Impact of myocardial structure and function postinfarction on diastolic strain measurements: implications for assessment of myocardial viability

Tae-Ho Park, Sherif F. Nagueh, Dirar S. Khoury, Helen A. Kopelen, Spyridon Akrivakis, Kamal Nasser, Guofeng Ren, and Nikolaos G. Frangogiannis. Impact of myocardial structure and function postinfarction on diastolic strain measurements: implications for assessment of myocardial viability. *Am J Physiol Heart Circ Physiol* 290: H724–H731, 2006. First published September 23, 2005; doi:10.1152/ajpheart.00714.2005.—We sought to assess the role of regional diastolic function by Doppler echocardiography in predicting myocardial viability. Sixteen dogs underwent left anterior descending coronary artery (n = 8) or circumflex (n = 8) occlusion. All animals were imaged at baseline and 1–8 wk postinfarction (post-MI). In 10 dogs, invasive hemodynamic monitoring with a conductance catheter placed in the left ventricle (LV) was performed at the above time points. Dobutamine was infused at 1–8 wk post-MI to determine LV contractile reserve. Histomorphological analysis was performed to determine the presence of viable myocardium and changes in interstitial matrix. Post-MI, diastolic strain rate measurements (in radial and longitudinal planes) decreased significantly in the distribution of the diseased artery (P < 0.01) and on multiple regression analysis were determined by time constant of LV relaxation, end-diastolic pressure, regional stiffness, and the ratio of cellular infiltration to collagen deposition in the interstitial matrix. Among several indexes, diastolic strain rate during dobutamine infusion readily identified segments with >20% transmural infarction and related best to the extent of interstitial fibrosis (r = −0.86, P < 0.01). In an animal model of healing canine infarcts, diastolic strain rate by Doppler echocardiography appears to be a promising novel index of myocardial viability.

THE PROGNOSIS OF PATIENTS with coronary artery disease is largely dependent on the presence and extent of myocardial viability (14). Accordingly, the accurate assessment of viable myocardium is needed for proper patient management. Echocardiographic techniques, in particular dobutamine echocardiography (14), have emerged as important diagnostic modalities that can identify residual viable myocardium in patients with coronary artery disease. There is, however, a paucity of data on the utility of assessment of regional diastolic function in these patients. This approach is important given the recent reports on diastolic function assessment during stress echocardiography (1, 12, 20).

Depending on the extent of ischemia, regional expansion may be delayed at a time when systolic function is normal (1, 21). Alternatively, it is possible for regional stiffness to be relatively unchanged despite the presence of systolic dysfunc-

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Diastolic strain rate for myocardial viability

1-8 wk postinfarction as detailed above, but in 10 animals (5 with LAD and 5 with circumflex occlusion), invasive hemodynamic studies and dobutamine infusion were carried out before euthanization.

Instrumentation. The dogs were anesthetized with pentobarbital sodium (30 mg/kg), intubated, and mechanically ventilated. All examinations were performed under anesthesia and with the same anesthesia. After calibration, a high-fidelity 5-F, 12-electrode conductance catheter (Millar) was advanced into the LV by crossing the aortic valve. The latter catheter was connected to a dedicated system (Cardiodynamics BV, Leycom-CFL-512, Argenstraat, the Netherlands) that continuously acquired and displayed pressure, volume, and ECG signals. Proper positioning of the conductance catheter along the long axis of the LV was guided by fluoroscopy and confirmed by segmental volume signals. With the use of fluoroscopic guidance, a Swan Ganz catheter was advanced from the right femoral vein to the pulmonary circulation. This catheter was used to measure cardiac output by thermodilution and determine parallel conductance with hypertonic saline injection. Further, to alter myocardial function, the proximal segment of the left circumflex coronary artery or the mid-segment of the LAD were occluded to result in myocardial infarction. Flow through the inferior vena cava (IVC) was gradually reduced by external compression to allow for alteration of loading conditions. To avoid the confounding effect of reflex sympathetic stimulation on myocardial function, the analysis of the effect of preload on strain measurements was limited to the early cycles showing no or minimal change in heart rate after IVC occlusion.

Hemodynamic measurements. To convert the conductance signals to volume data, blood resistivity was measured, and parallel conductance was determined by injecting 10 ml of hypertonic saline into the pulmonary artery through the distal port of the thermodilution catheter. Because the conductance method can underestimate true LV volume, stroke volume by the conductance catheter was compared with stroke volume by thermodilution. The ratio of the two methods defines the slope factor, α. The slope factor α, along with blood resistivity and parallel conductance volume, are then used to obtain true LV volume. All recordings of pressure and volume data were obtained at end expiration. LV volumes and pressures at end diastole (EDV, EDP) and end systole (ESV, ESP) were obtained from the conductance catheter (2). The time constant of LV relaxation (τ) was derived (4, 23). Using pressure-volume loops, end-systolic elastance (Ees; slope of ESP/ESV) was calculated. Meridional and circumferential end-systolic wall stress were derived (8) using two-dimensional echocardiographic measurements and ESP. The diastolic pressure (P)-wall thickness (h) data were fitted to a power function (5), where P = B × h^−α, to compute regional myocardial stiffness constant (θ).

Echocardiographic studies. Transthoracic imaging was performed using a System FIVE GE Vingmed ultrasound system (simultaneous with hemodynamic data acquisition in the animals that underwent invasive studies). Three short-axis tomograms were acquired at the level of the mitral valve, papillary muscles, and LV apex. In addition, the standard apical (4, 2, and 5 chamber) views were acquired. During tissue Doppler imaging, a narrow sector angle was used, and image depth was adjusted to allow for maximal acquisition frame rate (>120 frames/s) with care taken to avoid angulation. Digital loops were transferred to a dedicated computer for offline analysis.

Echocardiographic analysis. All analyses were performed by a single investigator blinded to all other data. The Doppler strain measurements were acquired at baseline and 1–8 wk postinfarction. Measurements were performed using reconstructed curves from data stored digitally. For animals undergoing mid-LAD occlusion, the velocity and strain rate were measured from the anterior and posterior (control segment) walls at two myocardial levels in the short-axis tomograms corresponding to the mid- and apical thirds of the LV.

For animals undergoing proximal circumflex occlusion, the velocity and deformation indexes were measured from the anterior (control segment) and posterior walls at three myocardial levels in the short-axis tomograms corresponding to the base, mid-, and apical thirds of the LV.

Two-dimensional and M-mode echocardiography were used to record aortic valve closure and mitral valve opening, which were used with LV pressure and ECG signals for timing events during the cardiac cycle. The following parameters were measured and averaged over three cycles: systolic strain rate, early diastolic velocity, and early and late diastolic strain rates. Velocity and strain rate measurements assessed in the radial and longitudinal directions (Fig. 1) had a low intra- and interobserver variability (3.8 ± 4 to 4.5 ± 3.5%). For the above Doppler measurements, variability was assessed using previously acquired recordings but with repeat measurements at a later date by the same observer and a second blinded observer (in 6 animals using baseline and postinfarction recordings).

Histopathological analysis. At the end of the experiment (1–8 wk post-MI), the animals were euthanized using a rapid intravenous injection of KCl (30 meq). Subsequently, the hearts were removed from the chest and sectioned in three transverse rings, which were used for determination of the extent of MI. Sections were stained with hematoxylin/eosin and Verhoeff-Van Gieson stain to identify cellular and extracellular matrix components in the healing infarct. Serial sections were stained immunohistochemically with antibodies to

<table>
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<tr>
<th>Table 1. Diastolic strain rate at baseline and 1–8 wk post-MI</th>
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<tr>
<td>Radial</td>
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<tr>
<td>Early diastolic strain rate, s⁻¹</td>
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<tr>
<td>Late diastolic strain rate, s⁻¹</td>
</tr>
<tr>
<td>Longitudinal</td>
</tr>
<tr>
<td>Early diastolic strain rate, s⁻¹</td>
</tr>
<tr>
<td>Late diastolic strain rate, s⁻¹</td>
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Values are means ± SD. Data are derived from the average of all 16 animals at each session. The strain rate measurements in the radial direction represent the absolute (and not vector) measurements with the mean values of the dysfunctional walls (anterior for left anterior descending coronary artery (LAD) stenosis and posterior for circumflex stenosis) shown. The strain rate measurements in the longitudinal direction represent the mean values of the dysfunctional walls (anterior and septal for LAD stenosis and posterior for circumflex stenosis). MI, myocardial infarction. *P < 0.05 vs. baseline measurements.
α-smooth muscle actin (α-SMA) (Sigma, St. Louis, MO), the matricellular protein tenasin (Chemicon International, Temecula, CA), and collagen (IGN Biomedicals, Aurora OH) (3, 10). For quantitative analysis, each section was scanned at 200× magnification using a Leaf Lumina digital camera (Leaf Systems, Southboro, MA). To evaluate the extent of infarction, the area of cardiomyocyte replacement by granulation tissue or scar was quantitatively assessed for each myocardial segment and expressed as a percentage of the total area of the segment. The myocardial segments were divided according to the presence of systolic thickening into two groups. Group I had systolic hypokinesis with transmural MI <20%, whereas group II segments were akinetic or dyskinetic with transmural MI >20%.

Percent collagen staining was assessed for each infarcted segment using Zeiss Image analysis software and expressed as the percentage of the total area of the infarct. Total cell density (the number of hematoxylin-stained nuclei in the area of infarction) and myofibroblast density (the number of α-SMA-positive myofibroblasts in the infarcted area) were quantitated in infarcted segments and were used as indexes of the cellular content of healing infarcts. In addition, the ratio of total nucleated cell density to percent collagen staining was calculated for all infarcted myocardial segments.

Statistical analysis. Data are presented as means ± SD. ANOVA was used for histopathological data analysis. Pairwise comparisons were performed by t-tests using the Bonferroni correction. Regression analysis was applied to relate Doppler measurements to hemodynamic and histopathological data in a pooled analysis including all time points. Statistical significance was considered for P < 0.05.

RESULTS

Changes in regional function by strain Doppler echocardiography after MI. After occlusion of the LAD, systolic strain rate and early diastolic velocity and strain rate were significantly reduced in the radial and longitudinal planes of the mid- and distal segments of the anterior and septal walls. Likewise, occlusion of the left circumflex coronary artery resulted in a significant decrease of systolic and early diastolic strain rate of the posterior wall (Table 1). The decrease in early diastolic strain rate was more in the longitudinal than in the radial direction (65% vs. 44%, P < 0.05).

Haemodynamic changes post-MI. As animals were examined at 1–8 wk post-MI, significant changes were noted as LV volumes increased, and Ees decreased; τ was significantly prolonged. Meridional and circumferential end-systolic wall stress were significantly increased in animals euthanized 1–8 wk post-MI (Table 2). The ratio of meridional to circumferential
tial wall stress was also significantly increased compared with baseline (0.5 ± 0.12 vs. 0.81 ± 0.14, P < 0.01).

The regional myocardial stiffness constant θ in normal segments showed no change post-MI (28 ± 8 vs. 28 ± 8, P > 0.1). On the other hand, θ of dysfunctional segments increased significantly after MI (28 ± 8 vs. 110 ± 8, P < 0.01).

Effect of preload on velocity and strain-rate measurements. At all experimental stages (baseline and 1–8 wk post-MI), IVC occlusion led to a significant decrease in systolic strain rate and early diastolic velocity and strain rate (for early diastolic strain rate: %decrease in radial strain with IVC occlusion ranging between 50 ± 8% at baseline to 32 ± 9% post-MI; %decrease in longitudinal strain ranging from 48 ± 5% at baseline to 33 ± 8% post-MI).

Myocardial response to dobutamine post-MI. When infused post-MI, dobutamine increased myocardial contractility (E₀w: 2.5 ± 1.2 vs. 3.3 ± 1.3 mmHg/ml, P < 0.05), stroke volume (27 ± 8 vs. 35 ± 9 ml, P < 0.05), ESP (80 ± 11 vs. 90 ± 13 mmHg, P < 0.05), and heart rate (112 ± 10 vs. 122 ± 13/min, P < 0.05) and improved LV relaxation (τ: 48 ± 5 vs. 35 ± 5 ms, P < 0.05). The average decrease in R-R interval with dobutamine was 8%, whereas τ was shorter by 27%, suggesting that an actual improvement in LV relaxation, and not only faster heart rate, played an important role in the shortening of τ with dobutamine infusion.

In some dysfunctional segments (for both LAD and circumflex occlusion) with >20% transmural infarction, systolic expansion was noted at 1–8 wk post-MI (pre-MI 5.2 ± 1.3 vs. post-MI 1.3 ± 1.5 s⁻¹, P < 0.01). In segments with <20% transmural infarction, dobutamine infusion resulted in a significant increase in radial systolic strain rate (pre-dobutamine 1.5 ± 0.5 vs. post-dobutamine 3.1 ± 1.3 s⁻¹, P < 0.05). Likewise, radial early diastolic velocity (4.8 ± 2.8 vs. 5.5 ± 2.3 cm/s, P < 0.05) and early diastolic strain rate (4.5 ± 2.3 vs. 5.4 ± 2.8 s⁻¹, P < 0.05) increased significantly with dobutamine infusion.

Similar significant changes were noted in the longitudinal plane with dobutamine as the early diastolic velocity (4.5 ± 3.1 vs. 5.2 ± 3.3 cm/s, P < 0.05) and early diastolic strain rate (2.8 ± 2.4 vs. 3.3 ± 2.1 s⁻¹, P < 0.05) increased significantly.

Histopathological changes post-MI. Early post-MI (1–2 wk), healing infarcts exhibited a high cellular content (Fig. 2) and limited deposition of collagen (Table 3, data derived using abnormal segments as units of analysis). Four to eight weeks post-MI, cellular density significantly decreased (P < 0.01) and the amount of collagen markedly increased, reflecting the

Table 3. Changes in histopathology

<table>
<thead>
<tr>
<th>Post-MI</th>
<th>1 wk</th>
<th>2 wk</th>
<th>4 wk</th>
<th>8 wk</th>
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</thead>
<tbody>
<tr>
<td>Collagen, %</td>
<td>3.9±3.7</td>
<td>12.7±14.3</td>
<td>30.7±13.5*</td>
<td>56.4±15†</td>
</tr>
<tr>
<td>Number of nucleated cells, cells/mm²</td>
<td>5.131±874‡</td>
<td>4.955±1.006‡</td>
<td>2.840±971</td>
<td>2.160±588</td>
</tr>
<tr>
<td>Number of myofibroblasts, cells/mm²</td>
<td>669±170§</td>
<td>547±85§</td>
<td>216±105</td>
<td>143±84</td>
</tr>
<tr>
<td>Cells/collagen ratio</td>
<td>2.633±1876§</td>
<td>643±325</td>
<td>157±238</td>
<td>40±13</td>
</tr>
</tbody>
</table>

Values are means ± SD. Analysis performed using dysfunctional segments as units of analysis. *P < 0.05 vs. 1 and 2 wk post-MI; †P < 0.05 vs. 1, 2, and 4 wk post-MI; ‡P < 0.05 vs. 4 and 8 wk post-MI; §P < 0.05 vs. 2, 4, and 8 wk post-MI.

Fig. 3. α-Smooth muscle actin (α-SMA) staining identifies myofibroblasts in healing canine infarcts after 7 days (A and B), 4 wk (C and D), and 8 wk (E and F). Magnification: ×200 (A, C, and E) and ×400 (B, D, and F). After 7 days, α-SMA immunoreactivity is predominantly localized in myofibroblasts, phenotypically modulated fibroblasts, which express contractile proteins such as α-SMA (A and B, arrows). After 4 wk (C and D), the number of myofibroblasts decreases. At this stage, α-SMA staining in the infarct is predominantly found in the muscular wall of maturing neovasculature (C and D, arrows). The mature scar (E and F) contains relatively few myofibroblasts and a large number of pericyte-coated vessels (arrows). Counterstained with eosin. Scale bar, 50 μm.
progressive formation of a mature scar in the infarcted area. In addition, at the early stages of infarct healing (1–2 wk post-MI), a large number of phenotypically modulated fibroblasts expressing contractile proteins, such as α-SMA (Fig. 3A, Table 3), infiltrated the infarcted area. Myofibroblast density significantly decreased in the maturation phase of infarction (Fig. 3, B and C). In addition, expression of the remodeling-associated protein tenascin was noted in the border zone of the infarct during the first 2 wk post-MI but was not found in mature scars.

**Relation of diastolic velocity and strain rate measurements to LV hemodynamics.** To explore the hemodynamic determinants of the tissue Doppler indexes measured in this study, we entered the average value of the dysfunctional segments (anterior or posterior) per animal, including the data acquired during load-altering maneuvers. Several significant correlations were observed between diastolic velocities and strain rate (both in radial and longitudinal planes) and indexes of LV systolic function (Fig. 4 and Table 4) with diastolic velocities and strain rates decreasing as LV contractility decreased and end-systolic wall stress increased. Significant correlations were present between early diastolic Doppler measurements and τ. Importantly, early strain rate was positively related to LV EDP. The above diastolic Doppler measurements were also significantly related to regional myocardial stiffness constant (θ), albeit the relation was influenced by the skewed distribution in the number of segments with particularly increased θ.

**Relation of diastolic velocity and strain rate measurements to LV histopathology.** Several significant correlations were present between the Doppler indexes of regional diastolic function and myocardial pathology. Overall positive correlations were present between diastolic velocity, strain rate, and extent of infarct cellularity, myofibroblast density, and the ratio of cellular infiltration to collagen deposition (Fig. 5), albeit influenced with the skewed distribution in the number of segments with particularly increased cellularity. The overall change observed was higher velocities and strain rate in the early stages of healing (1–2 wk) of infarcted segments, corresponding to a high cellular content and a large number of α-SMA-positive myofibroblasts compared with mature infarcts (4–8 wk) showing scars with lower cellularity and extensive collagen deposition.

On multiple regression analysis, regional myocardial stiffness (θ), LV EDP, τ, and the ratio of cellular infiltration to interstitial collagen were the independent predictors of both radial early diastolic velocity ($R^2 = 0.71$, $P < 0.001$) and strain rate ($R^2 = 0.9$, $P < 0.001$). For longitudinal early diastolic velocity ($R^2 = 0.75$, $P < 0.001$) and strain rate ($R^2 = 0.95$, $P < 0.001$), regional myocardial stiffness (θ), LV EDP, τ, and the ratio of cellular infiltration to interstitial collagen were the independent predictors.

**Identification of viable myocardium.** Systolic strain rate increased with low-dose dobutamine in all group I segments (infarction extending for <20% of wall thickness, $n = 38$; table 4).

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<thead>
<tr>
<th>Radial</th>
<th>Longitudinal</th>
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<tbody>
<tr>
<td></td>
<td>Early diastolic velocity</td>
</tr>
<tr>
<td>LV SV</td>
<td>0.73*</td>
</tr>
<tr>
<td>LV EDP</td>
<td>0.69*</td>
</tr>
<tr>
<td>$\tau$</td>
<td>$-0.64*$</td>
</tr>
<tr>
<td>Wall stress</td>
<td>$-0.68*$</td>
</tr>
<tr>
<td>Regional myocardial stiffness (θ)</td>
<td>$-0.7*$</td>
</tr>
<tr>
<td>Number of nucleated cells</td>
<td>0.48*</td>
</tr>
<tr>
<td>Cells/collagen ratio</td>
<td>0.61*</td>
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Values are correlation coefficients. * $P < 0.01$.  

![Fig. 5. Relation of interstitial cells/collagen ratio to radial early diastolic strain rate](http://ajpheart.physiology.org/10.1152/ajpheart.00579.2005)
radial systolic strain rate: pre-dobutamine \(1.5 \pm 0.5\) vs. post-dobutamine \(3.1 \pm 1.3\) s\(^{-1}\); \(P < 0.05\), but only in 52% of group II segments (infarction extending for >20% of wall thickness; \(n = 33\); radial systolic strain rate: pre-dobutamine \(0.83 \pm 0.6\) vs. post-dobutamine \(1 \pm 0.8\) s\(^{-1}\); \(P = 0.13\)). This occurred despite the presence of viable myocytes in the epicardial layer. Significant correlations (based on segmental analysis) were present between the extent of interstitial fibrosis and radial systolic strain rate at baseline \((r = -0.5, P < 0.05)\) and with dobutamine \((r = -0.63, P < 0.05)\). A stronger relation was observed however with early diastolic strain rate at rest \((r = -0.75, P < 0.01)\) and with dobutamine (Fig. 6, \(r = -0.86, P < 0.01\)). In segments with severe resting dysfunction, dobutamine uncovered the presence of lusitropic reserve where early diastolic strain rate increased from \(1 \pm 0.2\) to \(1.6 \pm 0.3\) s\(^{-1}\) \((P < 0.01)\), highlighting the role of low-dose dobutamine in examining segments with severe resting dysfunction. Similar correlations were noted when strain rate measurements in the longitudinal plane were examined (ranging from \(r = -0.45\) to \(r = -0.82\), all \(P < 0.01\)).

Effect of LV geometry on systolic and diastolic strain rate measurements. To examine the effect of LV geometry on the ability of regional systolic and diastolic strain rate to identify viable myocardium, we compared systolic and diastolic strain rate, wall stress, and extent of infarction in segments with and without inotropic reserve with dobutamine. As expected, segments without inotropic reserve had a significantly lower radial systolic strain rate at rest \((0.5 \pm 0.4)\) vs. \(0.86 \pm 0.5\) s\(^{-1}\); \(P = 0.03\) and with dobutamine \((0.8 \pm 0.5)\) vs. \(1.4 \pm 0.3\) s\(^{-1}\); \(P = 0.02\). This occurred despite the presence of a similar extent of infarction \((P = 0.4)\) and LV EDP \((P = 0.1)\), but in association with a significantly higher end-systolic circumferential wall stress \((128 \pm 16)\) vs. \(95 \pm 13\) kdyn/cm\(^2\); \(P = 0.02\). On the other hand, early diastolic strain rate at rest \((0.83 \pm 0.2\) vs. \(1.1 \pm 0.3\) s\(^{-1}\); \(P = 0.09)\) and with dobutamine were not significantly different \((1.55 \pm 0.3)\) to \(1.65 \pm 0.2\) s\(^{-1}\); \(P = 0.11\). Similar observations were noted with respect to longitudinal strain rate measurements.

DISCUSSION

The results of this investigation support the hypothesis that diastolic function assessment by strain Doppler echocardiography can be applied for the identification of myocardial viability post-MI. We have shown that regional diastolic function can readily identify segments with viable myocardium despite the presence of >20% myocardial necrosis. In addition, our observations support the strong impact of LV relaxation and regional stiffness on early diastolic velocity and strain rate in both radial and longitudinal planes. However, all of the above measurements are significantly dependent on preload. Finally, the composition of the interstitial matrix proved to be an important determinant of the diastolic deformation indexes.

Hemodynamic determinants of regional Doppler-derived diastolic measurements. We assessed myocardial diastolic velocities and strain rate to evaluate their utility in studying regional diastolic function. Previous canine (7, 19) and human (9, 13) studies with respect to systolic function have shown that the use of strain rate and strain parameters is advantageous over velocity measurements. Likewise, in this investigation, while early diastolic velocity and strain rate, both in the longitudinal and radial planes, were significantly reduced with coronary occlusion, the decrease in early diastolic strain rate (mean \(38 \pm 8\%), range 18–53\%) was significantly \((P < 0.05)\) larger than the decrement in early diastolic velocity (mean \(18 \pm 8\%), range 3–28\%), likely related to the confounding effects of tethering and translation on velocity measurements.

When the hemodynamic determinants of the diastolic Doppler indexes of myocardial function were examined, early diastolic strain rate was significantly related to the time constant of LV relaxation and regional stiffness. While these Doppler indexes readily detected the deterioration and improvement in LV relaxation with coronary occlusion and dobutamine, respectively, they were also positively influenced by filling pressures.

Nevertheless, there are advantages for examining diastolic strain rate over mitral early and late diastolic velocities in the clinical setting. Mitral inflow provides information on global function, whereas diastolic strain rate provides insight into regional diastolic function. Accordingly, segmental diastolic strain rate can readily uncover the presence and extent of regional ischemia and viability and therefore can appropriately guide plans for revascularization. However, similar to systolic strain measurements (19), the effect of preload on diastolic strain rate is a potential limitation if one were to use these regional measurements to draw conclusions about global LV diastolic function. On the other hand, it is possible to gain incremental information about potential recovery of function when one considers both mitral inflow and regional diastolic strain rate. For example, in the presence of a restrictive mitral inflow pattern, which reliably predicts highly increased LV filling pressures in patients with depressed ejection fraction, the presence of a markedly reduced early diastolic strain rate in a given segment provides a high negative predictive value for...
segmental recovery, given the positive relation between EDP and diastolic strain rate.

Other determinants included $E_{es}$. The positive relation between parameters of diastolic function and LV contractility can be accounted for by the interaction between systolic and diastolic function, whereby the elastic energy stored in systole is released in early diastole contributing to myocardial expansion.

The larger decrement in longitudinal diastolic strain rate measurement vs. the radial one (65% vs. 44%, $P < 0.05$) in this animal model suggests that assessment of regional diastolic function in the longitudinal plane may be a more robust parameter to study in patients with coronary artery disease. This finding is probably accounted for by the LV geometric changes as it was well related to the increase in meridional to circumferential wall stress ratio post-MI ($R^2 = 0.68$, $P < 0.05$).

**Effects of MI on regional diastolic function.** As expected, in this animal model, myocardial necrosis resulted in a significant deterioration of regional function. Both systolic and diastolic indexes were altered in dysfunctional segments when compared with their own baseline function (before MI) as well as with remote segments.

Given the known sequential changes that occur in interstitial structure after MI, we examined a number of animals at variable time intervals post-MI. In the early proliferative stage of healing, inflammatory cells infiltrate the infarct, leading to formation of granulation tissue, containing a large number of phenotypically modulated fibroblasts expressing α-SMA. These cells, termed myofibroblasts (6, 24), are primarily responsible for extracellular matrix deposition in the infarct. In the late stages, a number of inflammatory cells and myofibroblasts become apoptotic, leading to formation of a mature scar with extensive collagen deposition and a low cellular content.

The structural dynamic changes described above have important effects on regional stiffness. At an early stage, myofibroblasts expressing the contractile protein α-SMA and the transient deposition of extracellular matrix proteins with elastic properties, such as tenascin and fibronectin (15, 25), result in a more compliant myocardium. Older scars, on the other hand, contain large amounts of mature cross-linked collagen and a small cellular component (18), contributing to increased myocardial stiffness. Given the strong inverse correlation between diastolic deformation indexes and regional stiffness, the Doppler-derived diastolic expansion rate showed significant changes that paralleled those in myocardial structure.

**Assessment of myocardial viability.** The presence of viable myocardium can be identified using several echocardiographic parameters. At the present time, this is largely done semiquantitatively, whereby a visual assessment is made of baseline systolic function and in response to dobutamine infusion (14). The recent application of systolic strain measurements in this field appears promising based on animal (22) and human studies (11). The objective aspect of tissue Doppler is partially appealing. However, as shown in this and previous studies (17), the important negative effect of end-systolic stress on systolic strain rate may preclude its utility (systolic strain rate) in detecting viable myocardium once a critical threshold of wall stress is reached.

In this study, we show the utility of diastolic function assessment in the identification of viable myocardium as determined histologically. Diastolic strain rate measurement appears promising because, compared with systolic indexes, it is more indicative of the presence of viable myocardium in segments with >20% transmural infarcts (no significant change in systolic strain rate with dobutamine, whereas diastolic strain rate increased significantly from 0.9 ± 0.23 to 1.25 ± 0.3 $s^{-1}$, $P < 0.05$). The ultimate clinical application of this approach however, remains to be investigated in future clinical studies.

**GRANTS**

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