Effect of Angina on the Left Ventricular Diastolic Pressure-Volume Relationship

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SUMMARY The increased left ventricular end-diastolic pressure associated with myocardial ischemia was studied in 19 patients at cardiac catheterization. Single plane left ventriculograms were performed using high fidelity micromanometer tipped catheters before and immediately following rapid atrial pacing. Left ventricular diastolic properties were evaluated by constructing diastolic pressure-volume curves from the simultaneous pressure and volume data. In seven control patients, there was no significant change in left ventricular hemodynamics or the diastolic pressure-volume curve after atrial pacing. Twelve patients with significant coronary artery disease developed angina during pacing and had an increased left ventricular end-diastolic pressure (18 ± 2 mm Hg, control, vs 30 ± 2 mm Hg, angina, \( P < 0.01 \)) in the immediate post-pacing period. In these patients, the post-pacing ejection fraction was modestly decreased (0.63 ± 0.03, control, vs 0.57 ± 0.03, angina \( P < 0.01 \)), and left ventricular volumes at end systole (59 ± 8 cc, control, vs 74 ± 9 cc, angina, \( P < 0.01 \)) and end diastole (158 ± 10 cc, control, vs 170 ± 11 cc, angina, \( P < 0.0125 \)) were increased. The post-pacing diastolic pressure-volume curves in all 12 patients were shifted upward as compared with control so that for any given diastolic volume, pressure was higher during angina. The data indicate that the increased left ventricular diastolic pressure during myocardial ischemia is the result of both impaired left ventricular systolic performance and altered left ventricular diastolic properties.

ELEVATED LEFT VENTRICULAR DIASTOLIC PRESSURES are commonly observed during myocardial ischemia in patients with coronary artery disease, but the pathophysiology involved is not well understood.\(^1\)\(^-\)\(^3\) Impaired left ventricular systolic performance has been demonstrated during myocardial ischemia\(^4\)\(^-\)\(^8\) and the resulting increased left ventricular end-diastolic volume is thought to contribute to the increased end-diastolic pressure.\(^9\)\(^-\)\(^14\) In addition, several studies have suggested that altered left ventricular diastolic properties with reduced compliance may be an important factor in producing the elevated filling pressures.\(^15\)\(^-\)\(^20\) Documentation of the latter potential mechanism has been limited by the difficulty in measuring the diastolic compliance of the left ventricle.\(^16\)\(^-\)\(^21\)\(^-\)\(^22\)

The purpose of this study was to evaluate the mechanisms responsible for the elevated filling pressure seen during myocardial ischemia. Diastolic left ventricular pressure-volume curves were constructed from data obtained before and during angina pectoris induced by rapid atrial pacing. The data indicate that there is an upward shift of this diastolic pressure-volume curve during angina compared with control, suggesting that altered left ventricular diastolic properties contribute significantly to the elevated left ventricular filling pressure. Increased left ventricular end-diastolic volume due to impaired left ventricular systolic performance was also demonstrated.

Methods

The study was performed in a group of patients undergoing elective cardiac catheterization and coronary angiography for evaluation of chronic chest pain. Patientes with unstable angina pectoris, recent myocardial infarction, congestive heart failure, hypertension, valvular heart disease, left ventricular aneurysm, and the mitral valve prolapse syndrome were specifically excluded from the study. Nitrate preparations were held six hours prior to the procedure in all patients, and propranolol was held 12 to 24 hours prior to the procedure in most. The study was approved by this institution’s Committee for the Protection of the Rights of Human Subjects and informed consent was obtained in all cases.

Cardiac catheterization was performed using the brachial artery approach in a fasting state after premedication with diazepam. Systemic arterial pressure was recorded from the femoral artery. A Gorlin pacing catheter, used for the right heart catheterization, was positioned in the high right atrium for pacing after collection of initial hemodynamic data. Left ventricular pressures were recorded using a high fidelity micromanometer tipped catheter (Millar Instruments). The high fidelity left ventricular diastolic pressure was superimposed at high gain on the pressure measured through the catheter lumen prior to each cineangiogram, and the two pressures were compared immediately after the cineangiogram to ensure that there was no drift of the high fidelity pressure. Coronary arteriography was performed in all patients using the Sones technique.

Single plane (RAO) left ventricular cineangiography was performed using 30–50 ml of sodium diatrizoate injected through the Millar angiographic catheter at 10–15 ml/sec. Cineangiograms were recorded at 56 frames per second using a Siemens cesium iodide image intensifier system. A movable marker synchronized with the QRS complex of the electrocardiogram was used to identify end diastole on the cineangiogram. During each cineangiographic study, high fidelity left ventricular pressure, \(dP/dt\), mean femoral artery pressure, electrocardiogram, cineangiographic frame markers and an injection marker were simultaneously recorded at 200 mm/sec paper speed (fig. 1). The possibility of patients performing the Valsalva maneuver was evaluated by measurement of right atrial pressure or observation of diaphragm movement during the cineangiography.

Each study was performed before coronary angiography.
Control left ventricular cineangiography with simultaneous pressures was initially obtained. After left ventricular pressure had returned to baseline, the heart rate was incrementally increased with atrial pacing by 25 beats/minute every two minutes until a ventricular rate of 140-160 beats/minute was obtained, all patients maintaining 1:1 A-V conduction. Pacing was continued at this rate for 10 min or until typical angina pectoris developed, at which time the pacing was abruptly discontinued. Repeat left ventriculography was performed during the first 10-15 beats after cessation of pacing at the time left ventricular end-diastolic pressure was maximally elevated in patients who developed angina. Care was taken to insure that X-ray tube and patient position as well as injection volume and rate were identical during the two angiographic studies.

Twelve patients with coronary artery disease were selected for inclusion in the study on the basis of the following criteria: 1) significant coronary lesions as defined by 75% or greater narrowing of the luminal diameter of one or more vessels, 2) development of typical angina pectoris during pacing associated with a post pacing rise in left ventricular end-diastolic pressure, 3) high quality ventriculograms before and during atrial pacing induced angina, and 4) no Valsalva maneuver during left ventricular cineangiography. Seven patients with chest pain syndromes who had technically adequate studies and who did not have significant coronary artery lesions were selected as controls.

Left ventricular pressure-volume curves were constructed throughout diastole from data obtained before and after atrial pacing in each patient. Diastoles following ventricular premature beats as well as those following the postextrasystolic beat were excluded. Left ventricular single plane (RAO) volumes were calculated using the area-length method of Kasser and Kennedy. Volumes were determined throughout diastole every 0.036 seconds (every other cineangiographic frame) from early diastole, defined as the cine frame immediately before the mitral valve opening movement, to end diastole, defined as that cine frame on which the QRS marker first moved. Left ventricular end diastolic pressure was identified and each volume related to a corresponding pressure using end diastole and the cine frame markers as a guide.

Control diastolic pressure-volume curves were compared with those obtained in the post-pacing period. Hemodynamic and angiographic data before and after pacing were compared using Student's t-test for paired data. The left ventricular cineangiograms before and after pacing were analyzed qualitatively for segmental wall motion abnormalities by two independent observers; differences of opinion were arbitrated by a third observer.

**Results**

**Patients Without Coronary Artery Disease**

Data obtained from the seven patients with normal coronary angiography are listed in table 1. Atrial pacing was performed for ten minutes in each patient without the development of chest pain. Left ventricular end-diastolic pressure was unchanged after the atrial pacing. Left ventricular minimal diastolic pressure, heart rate, ventricular volumes, ejection fraction, and peak negative dP/dt were also not significantly different after atrial pacing as compared to control values. Mean systemic arterial pressure rose from 104 ± 4 mm Hg to 108 ± 4 mm Hg after the pacing (P < 0.05). Left ventriculograms remained normal after pacing without the development of segmental contraction abnormalities.

The pressure-volume curves for the seven patients with normal coronary arteries are shown in figure 2. In all patients the control and post-pacing curves were similar. In one of these patients (2), the left ventricular end-diastolic pressure was increased over control after pacing. This patient had a post-pacing bradycardia with reduced ejection fraction.

Table 1. Hemodynamic Data Before and After Pacing in Patients without Coronary Artery Disease

<table>
<thead>
<tr>
<th>Pt/Age/Sex</th>
<th>HR (beats/min)</th>
<th>MAF (mm Hg)</th>
<th>Vdp (ml)</th>
<th>Vve (ml)</th>
<th>EF</th>
<th>Pdp (mm Hg)</th>
<th>Pve (mm Hg)</th>
<th>dp/dt (mm Hg/sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/35/M</td>
<td>60 109</td>
<td>95 110</td>
<td>182 154</td>
<td>81 66</td>
<td>0.55 0.57</td>
<td>12 5</td>
<td>6 1</td>
<td>2486 2841</td>
</tr>
<tr>
<td>2/52/M</td>
<td>61 68</td>
<td>110 110</td>
<td>148 187</td>
<td>51 82</td>
<td>0.66 0.55</td>
<td>8 21</td>
<td>5 6</td>
<td>2303 2061</td>
</tr>
<tr>
<td>3/37/F</td>
<td>65 80</td>
<td>115 120</td>
<td>188 190</td>
<td>90 88</td>
<td>0.52 0.51</td>
<td>16 14</td>
<td>7 8</td>
<td>1732 1905</td>
</tr>
<tr>
<td>4/58/F</td>
<td>75 75</td>
<td>110 110</td>
<td>165 174</td>
<td>39 42</td>
<td>0.62 0.59</td>
<td>14 17</td>
<td>4 4</td>
<td>2216 2021</td>
</tr>
<tr>
<td>5/54/F</td>
<td>72 73</td>
<td>98 102</td>
<td>185 194</td>
<td>52 52</td>
<td>0.72 0.73</td>
<td>12 14</td>
<td>3 3</td>
<td>2803 2086</td>
</tr>
<tr>
<td>6/41/F</td>
<td>61 103</td>
<td>110 115</td>
<td>118 110</td>
<td>47 45</td>
<td>0.61 0.62</td>
<td>17 20</td>
<td>7 8</td>
<td>1699 1923</td>
</tr>
<tr>
<td>7/63/F</td>
<td>56 61</td>
<td>90 90</td>
<td>127 136</td>
<td>25 27</td>
<td>0.50 0.50</td>
<td>10 10</td>
<td>1 1</td>
<td>2336 2434</td>
</tr>
<tr>
<td>Mean</td>
<td>67 85</td>
<td>104 108</td>
<td>150 162</td>
<td>55 57</td>
<td>0.64 0.62</td>
<td>13 14</td>
<td>5 4</td>
<td>2221 2182</td>
</tr>
<tr>
<td>SEM</td>
<td>3 7</td>
<td>4 4</td>
<td>11 12</td>
<td>9 9</td>
<td>0.04 0.04</td>
<td>1 2</td>
<td>1 1</td>
<td>152 128</td>
</tr>
<tr>
<td>P</td>
<td>NS</td>
<td>&lt;.05</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

Abbreviations: HR = heart rate; MAP = mean arterial pressure; Vdp/ve = end-diastolic volume; End-systolic volume; EF = ejection fraction; Pdp = end-diastolic pressure; Pve = beginning (minimal) diastolic pressure; e = control; pp = post-pacing.
fraction, and his pressure-volume curve (2) indicates that the increased pressure was due to an increase in left ventricular volume.

Patients With Coronary Artery Disease

An example of the recording of hemodynamic data obtained during catheterization in a patient who developed angina with atrial pacing is shown in figure 3. Data from all 12 patients with coronary artery disease are listed in table 2.

Three of these patients had three vessel disease, seven of these patients had two vessel disease, and two patients had single vessel disease. In all 12 patients atrial pacing was discontinued before ten minutes had elapsed because of the development of typical angina pectoris. Eleven of the 12 patients developed or had worsening of their segmental contraction abnormalities on the post-pacing ventriculogram compared with the control ventriculogram.

Left ventricular end-diastolic pressure increased from
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so
upward
an
10
10/80/M 2 74 76 120 120 118 123 51 62 0.57 0.50 23 32 11 21 2440
39 104 121 123 46 44 0.33 0.32 22 24 23 24 1943
55 80 100 191 190 55 78 0.71 0.61 18 27 6 10 1491
6/56/M 2 80 82 110 120 115 146 41 50 0.64 0.66 13 24 6 12 2361
10/80/M 2 74 75 76 120 120 118 123 51 62 0.57 0.50 23 32 11 21 2440
11/48/F 2 94 92 105 110 157 157 30 36 0.81 0.77 11 16 3 7 1690
12/51/M 2 65 57 115 145 194 217 72 108 0.59 0.50 21 39 8 27 1997
Mean
74 75 104 117 158 170 59 74 0.63 0.57 18 30 8 15 1844
56
4 4
4 5
10 11
8 9
0.03 0.03
2 2
1 2
127 96
NS
Abbreviations: See table 1. a = angina; CA = coronary artery.

18 ± 2 mm Hg, control, to 30 ± 2 mm Hg, during angina
(P < 0.01). Minimal diastolic pressure also increased
significantly (8 ± 1 mm Hg, control, vs 15 ± 2 mm Hg, angina, P < 0.01). Both left ventricular end-diastolic (158 ±
10 cc, control, vs 170 ± 11 cc, angina, P < 0.0125) and end
systolic (59 ± 8 cc, control, vs 74 ± 9 cc, angina, P < 0.01)
volumes increased during angina; ejection fraction decreased
from 0.63 ± 0.03 to 0.57 ± 0.3 (P < 0.01). Mean arterial
pressure was increased over control during angina (104 ± 4
mm Hg, control, vs 117 ± 5 mm Hg, angina, P < 0.01).
Heart rate during angina was unchanged from control. Peak
negative dP/dt decreased during angina but this was not
statistically significant.

The pressure-volume curves of the 12 patients who de veloped angina are shown in figure 4. In each patient there was
an upward shift of the pressure-volume curve during angina,
so that for any given diastolic volume, pressure was higher
during angina compared with control. The curve is also
shifted slightly to the right, reflecting the larger diastolic
volumes during angina.

Discussion

Elevated left ventricular diastolic pressures are a charac teristic hemodynamic feature observed during angina pectoris in patients with coronary artery disease. In a group of
patients in which angina was provoked by dynamic exercise,
left ventricular end-diastolic pressure rose significantly
before the onset of angina, peaked 180% higher than the con trol resting value, and promptly returned to control levels
after resolution of chest pain. Similarly, when angina is in duced by rapid atrial pacing, left ventricular end-diastolic
pressure usually increases with the onset of angina during the pacing tachycardia and becomes maximally elevated in the post-pacing period for a brief period of time until angina resolves.

The pathophysiologic mechanism responsible for the in creased left ventricular end-diastolic pressure during angina remains controversial. Impaired myocardial performance
during ischemia has been demonstrated in isolated papillary muscle and intact experimental heart preparations, and in man. It has thus been postulated that the increased left ventricular end-diastolic pressure during ischemia is due to

an increased left ventricular end-diastolic volume resulting from transient left ventricular failure. McCans and Parker, using echocardiographically measured left ventricular volume data in patients with atrial pacing induced angina, and Sharma et al., using angiographically determined volumes in patients with angina induced by dynamic exercise, both demonstrated an increased left ventricular end-diastolic volume during angina.

It is probable however, that impaired left ventricular systolic performance is not solely responsible for this rise in
left ventricular end-diastolic pressure during angina.

Several investigators have noted that the increased left
ventricular end-diastolic pressure in patients with coronary
artery disease appeared out of proportion to changes in ventricular end-diastolic volume. Other studies have
suggested that left ventricular compliance may be transiently reduced during myocardial ischemia. Dwyer noted a significant decline in the LVEDV/LVEDP ratio during angina as compared with control. Barry et al. demonstrated an upward shift of the log of pressure versus volume curves during angina pectoris. Flessas et al. noted that isometric hand grip resulted in an upward shift of the diastolic pressure-volume curve in some patients with cor onary artery disease.

In the present study, left ventricular systolic and diastolic
properties were evaluated during angina pectoris in the period immediately following atrial pacing. During angina,
significant segmental wall motion abnormalities appeared in
11 of 12 patients, left ventricular end-systolic volume was
substantially increased over control in all patients, and ejection fraction was slightly but significantly reduced. These
changes in left ventricular systolic performance were associated with a small overall increase in left ventricular end-diastolic volume which contributed to the increased end-diastolic pressure. The increase in left ventricular end-diastolic volume was not the sole factor responsible for the increased left ventricular end-diastolic pressure, however, since the left ventricular diastolic pressure-volume curve was shifted upward during angina in each patient. For any given diastolic volume, left ventricular pressure was higher during
angina compared with control, thus defining a change in left
ventricular diastolic properties.
One explanation for the observed shift in the diastolic pressure-volume curve is that ischemia may impair left ventricular relaxation. A striking prolongation of tension duration has been demonstrated during the period of recovery from hypoxia in isolated papillary muscle preparations and during regional ischemia in the isovolumic canine heart.\textsuperscript{7, 24, 38} Watanabe et al. demonstrated an immediate decline in peak negative dP/dt after LAD occlusion in dogs, the degree of which was related to the extent of ischemic injury.\textsuperscript{38} McLaurin et al. found a similar decline in peak negative dP/dt in patients during atrial pacing-induced ischemia.\textsuperscript{27} The fall in negative dP/dt was associated with a rise in left ventricular end-diastolic pressure and an insignificant change in echocardiographic left ventricular diameter. In the present study peak negative dP/dt, measured after the cessation of pacing, did not decrease significantly. However, peak negative dP/dt is highly dependent on left ventricular systolic pressure and the increase in systolic pressure during angina in our patients would tend to increase peak negative dP/dt.\textsuperscript{28, 30} It is thus possible that the unchanged negative dP/dt in our study is the net result of both increased left ventricular systolic pressure and impaired ventricular relaxation.\textsuperscript{28, 30}

The shift of the diastolic pressure-volume curve during angina could also be related to a change in one of the external constraints acting upon the left ventricle.\textsuperscript{14, 80} It has been postulated that an increased aortic diastolic pressure may increase coronary artery perfusion pressure and flow and result in an increase in left ventricular chamber stiffness.\textsuperscript{31, 32} Templeton et al. were unable to demonstrate a change in the ventricular pressure-volume relation by altering coronary perfusion pressure and flow in dogs, and thus the effect of increased aortic pressure on the left ventricular pressure-volume relationship remains unclear.\textsuperscript{48} In the present study, mean arterial pressure was higher during angina than control and this remains a potential factor responsible for the altered diastolic properties in our patients.

An important technical limitation of the present study involves the use of single plane left ventricular cineangiography to determine left ventricular volumes. In coronary artery disease, segmental contraction abnormalities may result in inaccurate single-plane volume calculations.\textsuperscript{46}
but since these abnormalities should not significantly distort the ventricle during late diastole, the potential error in diastolic volumes should be minimal.

In summary, the results of this study suggest that the increased left ventricular end-diastolic pressure during angina pectoris is the result of two pathophysiologic mechanisms. Left ventricular systolic performance is impaired, causing increased left ventricular diastolic volume which is reflected by a rise in diastolic pressure. In addition, left ventricular diastolic properties are altered so that for any given diastolic volume the ventricular pressure is higher during myocardial ischemia as compared to the control state.

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References

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