Comparative Effects of Pacing-Induced and Balloon Coronary Occlusion Ischemia on Left Ventricular Diastolic Function in Man

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Background. Effects of pacing-induced and coronary occlusion myocardial ischemia on left ventricular (LV) function have been compared only in anesthetized dogs. Diastolic properties of the same LV anterior wall segment were therefore compared in 12 patients with single-vessel proximal left anterior descending coronary artery stenosis at rest, immediately after 7±1.2 minutes of pacing, and at the end of a 1-minute balloon occlusion of coronary angioplasty (CO).

Methods and Results. Shifts of the diastolic LV pressure–length relation, derived from simultaneous tip-micromanometer LV pressure recordings and digital subtraction LV angiograms, were used as an index of regional diastolic LV distensibility of the anterior wall segment. Immediately after pacing, LV end-diastolic pressure rose from 13.5±3.5 to 23.8±7.0 mm Hg (p<0.01 versus at rest) without a significant change of the LV end-diastolic volume index (83.1±18.9 versus 88.4±16.5 ml/m²), percentage systolic shortening (%SS) of the ischemic segment fell from 40.1±10.6% to 25.2±8.6% (p<0.01), and the diastolic LV pressure–radial length (P–RL) plot of the ischemic segment was shifted upward by 7.1±5.0 mm Hg for portions of the plot that overlapped with the diastolic LV P–RL plot at rest. At the end of CO, LV end-diastolic pressure rose to 20.8±7.8 mm Hg (p<0.01 versus at rest) and the LV end-diastolic volume index rose to 95.6±16.3 ml/m² (p<0.05 versus at rest, p<0.05 versus after pacing). Ejection fraction and %SS of the ischemic segment fell respectively from 76.6±6.8% to 46.6±11.4% (p<0.01 versus at rest, p<0.01 versus after pacing) and from 40.1±10.6% to 6.4±8.6% (p<0.01 versus at rest, p<0.01 versus after pacing). The diastolic LV P–RL plot of the ischemic segment was shifted upward by 3.1±2.3 mm Hg for portions of the plot that overlapped with the diastolic LV P–RL plot at rest. This upward shift at the end of CO was significantly smaller (p<0.05) than that immediately after pacing. At the end of CO, a correlation (p<0.03) was observed for the ischemic segment between %SS and upward shift of the diastolic LV P–RL plot.

Conclusions. The upward shift of the diastolic LV P–RL plot, which was used as an index of decreased regional diastolic LV distensibility, was larger immediately after pacing than at the end of CO. Persistent systolic shortening of ischemic myocardium seems to be a prerequisite for a decrease in diastolic distensibility of the ischemic segment because of the higher %SS of the ischemic segment immediately after pacing, and because of the correlation at the end of CO between the upward shift of the diastolic LV P–RL plot and %SS of the ischemic segment. (Circulation 1991;84:211–222)

Pacing tachycardia in the presence of coronary stenoses and brief coronary occlusion have opposite effects on diastolic properties of ischemic left ventricular myocardium in anesthetized dogs. Increased myocardial oxygen demand caused by pacing tachycardia in the presence of coronary stenoses results in an upward shift of the diastolic pressure–segment length or pressure–wall thickness relations of ischemic myocardium. During brief coronary occlusion, the ischemic region shows no change...
or a shift to the right of these relations. In contrast to these experimental findings, observations in man reveal pacing-induced angina, spontaneous coronary angina, and balloon coronary occlusion to have similar effects on left ventricular diastolic properties of ischemic myocardium. Under these conditions, myocardial ischemia results in an upward shift of the diastolic pressure-volume relation, of the diastolic pressure–wall thickness relation, and of the diastolic pressure–radial length relation. No previous study has directly compared regional diastolic pressure–radial length relations in the same patient during both pacing-induced ischemia and balloon occlusion of coronary angioplasty. In the present study we therefore investigated diastolic pressure–radial length relations of the same anterior wall segment in patients with single-vessel proximal tight left anterior descending coronary artery (LAD) stenosis immediately after pacing and during balloon occlusion of coronary angioplasty.

Methods

Patients

Twelve patients (10 men, two women; mean age 53.8 [range 42–77] years) are included in this study. All patients had exercise-induced angina in the absence of angina at rest or previous myocardial infarction as evident from their electrocardiogram at rest and normal wall motion on the left ventricular angiogram. In all patients, diagnostic left heart catheterization and coronary angiography revealed normal left ventricular function at rest and single-vessel coronary disease consisting of a significant (>80%) proximal LAD stenosis. There were no visible collaterals to the distal LAD on contralateral coronary injection before balloon inflation. All positively and negatively inotropenic drugs were withheld prior to the study, and only vasodilator medication was continued at the time of the procedure. Premedication consisted of 10 mg diazepam. The study was approved by the ethical committee of St. Antonius Hospital, Nieuwegein, The Netherlands, and of the O.L.V. Hospital, Aalst, Belgium. All patients gave informed consent, and there was no complication related to the procedure or study protocol.

Study Protocol

A 7-French pigtail Sentron tip-micromanometer (Cordis Europe, Rooden, The Netherlands) was advanced from the left femoral artery to the left ventricle. The guiding catheter for the angioplasty procedure was advanced from the left femoral artery. The high-fidelity tip-micromanometer left ventricular pressure signal and a left ventricular angiogram derived by digital subtraction ventriculography were simultaneously recorded in the resting state using angiographic frame markers and an injection marker. The first left ventricular angiogram was performed in the 30° right anterior oblique projection and obtained by the injection of 0.5 ml/kg ioxaglate with a low iodine content (160 mg/ml) and low osmolarity. Right ventricular pacing was initiated at a rate of 90 beats/min and was increased in a stepwise manner by 30 beats/min every 2 minutes. Pacing was continued until the appearance of angina. The second left ventricular angiogram was obtained immediately upon cessation of pacing (after 7.0±1.2 minutes) during the first 10 beats of restored sinus rhythm. The third left ventricular angiogram was obtained just prior to balloon deflation at the end of a fourth (patients 1–9) or second (patients 10–12) angioplasty balloon inflation of 60 seconds’ duration. End-diastolic pressure had returned to the baseline value prior to the pacing stress test or the angioplasty procedure. All patients had chest pain and ischemic ST segment changes during both the pacing stress test and the balloon occlusion of coronary angioplasty. Coronary angioplasty was successful in all 12 patients, with minimal residual coronary stenosis.

Data Acquisition and Analysis

Left ventricular volumes and pressures were matched using cine frame markers. Left ventricular volumes were calculated according to the area–length method and the regression formula of Kennedy et al. A Philips DVI-CV digital radiographic unit (Eindhoven, The Netherlands) acquired all images during held inspiration at 25 frames/sec in a continuous interlaced mode and stored them on 0.3-in. U-Matic videotape. An average mask frame was composed from the cardiac cycle before the appearance of contrast. Frame-by-frame analysis was performed on the third to fourth beat after contrast appearance. All nonsinus rhythm or potentiated beats were excluded from the analysis. All the ventriculograms studied had adequate subtraction and contrast opacification. The Philips DVI-CV unit analyzed regional wall motion using the end-diastolic center of mass as a reference point and 28 sectors emerging from the center of mass. Radial length was calculated for each frame as the distance from the center of mass to the endocardial contour of an ischemic and nonischemic sector. Percentage systolic shortening was expressed as the ratio of the difference between the end-diastolic and end-systolic radial lengths divided by the end-diastolic radial length. One unblinded investigator manually traced all the ventricular contours. Each individually reported angiographic value is the mean of three measurements. Intraobserver variabilities for left ventricular volume and radial length measurements were 1.5% and 1.6%, respectively. Two time constants of left ventricular pressure decay were derived from the left ventricular tip-micromanometer pressure signal, which was digitized from the moment of minimum left ventricular dP/dt to a left ventricular pressure that equaled left ventricular end-diastolic pressure plus 5 mm Hg. The time constant T1 was derived from a monoexponential curve fit to a 0 mm Hg asymptote pressure. The time constant T2 was calculated from a monoexponential curve fit to a nonzero asymptote pressure.
Diastolic left ventricular pressure–radial length plots of the ischemic segment were constructed by matching corresponding points of left ventricular pressure and radial length of an ischemic sector. Shifts of the diastolic left ventricular pressure–radial length plot during the ischemic episodes were quantified to provide an index of diastolic distensibility of the segment. An upward shift of the diastolic left ventricular pressure–radial length plot was expressed by a mean pressure value over which the overlapping portion of the diastolic left ventricular pressure–radial length plot had moved upward \( P_m \). \( P_m \) was obtained by planimetry of an area enclosed by the two left ventricular pressure–radial length plots and by two lines perpendicular to the radial length axis at the outer borders of a radial length zone for which there was overlap between the two left ventricular pressure–radial length plots (Figure 1). This area was subsequently divided by the distance between the two perpendicular lines to yield \( P_m \).

To assess material properties of the ischemic myocardium, a radial myocardial stiffness modulus for the ischemic segment \( E_R \) was calculated at rest, during pacing-induced angina, and after 1 minute of balloon coronary occlusion. \( E_R^{1,11,17} \) was defined as

\[
E_R = \Delta \sigma_R / \Delta \varepsilon_R = - \Delta P / (\Delta h / h) = - \Delta P / \Delta \ln h
\]

The increment in radial stress \( \Delta \sigma_R \) was equal but opposite in sign to the increment in left ventricular pressure at the endocardium, and the increment in radial strain \( \Delta \varepsilon_R \) was equal to the increment in wall thickness \( \Delta h \) relative to the instantaneous wall thickness \( h \). Because \( \Delta h / h = \Delta \ln h \), \( E_R \) was equal to the slope of a \( P \) versus \( \ln h \) plot. The value of \( h \) was derived from the instantaneous diastolic ischemic radial length, assuming a constant left ventricular wall mass. \( E_R \) values must be compared at a common radial stress or left ventricular pressure level. When comparing \( E_R \) at rest with \( E_R \) after pacing, a common radial stress level could be defined in six patients. When comparing \( E_R \) at rest with \( E_R \) at the end of balloon occlusion, a common radial stress level could be defined in four patients. When comparing \( E_R \) after pacing with \( E_R \) at the end of balloon occlusion, a common radial stress level could be defined in seven patients.

**Statistical Analysis**

Results \((n=12)\) are given as mean±standard deviation. The level of statistical significance was set at \( p<0.05 \), and the probability value was obtained by Student’s \( t \) test for paired data and Bonferroni’s method of multiple comparison.

**Results**

**Left Ventricular Hemodynamics**

Individual values of left ventricular end-diastolic pressure (LVEDP), maximum left ventricular \( dp/dt \), left ventricular end-diastolic volume index (LVEDVI), ejection fraction (EF), heart rate, and left ventricular peak systolic pressure obtained at rest, upon cessation of pacing, and at the end of balloon coronary occlusion just prior to balloon deflation are shown in Table 1.

LVEDP rose from 13.5±3.5 mm Hg at rest to 23.8±7.0 mm Hg immediately following pacing \((p<0.01)\) and to 20.8±7.8 mm Hg \((p<0.01)\) at the end of balloon coronary occlusion. LVEDVI rose from 83.1±18.9 ml/m² at rest to 88.4±16.5 ml/m² \((p<0.01)\) immediately following pacing and to 95.6±16.3 ml/m² \((p<0.05)\) versus at rest and after pacing) at the end of balloon coronary occlusion. EF decreased from 76.7±6.8% at rest to 70.8±8.9% immediately following pacing \((p<0.01)\) and to 46.6±11.4% at the end of coronary occlusion \((p<0.01)\) versus at rest and after pacing.

**Left Ventricular Hemodynamic Relaxation Indices and Global Diastolic Left Ventricular Properties**

Hemodynamic left ventricular relaxation indices measured at rest, immediately following pacing, and at the end of balloon coronary occlusion are shown in Table 2.

LVEDP rose to comparable levels at the end of balloon coronary occlusion and immediately following pacing, but LVEDVI was significantly greater at the end of balloon coronary occlusion than following pacing \((p<0.05)\) or at rest \((p<0.05)\) (Table 1). These findings are consistent with pacing-induced ischemia causing an upward shift of the end-diastolic left ventricular pressure–volume relation and balloon coronary occlusion ischemia causing an upward and rightward shift of the relation. Two examples (pa-
TABLE 1. Effects of Pacing-Induced Ischemia and of Balloon Coronary Occlusion on Left Ventricular Hemodynamics

<table>
<thead>
<tr>
<th>Pt</th>
<th>Rest LVEDP (mm Hg)</th>
<th>dP/dt max (mm Hg/sec)</th>
<th>Rest LVEDVI (ml/m²)</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>8</td>
<td>1,100</td>
<td>540</td>
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<td>2</td>
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<tr>
<td>4</td>
<td>15</td>
<td>2,100</td>
<td>1,400</td>
</tr>
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<td>5</td>
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<td>1,750</td>
<td>1,400</td>
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<td>1,300</td>
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<td>7</td>
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<td>1,550</td>
<td>1,300</td>
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<tr>
<td>11</td>
<td>15</td>
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</tr>
<tr>
<td>12</td>
<td>13</td>
<td>1,760</td>
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</table>

Mean±SD 13.5±3.5 23.8±7.0* 20.8±7.8* 1,444.2±381.2 1,582.9±353.9† 1,164.6±298.8‡ 83.1±18.9 88.4±16.5 95.6±16.3§

<table>
<thead>
<tr>
<th>Pt</th>
<th>Rest EF (%)</th>
<th>Rest HR (beats/min)</th>
<th>Rest LVPSP (mm Hg)</th>
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<tr>
<td>1</td>
<td>83</td>
<td>66</td>
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<td>96</td>
</tr>
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<td>62</td>
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</tr>
<tr>
<td>12</td>
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<td>89</td>
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</tr>
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</table>

Mean±SD 76.7±6.8 70.8±8.9 46.6±11.4* 69.1±7.9 82.4±11.8‡ 82.7±11.4‡ 125.6±27.7 136.8±23.3† 127.4±31.5

Pt, patient number; PI, pacing-induced ischemia; CO, coronary occlusion; LVEDP, left ventricular end-diastolic pressure; LVEDVI, left ventricular end-diastolic volume index; EF, ejection fraction; HR, heart rate; LVPSP, left ventricular peak systolic pressure.

*tp<0.01, 0.05, respectively, different from rest.
†‡tp<0.01, 0.05, respectively, different from PI.

Pacing-induced ischemia caused large reductions (68% and 58%) of segmental shortening in patients 4 and 5, respectively. At the end of balloon coronary occlusion, the diastolic left ventricular pressure–radial length plot was superimposable on the plot at rest in six patients (Figure 3: patient 2; Figure 4: patients 6 and 8; and Figure 5: patients 10, 11, and 12). In six patients (Figure 3: patients 1, 3, and 4; Figure 4: patients 5 and 7; and Figure 5: patient 9), the diastolic left ventricular pressure–radial length plot was shifted upward at the end of balloon coronary occlusion.

The upward shift of the diastolic left ventricular pressure–radial length plot was quantified by P_m. The shift of the diastolic left ventricular pressure–radial length plot was used as an index of regional diastolic distensibility. The higher P_m, the lower regional diastolic distensibility. Following pacing P_m equaled 7.1±5.0 mm Hg, and at the end of balloon coronary occlusion it equaled 3.1±2.3 mm Hg (p<0.05). At the
end of balloon coronary occlusion, a correlation was observed between the upward shift of the diastolic left ventricular pressure–radial length plot of the ischemic segment, quantified by $P_m$ and segmental shortening of the ischemic segment, expressed as a fraction of the value at rest (fSS) ($P_m = 7.6 \times fSS + 1.8; r = 0.64$,
$p < 0.03$).

Values for $E_R$ were calculated at rest, following pacing, and at the end of balloon coronary occlusion. For each patient, $E_R$ at rest, $E_R$ following pacing, and $E_R$ at the end of balloon coronary occlusion can be compared only at similar diastolic left ventricular pressures. At a diastolic left ventricular pressure of 10.8±3.0 mm Hg (n=6), $E_R$ was comparable at rest (68±55 mm Hg) and following pacing (51±56 mm Hg). At a diastolic left ventricular pressure of 10.0±3.6 mm Hg (n=4), $E_R$ was similar at rest (115±81 mm Hg) and at the end of a 1-minute balloon coronary occlusion (121±98 mm Hg). At a diastolic left ventricular pressure of 14.6±5.6 mm Hg (n=7), $E_R$ showed a nonsignificant change from 61±50 mm Hg following pacing to 106±113 mm Hg at the end of balloon coronary occlusion.

**Discussion**

*Diastolic Distensibility of Ischemic Myocardium*

The initial effect of ischemia on diastolic distensibility of the left ventricle has been the subject of intense research in patients with coronary artery
disease. In patients with triple-vessel coronary disease, pacing angina caused an upward shift of the diastolic left ventricular pressure–volume relation\(^8\)–\(^10\) and an upward shift of the diastolic left ventricular pressure–radial length\(^11\) or diastolic left ventricular pressure–wall thickness\(^11\) relations of the ischemic myocardium. Coronary occlusion during transluminal angioplasty caused a comparable decrease in diastolic distensibility of the ischemic region.\(^15\) Hence, in humans the effects of pacing angina and of brief coronary occlusion on regional diastolic distensibility appear to be similar. No study so far has analyzed diastolic distensibility of the same ischemic region during both pacing angina and balloon occlusion of coronary angioplasty. In the present study, therefore, we compared in the same patient diastolic distensibility of the same anterior wall segment during both pacing-induced ischemia and balloon occlusion of a proximal LAD stenosis. A shift of the diastolic left ventricular pressure–radial length plot was used as an index of regional left ventricular distensibility.

In the present study, LVEDP rose to similar levels during pacing-induced ischemia and at the end of balloon coronary occlusion. LVEDVI remained comparable to resting values during pacing-induced ischemia but rose significantly at the end of a 1-minute balloon coronary occlusion. These findings are consistent with an upward shift of the end-diastolic left ventricular pressure–volume relation during pacing-induced ischemia and an upward but rightward shift of the same relation after 1 minute of balloon coronary occlusion. Regional left ventricular diastolic distensibility of the ischemic segment followed a similar trend when considering pooled patient data: overlapping portions of the diastolic left ventricular pressure–radial length plot shifted upward to a greater extent during pacing-induced ischemia (7.1±5.0 mm Hg) than at the end of a 1-minute balloon coronary occlusion (3.1±2.3 mm Hg, \(p<0.05\)).

When considering individual patient data (Figures 3, 4, and 5) on diastolic distensibility of the ischemic segment during pacing-induced ischemia and at the end of a 1-minute balloon coronary occlusion, a variable response becomes evident. Pacing-induced ischemia caused an upward shift of the diastolic left ventricular pressure–radial length relation of the ischemic region during all of diastole in six patients and during early-to-mid diastole in four. There was no shift of the diastolic left ventricular pressure–radial length relation in two patients. Following pacing, there was a 34±26% reduction of systolic shortening of the ischemic region. In contrast to previous studies on regional left ventricular diastolic distensibility,\(^11\) the upward shift of the diastolic left ventricular pressure–radial length relation observed in the present study was limited to early and mid diastole in four of 12 patients. Previous reports examined the effects of pacing angina on diastolic left ventricular function in patients with triple-vessel coronary disease,\(^9\)–\(^11\) whereas we studied patients with single-vessel coronary disease. In patients with triple-vessel coronary disease, pacing-induced angina resulted in an upward shift of the entire diastolic left ventricular pressure–volume or pressure–wall thickness relations. The smaller amount of myocardium at risk\(^23\) in single-vessel coronary disease could explain the limitation to early and mid diastole of the upward shift of the diastolic left ventricular pressure–radial length relation observed in some patients of the present study. In a recent study\(^24\) on conscious dogs with a single-vessel coronary stenosis of the left circumflex artery, a similar upward shift limited to the early portion of the left ventricular diastolic pressure–volume relation was observed during exercise. In two patients (Figure 3;
patient 4 and Figure 4: patient 5) pacing-induced ischemia resulted in a profound depression of systolic performance and no change in regional diastolic distensibility of the ischemic myocardium. One of these patients had an electrocardiographically and scintigraphically strongly positive exercise stress test in the absence of anginal symptoms. A high threshold for anginal pain perception explained the patient’s tolerance to prolonged pacing in the present study. In these two patients, in whom systolic performance was severely depressed following pacing, the diastolic left ventricular pressure–radial length plot remained unaltered. In previous experiments on pacing tachycardia in anesthetized dogs with coronary stenoses, a similar relation between systolic performance and diastolic distensibility was observed; when systolic performance was severely depressed the diastolic pressure–radial length relation failed to change.1

At the end of balloon coronary occlusion, we observed no change of the diastolic left ventricular pressure–radial length plot of the ischemic segment in six of 12 patients; in the other six patients the diastolic left ventricular pressure–radial length plot was shifted upward. At the end of balloon coronary occlusion, a correlation ($p<0.03$) was observed between the upward shift of the diastolic left ventricular pressure–radial length plot and segmental shortening expressed as a fraction of the value at rest for the ischemic segment. This correlation reconciles some of the contradictory findings on the initial effect of balloon coronary occlusion on diastolic properties of ischemic myocardium. Bertrand et al17 observed a marked decrease in EF from 72±6% to 46±10% and no significant change in left ventricular diastolic properties during balloon coronary occlusion. In contrast, Wijns et al15 and Kass et al125 found smaller depressions of systolic performance during balloon coronary occlusion (a 20% decrease in systolic segmental shortening and a fall in EF from 69±8% to 54±12%, respectively) and reported an upward shift of the diastolic left ventricular pressure–radial length plot of the ischemic zone and an upward shift of the diastolic left ventricular pressure–volume relation. These different responses to balloon coronary occlusion.
sion are probably related to the presence of clinical and objective evidence of myocardial ischemia during the balloon inflations. In the present study and in the study by Bertrand et al., all patients had angina and significant ischemic ST segment changes at the time of the measurements. In the present study the balloon inflation time (60 seconds) was longer than in the study by Wijns et al. (20 or 50 seconds). In the present study the fourth or second balloon inflation was used, whereas in the study by Wijns et al. the balloon inflation during which the left ventricular angiogram was obtained varied from the third to the tenth. Bertrand et al. consistently used the first balloon inflation, and despite an inflation time shorter than that in the present study, they observed a similar depression of left ventricular systolic function. A recent study on the reproducibility of sequential balloon inflations, however, found the duration of the first inflation to be unreliable because of a variable degree of occlusion by the deflated balloon preceding the actual first inflation.

Pathophysiological Mechanisms

In the present study, pacing-induced ischemia caused a smaller reduction in systolic left ventricular performance and a larger decrease in global and regional diastolic left ventricular distensibility than 1 minute of balloon coronary occlusion. Several pathophysiological mechanisms could contribute to the difference in regional diastolic function of these two interventions.

Following pacing-induced ischemia, diastolic left ventricular function is assessed during initial relief of the ischemic stress (i.e., upon cessation of pacing) in contrast to following coronary occlusion, when function is assessed at the nadir of the ischemic stress. During experimental exercise or isoproterenol-induced ischemia, there is subendocardial hypoperfusion followed by increased blood flow to the ischemic region after the ischemic stress episode, even when residual stenosis permits no change in total coronary blood flow. During the postpacing episode, a similar reactive hyperemia in the ischemic region could contribute to the observed decrease in diastolic blood flow.

**FIGURE 4.** Diastolic left ventricular (LV) pressure–radial length plots at rest, during pacing-induced ischemia (PI), and at end of balloon coronary occlusion (CO) in patients 5–8.
left ventricular distensibility because of a reperfusion effect.\textsuperscript{29} This explanation implies that the decrease of diastolic distensibility of the ischemic region starts immediately upon cessation of pacing and is absent during the pacing episode itself. Studies on left ventricular pressure–volume relations during pacing tachycardia in patients with coronary artery disease, however, revealed a progressive upward shift of the relation that started during the pacing episode.\textsuperscript{30}

Absence or presence of tissue metabolites during the initial stages of myocardial ischemia could also modulate the mechanical response of ischemic myocardium.\textsuperscript{31,32} Washout of tissue metabolites is more likely to occur during pacing-induced ischemia than during brief coronary occlusion.

Different intensities and durations of ischemia during pacing-induced angina and balloon coronary occlusion could have influenced the different responses of the global left ventricle and of the ischemic segment to both interventions. In a recent study by Applegate et al,\textsuperscript{33} postspacing and coronary occlusion ischemia produced similar changes in systolic and diastolic function of the ischemic region when both ischemic stresses resulted in a comparable hemodynamic end point (i.e., LVEDP). The present study did not achieve in each individual patient such equal hemodynamic end points, so unequal degrees of ischemia as a result of the two ischemic stress episodes cannot be excluded. Nevertheless, for the pooled patient data the finding of widely different decreases in left ventricular EF but similar elevations of left ventricular filling pressure is incompatible with unequal severity of ischemia modulating the same type of left ventricular failure and is more likely explained by different types of left ventricular failure during the two interventions. Determination of the adenosine triphosphate and creatine phosphate contents of the ischemic myocardium, such as performed in dogs under similar conditions by Momomura et al,\textsuperscript{2} could resolve the issue of unequal intensities of myocardial ischemia during the two interventions.

\textbf{Study Limitations}

Left ventricular volumes and radial lengths of ischemic and nonischemic segments were derived
from single-plane right anterior oblique ventriculograms and a moving reference point angiographic method. These methodological limitations influence regional wall motion measurements during the ischemic episode because of absent visualization of the interventricular septum and because of motion of the center of mass toward the area of akinesia. The latter artifact leads to overestimation of systolic shortening of the ischemic segment, underestimation of systolic shortening of the nonischemic segment, and reduction of an eventual rightward shift of the diastolic left ventricular pressure–radial length relation. This motion of the center of mass at the end of the balloon coronary occlusion probably accounts for the decrease in percentage systolic shortening of the nonischemic segment and for the absence of a rightward shift of the diastolic left ventricular pressure–radial length relations as previously described in animal studies with somewhat longer periods of coronary occlusion.3-7

In the present study, diastolic properties of ischemic myocardium were characterized by shifts of the diastolic left ventricular pressure–radial length plot and by $E_R$. Such a shift of the diastolic left ventricular pressure–radial length relation of the ischemic segment was quantified by $P_{ms}$, which was no measure of myocardial stiffness or of the slope of the diastolic left ventricular pressure–radial length relation. Material properties of ischemic myocardium were analyzed by $E_R$, which was compared at common radial stress or left ventricular pressure levels.11,17 There was a trend, although statistically nonsignificant, for a higher $E_R$ at the end of balloon coronary occlusion than at rest and during pacing-induced ischemia. Using the same method a similar trend, which also failed to reach statistical significance, was observed by Bertrand et al17 during balloon coronary occlusion. In contrast to a previous study by Bourdillon et al,11 $E_R$ remained unaltered during pacing-induced ischemia. In the present study, however, $E_R$ was derived from instantaneous diastolic left ventricular pressure and not (as in the previous study) from passive diastolic left ventricular pressure. Passive diastolic left ventricular pressure equaled the difference between the instantaneous diastolic left ventricular pressure and the active diastolic left ventricular relaxation pressure, which was extrapolated from the time constant of isovolumic left ventricular pressure decay. Such extrapolation seems questionable because of a recently demonstrated interaction between myocardial reextension, as occurs during left ventricular filling, and residual cardiac muscle force development.34 A decrease in diastolic distensibility of the myocardium without an increase in $E_R$, as observed in the present study during pacing-induced ischemia, resembles the increase in cardiac muscle resting tension during reoxygenation contracture.35 Such an increase in cardiac muscle resting tension occurred without a change in muscle stiffness and was explained by reversible diastolic cross-bridge cycling in the absence of rigor bonds.

In the present study, right ventricular diastolic pressure was not measured. During pacing-induced ischemia and balloon coronary occlusion, left ventricular filling pressures rose to similar values. Reactive pulmonary hypertension and altered right ventricular loading were therefore probably comparable during the two interventions. Eventual biventricular interaction because of pericardial constraint should have had a similar effect on the left ventricular diastolic pressure–volume relations and therefore does not explain the divergent mechanical responses.

In the present study, regional diastolic distensibility during pacing-induced ischemia was investigated in patients with single-vessel LAD coronary stenosis. Most previous studies on left ventricular performance during pacing-induced angina analyzed left ventricular wall motion and hemodynamics in patients with triple-vessel coronary disease. Recently, a study by Dawson and Gibson36 included patients with single- and double-vessel coronary disease, and another recent study by Yamanishi et al37 comprised only patients with stable effort angina related to either single-vessel LAD stenosis or single-vessel right coronary artery stenosis. The present results on the effects of pacing-induced ischemia on left ventricular performance are similar to the last two studies and differ from previous studies on patients with multivessel involvement9-11 insofar that the present study failed to observe significant decreases in global left ventricular systolic performance indices such as maximum left ventricular dP/dt and left ventricular EF during pacing ischemia. In the study by Dawson and Gibson36 maximum left ventricular dP/dt was also unaltered during pacing ischemia. In their study left ventricular EF changed from 73±7% to 68±8%, which equals the 5% decrease in left ventricular EF observed in the present study. During pacing-induced ischemia in the present study, percentage systolic shortening of the ischemic segment fell from 40.1±10.6% to 25.2±8.6% ($p<0.01$). The decrease in percentage systolic shortening of the ischemic segment observed in the present study exceeded that previously reported during pacing angina in patients with single-vessel LAD stenosis (from 36±6% to 24±8%)37 and the decrease in anterior wall segmental shortening (from 16.7±2.6% to 12.7±1.5%) observed during pacing ischemia in a two-vessel coronary stenosis animal model.1,2,38 In the present study, systolic bulging was observed in the three patients (10–12) in whom measurements were obtained at the end of the second balloon coronary occlusion and not in the nine patients (1–9) in whom measurements were obtained at the end of the fourth balloon coronary occlusion. A recent study on the reproducibility of sequential balloon inflations26 found all inflations except the first one to cause similar ischemic stresses. The observation that systolic performance at the end of the fourth balloon inflation was better preserved than at the end of the second balloon inflation despite similar ischemic stresses could therefore be consistent with myocardial constraints.
dial preconditioning to ischemic stress by previous balloon inflations.39

Coronary occlusion depressed systolic shortening of the ischemic segment more profoundly than pacing-induced ischemia, even leading in some patients (Table 3, patients 10–12) to systolic bulging and early diastolic recoil. This segmental asynchrony40,41 observed in patients 10–12 at the end of balloon coronary occlusion could contribute to the greater prolongation of the time constant of left ventricular pressure decay during balloon coronary occlusion than during pacing-induced ischemia.

Coronary occlusion resulted in a variable depression of segmental shortening, probably because of unequal recruitment of collateral flow. Such a recruitment occurred despite the absence of visible collaterals on contralateral coronary injection at the time of diagnostic coronary angiography. This illustrates the need for assessment of collateralization by a quantitative measure such as coronary wedge pressure.42,43 Such measurement would have facilitated interpretation of regional left ventricular performance during both pacing-induced angina and balloon occlusion of coronary angioplasty. Similarly, measurement of coronary sinus washout of hydrogen and other metabolites could confirm the potential role of tissue metabolites as determinants of systolic performance and diastolic distensibility during the initial stages of myocardial ischemia. Future studies are therefore needed to correlate regional performance of ischemic myocardium with simultaneous measurements of coronary wedge pressure and coronary sinus concentrations of hydrogen and tissue metabolites.

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