Effects of modulation of left ventricular contractile state and loading conditions on tissue Doppler myocardial performance index

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Cannesson, Maxime, Didier Jacques, Michael R. Pinsky, and John Gorcsan III. Effects of modulation of left ventricular contractile state and loading conditions on tissue Doppler myocardial performance index. Am J Physiol Heart Circ Physiol 290: H1952–H1959, 2006. First published December 16, 2005; doi:10.1152/ajpheart.01090.2005.—The myocardial performance index (MPI), first described by Tei et al. (34) in 1995, has been shown to be a predictor of global left ventricular (LV) (35) and right ventricular (1, 4, 11) function in various clinical settings. MPI combines elements of systolic and diastolic function and has been shown to quantify LV contractility and has been reported to be relatively independent of heart rate (16, 27), ventricular geometry (5), and blood pressure in steady states (34). An important limitation of MPI is that it is derived from LV inflow and outflow Doppler velocities from two separate imaging planes that cannot be recorded simultaneously (Fig. 1). Accordingly, MPI may be affected by changes in cardiac cycle length that may occur from data acquisition in one view to the other. Furthermore, rapid changes in contractility cannot be readily assessed. A new approach using tissue Doppler (TD) of the mitral annulus can rapidly calculate the MPI from a single cardiac cycle, and it has been shown to predict global LV performance similar to the Tei index (9, 10, 36). However, the proposed load independence of MPI has remained controversial, and potential effects of alterations in loading conditions and contractile state on TD MPI are unclear. Accordingly, the aims of this study were to test the hypotheses that TD MPI 1) can quantify LV contractile state and 2) is affected by acute alterations in preload and afterload by using invasive hemodynamic measurements of LV pressure-volume relations in an animal model.

METHODS

Preparation. Eight mongrel male dogs, weighting 22.8 kg (SD 1.5), were studied. The protocol was approved by the Institutional Animal Care and Use Committee and conformed to the position of the American Heart Association on Research Animal Use. All dogs were anesthetized with pentobarbital sodium (30 mg/kg induction, 1.0 mg·kg⁻¹·h⁻¹ maintenance with intermittent boluses, if needed), underwent endotracheal intubation (7-Fr-cuffed endotracheal tube), and placed on mechanical ventilation (tidal volume, 8 ml/kg; FiO₂, 0.21; and frequency adjusted to maintain a Pao₂, between 35 and 40 mmHg). A 6-Fr 11-pole multielecctrode conductance catheter (Webster; Irvine, CA) was inserted via the right internal carotid artery with its tip positioned in the LV apex using fluoroscopy guidance. A LV micromanometer catheter (MPC-500; Millar; Houston, TX) was placed from the left common carotid artery. A second micromanometer-tipped catheter was introduced in a femoral artery and placed in the descending thoracic aorta. A 20-mm Fogarty balloon catheter was inserted via the right femoral vein to the inferior vena cava (IVC). This balloon was partially filled with saline solution to intermittently occlude IVC flow and to decrease preload to determine sequential pressure-volume relations (7, 13). A second 20-mm balloon catheter was inserted via the femoral artery and placed at the level of the descending thoracic aorta. This balloon was partially filled with saline solution to intermittently occlude aortic flow and to increase LV afterload. A median sternotomy was performed, and the heart was suspended in a pericardial cradle. A 5-MHz multiplane echocardiographic transducer was placed at the LV apex and adjusted to image the maximal longitudinal dimension, analogous to the apical four-chamber view used in transthoracic imaging (Fig. 2). The transducer was interfaced with an echocardiographic system with TD echocardiography capabilities (PV 6000; Toshiba Medical System; Tochigi, Japan). The pulsed-Doppler sample volume was opened to 10 mm and placed on the medial mitral annular sites as previously described (8). High-pass filtering was removed, and system settings were adjusted to optimize TD data. TD data were recorded on videotape for subsequent analog-to-digital conversion and quantitative analysis. An ECG was recorded continuously with limb electrodes. An epicardial pacing electrode was sewn on the right atrium to induce an electrical spike used to synchronize analysis of simultaneous Doppler echocardiogra-
phy and hemodynamic data. For the conductance catheter, a 20-kHz constant-amplitude current of 0.03-mA root mean square between proximal distal electrode pairs was used with a data processor as described previously (Sigma 5DF; Leycom; Leyden, Netherlands) (7, 13). Changes in volume were sensed as a change in resistance in the cross-sectional area of each electrode pair, with the sum of all segments reflecting total volume. Parallel conductance was calculated by the hypertonic saline solution method and subtracted to measure left ventricular volume. All physiological signals were digitized at 150 Hz (WINDAQ Software; DATAQ Instruments; Akron, OH) and recorded on a computer.

Protocol. Hemodynamic and echocardiographic data were obtained simultaneously during end-expiratory apnea. The measurements were obtained during the following sequences: 1) baseline (control period), 2) transient IVC occlusion to decrease preload to minimum LV volume, 3) transient aortic occlusion to increase afterload by a 30- to 40-mmHg pressure elevation, 4) dobutamine infusion (5 μg·kg⁻¹·min⁻¹) to increase contractility, and 5) esmolol infusion (bolus of 500 μg and continuous infusion of 100 μg·kg⁻¹·min⁻¹) to decrease contractility. During each sequence, mitral annular velocities were recorded. The time for physiological data to return to baseline was observed between each manipulation.

Data analysis. Pressure-volume data were analyzed off-line. The maximal slope (left upper shoulder) of the end-systolic pressure-volume relation, maximal elastance (Ees) during caval occlusion, LV end-diastolic volume, and peak positive and negative first derivative of LV pressure (dP/dt max and dP/dt min, respectively) were calculated. The time constant of isovolumic relaxation (τ) was calculated by the Weiss method (38). TD MPI was calculated as previously described (9). Accordingly, the TD MPI was calculated as (a' − b')/b', where

**Fig. 1.** Spectral Doppler recordings of mitral inflow and left ventricular (LV) outflow used for calculation of conventional Tei or myocardial performance index (MPI). These data need to be recorded sequentially from the 4-chamber (top, left) and 5-chamber view (bottom, left). Conventional MPI index is defined as (a − b)/b, where a is time interval from end of late diastolic mitral inflow (E wave) and b is ejection time (ET) interval from LV outflow velocity. ICT, isovolumic contraction time; IRT, isovolumic relaxation time.

**Fig. 2.** Pulsed tissue Doppler (TD) recording of mitral annular velocity (left) and corresponding apical 4-chamber view (right) with sample volume in medial site from 1 dog. TD MPI was calculated as (a' − b')/b', where a' is total isovolumic time, which is interval from end of late diastolic mitral annular velocity (Am wave) to onset of subsequent early diastolic mitral annular velocity (Em wave), and b' is ET interval, which is duration of mitral annular systolic wave (Sm). LA, left atrium.
RESULTS

Validation of ET for TD MPI. Simultaneous TD mitral annular velocity data were compared with aortic pressure data to confirm the correct timing and interpretation of the mitral annular systolic wave, because the TD mitral annular velocity profile in our open-chest animal model had a slightly different morphology with a more prominent isovolumic relaxation velocity than that usually observed in humans. The duration of the mitral annular systolic wave was compared with the time interval between the onset of the aortic pressure and the dicrotic notch on the aortic pressure tracing (Fig. 3) and correlated favorably [r = 0.92, P < 0.001, Bland-Altman analysis bias = 16 ms (SD 15)].

Effects of inotropic modulation. Dobutamine infusion induced a significant increase in both dP/d\text{max} [1,892 (SD 504) to 4,713 mmHg/s (SD 1,008), P < 0.001] and E\text{es} [4.1 (SD 1.4) to 7.0 mmHg/ml (SD 1.8), P = 0.01], consistent with an increased contractile state (Fig. 4 and Table 1). Heart rate was also increased [108 (SD 14) to 135 beats/min (SD 21); P = 0.01]. We also observed a decrease in dP/d\text{min} and \tau [−1,846 (SD 500) to −2,970 mmHg/s (SD 684), P = 0.004; and 40 (SD 6) to 30 ms (SD 10), P = 0.003, respectively], indicative of improved diastolic relaxation consistent with the lusitropic properties of dobutamine. TD MPI demonstrated a significant decrease from 0.83 (SD 0.19) to 0.62 (SD 0.2) (P = 0.004), indicative of increased contractile state, associated with a significant decrease in total isovolumic time [from 164 (SD 33) to 114 ms (SD 44); P = 0.005] and total isovolumic time/(R-R interval)\textsuperscript{1/2} [from 219 (SD 37) to 166 ms (SD 51); P = 0.01]. No change in either ET [from 198 (SD 23) to 182 ms (SD 27); P = 0.14] or ET/(R-R interval)\textsuperscript{1/2} [from 265 (SD 25) to 269 ms (SD 30); P = 0.53] was observed (Fig. 5). Esmolol infusion resulted in a significant decrease in both dP/d\text{max} and E\text{es} [1,892 (SD 504) to 1,155 mmHg/s (SD 413), P = 0.01; and 4.1 (SD 1.4) to 2.6 mmHg/ml (SD 1.1), P = 0.038, respectively], consistent with a decrease in contractile state and associated with a significant decrease in heart rate from 108 (SD 14) to 96 beats/min (SD 9) (P = 0.03). Similarly, both \tau and dP/d\text{min} were increased [40 (SD 6) to 70 ms (SD 18), P = 0.001; and −1,846 (SD 500) to −1,206 mmHg/s (SD 433), P = 0.01, respectively]. TD MPI was significantly increased from 0.83 (SD 0.19) to 1.14 (SD 0.19) (P = 0.004), consistent with decreased contractile state, with a significant increase in total isovolumic time [from 164 (SD 33) to 258 ms (SD 48); P < 0.001] and total isovolumic time/(R-R interval)\textsuperscript{1/2} [from 219 (SD 37) to 324 ms (SD 50); P < 0.001]. No change in either ET [from 198 (SD 23) to 195 ms (SD 30); P = 0.21] or ET/(R-R interval)\textsuperscript{1/2} [from 265 (SD 25) to 277 ms (SD 35); P = 0.51] was observed (Fig. 5). TD MPI correlated significantly with dP/d\text{max} (r = −0.76; P < 0.001) and E\text{es} (r = −0.68; P = 0.001) (Fig. 6), as well as −dP/d\text{min} (r = −0.82; P < 0.001) and \tau (r = 0.78; P < 0.01) (Fig. 7).

Effects of acute alterations in preload and afterload. Acute decreases in preload induced by IVC occlusion were associated with a significant decrease in LV end-diastolic volume [123 (SD 33) to 111 mmHg (SD 33); P < 0.001] and mean arterial
Fig. 4. Sequential pressure-volume loops (A–C, left) and corresponding mitral annular velocity recordings (A–C, right) at baseline (A), during dobutamine infusion (B), and during esmolol infusion (C) in 1 illustrative dog. TD MPI was inversely correlated to end-systolic elastance ($E_{es}$).

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<tr>
<th>Table 1. Changes in left ventricular tissue Doppler MPI and hemodynamic indexes during inotropic modulation</th>
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<td><strong>Baseline</strong></td>
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<tr>
<td>Tissue Doppler-MPI</td>
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<td>End-systolic elastance, mmHg/ml</td>
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<td>Left ventricular dP/dt min, mmHg/s</td>
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<td>Time constant of relaxation, ms</td>
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Values are means (SD). MPI, myocardial performance index; R-R, R-R time interval; dP/dt max and dP/dt min, peak positive and negative first derivative of pressure. *$P < 0.05$ compared with baseline.
pressure [133 (SD 22) to 97 mmHg (SD 18); \( P < 0.001 \)], as expected, with no change in heart rate [108 (SD 14) to 109 beats/min (SD 15); \( P = 0.67 \)] and a significant decrease in \(\frac{dP}{dt_{\text{max}}} \) [1,892 (SD 504) to 1,326 mmHg/s (SD 345); \( P < 0.01 \)] (Table 2). During IVC occlusion, TD MPI significantly increased from 0.83 (SD 0.19) to 1.09 (SD 0.36) (\( P < 0.05 \)). This increase was related to a significant decrease in ET [from 198 (SD 23) to 175 ms (SD 15); \( P = 0.004 \)] and ET/(R-R interval)\(^{1/2} \) [from 265 (SD 25) to 234 ms (SD 28); \( P = 0.004 \)] with no change in either total isovolumic time [from 164 (SD 33) to 188 ms (SD 53); \( P = 0.011 \)] or total isovolumic time/(R-R interval)\(^{1/2} \) [from 219 (SD 37) to 248 ms (SD 54); \( P = 0.08 \)].

Acute increases in afterload induced by partial aortic occlusion significantly increased LV systolic pressure [138 (SD 28) to 176 mmHg (SD 43); \( P = 0.001 \)] and mean arterial pressure [133 (SD 22) to 154 (SD 17) mmHg; \( P = 0.03 \)], as expected, with no significant change in heart rate [108 (SD 14) vs. 97 beats/min (SD 12); \( P = 0.10 \)] and no significant change in \(\frac{dP}{dt_{\text{max}}} \) [1,892 (SD 504) to 1,791 mmHg/s (SD 431); \( P = 0.76 \)]. Increased afterload increased TD MPI from 0.83 (SD 0.19) to 1.23 (SD 0.17) (\( P < 0.001 \)) and total isovolumic time/\(\frac{(R-R \text{ interval})^{1/2}}{ \text{ET}} \) [from 219 (SD 37) to 305 ms (SD 54); \( P = 0.003 \)] and no change in either ET [from 198 (SD 23) to 198 ms (SD 30); \( P = 0.83 \)] or ET/(R-R interval)\(^{1/2} \) [from 265 (SD 25) to 251 ms (SD 31); \( P = 0.33 \)].

**DISCUSSION**

This study demonstrates that TD MPI can reliably detect alterations in LV function induced by inotropic modulation. TD MPI correlated favorably with invasive hemodynamic pressure-volume loop measurements of LV contractile state and diastolic relaxation in an experimental animal model. In addition, calculation of TD MPI was rapidly acquired and reproducible. We also observed that TD MPI was directly affected by acute changes in preload and afterload induced by IVC occlusion and partial aortic occlusion. Accordingly, TD MPI may have limitations in clinical scenarios associated with rapidly changing hemodynamic conditions.

The conventional MPI, first described by Tei et al. (34), is based on the recording of both mitral and aortic flows using pulsed Doppler. This index has been shown to be a useful clinical index of LV and right ventricular function (4, 33, 35). It is a unitless ratio of total isovolumic time (isovolumic contraction time + ET + isovolumic relaxation time) to ET, which can be recorded and measured by using routine conventional pulsed Doppler. Conventional MPI has gained clinical acceptance in assessing congenital cardiac disease (1, 22, 28, 29, 31, 39) and acquired cardiac disease, in particular as a useful predictor of clinical outcome in patients with cardiac disease.

Intraobserver and interobserver variability. We found a 1.0% (SD 7.7) intraobserver and a 6.2% (SD 7.4) interobserver variability of measurement of TD MPI.
amyloidosis (33), myocardial infarction (20), and dilated cardiomyopathy (26). The main advantages of this index are that it appears to be independent from ventricular geometry (5) and heart rate (16, 27, 34). Furthermore, it is a unique index of both systolic and diastolic (global) ventricular function (34). The MPI combines elements of LV systolic and diastolic function by reflecting systolic dysfunction in a shortened ET and a lengthened isovolumic contraction time and diastolic dysfunction in a lengthened isovolumic relaxation time (30). Consequently, an increased MPI indicates worsened LV performance, whereas a decreased MPI will indicate improved performance. An important feature of these previous investigations of MPI is that patients were studied during clinical stability with chronic disease states and steady-state hemodynamic conditions, unlike the acute loading alterations induced in our present animal study. One of the main limitations of the conventional MPI is that it cannot be calculated over a single cardiac cycle because the interval between the end and the onset of mitral inflow and the ET are measured sequentially. Accordingly, single beat analysis cannot be done. Cheung et al. (3) have recently shown that LV MPI was unable to detect acute change in LV contractile function induced by dobutamine or esmolol infusion in a porcine model (3). Because simultaneous LV inflow and outflow data cannot be recorded simultaneously, this limitation may account for these findings, although the precise reason is unknown.

Fig. 6. Relationship of LV TD MPI to positive peak first derivative of pressure ($dP/dt_{\text{max}}$) $dP/dt_{\text{max}}$ (A) and $E_{\text{es}}$ $E_{\text{es}}$ (B) during baseline (○), dobutamine infusion (■), and esmolol infusion (▲).

Fig. 7. Relationship of LV TD MPI to negative peak first derivative of pressure ($-dP/dt_{\text{min}}$; A) and time constant of relaxation ($\tau$; B) during baseline (○), dobutamine infusion (■), and esmolol infusion (▲).
(LV relaxation and contraction), clearly relating the routine MPI to the TD MPI. However, cardiac dysfunction may affect the coupling of the time intervals. For example, the difference in time to onset of early diastolic velocity of the mitral annulus and time to onset of mitral inflow is increased in the case of abnormal relaxation (30), suggesting that the assessment of isovolumic relaxation time using TD may be more sensitive of abnormal relaxation than conventional pulsed Doppler. Our data reported (see RESULTS) support a strong relationship and close agreement between time duration of the mitral annular systolic wave and ET assessed with the use of aortic pressure recordings at baseline and during dobutamine and esmolol infusion. TD MPI, however, appears to be similarly affected by changes in loading as does conventional MPI.

**Study limitations.** The animals in this study did not maintain a constant heart rate, and significant changes occurred during dobutamine and esmolol infusion. However, previous investigators (16, 27) have shown that MPI is relatively unaffected by heart rate. Furthermore, we attempted to correct ET and total isovolumic time values for R-R intervals to minimize confounding effects. In addition, potential effects of heart rate on total isovolumic time and ET are likely to be mathematically canceled when expressed as a ratio:

\[
\frac{\text{ET}/(R-R \text{ interval})^{1/2}}{\text{total isovolumic time}} = \frac{\text{total isovolumic time}}{\text{ET}/(R-R \text{ interval})^{1/2}}
\]

Another limitation is that a direct comparison of routine MPI with TD MPI was not performed, although previous investigations have established this relationship. Another possible limitation of our study is that the values for TD MPI were higher than those reported in humans. We postulate that this was due, in part, to the myocardial depressing action of the anesthetic drugs in our open-chest preparation. Mancini et al. (19) observed similar elevated indexes at baseline with long isovolumic relaxation times in a canine model. Thus we can postulate that MPI and TD-MPI values may possibly be higher in dogs than in humans, although this is unknown. Because we examined changes in TD MPI from baseline using each animal as its own control, potential interspecies variations in the absolute value do not appear to affect our conclusions. Finally, we focused only on acute changes in loading, and the potential effects of chronic adaptation to loading on TD MPI remain unknown.

In conclusion, TD MPI is a simple and rapidly calculated index that can quantify alterations in LV contractile state. It has an advantage over the traditional MPI because it may be performed on a single beat from a single echocardiographic view. However, TD MPI is directly influenced by acute decreases in preload and acute increases in afterload, and both maneuvers are associated with increases in TD MPI. Accordingly, TD MPI may have limitations in comparing contractile states in patients with different loading conditions or in clinical scenarios associated with rapidly changing hemodynamic conditions, such as critically ill or hemodynamically unstable patients. In view of the significant preload and afterload sensitivity, the utility of this index for clinically assessing contractile state may potentially be limited. Accordingly, these data suggest that the TD MPI may be best suited as a measure of cardiac function in patients in steady-state hemodynamic conditions. Further analysis in humans is needed to show that the range of afterloads and preloads encountered clinically is within a narrow enough range that the impact of these factors is negligible compared with the impact of changes in contractility.

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**GRANTS**

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**REFERENCES**


**Table 2. Changes in left ventricular tissue Doppler MPI and hemodynamic indexes during changes in loading conditions**

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<th>Preload Decrease</th>
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<td>0.83 (SD 0.19)</td>
<td>1.09 (SD 0.36)*</td>
<td>1.23 (SD 0.17)*</td>
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<td>Heart rate, beats/min</td>
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<td>234 (SD 28)*</td>
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<td>Left ventricular dP/dmax, mmHg/s</td>
<td>1.892 (SD 504)</td>
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<td>42 (SD 14)</td>
<td>55 (SD 9)*</td>
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</table>

Values are means (SD). *P < 0.05 compared with baseline.


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