Journal of the American College of Cardiology
© 2001 by the American College of Cardiology
Published by Elsevier Science Inc.

Vol. 38, No. 6, 2001
ISSN 0735-1097/01/$20.00
PII S0735-1097(01)01598-4

Intracardiac Measurement of Pre-Ejection Myocardial Velocities Estimates the Transmural Extent of Viable Myocardium Early After Reperfusion in Acute Myocardial Infarction

Cristina Pislaru, MD,* Charles J. Bruce, MD,† Marek Belohlavek, MD, PHD, FACC,† James B. Seward, MD, FACC,† James F. Greenleaf, PHD*

Rochester, Minnesota

OBJECTIVES We hypothesized that wall motion velocity during pre-ejection is proportional to the regional content of viable myocardium after reperfusion for acute myocardial infarction (AMI).

BACKGROUND Pre-ejection wall motion consists of short and fast inward and outward movement towards and away from the center of the left ventricle (LV) and is altered during regional ischemia. This short-lived event can be accurately quantified by Doppler myocardial imaging (DMI).

METHODS Fourteen open-chest pigs underwent 60 to 120 min of left anterior descending coronary artery occlusion followed by 30 min of reperfusion. The DMI data were collected using a phased-array intracardiac catheter (LV cavity) from ischemic and nonischemic myocardium encompassed within a plane passing through two epicardial bead markers. Peak tissue velocities during isovolumic contraction (IVC) (peak positive and peak negative), ejection (S) and early filling (E) were measured. The cardiac specimen was sliced through the epicardial markers in a plane approximating the ultrasound imaging plane. The transmural extent of necrosis (TEN) (%) was measured by triphenyltetrazolium chloride staining.

RESULTS During ischemia, positive IVC velocity was zero in ischemic walls with TEN >20%. At reperfusion, positive IVC velocity correlated better with TEN ($r = -0.94$, $p < 0.0001$) than it did S ($r = -0.70$, $p < 0.01$) and E ($r = -0.81$, $p < 0.01$). Differential IVC (the difference between peak positive and peak negative velocity) highly correlated with TEN, during ischemia ($r = -0.78$, $p < 0.001$) and during reperfusion ($r = -0.93$, $p < 0.0001$).

CONCLUSIONS Pre-ejection tissue velocity, as measured by intracardiac ultrasound, allows rapid estimation of the transmural extent of viable myocardium after reperfusion for AMI. (J Am Coll Cardiol 2001;38:1748–56) © 2001 by the American College of Cardiology

Asynchronous and rapid onset of myocardial contraction occurs after ventricular activation and before aortic valve opening, resulting in minor changes in left ventricular (LV) cavity dimensions and in wall thickness (1–3). At the regional level, the onset of regional contraction is the result of a complex interaction between electrical activation, myofiber orientation and load (4). The resulting pattern of contraction ultimately depends on regional wall stress, which is directly related to myocardial oxygen demand (5).

During ischemia, regional contraction is the result of a mosaic of contracting and noncontracting myofibers. An acutely ischemic segment suffers a loss of contractility and a decrease in stiffness, being unable to generate or sustain tensile stress. Mathematical models of regionally ischemic myocardium have suggested that the pattern of contraction is related to the rate of wall tension development, which is proportional to the degree of ischemia (6). In this study, we hypothesized that tissue velocities of the pre-ejection inward motion are proportional to the content of viable myocardium in the region.

Regional wall motion abnormalities during ejection have been extensively studied in ischemic heart disease, but those during pre-ejection (i.e., time from the onset of ventricular activation to the end of the isovolumic contraction phase) have received little attention. Early systolic wall bulging during ischemia has been documented by various techniques such as cine-ventriculography (7,8), sonomicrometry (9,10) and two-dimensional echocardiography (11,12). Doppler myocardial imaging (DMI) is a new noninvasive method that can accurately measure small changes in the myocardial wall velocities during short-lived events (13,14). The normal multiphasic pattern of tissue velocities during pre-ejection has been recently described (15,16). Most previous studies using DMI focused on peak systolic velocities during the ejection phase as a measure of regional contractile function (17–19). The changes in pre-ejection tissue velocities during acute myocardial infarction (AMI) have not yet been reported.

Identification of the extent of viable myocardium early after reperfusion is important in the management of patients and carries prognostic information (20). Because the return of regional contraction is delayed in a stunned myocardial wall, quantification of viable myocardium based on conven-

From the *Department of Physiology and Biophysics and the †Division of Cardiovascular Diseases Internal Medicine, Mayo Clinic and Foundation, Rochester, Minnesota. Supported by a grant from the National Heart, Lung and Blood Institute (HL41046), Bethesda, Maryland.

Manuscript received March 2, 2001; revised manuscript received July 12, 2001, accepted August 9, 2001.

Abbreviations and Acronyms

AMI = acute myocardial infarction
DMI = Doppler myocardial imaging
E = myocardial velocity due to early left ventricular filling
IVC = isovolumic contraction
LAD = left anterior descending coronary artery
LV = left ventricle or left ventricular
MI = myocardial infarction
S = myocardial velocity during ejection
SWT = systolic wall thickening
TEN = transmural extent of necrosis
TTC = 2,3,5-triphenyltetrazolium chloride

tional wall motion analysis at rest is not reliable (21,22). Dobutamine echocardiography can identify the extent of salvageable myocardium (23,24), but it is based on the detection of wall motion abnormalities induced during demand ischemia. A parameter that could assess the extent of viable myocardium at rest would be preferable, particularly during the acute phase of myocardial infarction (MI).

The aim of this study was to evaluate changes that occur in pre-ejection myocardial velocities in normal, ischemic (but viable) and nonviable myocardium in a controlled experimental setting using high-spatial resolution offered by intracardiac ultrasound (25,26) combined with high-temporal resolution DMI.

METHODS

Animal preparation. All animal experiments conformed to the "Position of the American Heart Association on Research Animal Use" and were approved by the Institutional Animal Care and Use Committee of the Mayo Clinic. Pigs weighing 40 kg to 50 kg were anesthetized with an infusion of Ketamine, Fentanyl and Amidate, intubated and mechanically ventilated with room air. A sternotomy was performed and the heart exposed in a pericardial cradle. All animals received intravenous heparin. Two epicardial bead markers were placed on the anterior LV wall: one in the anticipated ischemic zone and the other in the adjacent normal zone (Fig. 1). An intracardiac ultrasound catheter was placed into the LV cavity for repetitive ultrasound measurements from the normal and ischemic wall (described in the following text). Myocardial infarcts with varying transmural extents were induced by percutaneous transluminal coronary angioplasty balloon occlusion of the mid- or distal left anterior descending coronary artery (LAD) for 60 min to 120 min. Total occlusion was confirmed by angiography. Before balloon deflation, the site of the occlusion was marked by India ink injection on the epicardial surface. Reperfusion was allowed for 30 min.

At the end of the experiment, the animal was euthanized and the heart excised. The LAD at the site of the occlusion was ligated and cannulated. Myocardium at risk was delineated by injecting Evans blue solution into the proximal coronary arteries and saline into the LAD at the site of the occlusion. Each heart was sliced through the epicardial markers in a plane approximating the ultrasound imaging plane (Fig. 2A and 2B). Slices were immersed in triphenyltetrazolium chloride (TTC) solution to differentiate infarcted from viable myocardium (Fig. 2A). Samples were taken from the nonischemic, viable and infarcted tissue to confirm the TTC findings by light and electron microscopy.

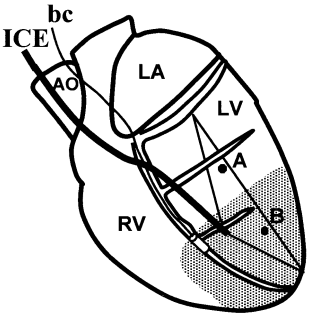

Figure 1. Schematic representation of the placement of the epicardial markers and intracardiac ultrasound interrogation plane. A and B = epicardial markers; AO = aorta; bc = percutaneous transluminal coronary angioplasty balloon catheter; ICE = intracardiac ultrasound catheter; LA = left atrium; LV = left ventricle; RV = right ventricle.

Intracardiac ultrasound. Ultrasound scanning was performed with a SEQUOIA system and using a 10F, 8.5 MHz phased-array intracardiac catheter (AcuNav, Acuson, a Siemens Company, Mountain View, California). The catheter tip was maneuvered to allow imaging in a plane passing through both epicardial markers in an approximately long-axis section through the LV (Fig. 2B). The intracardiac approach allowed measurements of wall motion velocities towards and away from a virtual center of the LV. Care was paid to align the vector motion of the anterior wall parallel with the central ultrasound beam. Data were acquired at baseline, at the end of the occlusion period and 30 min after reperfusion. Guided by the position of the epicardial markers, the anterior LV wall was systematically interrogated (M-mode and pulsed DMI) at three locations, equally spaced from the centrally dysfunctional area to the adjacent nonischemic area (Fig. 2A and 2B). Digital data were acquired in gray-scale M-mode, and color two-dimensional ($\backsim$150 frames/s), color M-mode and pulsed DMI. A sample length of 4 mm to 5 mm was used for pulsed DMI. The Nyquist limit was set to include the low velocities but avoid aliasing. Data were recorded on videotape and magneto-optical disk.

Echocardiographic measurements. Tissue velocities were analyzed offline using customized software. Peak velocities during isovolumic contraction (IVC) (peak positive and, where visible, peak negative), myocardial velocity during ejection (S) and myocardial velocity due to early left ventricular filling (E) were measured from pulsed DMI strips (15,16). Duration of positive IVC velocity wave was measured from color M-mode DMI. To quantify the progres-

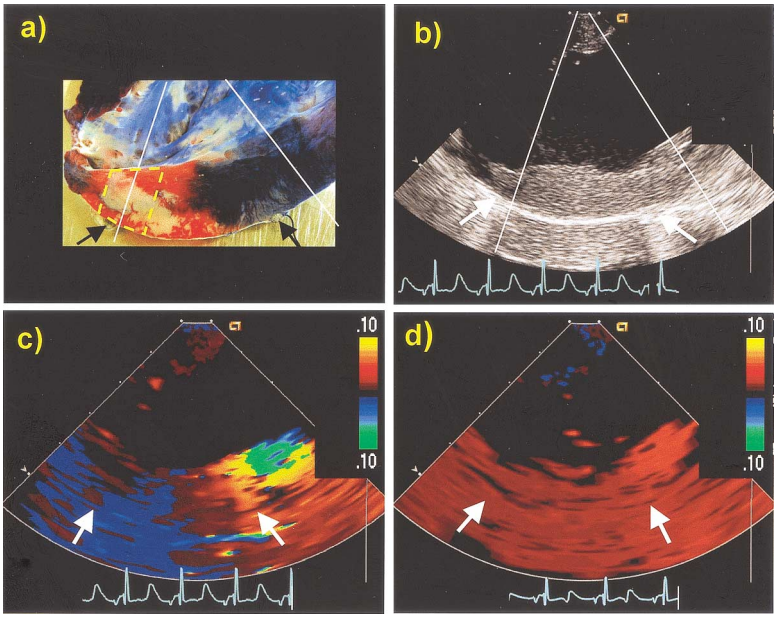

Figure 2. Cardiac specimen image and corresponding gray-scale and color Doppler myocardial imaging (DMI) images of the anterior wall from intracardiac echocardiography. **(a)** The cardiac specimen was sliced through the plane that included both epicardial markers **(arrows)** and double-stained with Evans blue and 2,3,5-triphenyltetrazolium chloride. Nonischemic myocardium is stained in **blue,** ischemic, but viable, myocardium in **red** and infarcted myocardium in **yellow-white.** The apex of the heart is toward the left, base of the heart toward right. The **white lines** correspond with the location of M-mode lines (or gate in pulsed DMI). The **yellow polygon** indicates the region of interest selected for analysis of the transmural extent of necrosis in the region (transmural extent of necrosis = 100 · number of white pixels / total number of pixels). **(b)** The corresponding **gray scale** image shows the location of the epicardial markers, helping in the registration of the gross pathology images with the DMI images. **(c)** Color DMI frame during ischemia shows tissue velocities during the isovolumic contraction (IVC) period. Note the high-positive velocities in the nonischemic myocardium and negative velocities in the ischemic myocardium. **(d)** Selected color DMI frame displaying tissue velocities during the ejection phase (at the time of the peak values). Note that the difference in tissue velocities between the normal and ischemic regions is less obvious than it is for IVC tissue velocities.

sion from positive to negative IVC velocities during ischemia, we defined a new parameter, differential IVC, as:

$$\text{Differential IVC} = \text{positive IVC velocity} - \text{negative IVC velocity}$$

Values from two to three heartbeats in sinus rhythm were averaged for each parameter. The time of the aortic valve closure and opening were identified on the color M-mode and pulsed DMI strips as brief velocity spikes produced by the aortic valve on the ultrasound catheter (confirmed in two animals by simultaneous phonocardiogram recording and gray-scale M-mode through the aortic leaflets).

Systolic wall thickening [SWT (%) = 100 · (end-diastolic − end-systolic) / end-diastolic wall dimension] was calculated from gray-scale M-mode recordings. End-diastole was considered at the electrocardiographic peak R-wave and end-systole at the time of the aortic valve closure. Regional wall motion was interpreted from gray-scale cineloops and M-mode strips and blinded to animal data. Normokinesis was defined as SWT >30%, hypokinesis SWT 10% to 25%, akinesis SWT 0% to 10% and dyskinesis SWT <0% with systolic outward motion.

Gross specimen data. Guided by the epicardial markers, the location of the line of M-mode or sample gate in DMI strips was marked on the cardiac specimen image (Fig. 2). A 1-cm wide region of interest was selected, centered by the identified line and using the full thickness of the wall (Fig. 2A). The transmural extent of necrosis (TEN) (%) within the region of interest was computed as the fraction of pixels in the TTC-unstained area (infarct, white area) from the total number of pixels in the region.

Statistical analysis. Peak velocities measured at baseline, during ischemia and reperfusion in nonischemic and ischemic regions were compared using repeated measures analysis of variance and multiple pairwise comparisons. Normal distribution was tested, and, when necessary, parameters were normalized to baseline values (positive IVC velocity and differential IVC). The influence of wall thickness, blood pressure, heart rate and TEN on tissue velocity parameters was tested with multiple stepwise regression analysis. Pearson's correlation coefficient was used to test the relationship between velocity parameters and TEN. A p value <0.05 was considered statistically significant. The results are presented as mean ± SEM.

RESULTS

A total of 20 animals was used in the study. Four animals developed ventricular fibrillation and died during LAD occlusion. Two animals developed an infarct outside the imaging plane, and, therefore, data were considered inconclusive and were excluded. Fourteen animals entered the final analysis. Heart rate did not change significantly from baseline to ischemia and reperfusion (73 ± 4 beats/min, 78 ± 5 beats/min and 85 ± 6 beats/min, respectively). Mean blood pressure was slightly lower during reperfusion (98 ± 5 mm Hg, 95 ± 6 mm Hg and 80 ± 6 mm Hg,

Table 1. Tissue Velocities and Wall Thickening in the Ischemic and Nonischemic Regions Throughout the Experiment

Parameter	Baseline		60-Min Occlusion		30-Min Reperfusion	
	Ischemic	Nonischemic	Ischemic	Nonischemic	Ischemic	Nonischemic
Positive IVC (cm/s)	8.7 ± 0.7	11.1 ± 1.0	3.0 ± 1.1*	12.4 ± 0.8	4.1 ± 0.9*	11.8 ± 1.1
Negative IVC (cm/s)	2.5 ± 1.3	1.0 ± 1.0	5.5 ± 1.3	2.3 ± 0.9	6.0 ± 1.2*	0.0 ± 0.0
S (cm/s)	6.4 ± 0.4	7.0 ± 0.5	3.8 ± 0.5*	6.2 ± 0.5	3.6 ± 0.5*	5.6 ± 0.5
E (cm/s)	10.2 ± 0.9	12.0 ± 1.4	7.2 ± 1.0*	9.9 ± 1.3	5.6 ± 1.5*	10.0 ± 1.2
Δt positive IVC (ms)	46.8 ± 2.2	49.4 ± 2.7	14.8 ± 5.7*	48.5 ± 2.6	25.7 ± 4.6*	57.2 ± 2.9
Diff. IVC (ms)	7.0 ± 1.4	9.5 ± 1.2	−2.5 ± 2.1*	9.6 ± 1.4	−1.6 ± 2.0*	9.8 ± 1.2
SWT (%)	35.0 ± 4.3	37.3 ± 4.4	−1.5 ± 3.1*	36.0 ± 6.2	5.7 ± 3.4*	38.5 ± 6.3

*$p < 0.05$ versus baseline. Data as mean ± SEM.

Δt positive IVC = duration of positive IVC velocity wave; Diff. IVC = differential IVC velocity; E = tissue velocity due to early filling; IVC = tissue velocity during isovolumic contraction; S = tissue velocity during ejection; SWT = systolic wall thickening.

respectively). The TEN in the ischemic region was 42 ± 8% (range: 0% to 98%).

Wall motion analysis. Systolic wall thickening was severely reduced during ischemia and did not recover after reperfusion (Table 1). There was no correlation between SWT and TEN, neither during ischemia nor at reperfusion (p = NS for both). The TEN in the reperfused infarcted region was 15 ± 3%, 56 ± 9% and 29 ± 9% in hypokinetic (n = 4), akinetic (n = 6) and dyskinetic walls (n = 4), respectively.

Changes in myocardial velocities during ischemia and reperfusion. Tissue velocity parameters in the ischemic region were significantly reduced during ischemia and reperfusion as compared with baseline (Table 1). Multiple pairwise comparisons showed that positive IVC, S, E and differential IVC velocities during ischemia and during

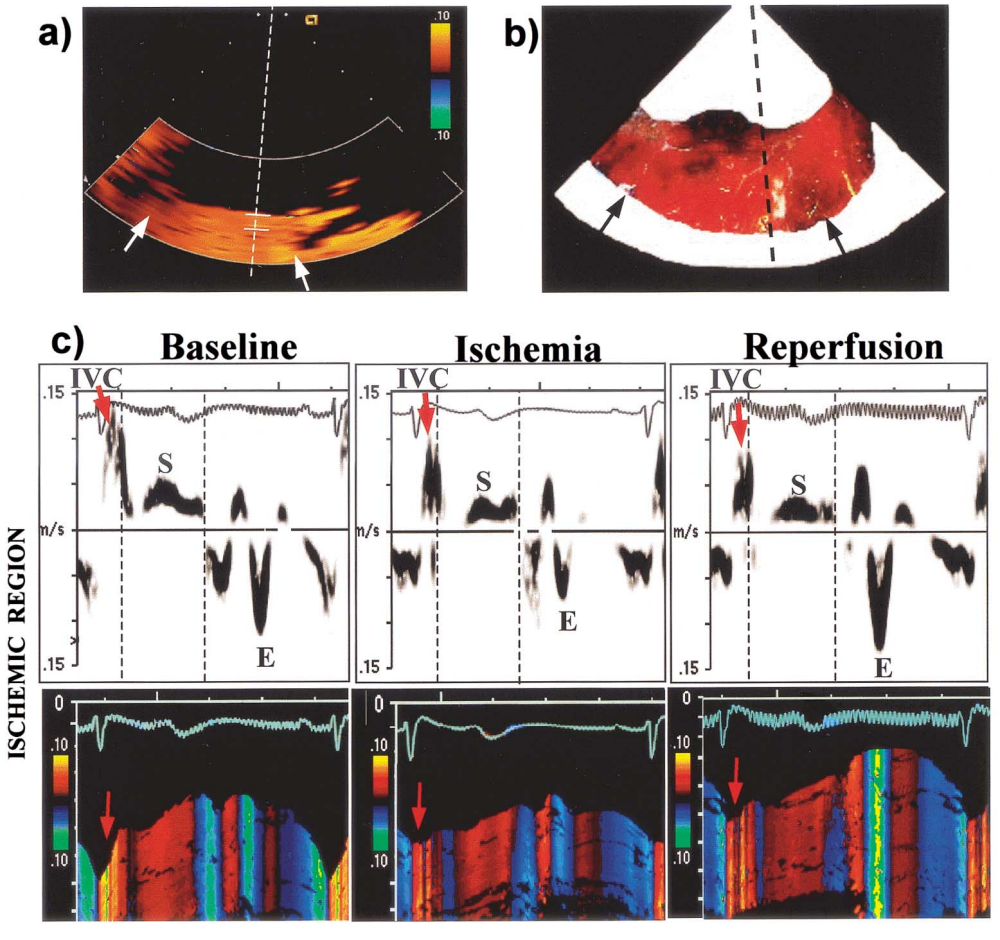

Figure 3. Data from one animal with a small anterior infarct. **(a)** A color Doppler myocardial imaging (DMI) frame during isovolumic contraction phase and showing the location of sample in pulsed DMI mode; epicardial markers are located at the **tip of the arrows. (b)** Shows a corresponding stained cardiac specimen image. The transmural extent of necrosis measured at the location of the sample gate was 6%. **(c)** Pulsed and color M-mode DMI at baseline, at the end of the occlusion (60 min) and after reperfusion (30 min). Note the reduced systolic (S) velocities during the ejection phase but the presence of high positive isovolumic contraction (IVC) velocity **(red arrows)**, identifying ischemic, but viable, myocardium. The **dashed vertical lines** indicate the time of the aortic valve opening and closure.

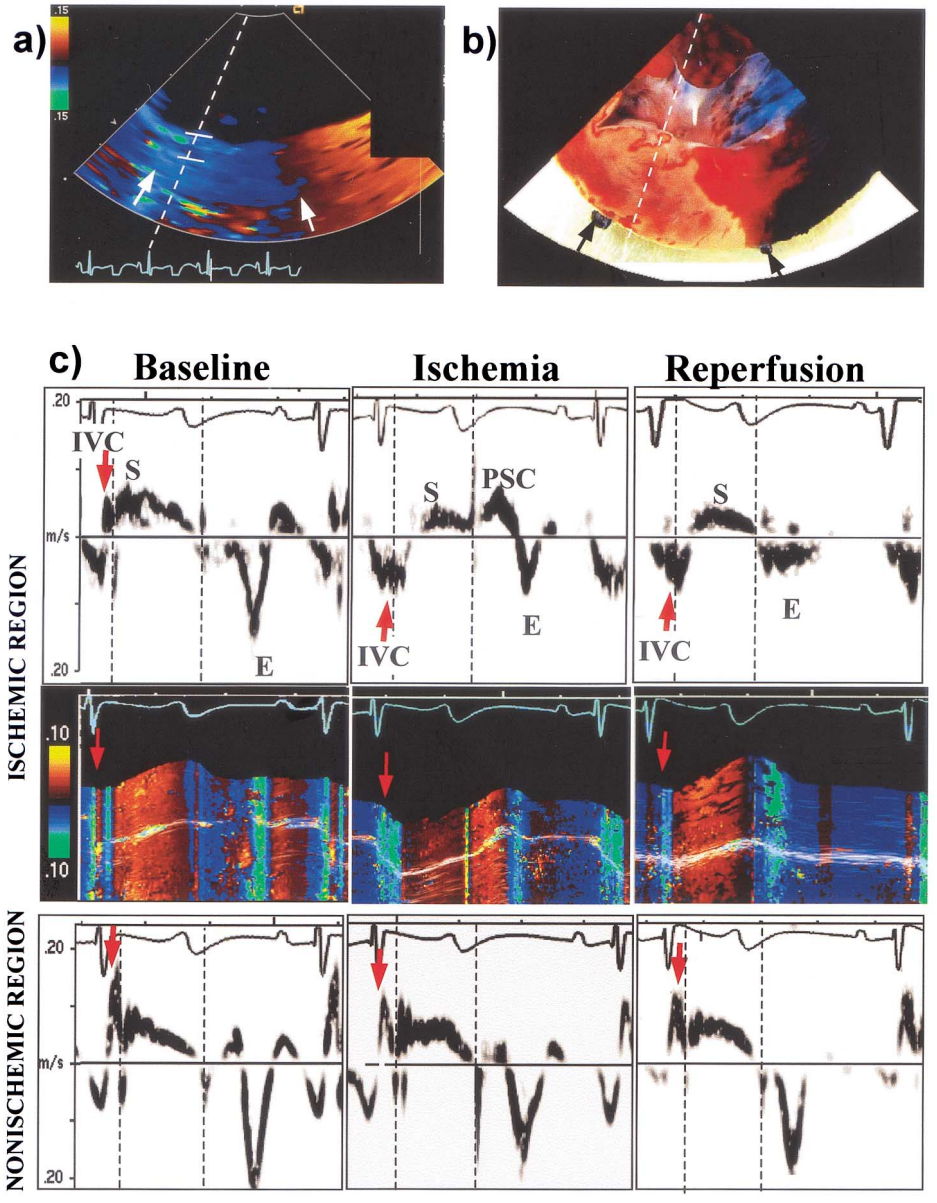

Figure 4. Data from one animal with anterior transmural infarction. **(a)** Shows the color Doppler myocardial imaging (DMI) frame during the isovolumic contraction phase and the location of sample in pulsed DMI mode; epicardial markers are located at the **tip of the arrows. (b)** Corresponding 2,3,5-triphenyltetrazolium chloride and Evans blue-stained cardiac specimen image. **(c)** Pulsed and color M-mode DMI at baseline, at the end of the occlusion (120 min) and after reperfusion (30 min) in the ischemic and nonischemic regions (pulsed DMI). Note in the ischemic region the reduced, but present, velocities during the ejection (S) (suggesting tethering effect) but different patterns of isovolumic contraction (IVC) velocities **(red arrows)**, which clearly identify ischemic myocardium. No change occurred in the nonischemic region. The **dashed vertical lines** indicate the time of the aortic valve opening and closure. E = myocardial velocity due to early left ventricular filling; PSC = tissue velocities due to postsystolic contraction.

reperfusion were significantly different from baseline ($p < 0.05$) but not different between ischemia and reperfusion (p = NS). There were no changes in velocity parameters in the nonischemic region (p = NS). Data from two animals with a small and a large transmural infarct are shown in Figures 3 and 4.

The positive IVC velocity wave was absent during ischemia in walls with TEN >20% but present in walls with TEN <20% (Fig. 5A). Positive IVC velocity at reperfusion highly correlated with TEN (Fig. 5B). Similarly, the duration of positive IVC velocity wave became shorter or zero as more necrosis was present transmurally ($r = -0.84$, $p < 0.0001$). Negative IVC velocity also correlated with TEN during ischemia ($r = -0.75$, $p < 0.05$) and reperfusion ($r = -0.80$, $p < 0.05$). Negative IVC velocity waves often extended into the early ejection period. Viable border zones showed a transition of IVC velocity values (usually >5 cm/s).

Differential IVC highly correlated with TEN during ischemia and reperfusion (Fig. 6). Generally, differential IVC was positive at baseline, except in two animals: one negative, the other zero; both animals had low positive IVC

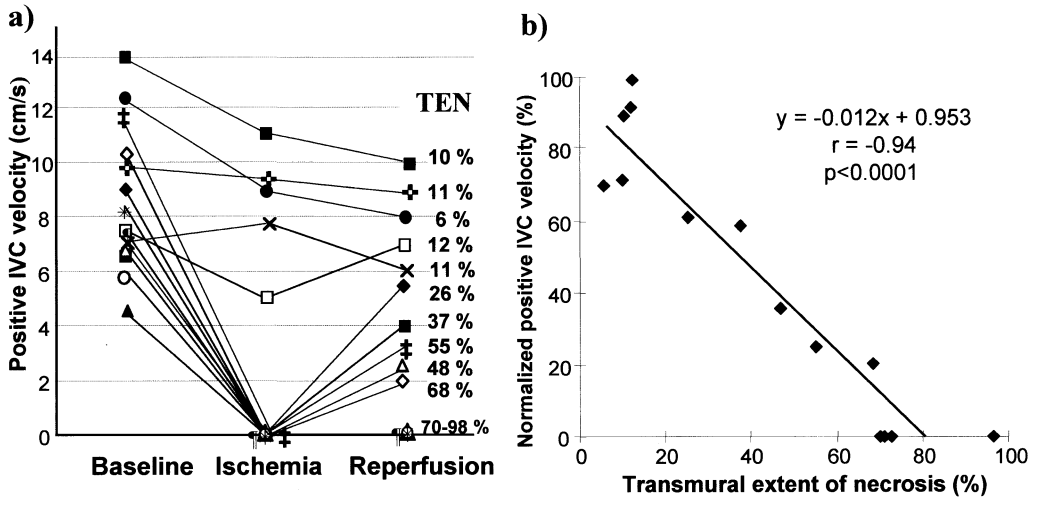

Figure 5. Positive isovolumic contraction (IVC) velocity in the ischemic region throughout the experiment and its correlation with the transmural extent of necrosis (TEN). **(a)** Different positive IVC velocity values were found in walls with small and large transmural infarcts during ischemia and reperfusion. **(b)** To compensate for the large variation in positive IVC velocity between animals, the values at reperfusion were normalized to baseline. Normalized positive IVC velocity highly correlated with TEN. The line of regression is indicated.

velocity (<6 cm/s) and both developed extensive infarction (TEN >70%) after 1 h of LAD occlusion.

Conversely, S velocity was significantly reduced during both ischemia and reperfusion (Table 1) and was only modestly correlated with TEN ($r = -0.72$ and -0.70, respectively; $p < 0.01$ for both). The E velocity correlated well with TEN only at reperfusion ($r = -0.81$, $p < 0.01$) but not during ischemia (p = NS).

Stepwise regression analysis revealed that positive IVC velocity was mainly influenced by TEN during ischemia ($r^2 = 0.72$, $p < 0.05$) and reperfusion ($r^2 = 0.88$, $p < 0.001$) but not by blood pressure, heart rate or wall thickness (p = NS for all). During ischemia, S velocity was influenced by TEN and by blood pressure ($r^2 = 0.49$ and 0.70 after inclusion into the model; $p < 0.05$), a relation that persisted with reperfusion.

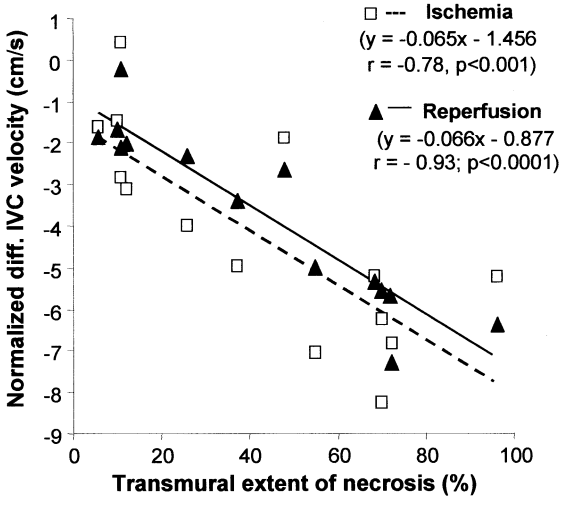

Figure 6. Differential isovolumic contraction (IVC) velocity versus transmural extent of necrosis (TEN). Differential IVC during ischemia **(open square)** and reperfusion **(solid triangle)** was normalized by subtracting the baseline value. A good correlation was found between differential IVC and TEN. The lines of regression are indicated for both ischemia **(broken line)** and reperfusion **(solid line)**.

DISCUSSION

This study demonstrates that pre-ejection tissue velocity can be used to rapidly estimate the transmural extent of necrosis in the reperfused infarcted wall. Isovolumic contraction tissue velocities were more sensitive to the transmural extent of necrosis than other systolic or diastolic regional velocity parameters. The presence of a positive IVC velocity wave in the ischemic wall was a marker of a less severe ischemic insult, while its absence identified a more severe ischemia.

Theoretical aspects of pre-ejection wall motion. The small increase in wall thickness that occurs in normal myocardium after ventricular activation and before aortic valve opening (1–4) corresponds to the brief and ample positive IVC velocity wave. These IVC velocities represent rapid excursions, smaller than 1 mm, frequently seen as small notches in high-quality gray-scale M-mode recordings. Pellerin et al. (15) and Garcia et al. (16) have shown that peak positive IVC tissue velocity occurs approximately at the time of mitral valve closure.

Mathematical models have predicted that the rate of the developed wall tension is proportional to the degree of ischemia; when the balance between the rate of the developed tension and the rate of rise in the internal LV pressure is disrupted, bulging occurs (6). In our study, the positive IVC velocity wave was reduced in amplitude and eventually disappeared during ischemia. Subsequently, the negative IVC velocity wave became apparent and increased in amplitude, thus reflecting bulging. Our findings of the progression from positive to negative IVC velocities in the ischemic walls are in agreement with the theoretical predictions.

JACC Vol. 38, No. 6, 2001
November 15, 2001:1748–56

Pre-ejection tissue velocities during ischemia. An important finding of our study was that positive IVC velocity wave was absent during ischemia in walls that finally developed more than 20% infarcted tissue in transmurality. In contrast, the persistence of positive IVC velocity during ischemia was associated with smaller infarcts (Figs. 3 and 5). The normal adjacent myocardium consistently showed large positive IVC velocity waves, occasionally with higher amplitude than at baseline (Table 1). This mechanical disadvantage imposed by the ischemic regions on the nonischemic regions has been shown to be more an isovolumic event (10) and caused by intraventricular unloading (27). In our study, the compensatory increase in IVC velocity observed in normal myocardium emphasized the distinction between normal and ischemic regions and easily identified the extent of ischemic myocardium (Fig. 2C and 4A).

The negative IVC velocities often extended into the early ejection period, reflecting bulging, as a result of the increased wall stress in the ischemic regions. Consequently, delayed onset of contraction occurred in some animals, similar to previous observations (7,8,28).

Pre-ejection tissue velocities during reperfusion. A second important finding of this study is that positive IVC velocity at reperfusion was inversely correlated with TEN and, therefore, proportional to the content of viable myocardium in the region. This finding suggests that viable stunned myocardium may contract at rest when LV pressure and wall stress are low (e.g., during pre-ejection), while it cannot sustain the load during ejection. Indeed, contraction during the isovolumic relaxation phase (i.e., post-systolic contraction [28,29]) was observed in the ischemic regions (Figs. 3 and 4). Our findings are in close agreement with the study of Zeiher et al. (11) who showed that early systolic contraction was preserved in patients with unstable angina but absent in patients with MI.

Interestingly, a return of positive IVC velocity was observed in four of nine animals after reperfusion, proportional with TEN (Fig. 5B). However, positive IVC velocity at reperfusion was not significantly different from ischemia due to opposite change in velocity values in small and large transmural infarcts. Derumeaux et al. (30) reported a small increase in IVC velocity during short-term ischemia, similar to our findings in small infarcts (Fig. 5). A similar return in regional isovolumic contraction was observed in patients with AMI treated with thrombolysis (8). On the contrary, the absence of positive IVC velocity wave during ischemia and reperfusion identified transmural infarcts (Fig. 5B). If proven by further studies, the return in positive IVC velocity might become a maker of successful reperfusion in viable myocardial walls.

Positive IVC velocity did not vary with wall thickness, mean blood pressure or heart rate. Although good correlation was found between normalized IVC velocities and TEN, baseline values are not available in clinical settings. Further studies are necessary to establish the normal distribution of tissue IVC velocities along the cardiac segments.

Value of differential IVC velocity. Differential IVC combined information on both positive and negative IVC velocities and showed the highest correlation with TEN during ischemia and during reperfusion. The near zero values of differential IVC in two animals at baseline imply that this parameter alone is still not ideal. Interestingly, both animals developed extensive infarcts. Whether or not lower differential IVC value may reflect increased regional wall stress, therefore, a predisposition to develop an extensive infarct, warrants further investigation.

IVC velocity versus conventional wall motion analysis. Wall thickening did not recover with reperfusion, indicating the presence of stunning (21) and did not help with quantification of TEN (23). Nevertheless, differential IVC and positive IVC velocities (at reperfusion) were able to distinguish segments with different degrees of necrosis. Preserved IVC velocity waves in hypokinetic or akinetic ischemic walls were associated with small infarcts (Fig. 5). Conversely, animals with extensive infarcts and akinetic or dyskinetic walls exhibited higher amplitudes of negative IVC velocity during ischemia that persisted during reperfusion.

Tissue velocities during ejection and early filling phases. The lower correlation found for the ejection and early filling tissue velocities with TEN suggests the influence of other factors on these two parameters, such as tethering, cardiac rotation (theoretically higher during ejection than during pre-ejection) or loading. To overcome the influence of tethering, myocardial velocity gradient can be calculated (31). Derumeaux et al. (32) have used myocardial systolic velocity gradient to differentiate transmural from nontransmural infarcts, but the authors did not separate the gradients during pre-ejection.

The lack of a significant compensatory increase in systolic indexes in nonischemic regions in our study may disagree with experimental or clinical observations; this difference could be explained by tethering of the normal region that may have been located too close to the ischemic region. Ning et al. (27) have demonstrated that the augmented contraction in nonischemic wall is more an isovolumic event rather that an ejection phase event and depends on the size of the ischemia. We observed this compensatory increase in IVC tissue velocities only in some animals.

Implications. Nuclear perfusion techniques, dobutamine stress echocardiography, ultrafast computed tomography or magnetic resonance imaging are current clinical tools for the assessment of myocardial viability, but all are expensive, not in real-time and not available for all patients. Development of a less expensive, widely available and rapid tool for prediction of the amount of viable myocardium would represent a distinct advantage over the existing technology. The observation of a positive IVC tissue velocity in a stunned myocardium suggests preserved viability without the need of a stress test, with data being instantly available at bedside. It might be possible to select appropriate treatment or to follow the results of revascularization procedures on the basis of the pattern of wall motion (29).

The lack of positive IVC velocity wave may facilitate accurate sizing of regional ischemia and patient follow-up for infarct extension and expansion. The recognition of the mechanical disadvantage imposed by the ischemic myocardium on the normal myocardium is important because asynchronous and opposite direction of motion results in waste of energy developed in the normal region and possibly impairment in coronary blood flow reserve (33). Nevertheless, our findings may become useful if they are reproduced in humans using a transthoracic approach.

The small amount of wall thickening during pre-ejection precluded its accurate measurement in the past. Pulsed DMI is a rapid, noninvasive and quantitative method that can track local function with high spatial and temporal accuracy, being independent of endocardial border detection (19). Wall thickening is calculated using the end-diastolic and end-systolic wall dimensions; however, the pattern of contraction that occurs between these time points is ignored. Detailed analysis of the entire contraction/relaxation sequence may offer valuable information (11,12,28,29). Conventional assessment of endocardial motion is subjective and experience-dependent and does not allow discernment of small differences in wall motion. Therefore, reproducible, quantitative and sensitive indicators of regional ischemia are required.

The intracardiac ultrasound enables systematic interrogation of all cardiac segments with high-spatial resolution, minimizing limitations from other approaches. Our findings can be directly tested in a selected patient population undergoing open-heart surgery.

Study limitations. Angle dependency of the Doppler technique can affect the measurement of tissue velocity, a limitation that may restrict this method to fewer segments when transthoracic or transesophageal approaches are to be used. Only anterior wall ischemia was tested in this study, with no residual stenosis after reperfusion. The effect of myocardial blood flow reduction on pre-ejection wall motion has to be further studied. The placement of epicardial markers required the use of an open-chest model, eliminating the restraint of the pericardium (4); however, no change in IVC tissue velocity was found in closed-chest versus open-chest preparation (30). The influence of loading (10), myocardial fiber orientation and asynchronous ventricular activation on pre-ejection tissue velocities has to be further studied. The change in LV end-diastolic pressure (34) or wall stiffness (35) during ischemia and reperfusion may affect wall motion; in our study, less IVC bulging was observed in one animal with a transmural infarct. Whether our findings apply to myocardial walls with chronic infarction (36) needs to be further tested.

CONCLUSIONS

Intracardiac ultrasound measurement of radial pre-ejection tissue velocity is a rapid means for estimating the content of viable myocardium early after reperfusion in AMI. Isovolumic contraction tissue velocities were more sensitive to the transmural extent of necrosis than other systolic or diastolic regional velocity parameters. The presence of a positive IVC velocity wave in the ischemic wall was a marker of a less severe ischemic insult, while its absence identified a more severe ischemia. In the stunned myocardium, the amplitude of positive IVC velocity was inversely proportional to the transmural extent of infarcted myocardium, therefore, indirectly reflecting the content of viable myocardium in the region. Further studies are required to evaluate this method for transthoracic and transesophageal ultrasound imaging.

Acknowledgment

The authors thank Acuson for providing the ultrasound catheters and scanner.

Reprint requests and correspondence: Dr. Cristina Pislaru, Mayo Clinic, Ultrasound Research Laboratory, 200 First Street SW, Rochester, Minnesota 55905. E-mail: Pislaru.Cristina@mayo.edu.

REFERENCES

1. Rushmer RF. Initial phase of ventricular systole: asynchronous contraction. Am J Physiol 1956;184:188–94.
2. Feigl EO, Fry DL. Myocardial mural thickness during the cardiac cycle. Circ Res 1964;14:541–5.
3. Bove AA. Radiographic evaluation of dynamic geometry of the left ventricle. J Appl Physiol 1971;31:227–34.
4. Rankin JS, McHale PA, Arentzen CE, et al. The three-dimensional dynamic geometry of the left ventricle in the conscious dog. Circ Res 1976;39:304–13.
5. Maroko PR, Braunwald E. Modifications of myocardial infarction size after coronary occlusion. Ann Intern Med 1973;79:720–33.
6. Elings VB, Jahn GE, Vogel JHK. A theoretical model of regionally ischemic myocardium. Circ Res 1977;41:722–9.
7. Gibson DG, Doran JH, Trail TA, Brown DJ. Abnormal left ventricular movement during early systole in patients with angina pectoris. Br Heart J 1984;51:70–6.
8. Gibson D, Mehmel H, Scharz F, et al. Changes in left ventricular regional asynchrony after intracoronary thrombolysis in patients with impending myocardial infarction. Br Heart J 1986;56:121–30.
9. Theroux P, Ross J, Franklin D, et al. Regional myocardial function in the conscious dog during acute coronary occlusion and response to morphine, propranolol, nitroglycerine and lidocaine. Circulation 1976; 53:302–14.
10. Lew WYW, Chen Z, Guth B, Covell JW. Mechanisms of augmented segment shortening in nonischemic areas during acute ischemia of the canine left ventricle. Circ Res 1985;56:351–8.
11. Zeiher AM, Wollschlaeger H, Bonzel T, et al. Hierarchy of levels of ischemia-induced impairment in regional left ventricular systolic function in man. Circulation 1987;76:768–76.
12. Weyman AE, Franklin TD, Hogan RD, et al. Importance of temporal heterogeneity in assessing the contraction abnormalities associated with acute myocardial ischemia. Circulation 1984;1:102–12.
13. Isaaz K, Thompson A, Ethevenot G, et al. Doppler echocardiographic measurement of low velocity motion of the left ventricular posterior wall. Am J Cardiol 1989;64:66–75.
14. Sutherland GR, Stewart MJ, Groundstroem KWE, et al. Color Doppler myocardial imaging: a new technique for the assessment of myocardial function. J Am Soc Echocardiogr 1994;7:441–58.
15. Pellerin D, Berdeaux A, Cohen L, et al. Pre-ejectional left ventricular wall motions studied on conscious dogs using Doppler myocardial imaging: relationships with indices of left ventricular function. Ultrasound Med Biol 1998;24:1271–83.
16. Garcia MJ, Rodriguez L, Ares M, et al. Myocardial wall velocity

assessment by pulsed Doppler tissue imaging: characteristic findings in normal subjects. Am Heart J 1996;132:648–56.
17. Gorcsan J, III, Strum DP, Mandarino WA, et al. Quantitative assessment of alterations in left ventricular contractility with color-coded tissue Doppler echocardiography: comparison with sonomicrometry and pressure-volume relations. Circulation 1997;95:2423–33.
18. Wilkenshoff UM, Sovany A, Wigstrom L, et al. Regional mean systolic velocity estimation by real-time color Doppler myocardial imaging: a new technique for quantifying regional systolic function. J Am Soc Echocardiogr 1998;11:683–92.
19. Hatle L, Sutherland GR. Regional myocardial function—a new approach. Eur Heart J 2000;21:1337–57.
20. Bolognese L, Cerisano G, Buonamici P, et al. Influence of infarct-zone viability on left ventricular remodeling after acute myocardial infarction. Circulation 1997;96:3353–9.
21. Pfisterer M, Zuberg M, Wenzel R, et al. Prolonged myocardial stunning after thrombolysis: can left ventricular function be assessed definitely at hospital discharge? Eur Heart J 1991;12:214–7.
22. Lieberman AN, Weiss JL, Jugdutt BI, et al. Two-dimensional echo infarct size. Circulation 1981;63:739–46.
23. Sklenar J, Ismail S, Villanueva FS, et al. Dobutamine echocardiography for determining the extent of myocardial salvage after reperfusion: an experimental evaluation. Circulation 1994;90:1502–12.
24. Garot J, Bluemke DA, Osman NF, et al. Transmural contractile reserve after reperfused myocardial infarction in dogs. J Am Coll Cardiol 2000;36:2339–46.
25. Pandian NG. Intravascular and intracardiac ultrasound imaging. Circulation 1989;80:1091–4.
26. Bruce CJ, Packer DL, Belohlavek M, Seward JB. Intracardiac echocardiography: newest technology. J Am Soc Echocardiogr 2000;13:788–95.
27. Ning XH, Zweng TN, Gallagher KP. Ejection and isovolumic contraction-phase wall thickening in non-ischemic myocardium during coronary occlusion. Am J Physiol 1990;258:H490–9.
28. Pislaru C, Belohlavek M, Bae R, et al. Regional asynchrony during acute myocardial ischemia quantified by ultrasound strain rate imaging. J Am Coll Cardiol 2001;37:1141–8.
29. Jamal F, Kukulski T, D'hooge J, et al. Abnormal post-systolic thickening in acutely ischemic myocardium during coronary angioplasty: a velocity, strain, and strain rate Doppler myocardial imaging study. J Am Soc Echocardiogr 1999;12:994–6.
30. Derumeaux G, Ovize M, Loufoua J, et al. Doppler tissue imaging quantitates regional wall motion during myocardial ischemia and reperfusion. Circulation 1998;97:1970–7.
31. Uematsu M, Miyatake K, Tanaka N, et al. Myocardial velocity gradient as a new indicator of regional left ventricular contraction: detection by a two-dimensional tissue Doppler imaging technique. J Am Coll Cardiol 1995;26:217–23.
32. Derumeaux G, Loufoua J, Pontier G, et al. Tissue Doppler imaging differentiates transmural from nontransmural acute myocardial infarction after reperfusion therapy. Circulation 2001;103:589–96.
33. Daher E, Dione DP, Heller EN, et al. Acute ischemic dysfunction alters coronary flow reserve in remote nonischemic regions: potential mechanical etiology identified in an acute canine model. J Nucl Cardiol 2000;7:112–22.
34. Lew WYW, Ban-Hayashi E. Mechanisms of improving regional and global ventricular function by preload alterations during acute ischemia in the canine left ventricle. Circulation 1985;5:1125–34.
35. Parmley WW, Chuck L, Kivovitz C, et al. In vitro length-tension relations of human ventricular aneurysms: relation of stiffness to mechanical disadvantage. Am J Cardiol 1973;32:889–94.
36. Radhakrishnan S, Ghista DN, Jayaraman G. Mechanics of left ventricular aneurysm. J Biomed Eng 1986;8:9–23.