Intraventricular Early Diastolic Filling During Acute Myocardial Ischemia
Assessment by Multigated Color M-Mode Doppler Echocardiography

Marie Stugaard, MD; Otto A. Smiseth, MD, PhD; Cecilie Risøe, MD; Halfdan Ihlen, MD, PhD

Background. Color M-mode Doppler echocardiography has been suggested as a new noninvasive technique for assessing left ventricular diastolic function. The present study investigated intraventricular filling pattern by color M-mode Doppler in patients during percutaneous transluminal coronary angioplasty (PTCA). In a dog model of myocardial ischemia, the color M-mode flow pattern was related to indices of global and regional myocardial function.

Methods and Results. From color M-mode images, the time difference (TD) between occurrence of peak velocity in the apical region and at the mitral tip was determined in 20 patients and eight anesthetized dogs during coronary occlusions. During PTCA, the timing of peak velocity was progressively delayed from mitral valve to apex. Consistent with this, the dog model showed delayed apical filling during coronary occlusion; TD increased from 18±4 to 71±9 milliseconds (P<.01). In the ischemic region, systolic shortening (sonomicrometry) decreased from 20±3% to −5±2% (P<.01). The one-third filling fraction decreased from 59±5% to 31±6% (P<.01) and correlated with TD (r=.85, P<.01). The time constant of isovolumic relaxation (τ) increased slightly and correlated with TD (r=.81, P<.01). Pacing tachycardia, caval constriction, and volume loading were performed to mimic the ischemia-induced changes in heart rate, stroke volume, and intracavitary filling pressure, respectively. There were no significant changes in TD or τ during these interventions.

Conclusions. Color M-mode Doppler echocardiography showed a marked delay of apical peak filling velocity during PTCA. The experimental data suggest that this reflects retarded filling of the ischemic ventricle. Thus, color M-mode Doppler may provide a useful method for assessing diastolic dysfunction. (Circulation. 1993;88:2705-2713.)

KEY WORDS • echocardiography • diastole • ventricles • ischemia

Recently, color M-mode Doppler echocardiography has been proposed as a method for assessing left ventricular (LV) filling in patients with myocardial dysfunction.1,2 This is a multigated technique that measures velocities at multiple sites simultaneously and with high time resolution. We have reported preliminary color M-mode data showing that intraventricular filling velocities fall during myocardial ischemia.3

In the present study, we used color M-mode Doppler echocardiography to measure differences in the timing of peak filling velocities at multiple sites between the mitral valve and the apex. In patients, we found that peak early filling velocity in the apical region was markedly delayed during percutaneous transluminal coronary angioplasty (PTCA). To investigate the hypothesis that this abnormal color M-mode pattern was due to retarded filling of the ischemic LV, a dog model was studied. We were able to reproduce the clinical observations with color M-mode Doppler and to relate the delay in apical filling to changes in global and regional LV function.

Methods

Clinical Material

Thirty-nine patients with symptomatic coronary artery stenosis and normal ejection fraction (EF) who were admitted for elective PTCA were evaluated consecutively by color M-mode Doppler echocardiography. Nineteen patients were excluded from the study because of technically inadequate recordings in the supine position despite adequate signals in the lateral rotated position. Thus, 20 patients with a mean age of 54 years were included (Table 1). No evidence of valvular disease was present by echocardiography or catheterization. All patients were in regular sinus rhythm. Most patients were treated with cardioactive drugs: nitrates (70%), β-adrenergic blockers (70%), calcium channel blockers (30%), and angiotensin-converting enzyme inhibitors (5%). The excluded patients were not significantly different from the included patients with respect to clinical and hemodynamic characteristics.

Color M-Mode Doppler Technique

A Vingmed CFM 700 cardiac ultrasound machine (Vingmed Sound, Horten, Norway) with a combined
TABLE 1. Clinical Characteristics and Results of the 20 Patients Treated With Coronary Angioplasty

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age, y</th>
<th>Sex</th>
<th>Stenosis</th>
<th>LV angio</th>
<th>EF, %</th>
<th>LVEDP, mm Hg</th>
<th>Occl</th>
<th>ST, mV</th>
<th>Pain</th>
<th>TD, ms</th>
<th>nTD, ms/cm</th>
</tr>
</thead>
</table>
| 1       | 58     | M   | LAD 90   | N       | 86    | 16          | LAD 0 | -     | 37   | 12    | 15          | 9  3  4  
| 2       | 48     | M   | LAD 90   | N       | 84    | 24          | LAD 0 | -     | 17   | 110   | 43          | 4  28 14 |
| 3       | 43     | M   | RCA 90, LAD 75, circumflex 100 | N | 79    | 12          | RCA 0 | -     | 22   | 25    | 12          | 5  6  3  
| 4       | 55     | M   | LAD 90   | N       | 91    | 16          | LAD 0 | -     | 27   | 138   | 17          | 7  35 4   
| 5       | 63     | M   | LAD 75, circumflex 75, RCA 75 | N | 85    | 4           | LAD 0 | -     | 42   | 173   | 18          | 10 43 5   
| 6       | 45     | M   | RCA 90, LAD 75 | N | 79    | 20          | RCA -1 | +    | 10   | 178   | 28          | 3 45 7   
| 7       | 44     | M   | Circumflex 90, LAD 75, RCA 100 | N | 73    | 15          | Circumflex -1 | -   | 52   | 168   | 23          | 13 41 8   
| 8       | 49     | F   | RCA 90   | Inf akin | 55    | 16          | RCA -1 | +    | 102  | 102   | 58          | 25 25 15  
| 9       | 60     | F   | Circumflex 75 | N | 78    | 20          | Circumflex -1 | +   | 43   | 168   | 58          | 14 42 14  
| 10      | 60     | M   | LAD 75, Circumflex 90 | N | 66    | 12          | LAD -1,5 | +   | 25   | 267   | 110         | 6 39 37  
| 11      | 58     | M   | LAD 90   | Inf akin | 10    | 2           | LAD -1,5 | +   | 50   | 153   | 45          | 13 38 11  
| 12      | 68     | F   | Circumflex 90 | N | 76    | 24          | Circumflex -3 | +  | 45   | 128   | 48          | 11 32 12  
| 13      | 45     | M   | R med 90, circumflex 90, RCA 75 | N | 83    | 6           | LAD 1 | +    | 13   | 160   | 35          | 3 53 12  
| 14      | 49     | M   | LAD 90   | N       | 82    | 15          | LAD 1 | +    | 22   | 285   | 13          | 5 95 3    
| 15      | 40     | M   | LAD 90   | N       | 65    | 12          | LAD 1 | +    | 33   | 112   | 7           | 8 28 2    
| 16      | 66     | M   | LAD 90   | N       | 91    | 8           | LAD 2 | -    | 37   | 195   | 25          | 9 49 6    
| 17      | 51     | M   | LAD 90   | N       | 81    | 18          | LAD 3 | +    | 20   | 288   | 35          | 5 72 9    
| 18      | 52     | M   | LAD 75   | N       | 91    | 8           | LAD 4 | +    | 12   | 88    | 38          | 3 22 10   
| 19      | 70     | M   | LAD 90   | N       | 82    | 18          | LAD 5 | +    | 17   | 208   | 18          | 4 69 5    
| 20      | 53     | M   | LAD 90   | N       | 72    | 10          | LAD 8 | +    | 50   | 160   | 47          | 17 53 16  
| Mean    | 54±2   |     |           |         |       | 78±2        | 14±1 |       | 34±5 | 156±16 | 35±5        | 9±1 43±5 10±2 |

| P       | <.001  | NS    | <.001 NS  | NS    |

Stenosis indicates % areal stenosis of coronary artery; LV angio, left ventricle angiography; EF, ejection fraction; LVEDP, left ventricular end-diastolic pressure; Occl, balloon-occluded artery; ST, ST segment change; TD, time difference between occurrence of peak velocity in the apical region and at the mitral tip; nTD, normalized TD; C, control; PTCA, percutaneous transluminal coronary angioplasty; A, 5 minutes after PTCA; LAD, left anterior descending artery; RCA, right coronary artery; Circumflex, left circumflex artery; R med, ramus medianus; N, Normal; Ant, anterior; Inf, inferior; hypo, hypokinesia; akin, akinesia; and P, paired t test vs control.

tissue imaging (3.75-MHz) and Doppler (2.5-MHz) transducer was used. The patients were examined in the supine position. LV inflow was imaged by two-dimensional color flow mode using the transthoracic apical long-axis view. This view was chosen to avoid disturbing signals from aortic outflow. The depth of the mitral tip was determined at maximum opening in early diastole, and color M-mode Doppler velocities were measured along a cursor line placed centrally in the two-dimensional color inflow map to include both mitral and apical flow. The transducer position was adjusted so that early diastolic filling was depicted as a continuous column of blood flow from mitral valve to apex, using a high-pass filter of 12 cm/s (Fig 1A). Care was taken that all recordings were performed from the same apical window and at the same site in the inflow part of the LV. Recordings with lack of continuity in the flow column were considered inadequate.

Clinical Procedure

PTCA was performed by the standard approach. The 30- to 60-second balloon inflations were repeated 2 to 13 times, interspaced by 1 to 5 minutes of reperfusion, until residual areal stenosis was <50%. Color M-mode Doppler and ECG (limb and V1 leads) were recorded before, during (within 40 seconds), and 5 minutes after PTCA.

The protocol was approved by the ethical committee of the hospital, and informed consent was obtained from all patients.

Experimental Material and Methods

Fourteen dogs of either sex (17 to 26 kg) were given thiopentone (25 mg/kg body weight IV), followed by an infusion of morphine (50 to 100 mg/h) and sodium
pentobarbital (50 mg every 1.5 hours). The animals were artificially ventilated with room air.

After a median sternotomy, the pericardium was widely split from apex to base. Peripheral veins were cannulated for infusion. Micromanometer-tipped catheters were placed in the left atrium (LA) and in the LV (models PC 350 and SPC 474A, Millar Instruments, Houston, Tex) via a pulmonary vein and a femoral artery, respectively. The LV micromanometer was zero-referenced to pressure via a fluid-filled line, and the LA manometer was referenced to LV pressure. Aortic pressure was monitored (model AE 840, SensoNor, Horten, Norway). A flow probe was placed around the ascending aorta (model T201, Transonics Systems Inc, Ithaca, NY). Vascular occluders (In Vivo Metric, Healdsburg, Calif) were placed on both venae cavae and on the left circumflex coronary artery (LCx) <2 cm from its origin and the left anterior descending coronary artery (LAD) proximal to the first diagonal branch.

Regional myocardial function was assessed in non-ischemic and ischemic regions by sonomicrometry. Two pairs of cylindrical transducers (Triton Technology, Inc, San Diego, Calif) were implanted in the midmyocardium to measure segment length in the distribution areas of the LCx and LAD. Each pair was aligned about 1 cm apart in the minor axis circumference approximately midway between the base and the apex. Pacing electrodes were sutured to the right atrial appendage.

Data were recorded by a Gould ES 2000 (Cleveland, Ohio) and were digitized for analysis by cvsoft (Odessa Computer, Calgary, Canada). Doppler recordings were performed as in the clinical study.

**Experimental Procedure**

Recordings were taken with the dogs in the left lateral position with the ventilator off. Because of acoustic interference, Doppler recordings were performed separately, followed within 5 seconds by measurement of ECG, pressures, dimensions, and aortic flow.

Myocardial ischemia was produced in eight dogs by occluding either the LCx \( n=8 \) or LAD \( n=3 \) for <8
minutes. Recordings were taken after about 4 minutes of ischemia. In three of the eight dogs, alternating LAD or LCx ischemia was produced, interspaced by 10 minutes of reperfusion. The hemodynamic variables had returned to preischemic values before the second occlusion.

Because ischemia was associated with tachycardia, reduction of stroke volume, and elevation of LV enddiastolic pressure (LVEDP), separate interventions were done to study how each of these variables influenced the color M-mode pattern. In the nonischemic ventricle, recordings were made during atrial pacing at three different rates (eight dogs), during reduction of stroke volume by constriction of both venae cavae (seven dogs), and during rapid intravenous infusion of saline to three different levels of LVEDP (eight dogs).

Data Analysis and Calculations

Color M-mode Doppler echocardiography. Each picture element (pixel) in the color M-mode picture represented a velocity, averaged over a 2.3-mm distance along the depth axis and over 5 milliseconds along the time axis. The velocities (-1.4 to +1.4 m/s) were digitized into 36 levels of color codes by use of a rainbow color system. The original recorded velocity, time, and depth values were digitized and transferred unchanged to an external computer. Image calculations were then performed by processing routines developed for this study (Vingmed Sound, Horten, Norway) as described below. To reduce the problem of velocity "dropouts" and noise in the flow recording, median filtering was performed: the velocity of each pixel was replaced by the median of the velocities in an area of five pixels in the depth axis and three pixels in the time axis around that pixel.

The area of early filling was defined, and the color data were decoded into numerical values (Fig 1B). An algorithm was used to locate the intraventricular peak velocity at every second pixel depth (0.46 cm) in the dogs and at every fourth pixel depth (0.92 cm) in the humans, from the mitral tip toward the apex. In the distal 1.5 to 2 cm of the ventricle, velocities were low and difficult to separate from noise artifacts. These velocities were therefore not included in the analysis. If peak velocity at a given depth was found in several adjacent pixels, the most centrally located pixel was chosen. In cases in which the flow column was divided into two phases in the apical region, the algorithm was constructed to determine peak velocity in the phase with the highest velocity at the dividing site. The time difference (TD) of peak velocity was defined as the TD between occurrence of peak velocity in the apical region and at the mitral tip (Fig 1C). Because of individual variability in mitral to apical distance, TD was normalized (nTD) by dividing by the distance. Data were read as the mean of three consecutive heartbeats.

Pressures. LA pressure was measured at the time of LV/LA pressure crossover in early diastole. The peak early diastolic transmitral pressure gradient was calculated. The time constant of isovolumic relaxation (τ) was calculated by the derivative method. Satisfactory r values for ln dP/dt versus pressure (>0.95) were obtained in all dogs.

Sonomicrometry. Regional filling was measured as one-third filling fraction, defined as the increase in myocardial segment length during the first third of diastole as a percentage of total lengthening. The onset
of diastole was defined as LA/LV pressure crossover. Percentage systolic shortening was calculated.

Statistics

Data are presented as mean±SEM or ranges. For univariate comparisons of the data, paired and unpaired t tests (two-tailed) and ANOVA were performed. We performed multiple regression analysis with dummy variables to account for between-subject variability. The level of statistical significance was P<.05.

Results

Clinical Study

During the balloon occlusions, 13 patients experienced chest pain and 15 patients had significant (>0.1 mV) ST segment changes (Table 1). Five minutes after the last balloon inflation, the patients had neither pain nor ECG changes. Heart rate was 59±2 beats per minute before, 63±3 beats per minute during, and 60±2 beats per minute 5 minutes after occlusion. In agreement with these observations, TD increased from 34±5 to 156±16 milliseconds (P<.001), indicating a marked delay of apical filling. The increase in TD was observed regardless of whether the LAD or LCX was occluded, whereas one of three right coronary artery occlusions induced increased TD. Five minutes after the procedure, TD was back to control values. The distance from the transducer to the mitral tip did not change during PTCA. In some patients, apical inflow was divided into two phases (Figs 1 and 2). Before PTCA, this occurred in 30% of the patients and during PTCA in 70%. At the dividing site, peak velocities were always found in the second phase; therefore, this phase was used to calculate TD. Occasionally, the initial phase reached more distally toward the apex and had higher distal velocities than the second phase, despite being lower at the dividing site.

Experimental Study

Coronary occlusion. Coronary occlusion caused systolic paradoxical motion in 10 of the 11 ischemic episodes (Table 2). In the nonischemic region, systolic shortening did not change. Stroke volume decreased by 20% (P<.05) and heart rate increased (P<.01), accompanied by a moderate increase in LVEDP (P<.01) and a nonsignificant increase in LA pressure. The one-third filling fraction decreased in the ischemic region from 59±5% to 31±6% (P<.01) but was unchanged in the nonischemic region. τ increased slightly with ischemia (P=.05). Traces from a representative dog are presented in Fig 3.

As in the clinical study, peak inflow velocity in each dog was progressively delayed from mitral tip toward apex during ischemia. Thus, TD increased from 18±4 to 71±9 milliseconds (P<.01). Representative color M-mode recordings and mean results are shown in Figs 4 and 5. The distance from the transducer to the mitral tip did not change significantly during the interventions.

| TABLE 2. Hemodynamic Results of the 11 Different Ischemic Episodes in the Eight Dogs at Control and During Acute Ischemia |
|------------|----------------|----------------|
| Variable   | Control        | Ischemia       |
| HR, bpm    | 107±7          | 131±10†        |
| SAP, mm Hg | 94±4           | 88±4           |
| LVEDP, mm Hg | 9±1          | 14±1†          |
| LAP, mm Hg | 11±1           | 14±2           |
| ΔP, mm Hg  | 4.6±0.6        | 3.9±0.6        |
| Time to ΔP, ms | 26±2          | 27±2           |
| SV, mL     | 15±2           | 12±2*          |
| τ, ms      | 33±1           | 36±2*          |
| TD, ms     | 18±4           | 71±1†          |
| nTD, ms/cm | 7±2            | 31±4†          |
| 1/3 FF/IR, % | 59±5         | 31±6†          |
| 1/3 FF/NR, % | 65±3         | 65±5           |
| SS/IR, %   | 20±3           | −5±2†          |
| SS/NR, %   | 30±3           | 27±2           |
| EDSL/IR, mm | 10.3±1.5      | 11.5±1.5†      |
| EDSL/NR, mm | 9.5±0.8       | 10.0±0.8       |

HR indicates heart rate; bpm, beats per minute; SAP, systolic arterial pressure; LVEDP, left ventricular end-diastolic pressure; LAP, left atrial pressure; ΔP, peak early diastolic transmural pressure gradient; Time to ΔP, time from LV/RA pressure crossover to ΔP; SV, stroke volume; τ, time constant of isovolumic relaxation; TD, time difference between occurrence of peak velocity in the apical region and at the mitral tip; nTD, normalized TD; 1/3 FF, one-third filling fraction; IR, ischemic region; NR, nonischemic region; SS, systolic shortening; and EDSL, end-diastolic segment length. Values are mean±SEM.

Two phases of apical inflow were present in 36% of the dogs at control and in 73% during coronary occlusion. At the dividing site, the highest filling velocities were always found in the second phase.

Effects of alteration in heart rate and loading. Pacing tachycardia at rates of 120, 135, and 150 beats per minute caused a slight, statistically nonsignificant decrease in TD. With caval constriction that reduced stroke volume by 25% (P<.05) and with volume loading to LVEDP of 13±1, 17±0, and 22±1 mm Hg, TD tended to increase, but these changes did not reach statistical significance (Table 3).

Relation between TD and other hemodynamic variables. Multiple regression analysis of values before and during ischemia showed that TD correlated positively with τ (r=.81, P<.01), end-diastolic segment length of the ischemic region (r=.92, P<.0001), and LVEDP (r=.78, P<.05). Furthermore, there was a negative correlation between TD and one-third filling fraction (r=.85, P<.01) (Fig 6). No other diastolic variables correlated significantly with TD.

Discussion

The present study shows that acute myocardial ischemia is associated with a marked change in the early diastolic intraventricular flow pattern. In the nonischemic ventricle, there was rapid early diastolic filling of the apical region, and peak filling velocities occurred
nearly simultaneously throughout the entire LV inflow tract. In the ischemic ventricle, the peak filling velocity in the apical region was markedly delayed. We could reproduce this pattern of delayed apical filling during coronary occlusion in a dog model. The delay of peak filling velocity was associated with a marked decrease in the one-third filling fraction of the ischemic myocardial segment. \( \tau \) was used as an index of global LV relaxation in the dog model. There were significant correlations between TD and \( \tau \) and between TD and one-third filling fraction. Taken together, these results suggest that the altered color M-mode flow pattern during coronary occlusion is related to retarded filling of the ischemic ventricle.

Few studies have been published using the color M-mode Doppler technique to study LV filling. Jacobs et al. found delayed propagation and prolonged duration of LV inflow in patients with dilated cardiomyopathy. Brun et al. recently reported low velocity of blood propagation during diastole in patients with LV hypertrophy or cardiomyopathy. The velocity of flow propagation was inversely related to \( \tau \). Brun et al measured the slope of the basal flow wave front, whereas we measured delay of peak velocities, which could be determined even in the apical part of the ventricle.

The pulsed Doppler technique might have been used for measuring the timing of intraventricular filling velocities. This technique displays the velocity spectrum, whereas color M-mode Doppler echocardiography measures mean spectral velocity. Pulsed Doppler echocardiography therefore may have a higher level of precision in determining the exact timing of peak velocity. However, if pulsed Doppler echocardiography were to be used, the time difference would have to be calculated from different heart beats, introducing an additional factor of variability.

The dog experiments showed that the delayed apical filling by color M-mode Doppler could not be attributed to a change in the early transmitral pressure gradient. This may suggest that the color M-mode flow pattern
during ischemia reflects alterations of intraventricular redistribution of blood. A change in redistribution is also suggested by the finding in several subjects that mitral inflow had ended when apical filling was still occurring. Courtois et al\(^9\) showed that early diastolic midventricular to apical pressure gradient decreased or slightly reversed after coronary artery occlusion in dogs. Our findings of rapid apical filling in the normal LV and retarded apical filling during ischemia might reflect such a change in intraventricular pressure gradients. Jacobs et al\(^1\) postulated that the prolonged duration of inflow in patients with dilated cardiomyopathy was secondary to formation of eddy currents at the apex. The existence of eddy currents during ischemia is supported by the study of Beppu et al\(^10\) who used echo contrast to show abnormal inflow patterns during coronary occlusion in dogs. Furthermore, Delemarre et al\(^11\) described circular apical flow patterns in patients with acute myocardial infarction and pump failure. Therefore, the retarded filling of the apical region in our study might reflect formation of eddy currents. With color M-mode Doppler echocardiography, two phases of early apical inflow were found, occasionally before and more often during ischemia. One might speculate that this reflects different waves of apical inflow and that the second wave is retarded during coronary occlusion because of impaired relaxation of the ischemic myocardium.

In the dog model, myocardial ischemia was accompanied by moderate tachycardia, moderate elevation of intracavitary filling pressure, and reduction of stroke volume. To investigate whether the change in filling pattern was caused by these changes rather than by ischemia as such, we assessed the effect of changes in heart rate and loading in the nonischemic ventricle.
Table 3.  Results of the Dogs at Control and During the Different Interventions of Pacing Tachycardia at Maximum Heart Rate, Caval Constriction, and Volume Loading at Maximum LVEDP

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control Before PT</th>
<th>PT</th>
<th>Control Before CC</th>
<th>CC</th>
<th>Control Before VL</th>
<th>VL</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR, bpm</td>
<td>86±5</td>
<td>150*</td>
<td>83±5</td>
<td>92±7</td>
<td>93±6</td>
<td>130±7*</td>
</tr>
<tr>
<td>SAP, mm Hg</td>
<td>93±7</td>
<td>98±3</td>
<td>88±7</td>
<td>86±5</td>
<td>95±5</td>
<td>101±3</td>
</tr>
<tr>
<td>LVEDP, mm Hg</td>
<td>8±1</td>
<td>6±1</td>
<td>8±1</td>
<td>6±1</td>
<td>9±1</td>
<td>22±1*</td>
</tr>
<tr>
<td>LAP, mm Hg</td>
<td>8±1</td>
<td>8±1</td>
<td>9±1</td>
<td>7±1*</td>
<td>9±1</td>
<td>20±3*</td>
</tr>
<tr>
<td>ΔP, mm Hg</td>
<td>4.2±0.3</td>
<td>4.6±0.4</td>
<td>3.9±0.4</td>
<td>2.9±0.3*</td>
<td>3.9±0.4</td>
<td>6.3±0.5*</td>
</tr>
<tr>
<td>SV, mL</td>
<td>17±2</td>
<td>10±1*</td>
<td>16±1</td>
<td>12±1*</td>
<td>15±2</td>
<td>21±1</td>
</tr>
<tr>
<td>τ, ms</td>
<td>34±2</td>
<td>32±2</td>
<td>36±2</td>
<td>36±2</td>
<td>35±2</td>
<td>35±2</td>
</tr>
<tr>
<td>TD, ms</td>
<td>18±8</td>
<td>16±6</td>
<td>24±11</td>
<td>32±18</td>
<td>23±12</td>
<td>33±9</td>
</tr>
<tr>
<td>nTD, ms/cm</td>
<td>6±3</td>
<td>6±2</td>
<td>8±4</td>
<td>13±8</td>
<td>8±4</td>
<td>12±3</td>
</tr>
<tr>
<td>EDSL/circumflex, mm</td>
<td>8.0±0.8</td>
<td>7.4±0.7*</td>
<td>8.0±0.9</td>
<td>7.4±0.8*</td>
<td>7.8±0.8</td>
<td>8.4±1.0*</td>
</tr>
<tr>
<td>EDSL/LAD, mm</td>
<td>7.6±0.5</td>
<td>7.1±0.5*</td>
<td>7.7±0.6</td>
<td>7.2±0.6*</td>
<td>7.5±0.6</td>
<td>8.1±0.7*</td>
</tr>
</tbody>
</table>

PT indicates pacing tachycardia; CC, caval constriction; VL, volume loading; HR, heart rate; bpm, beats per minute; SAP, systolic aortic pressure; LVEDP, left ventricular end-diastolic pressure; LAP, left atrial pressure; ΔP, peak early diastolic transmitral pressure gradient; SV, stroke volume; τ, time constant of isovolumic relaxation; TD, time difference between occurrence of peak velocity in the apical region and at the mitral tip; nTD, normalized TD; EDSL, end-diastolic segment length; Circumflex, area of left circumflex artery; and LAD, area of left anterior descending artery. Values are mean±SEM.

*P<.05 vs control.

Pacing tachycardia, volume loading, and caval constriction caused only minor and statistically nonsignificant changes in TD. Thus, the change in the color M-mode Doppler flow pattern during coronary occlusion apparently was not caused by these hemodynamic changes. A limitation of this experimental approach, however, is that each of these interventions induced several hemodynamic changes. Furthermore, we were not able to study the combined effect of a reduction in stroke volume and an increase in end-diastolic volume. Therefore, we cannot exclude that the changes in filling pattern are a result of depression of LV function rather than being specific to myocardial ischemia.

Some studies have shown that increased preload is accompanied by increased τ.11 Our study failed to demonstrate an increase in τ or TD with volume loading, possibly because of the accompanying tachycardia.

Limitations of the Study

The rather high exclusion rate in the patient group was a result of inadequate acoustic windows in the supine position. This, however, is more a reflection of the study conditions than of a problem with the color M-mode Doppler technique, since the excluded patients showed adequate recordings in the lateral rotated position. Furthermore, no differences in clinical characteristics were present between the included and the excluded patients.

A major problem with color M-mode Doppler echocardiography is that the ultrasonic beam interrogates only a limited part of the ventricle in a single dimension. Since spatial resolution is very limited, care should be exerted when conclusions are drawn regarding global filling of the LV cavity. Regional abnormality in wall motion, which is an early marker of ischemia, could have been detected from two-dimensional tissue imaging. The version of the ultrasound machine used in this study did not allow optimal imaging of the ventricle simultaneously with color Doppler flow. During the short period of occlusion in the patients, additional two-dimensional imaging of the ventricle was not feasible. One objection to our method is that the computer analysis is not yet commercially available.

The majority of the patients used ß-adrenergic blockers or calcium channel blockers, which may have modified LV diastolic function and contributed to the variability in the baseline values for TD. During PTCA, however, TD consistently increased regardless of which drug was used.

The animal preparation, of course, was influenced by the anesthetic and the rather extensive surgery. In particular, the thoracotomy and the pericardiectomy must have influenced extraventricular pressures.13 The main objective of this study, however, was not to characterize diastolic function in an intact preparation but rather to relate abnormal flow pattern in the ischemic ventricle to other indices of diastolic function. We do not believe that

Fig 6.  Graph showing relation between the time difference (TD) between occurrence of peak velocity in the apical region and at the mitral tip and one-third filling fraction (1/3 FF) of myocardial segment before and during ischemia. Arrowheads point to ischemia.
our findings regarding the relation between the color M-mode pattern and the other indices of LV diastolic function are invalidated in such a preparation.

Conclusions

During PTCA, color M-mode Doppler echocardiography showed a delay of LV early diastolic filling that increased progressively from mitral valve to apex. This color M-mode filling pattern could be reproduced during coronary occlusion in dogs and was associated with a prolongation of $\tau$ and a reduction of the one-third filling fraction in the ischemic myocardial segment. The findings suggest that the altered flow pattern reflects impairment of LV relaxation and filling. The color M-mode delay could not be attributed to changes in LV filling pressure or heart rate. Thus, color M-mode Doppler echocardiography may have potential as a clinical method for assessing diastolic dysfunction.

Acknowledgment

Marie Stugaard was a recipient of a research fellowship from the Norwegian Council on Cardiovascular Diseases.

References

Intraventricular early diastolic filling during acute myocardial ischemia, assessment by multigated color m-mode Doppler echocardiography.

M Stugaard, O A Smiseth, C Risøe and H Ihlen

Circulation. 1993;88:2705-2713
doi: 10.1161/01.CIR.88.6.2705

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/88/6/2705