-wave, etc.), like the E’-wave, usually have contours that can be closely approximated by the equation of motion for a damped SHO (Eq. 4). Furthermore, each successive oscillation exhibits a reduced amplitude from the prior oscillation in analogy to the kinematics of underdamped oscillation. Therefore, by modeling these oscillations as those of a damped linear spring released from rest (E’ = 0 at mitral valve opening), it should be possible to derive noninvasive indexes of longitudinal LV stiffness, relaxation (damping), and stored elastic strain from the contour of successive annular oscillations in analogy to the PDF formalism’s fit to transmural flow.

Increased damping in the diabetic heart. Although this study is the first application of the PDF formalism to longitudinal diastolic function of the normal and diabetic human heart, Dent et al. (11) applied the method to E-waves of rats with strepto-

**Table 1. Parameters and indexes derived from DTI**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control Group (n = 12)</th>
<th>Diabetic Group (n = 9)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak E’, cm/s</td>
<td>18.4±2.9</td>
<td>17.6±3.3</td>
<td>P = 0.58</td>
</tr>
<tr>
<td>Peak E”, cm/s</td>
<td>5.4±0.9</td>
<td>5.6±1.4</td>
<td>P = 0.80</td>
</tr>
<tr>
<td>E’/E”</td>
<td>3.44±0.60</td>
<td>3.30±0.44</td>
<td>P = 0.61</td>
</tr>
<tr>
<td>tE’− tE”, ms</td>
<td>131±25</td>
<td>104±24</td>
<td>P &lt; 0.024</td>
</tr>
<tr>
<td>c’, g/s²</td>
<td>19.8±5.6</td>
<td>28.7±11.1</td>
<td>P &lt; 0.025</td>
</tr>
<tr>
<td>k’, g/s²</td>
<td>421±113</td>
<td>516±142</td>
<td>P = 0.10</td>
</tr>
<tr>
<td>x’₀, cm</td>
<td>1.37±0.27</td>
<td>1.02±0.22</td>
<td>P &lt; 0.005</td>
</tr>
<tr>
<td>k’x’₀, dynes/cm</td>
<td>559±151</td>
<td>508±132</td>
<td>P = 0.43</td>
</tr>
<tr>
<td>1/2k’x’₀², ergs</td>
<td>392±129</td>
<td>271±84</td>
<td>P &lt; 0.025</td>
</tr>
<tr>
<td>β’, g/s²</td>
<td>−1.265±397</td>
<td>−1.131±650</td>
<td>P = 0.57</td>
</tr>
</tbody>
</table>

Values are means ± SD. E’ and E” peak amplitudes of E’- and E”-waves, respectively; tE’− tE”, separation in time between E’- and E”-wave peaks; c’, damping constant; k’, spring constant; x’₀, initial displacement of spring before release. *E’-waves were present in 7 of the diabetic subjects. Bold type indicates significance.
zotocin-induced diabetes and Riordan et al. (40) applied it to E-waves of diabetic humans, obtaining similar results. In partial concordance with this study, these investigators obtained significantly higher values for $c$ (global damping), $kx_0$ (force generated by peak atrioventricular pressure gradient), and $1/2kx_0^2$ (stored global strain energy) in their respective diabetic groups compared with non-diabetic controls, whereas no significant differences were observed for $k$ or $x_0$ (although $x_0$ was somewhat close to significance) (11). The index $\beta$ was increased (less negative) in the study of Riordan et al. Although we do not know whether the E-wave-derived parameters $c$ or $x_0$ or index $1/2kx_0^2$ are significantly greater in the diabetic subjects than in their non-diabetic cohorts in this study, the fact that $c'$ (longitudinal damping) is greater in the diabetic group than in the non-diabetic control group suggests that the same, or similar, pathophysiological mechanisms affect both longitudinal and global chamber function during filling in both the animal model of diabetes and the presence of historically established diagnosis of diabetes in normotensive humans. In essence, increased longitudinal damping should translate into increased global damping (as measured via the E-wave contour) under the assumption that damping in the radial dimension does not diminish.

In kinematic terms, the parameter $c'$ represents the lumped viscoelastic (resistive) properties associated with longitudinal expansion of the LV chamber. Its physiological analog includes sources of energy loss that oppose longitudinal motion during filling, which are discussed at length by Dent et al. (11) and Riordan et al. (40). Although $c'$ is influenced by a variety of factors, including blood viscosity, extracellular matrix viscosity, delayed relaxation, dynamic friction associated with sarcomere lengthening, and pericardial effects, the most probable explanation for its increase in the diabetic subjects is likely delayed myocyte relaxation and ventricular remodeling. Impairment of calcium reuptake by the sarcoplasmic reticulum may cause delay and damping in ventricular relaxation. In addition, alteration of LV molecular and cellular properties, manifesting as glycosylation of proteins and collagen and advanced glycosylation end products, is known to occur in the diabetic heart (20). Disorganization of the extracellular matrix has also been reported in the diabetic heart (43, 45).

The decreased values of $x_0$’ (which manifests as the E-wave VTI) and $1/2kx_0^2$ in the diabetic group suggest that the stored longitudinal strain in the myocardium at the end of isovolumic relaxation is less in diabetic subjects. The fact that $k'$ and $k'x_0'$ did not differentiate between groups is due to most of the difference being in $x_0'$ rather than $k'$, which was increased in the diabetic group (but not statistically significant). The decreased $x_0'$ and $1/2kx_0'^2$ in the diabetic subjects is counterintuitive considering that Dent et al. (11) and Riordan et al. (40) reported higher values for $x_0$ and $1/2kx_0^2$ in diabetic rats and humans, respectively. However, it may imply that increased radial strain energy is stored in the presence of increased longitudinal damping in the LV. In other words, radial diastolic function (recoil) may be enhanced as a compensatory mechanism in the presence of impaired longitudinal diastolic function. Future research is in progress to elucidate the relationship between radial and longitudinal diastolic function.

Some of the observed oscillations deviated in shape from damped sinusoidal patterns (Fig. 2B). Although these contours still appear reasonably sinusoidal, they sometimes are marked by a slightly longer AT than DT, slightly elongated (blunted) peaks, and various other features. Although this variation of shapes may in part be due to variation of sample volume location or the (unknown) contribution of torsion, shear, and inhomogeneity of relaxation to annular motion, it underscores that we do not fully understand the detailed (nonlinear) kinematics of annular motion that generate these patterns. However, even if the contours of some oscillations are not exactly sinusoidal, the dominant geometric features of these oscillations, such as amplitudes and durations, may still be used to derive indexes of longitudinal stiffness and relaxation independently of an idealized, piecewise linear spring model. For example, the duration of the E'-wave is effectively a statement of longitudinal stiffness, because the duration of the E'-wave is linearly related to the square root of the tissue stiffness ($m$ is set to 1) in healthy subjects without significant damping (23). Neglecting viscous effects (no damping), LV stiffness has previously been derived from the geometry of the E-wave (DT, specifically) (28). Accordingly, it is reasonable to expect that analysis of the geometric features of annular oscillation waveforms will similarly allow improved characterization of longitudinal stiffness and relaxation in the LV.

In examining the DTI images of other patients in our database, we observed a number of subjects in whom subsequent oscillations of the mitral annulus were nonexistent (only the E'-wave was visible). It should be noted that Isaz et al. (19) also observed normal subjects without oscillations follow-

Fig. 2. A: representative (damped sinusoidal shaped) annular motion pattern from a subject with normal diastolic function with superimposed model fit. E'-wave (oscillation) immediately following E'-wave. Waves are well fit piecewise by the model. Best-fit parameters for E'-wave are $c = 2.2$ g/s, $k = 530$ g/s², $x_0 = 1.0$ cm. Best-fit parameters for E-wave are $c = 18.2$ g/s, $k = 2.970$ g/s², $x_0 = 0.2$ cm. B: nonsinusoidally shaped pattern from a subject with normal diastolic function. Note asymmetric shape of E'-wave and blunt peak of E'-wave. Despite nonsinusoidal shape, geometric features of this nonsinusoidal pattern allow longitudinal indexes of left ventricular stiffness and relaxation to be derived as detailed in the text: $t_{E'} - t_{E''}$ denotes separation in time between E'- and E'-wave peaks. dur, Duration. See text for details.
ing the E'-wave. This absence of additional oscillations (non-ringing) of the mitral annulus in certain subjects with otherwise normal function may convey aspects of LV diastolic function in terms of stiffness and relaxation that have additional physiological correlates. These correlates remain to be fully elucidated. It is likely, however, that loss of the diastolic ringing feature in follow-up studies indicates alteration of diastolic function.

We do not yet know why certain patients exhibit oscillations of the mitral annulus and others do not. However, for every patient we have examined, with or without secondary (E') annular oscillations, relative to the QRS complex as a fiducial marker, the onset of the E- and E'-waves have coincided, although the E'-wave has always terminated before the E-wave (19). Because, for a SHO, \( \omega_0^2 = k/m \) and oscillation duration is \( D = 2\pi/\omega_0 \), stiffness is inversely proportional to E- and E'-wave duration. Because global stiffness \((K_{\text{global}})\) is the sum of parallel elastic elements having radial and longitudinal (anatomical) components (i.e., \( 1/K_{\text{global}} = 1/K_{\text{radial}} + 1/K_{\text{longitudinal}} \)), their algebraic sum requires that longitudinal stiffness be numerically greater than the global stiffness. This is what we observe, because the shorter E'-wave duration implies that the longitudinal stiffness of the LV (as measured by \( k' \)) is greater than its global stiffness \((k)\). Similarly, we predict that that the analog of radial stiffness of the LV should be numerically greater than the global stiffness.

Furthermore, in each of these patients, the E'-wave peaks before the peak of the E-wave (19) and the E'-wave terminates either before or simultaneously with the termination of the E-wave at the mitral valve annulus (Fig. 3). These preliminary observations naturally raise several physiologically and clinically interesting questions such as the following: 1) What is the relationship between longitudinal oscillations and prolonged or shortened DT? 2) Is it possible to have transmitial flow in the absence of longitudinal displacement and still adhere to the constant volume attribute of the heart (i.e., can the LV fill by radial displacement only)? 3) What is the physiological significance of additional oscillations following the E'-wave? 4) What is the role of the atrium in determining the presence or absence of subsequent oscillations?

Limitations. It is possible that the deviation of the shape of the E'-wave and its oscillations from that of a damped sinusoid in some patients may be due to sample volume positioning during DTI. However, neither the position nor the size of the sample volume should affect the existence of annular oscillations.

In this study, only DTI of the lateral annulus was obtained, rather than the septal, anterior, or posterior aspects because, in general, it is echocardiographically easier to localize the sample volume at this location and thereby minimize the likelihood of including tissue (myocardial) velocities. We caution that because of the known saddle shape of the annulus, the motion of its septal or other aspects may differ somewhat from the motion of the lateral annulus. Specifically, other investigators have found that the peak velocity of septal E'-waves is generally lower than that of lateral E'-waves (1, 19, 35). Our prior observations indicate that E' and oscillations of the septal aspect of the annulus are generally of lower amplitude than those of the lateral mitral annulus and sometimes are not observed, even though oscillations of the lateral mitral annulus may be seen in the same subject. Consequently, mitral annular oscillations during early filling are a likely feature of the septal side as well but may be more damped owing to the geometric and kinematic constraints imposed by adjacent structures such as the septum and the aortic root. It is important to note that our modeling approach (the model, equations, methodology of computing parameters, etc.) does not depend on which aspect of the annulus is imaged.

A limitation may be thought to arise from the fact that subjects with catheterization-proven CAD were included. The inclusion of subjects with CAD may affect diastolic filling through ongoing ischemia; however, none of the subjects had critical stenoses, active ischemia, or wall-motion abnormalities as evidenced by normal LVEF by ventriculography. Longitudinal damping and stored strain energy did not significantly differ between subjects with and without CAD, both in the normal and diabetic group, which strongly suggests that the presence of anatomical CAD did not bias our results. When patients with CAD were eliminated from both groups (the groups were still well matched demographically), the significant difference in longitudinal damping was maintained. In addition, we note that patients with other risk factors were excluded to maintain the historically established diagnosis of diabetes as the primary clinical differentiating feature between the two groups.

Unfortunately, the number of years since each diabetic subject had been diagnosed with diabetes was not available. Therefore, we cannot comment on the sensitivity of the longitudinal indexes of diastolic function to duration of diabetes.
In conclusion, by considering diastole in kinematic terms as being governed by the rules of damped oscillatory motion and invoking the (near) constant-volume attribute of the two-chambered heart, it is not only possible to extract model-based global indexes of chamber stiffness and relaxation/viscosity from the E-wave but also to extract analogous indexes accounting for longitudinal diastolic function. Furthermore, for non-rectified motion such as ringing of the annulus, the kinematic paradigm predicts and agrees with observed continued damped oscillations in subjects with normal diastolic function. This approach provides a new quantitative window on the physiology of diastole and offers a kinematic paradigm in which to view, analyze, and predict the motion of the mitral annulus: as damped, sinusoidal waves following (and continuous with) the E’-wave. By modeling the E’-wave according to the motion of a damped SHO, indexes of LV longitudinal stiffness (k’), relaxation/damping (c’), and stored elastic strain (x’0) can be determined. The clinical utility of longitudinal indexes of diastolic function was assessed in a subgroup exploratory analysis. The indexes c’, x’0, and 1/2k’x’02 differentiated between diabetic and non-diabetic subjects, whereas longitudinal diastolic stiffness (k’) did not. In cases in which DTI waveforms are not sufficiently sinusoidal, indexes of longitudinal stiffness and relaxation may still be derived from geometric aspects of the waveforms, such as their amplitudes and durations, as proposed.

This work is a necessary first step in expanding the previous descriptive observations of others (19, 21, 22, 46, 47, 49, 50) in achieving a new longitudinal kinematic diastolic function assessment approach (i.e., a model based on how things move) having practical clinical utility. The approach permits qualitative elucidation of the relationship between global, radial, and longitudinal indexes of diastolic function. By analyzing longitudinal and, later, radial diastolic function as components of global diastolic function, we can begin to understand the effects of certain pathologies (i.e., diabetes, ischemia, hypertrophy, etc.) on radial and longitudinal motion of the LV. Specifically, we can determine whether primarily radial function, longitudinal function, or both are compromised in these cases and the extent to which radial or longitudinal motion compromises for the impairment of the other. These relationships have not yet been elucidated. Future work should aim to account for the nondominant, radial, and azimuthal components of filling to fully characterize the relationship between global diastolic function and that of its components.

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