Peak systolic velocity of mitral annular longitudinal movement measured by pulsed tissue Doppler imaging as an index of global left ventricular contractility

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Seo JS, Kim DH, Kim WJ, Song JM, Kang DH, Song JK. Peak systolic velocity of mitral annular longitudinal movement measured by pulsed tissue Doppler imaging as an index of global left ventricular contractility. Am J Physiol Heart Circ Physiol 298: H1608–H1615, 2010. First published March 5, 2010; doi:10.1152/ajpheart.01231.2009.—We sought to test whether the peak systolic velocity of mitral annular longitudinal movement (S′) measured by pulsed tissue Doppler imaging technique is useful to assess global left ventricular (LV) contractility under various LV inotropic conditions, including regional wall motion abnormality. In addition, the accuracy of S′ relative to LV ejection fraction (EF), a conventional index of LV contractility, and its association with apical rotation, a new index of LV contractility, were also evaluated. We measured S′ at the medial mitral annulus and apical rotation in 11 open-chest anesthetized dogs at eight inotropic stages before and after ligation of either the anterior descending or circumflex coronary artery. Maximal positive dP/dt (dP/dtpeak) was measured using a high-fidelity pressure catheter and used as the standard measure of LV contractility. S′ showed dose-dependent increases and decreases after dobutamine and esmolol infusion, respectively. There was a stronger association between dP/dtpeak and S′ (R² = 0.665, P < 0.001) than between dP/dtpeak and EF (R² = 0.408, P < 0.001), and this trend was more apparent with coronary ligation, regardless of the ligation site. The strength of association between dP/dtpeak and S′ (R² = 0.665) was not different from that between dP/dtpeak and apical rotation (R² = 0.726, P < 0.001). The association between LV EF and S′ was modest (R² = 0.472, P < 0.001), whereas a good association between S′ and apical rotation was observed both with (R² = 0.552, P < 0.001) and without (R² = 0.674, P < 0.001) coronary ligation. S′ is a more sensitive index of global LV contractility than is LV EF, reflecting both LV longitudinal shortening and torsional deformation.

contractility; echocardiography; longitudinal movement; ventricular rotation

Despite early recognition of abundant longitudinal cardiac muscle fibers (31), the function of these longitudinal fibers could not be extensively investigated before successful clinical introduction of echocardiography. Initial M-mode recording of mitral annular descent or excursion reflecting left ventricular (LV) longitudinal shortening during ejection was reported to be a sensitive measure of LV systolic function, and the amplitude of long-axis motion during systole also correlates well with LV ejection fraction (EF) (12, 23, 28). Later, the development of tissue Doppler imaging (TDI) provided an easier way to measure peak systolic velocity of mitral annular longitudinal movement (S′), with S′ found useful in diagnosing global LV systolic dysfunction in many cardiac diseases (2, 4, 8, 16, 20, 27). Moreover, the prognostic implication of S′ has been documented in patients with heart failure, mitral regurgitation, or ischemic heart disease (1, 15, 21, 34, 35). Although S′ measurement by TDI shows great promise in routine clinical practice, several issues must be solved before its widespread clinical adoption. The accuracy of color-coded TDI for measuring annular displacement has been validated by invasive sonomicrometry (6), but the validation of pulsed TDI with respect to other established indexes of LV contractility has not been extensively investigated. In addition, the effect of regional ischemia or regional wall motion abnormality (RWMA) has not been specifically evaluated. Although S′ has been found to show significant correlation with EF, a widely used clinical index of LV systolic function, the accuracy of S′ relative to EF under a wide range of contractility conditions and RWMA has not been investigated extensively. Moreover, the relationship between S′, a measure of LV longitudinal movement, and LV rotation, a new index of LV contractility (9, 14), has not been established. Using an open-chest canine model with and without coronary artery ligation, we sought to determine whether S′ measured by pulsed TDI could be used as a noninvasive quantitative index of contractility under various conditions, including a wide range of LV inotropic status, including RWMA.

METHODS

Animal model. This study was reviewed and approved by the Institutional Animal Care and Use Committee of Asan Institute for Life Sciences, Asan Medical Center. The Committee abides by the Institute of Laboratory Animal Resources guide. Eleven adult mongrel dogs of either sex and an average body weight of 23.5 kg (range 23.0–25.5 kg) were anesthetized with intramuscular injection of atropine sulfate (0.05 mg/kg) and a mixture of zolazepam and tiletamine (7 mg/kg). The dogs were intubated with an endotracheal tube, mechanically ventilated (rate, 15/min; tidal volume 250–300 ml) using oxygen (1.0 l/min), and maintained with enflurane (2–2.5%). The dogs were placed on a water blanket controlled at 38°C. The right femoral artery, left carotid arteries, and the right jugular vein were isolated and cannulated with introducer sheaths. Arterial blood pressure was monitored via a fluid-filled catheter together with a single lead electrocardiogram to an oscilloscopic multichannel recorder. A 5-Fr catheter with dual high-fidelity pressure sensor (Millar Instruments) was advanced after adequate calibration from the left carotid artery to the LV under echocardiographic guidance. The dP/dtpeak, an invasive index of LV contractility, was continuously monitored during the whole experiment. Thoracotomy was done in the right lateral decubitus position for echocardiographic measurement, and pericardium was not opened.

Experimental protocol. A wide range of LV inotropy status was achieved by pharmacological modulation of β-adrenergic receptors

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(14). Each animal was treated with dobutamine (5, 10, and 20 \( \mu g \cdot kg^{-1} \cdot min^{-1} \)) and esmolol (100, 200, 300, and 400 \( \mu g \cdot kg^{-1} \cdot min^{-1} \)) with a 20- to 30-min period of stabilization after each treatment. After obtaining simultaneous hemodynamic and echocardiographic data without coronary ligation, coronary artery ligation was performed by tying a blind stitch over the left anterior descending (LAD, \( n = 6 \)) or left circumflex (LCX, \( n = 5 \)) artery. Hemodynamic (dP/dt) and echocardiographic data were again acquired simultaneously after the treatments described above. RWMA developed immediately after coronary ligation, with data acquired after confirmation of stable LV pressure by a high-fidelity pressure catheter and no change of RWMA by echocardiography. It usually took 10 min to have stable LV pressure and RWMA after coronary ligation.

Echocardiographic recordings and analysis. All echocardiographic examinations were performed with a Vivid 7 ultrasound machine (GE Medical System, Horten, Norway) with a multifrequency transducer (M3S) and second harmonic imaging. LV EF by two-dimensional echocardiography was obtained by the modified Simpson’s method from apical four- and two-chamber views. Pulsed wave TDI was performed by activating the TDI function in the same echocardiographic system. The filter settings were kept low (50 Hz), and gains were adjusted at the minimal optimal level to minimize noise and eliminate the signals produced by transmitral flow. A 6-mm sample volume was used. In the apical four-chamber view, the TDI cursor was placed at the septal side of the mitral annulus (Fig. 1). Speckle tracking imaging technique (14) was used for measurement of apical rotation at the parasternal short-axis plane (Fig. 2). Frame rates (84.8 ± 2.1, range 83.8–88.5 frames/s) and probe frequency (range 3–4 MHz) were adjusted during apnea for better image acquisition. The apical level was defined just proximal to the level with LV cavity obliteration at the end systole. Maximal efforts were made to make the LV as circular as possible. Great care was taken to get a high frame rate without significant loss of two-dimensional image quality by optimizing sector width and image depth. Three consecutive beats were digitally saved in cine loop format for offline analysis with a dedicated software package (EchoPAC workstation 7.0.1; GE Medical System).

LV apical rotation was determined as average angular displacements of six myocardial segments along the central axis (Fig. 2). Offline analyses were performed independently without any knowledge of dP/dt peak or LV EF.

Statistical analysis. Data are expressed as means ± SD or percentages, as appropriate. Linear mixed models were performed to examine the pharmacological effects of \( \beta \)-adrenergic modulation on various physiological parameters, the association between dP/dt peak and non-invasive indexes of LV contractility (\( S’ \), apical rotation, and EF), and
the association among noninvasive indexes. The generalized $R^2$ was used to compare strength of association for each pair of variables, since it measures how much variability of dependent variable is the result of the independent variable (18). To compare the generalized $R^2$ for each linear mixed model with the same dependent variable, we used a bootstrap technique (200 replicates) (3). All statistical analyses were performed with SAS software, version 9.1 (SAS Institute, Cary, NC) and a $P$ value $<0.05$ was considered statistically significant.

Fig. 2. Representative images showing measurement of apical rotation using speckle tracking echocardiography ($A$-$D$) and changes of apical rotation with pharmacological modulation of inotropy and after coronary artery ligation ($E$-$H$). Two-dimensional short-axis views from the beginning ($A$) and to the end ($B$) of ventricular contraction were used for speckle tracking ($C$ and $D$), and apical rotation was determined as average angular displacements of 6 myocardial segments along the central axis. Maximum angle during systole was used as a representative value of apical rotation. $E$: baseline. $F$: 10 g/kg min$^{-1}$ dobutamine. $G$: 200 g/kg min$^{-1}$ esmolol. $H$: LAD artery ligation.

Fig. 3. Inotropic effects on $dP/dt_{peak}$ ($A$ and $B$) and left ventricular (LV) ejection fraction (EF; $C$ and $D$). $A$ and $C$: without coronary ligation. $B$ and $D$: with coronary ligation. Nos. above bars represent the mean value of each variable explained by the y-axis.
RESULTS

Positive and negative inotropic effects on dP/dt_{peak} and LV EF resulting from pharmacological interventions are shown in Fig. 3. Mean values are given for each stage, and statistically significant differences between stages of pharmacological modulation were noted for both dP/dt_{peak} and LV EF, irrespective of coronary ligation. S' and apical rotation also showed significant differences during pharmacological modulation of β-adrenergic receptors with and without coronary ligation (Fig. 4). Dose-dependent changes were observed for both S' and apical rotation. Significant linear trends from baseline in S' were observed before (P<0.001 for both positive and negative inotropics) and after (P<0.001 for both positive and negative inotropics) coronary ligation.

S' changed in parallel to the pharmacological modulation of β-adrenergic receptor activity, and there was a strong association between dP/dt_{peak} and S' (R^2 = 0.665, P < 0.001; Fig. 5A). The association between LV EF and dP/dt_{peak} was less strong (R^2 = 0.408, P < 0.001; Fig. 5B), and the generalized R^2 values between S' and dP/dt_{peak} were significantly higher than those between LV EF and dP/dt_{peak} (P = 0.002; Table 1). The association between dP/dt_{peak} and apical rotation was also strong (R^2 = 0.726, P < 0.001; Fig. 5C), and the R^2 value between apical rotation and dP/dt_{peak} did not differ significantly from that between S' and dP/dt_{peak} (P = 0.350; Table 1).

The effect of coronary ligation on the association between dP/dt_{peak} and S' is shown in Fig. 6. There was a significant association between these parameters with (R^2 = 0.677, P < 0.001) and without (R^2 = 0.719, P < 0.001) coronary ligation. Before coronary ligation, the R^2 value between S' and dP/dt_{peak} did not differ significantly from that between LV EF and dP/dt_{peak} (P = 0.204; Table 1). After coronary ligation, however, the generalized R^2 value between S' and dP/dt_{peak} was significantly higher than that between LV EF and dP/dt_{peak} (P = 0.006; Table 1). The R^2 values between apical rotation and dP/dt_{peak} before and after coronary ligation did not differ significantly from the corresponding values for the association between S' and dP/dt_{peak} (P = 0.758 and P = 0.122, respec-

Fig. 4. Inotropic effects on S' (A and B) and apical rotation (C and D). A and C: without coronary ligation. B and D: with coronary ligation.

Fig. 5. Association of dP/dt_{peak} with S' (A), EF (B), and apical rotation (C).
A closer relationship between associations between dP/dt and ejection fraction; dP/dt to arteries are summarized in Table 2. LV contractility following the ligation of different coronary arteries is shown in Fig. 6. A modest association was observed during pharmacological modulation with (R\(^2\) = 0.431, P < 0.001) and without (R\(^2\) = 0.568, P < 0.001) coronary ligation. There was also a good association between S’ and apical rotation during pharmacological modulation, with (R\(^2\) = 0.552, P < 0.001) and without (R\(^2\) = 0.674, P < 0.001) coronary ligation.

**DISCUSSION**

In this controlled animal study, we found that S’ measured by pulsed TDI exhibited dose-dependent changes in response to pharmacological modulation of introtropic status. S’ was highly correlated with dP/dt\(_{peak}\), an invasive index of LV contractility, under a variety of LV inotropic conditions, irrespective of coronary ligation and development of RWMA. Although there was also a modest association between S’ and LV EF, a comparison of the R\(^2\) values demonstrated that S’ provides a more accurate measure of global LV contractility. Moreover, S’ also showed good correlation with apical rota-

**Table 1. R\(^2\) values of LV contractility indexes**

<table>
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<tr>
<th>S’ vs. EF</th>
<th>dP/dt(_{peak}) vs. S’ (R(^2) = 0.719) and EF (R(^2) = 0.580), before coronary ligation</th>
<th>0.204</th>
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<td>dP/dt(_{peak}) vs. S’ (R(^2) = 0.677) and EF (R(^2) = 0.318), after coronary ligation</td>
<td>0.006</td>
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<td>dP/dt(_{peak}) vs. S’ (R(^2) = 0.665) and EF (R(^2) = 0.408), total</td>
<td>0.002</td>
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**Table 2. R\(^2\) values of LV contractility indexes after coronary ligation**

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<th>After LAD ligation</th>
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<td>dP/dt(_{peak}) vs. S’ (R(^2) = 0.649) and EF (R(^2) = 0.350)</td>
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<td></td>
<td>dP/dt(_{peak}) vs. apical rotation (R(^2) = 0.774) and EF (R(^2) = 0.350)</td>
<td>0.015</td>
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<tr>
<td></td>
<td>dP/dt(_{peak}) vs. S’ (R(^2) = 0.649) and apical rotation (R(^2) = 0.774)</td>
<td>0.385</td>
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**Fig. 6.** Association of dP/dt\(_{peak}\) with S’ before and after coronary ligation. A: before coronary artery ligation. B: after coronary ligation [pooled data after ligation of LAD and left circumflex artery (LCX)]. C: individual data after LAD ligation. D: individual data after LCX ligation.
tion, a new index of global LV contractility. All of these observations suggest that TDI measurement of $S'$ provides a noninvasive assessment of global LV contractility.

Interestingly, the potential functional relationship between mitral annular movement and global LV performance was an important hypothesis during early echocardiographic assessments (5). Because the shortening of LV longitudinal fibers drives mitral annular movement, quantification of global LV contractility, and regional myocardial function, using TDI data has been of interest. Compared with LV EF by two-dimensional echocardiography, recording of mitral annular motion has several practical advantages, since it is devoid of trabeculas or myocardial dropouts and therefore is relatively independent of image quality. Moreover, because shortening velocity is an established functional measure in isolated cardiac muscle preparations (30), the ability of TDI to quantify LV longitudinal shortening in the intact heart provides a theoretical superiority over LV EF in evaluating LV contractility, because LV EF is at best an indirect measure of myocardial contractility. Another theoretical advantage of $S'$ over LV EF is related with asynchronus ventricular contraction during systole. During early systole, longitudinal fibers shorten before circumferential fibers shorten (25, 26). In several cardiac diseases, including subendocardial ischemia, impaired longitudinal shortening occurred before changes in the short-axis function (4, 12). In addition, at very-low-dose dobutamine infusion (1 to 3 μg·kg⁻¹·min⁻¹), resulting in no change of LV EF, $S'$ measured by TDI showed a linear dose-dependent increase (7). All of these previous observations support our finding that $S'$ assessed by TDI is more closely related to $dP/dt_{peak}$, an invasive gold standard of global LV contractility, than is LV EF under a wide range of pharmacologically modulated inotropic conditions and RWMA.

The finding that $S'$ is a more sensitive index of myocardial contractility than is LV EF has been well documented clinically, since $S'$ rather than LV EF was found to be useful in detecting early myocardial dysfunction in asymptomatic severe mitral regurgitation (1) and to be a valuable prognosticator in patients with heart failure resulting from severe LV systolic dysfunction (21). Considering the significantly lower measurement variability of $S'$ (4–8%) (21) and the relatively frequent dropout of endocardial borders in routine clinical practice, making measurements of LV EF more difficult, $S'$ may replace LV EF as a reliable noninvasive index of global LV contractility in routine clinical settings.

Since the successful clinical introduction of TDI (32), it has been used primarily to quantify regional myocardial thickening for estimation of segmental LV contractility, thus overcoming the subjective and semiquantitative visual interpretation of endocardial motion. In a well-controlled animal experiment, TDI determinations of mid-LV showed excellent correlation with alterations in both regional and global LV contractility, providing further evidence that TDI has the potential to quantify both regional and global function (6). Considering the normal velocity gradient between relatively fixed LV apex and actively moving mitral annulus, the velocity tracing of the mitral annulus by TDI may reflect global LV longitudinal movement during the entire cardiac cycle. This was confirmed by demonstration of a close relationship between global LV relaxation velocity and early diastolic mitral annular velocity ($E'$ velocity), with measurements of $E'$ velocity having become the cornerstone for the assessment of global LV diastolic function and estimation of LV filling pressure (19, 22, 29). We confirmed the strong association between $S'$ and $dP/dt_{peak}$ even after coronary ligation or development of RWMA, suggesting
that mitral annular motion can reflect global systolic LV function.

In this animal experiment, we could evaluate the relationship between longitudinal shortening and other mechanisms of LV systolic performance. The systolic motion of the mitral annulus is not entirely due to myocardial longitudinal shortening or contraction but rather is the summation of contraction and rotation (22). The helical configuration of a cardiac continuous muscle band has been recently documented (33), and apical rotation has shown to be a major component of LV torsional deformation (14), which generates the required pumping power. In this study, we documented a good association between S’ and apical rotation under a variety of LV inotropic conditions, irrespective of coronary ligation and development of RWMA, suggesting that both longitudinal shortening and apical rotation or LV torsion are closely related phenomena in a ventricular muscle band model (33). Moreover, apical rotation itself can be regarded as a main driving force of longitudinal shortening. LV torsion is a crucial component of LV performance and can be measured by a new echocardiographic technique (9). However, measurements of LV torsion have been reported to be notoriously difficult in routine clinical practice (13). Thus, because systolic mitral annular movement is a good measurement of both longitudinal shortening and LV torsional deformation, TDI measurement of S’ is an accurate and more practical approach to the assessment of global LV function.

The location of TDI sample volume is another issue in the assessment of global LV contractility. The major advantage of the medial (septal) mitral annulus is that the ultrasound beam is most parallel to the LV longitudinal movement, an advantage well documented in both animal and clinical studies. In an animal experiment using invasive dP/dt peak, S’ from the TDI assessment of the LV free wall was higher than that derived from the septal or medial annulus; however, the correlation coefficient between dP/dt peak and the S’ velocity was higher for the septal or medial annulus than for TDI assessment of the LV free wall (10). The excellent performance of the TDI data measured at the medial (septal) mitral annulus for estimation of LV relaxation and LV filling pressure has been demonstrated frequently (19, 22, 29). Thus it was not surprising that S’ from the medial (septal) annulus showed excellent association with dP/dt peak in our study.

A more challenging issue is whether medial annulus alone is good enough for estimation of global LV contractility in patients with RWMA. Compared with normal controls, patients with inferior or anterior myocardial infarction showed significantly reduced S’ velocities at all four sites (septal, anterior, lateral, and inferior) of the mitral annulus, regardless of the location of infarction (2). We also observed an excellent association between S’ from the medial annulus alone and dP/dt peak even with coronary ligation or RWMA. The stronger association between dP/dt peak and S’ from the medial annulus alone than between dP/dt peak and LV EF, irrespective of coronary ligation site, implies that the degree of LV damage induced by myocardial infarction determines the S’ value of the medial annulus and that TDI measurements of the medial annulus alone are sufficient for routine clinical assessment of global LV contractility. Taken together, these findings again indicate that longitudinal movement of the mitral annulus is largely determined by global LV contractility and that TDI measurements of the medial annulus, although recoded at the localized area of the LV, provide more information regarding global LV performance than expected.

Several potential limitations of our study need to be clarified. Measurement of annular longitudinal movement and apical rotation was done in two-dimensional echocardiography. Comprehensive three-dimensional measurement of apical rotation and annular movement would be more accurate to assess the impact of RWMA on LV performance. Possible shortcomings of the experimental conditions such as open thoracotomy and anesthesia should be considered when extrapolating our findings to intact humans. An open-chest anesthetized animal model factitiously reported absence of right ventricular isovolumic relaxation (17), which was later clearly documented in the intact awake state (24). Considering the fact that a highly unphysiological state and methods can significantly affect ventricular diastolic function (11), further investigations are necessary to test the potential impact of the experimental conditions on LV systolic function, including apical rotation and S’. Movement of septal mitral annulus can be affected by the right ventricular function. In this animal experiment, we could not induce right ventricular dysfunction alone. Thus the accuracy and feasibility of S’ in assessing LV function in cases with dominant right ventricular dysfunction could not be assessed.

In conclusion, we have shown here that S’ is an excellent noninvasive index of global LV contractility with excellent association with established indexes. This association was irrespective of coronary ligation, and S’ was found to be a better index of global LV contractility than LV EF. S’ measurement has potential as a reliable noninvasive index of global LV contractility in various clinical settings.

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DISCLOSURES
No conflicts of interest are declared by the authors.

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