Acute Changes in Left Ventricular Volume and Contractility during Ventricular Pacing in Patients with Complete Heart Block

By Fredarick L. Gobel, M.D., Charles R. Jorgensen, M.D., Kazuto Kitamura, M.D., and Yang Wang, M.D.

SUMMARY
To determine whether changes in preload and contractility may account for clinical improvement in patients with complete heart block (CHB) when the ventricular rate is increased by pacing, 10 hemodynamic studies were performed in nine patients with CHB. Left ventricular end-diastolic volume (EDV) was measured before and during pacing by the dye-dilution and the angiographic techniques. Changes in contractility were assessed from the first derivative of ventricular pressure divided by a common peak isovolumic pressure (CPIP) to correct for afterload and by EDV to correct for preload. EDV decreased during pacing, the mean value decreasing from 242 to 180 ml (P < 0.001). Since the left ventricular dp/dt is influenced by afterload and preload, improvement in contractility indices was consistent only after allowances were made for changes in aortic diastolic pressure and EDV. The mean dp/dt/CPIP divided by EDV increased from 0.120 to 0.160 (P < 0.005). The mean left ventricular end-diastolic pressure decreased from 17.0 to 9.7 mm Hg (P < 0.05) during pacing, while the mean cardiac index increased from 2.0 to 2.5 liters/min/m² (P < 0.025). The clinical improvement seen after pacing in patients with CHB results, in part, from an increase in contractility and a decrease in EDV and pressure.

Additional Indexing Words:
Catheterization Myocardial contractility Ventricular function

Patients with symptomatic complete heart block (CHB) usually improve clinically when the ventricular rate is increased by electric pacing, although the relief of congestive heart failure may be slow.1-4 Bradycardia per se is not a cause of heart failure but may be a major contributing factor in the patient with impaired myocardial function.2 The cardiac output is much more rate dependent in patients with CHB and previous evidence of myocardial disease than in those patients with CHB and no evidence of previous myocardial disease.2 During ventricular pacing there may be little or no change in the resting cardiac output,1-4 but there is, however, an increase in the exercise cardiac output, and elevated left and right ventricular filling pressures return toward normal during both rest and exercise.3 The reduction in elevated left ventricular filling pressure may account for the relief of dyspnea during ventricular pacing in patients with CHB. Changes in ventricular performance in patients with CHB have received less attention, and available data suggest that patients may be merely working on a lower portion of the same ventricular function curve,3 as occurs

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in normal subjects during atrial pacing. To understand better the effects of ventricular pacing on ventricular function in patients with CHB this study was undertaken to evaluate the acute changes in left ventricular volume and contractility during pacing.

It has been demonstrated in both man and animals that coronary blood flow and myocardial oxygen consumption per minute increase in response to increasing the heart rate by ventricular pacing. It is, therefore, somewhat surprising that angina pectoris is not a more common complaint during ventricular pacing in patients with CHB, since these patients are usually in an age group with a high incidence of coronary artery disease. Changes in ventricular work and contractility which influence myocardial oxygen demand must therefore be balanced by appropriate changes in myocardial oxygen supply during ventricular pacing. The influence of changes in ventricular performance during pacing on myocardial oxygen consumption is considered.

Material and Methods

Patient Material

This is a report of 10 studies in nine patients with complete atrioventricular block. None of the patients had recent myocardial infarction or congenital or surgically acquired heart block. Patient 4 had a positive Treponema pallidum immobilization test and aortic insufficiency. Patient 2 was studied twice (studies 2a and 2b); the second study was after an interval of 1 year at which time ventricular pacing was interrupted due to pacemaker wire breakage. Ages ranged from 55 to 86 years. The mean body surface area (BSA) was 1.8 m². All patients were symptomatic: one complained of angina pectoris, two of syncope, five of dyspnea, and two of exertional fatigue. Four patients were receiving digitalis at the time of the study, although none was acutely digitalized immediately before or during the study. Patients were divided into two groups according to their atrial mechanism: (1) those whose atrial mechanism was normal sinus rhythm (patients 1 to 4), and (2) those with atrial flutter or fibrillation (patients 5 to 9). Patient 8 was studied during both sinus rhythm and during atrial fibrillation induced by rapid atrial stimulation. Studies were done at two heart rates: the control rate of approximately 40 beats/min and during ventricular pacing at rates of approximately 78 beats/min. In patients 2 (study b) and 5 the control rate was accomplished by ventricular pacing at a rate approaching their idioventricular rhythm. Patients 1, 3, and 4 had aortic valvular disease. Patient 3 had moderately severe aortic stenosis. Ascending aortography in patients 1 and 4 demonstrated regurgitation of enough contrast material to faintly outline the left ventricle but less contrast than remained in the aorta (2+ on a 0 to 4+ scale). No patient had clinical evidence of mitral valve disease.

Methods

Right and left heart catheterization was performed in each patient. A bipolar pacing catheter was positioned with the tip of the catheter at the apex of the right ventricle. A 75-cm, 5F, Teflon arterial catheter with an inside diameter of 1.1 mm was positioned with the tip in the apex of the left ventricle (LV). A 50-cm, 5F, Teflon catheter of the same bore was positioned with the tip in the ascending aorta (Ao) 2 cm above the aortic valve. The left atrial (LA) mean pressure was not measured in study 2b, was measured directly through a transseptal catheter in four studies, and was estimated from the pulmonary artery wedge (PAW) pressure in five studies. The left ventricular end-diastolic pressure (LVEDP) was measured in all patients. The midchest level at the angle of Louis was used as the zero reference. An oscilloscopic photographic recorder was used for recording pressures and dye curves. Statham P23Db strain-gauge transducers were used. The catheter-manometer-recording systems used typically have a damped natural frequency between 15 and 25 cycles/sec.

Cardiac output (CO) was determined by the dye-dilution technique with the use of indocyanine green dye and a densitometer. Dye was hand injected into the pulmonary artery (PA) as a 5-mg bolus from a calibrated syringe. The ascending aorta was the sampling site in all cases. Each patient also had the cardiac output determined as the quotient of the oxygen consumption and the arteriovenous oxygen-content difference. Electric pacing was accomplished with an external pulse generator. The first derivative of the left ventricular pressure (LV dp/dt) (fig. 1) was determined in all patients with a resistance-capacitance differentiator. Measurements at the control rate preceded those done while pacing. A 20-min interval following
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Figure 1

Demonstrated is a high-speed recording of the left ventricular pressure and its first derivative (dp/dt) during a paced beat.

the onset of pacing preceded the second set of measurements.

Ventricular volume was measured by the dye-dilution technique in all patients. Left ventricular end-diastolic volume (EDV) was calculated as the quotient of the forward stroke volume and the factor \( 1 - (C_{n+1}/C_n) \), where \( C_n \) and \( C_{n+1} \) reflect dye concentration in the aortic blood at steps \( n \) and \( n+1 \), respectively.\(^9\) The forward stroke volume (FSV) was calculated as the quotient of the cardiac output and heart rate. Dye was hand injected into the apex of the left ventricle during diastole. Aortic sampling was done through a 50-cm Teflon catheter with an internal volume of 0.5 ml. Withdrawal rates were 40–66 ml/min. The ratio \( C_{n+1}/C_n \) was determined from an average of three to five successive beats depending upon the heart rate. To reduce error due to incomplete mixing the first deflection after the appearance of the dye was omitted. The ratio \( C_n/C_{n+1} \) was then constant for the next several beats. At least three acceptable ventricular volume curves were obtained on each patient during the control and during the paced study. Curves were rejected when we were unable to clearly define sharp changes in dye concentration with each systole.

Single-plane cineangiography in the right anterior oblique position was used to determine changes in ventricular dimensions in three patients.\(^10\) Angiograms were done at 60 frames/sec as 50 ml of 76% methylglucamine d'atrizate (Renografin) was injected into the left atrium through a transseptal catheter. Angiographic studies were done immediately following the control measurements and repeated following the paced study with the patient and X-ray equipment in an identical position. Reference to simultaneous graphic records of the electrocardiograms and the cineangiogram was used to avoid taking data on premature contractions which were rare with the left atrial injection. An outline of the ventricle with adjacent atrial border was traced on a sheet of paper marked with an identifying frame number. A long axis was drawn from the intersection of the left ventricular margin and the left atrial margin at the level of the mitral valve annulus to the apex of the ventricle. The long axis of the ventricle (L) and a short axis (M) at right angles to it at its midpoint were directly measured. Volume (V) then equals \((\pi/6)LM^2\).\(^10\) No corrections for the volume of the trabecular or papillary musculature were made. A circular disc (patients 3 and 4) and a 1-cm wire grid (patient 9) placed at the level of the left ventricle were used to correct for X-ray magnification.

Left ventricular minute-work index (LVMWI) in kilogram-meters per minute per square meter body surface area (kg-m/min/m² BSA) was calculated as the product of the cardiac index (liters/min/m²), the mean systolic aortic pressure (mm Hg), and 0.0144. Left ventricular stroke-work index (LVSWI) in gram-meters per beat per square meter of body surface area (g-m/beat/m² BSA) was the quotient LVMWI and the ventricular rate. In patient 3, who had aortic stenosis, the mean systolic left ventricular pressure replaced the aortic pressure in these calculations. Ejection time was determined from central aortic pressure tracings. The tension-time index (TTI) was computed as the product of the mean systolic aortic pressure and the ejection time per beat or the ejection time per minute and expressed in mm Hg-sec/beat or mm Hg-sec/min.\(^11\) Resistances were calculated as the quotient of the mean pressure times 80 and the cardiac output and expressed as dynes-sec-cm⁻².

Contractility was estimated from the left ventricular dp/dt with corrections for changes in afterload and preload. To correct for changes in aortic diastolic pressure (instantaneous afterload) during pacing the left ventricular dp/dt measured at a maximal isovolumetric pressure common to the control and paced beats was divided by this common peak isovolumetric pressure (CPIP) and expressed as \((dp/dt)/CPIP\).\(^12\) In patient 1, with aortic insufficiency, a low aortic diastolic pressure during the control study resulted in a very short period of isovolumetric contraction and prevented the determination of a meaningful CPIP. To correct for changes in ventricular volume, preload, we estimated contractility by dividing \((dp/dt)/CPIP\) by EDV as suggested by Mason.\(^12\)
Table 1

Mean Hemodynamic Data for Ten Studies in Patients with Complete Heart Block

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean control (±SD)</th>
<th>P value control to study</th>
<th>Mean study (paced) (±SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate (beats/min)</td>
<td>39.5 ± 6.8</td>
<td>&lt;0.001</td>
<td>78.2 ± 3.6</td>
</tr>
<tr>
<td>Cardiac index (liters/min/m²)</td>
<td>2.0 ± 0.4</td>
<td>&lt;0.025</td>
<td>2.5 ± 0.8</td>
</tr>
<tr>
<td>Stroke index (ml/beat/m²)</td>
<td>52.2 ± 11.4</td>
<td>&lt;0.001</td>
<td>32.0 ± 9.1</td>
</tr>
<tr>
<td>Aortic systolic pressure (mm Hg)</td>
<td>172 ± 38</td>
<td>&lt;0.4</td>
<td>160 ± 48</td>
</tr>
<tr>
<td>Aortic diastolic pressure (mm Hg)</td>
<td>61 ± 10</td>
<td>&lt;0.005</td>
<td>82 ± 22</td>
</tr>
<tr>
<td>Aortic mean pressure (mm Hg)</td>
<td>127 ± 25</td>
<td>&lt;0.5</td>
<td>124 ± 32</td>
</tr>
<tr>
<td>LVED pressure (mm Hg)</td>
<td>17.0 ± 9.3</td>
<td>&lt;0.05</td>
<td>9.7 ± 3.7</td>
</tr>
<tr>
<td>LA mean pressure (mm Hg)</td>
<td>16.9 ± 7.6</td>
<td>&lt;0.4</td>
<td>13.7 ± 6.4</td>
</tr>
<tr>
<td>PA mean pressure (mm Hg)</td>
<td>24.4 ± 6.7</td>
<td>&gt;0.5</td>
<td>25.2 ± 7.2</td>
</tr>
<tr>
<td>Ejection time/beat (sec)</td>
<td>0.38 ± 0.04</td>
<td>&lt;0.001</td>
<td>0.28 ± 0.03</td>
</tr>
<tr>
<td>Ejection time/min (sec)</td>
<td>14.8 ± 2.0</td>
<td>&lt;0.001</td>
<td>21.7 ± 2.3</td>
</tr>
<tr>
<td>LVSWI (g-m/m²)</td>
<td>101.7 ± 38.7</td>
<td>&lt;0.01</td>
<td>58.6 ± 20.0</td>
</tr>
<tr>
<td>LVMWI (kg-m/min/m²)</td>
<td>3.9 ± 1.3</td>
<td>&lt;0.05</td>
<td>4.6 ± 1.6</td>
</tr>
<tr>
<td>TTI/min (mm Hg-sec)</td>
<td>1887 ± 453</td>
<td>&lt;0.001</td>
<td>2714 ± 817</td>
</tr>
<tr>
<td>EDV (ml)</td>
<td>242 ± 60</td>
<td>&lt;0.001</td>
<td>180 ± 43</td>
</tr>
<tr>
<td>Peak LV dp/dt (mm Hg/sec)</td>
<td>1880 ± 273</td>
<td>&gt;0.5</td>
<td>1940 ± 474</td>
</tr>
<tr>
<td>LV dp/dt/CPIP (sec⁻¹)</td>
<td>27.1 ± 7.3</td>
<td>&gt;0.5</td>
<td>27.7 ± 4.9</td>
</tr>
<tr>
<td>LV dp/dt/CPIP LVEDV</td>
<td>0.120 ± 0.053</td>
<td>&lt;0.005</td>
<td>0.160 ± 0.052</td>
</tr>
</tbody>
</table>

See text for abbreviations.

Hemodynamic measurements were compared by the Student t-test for paired observations.

Results

Mean values and standard deviations are presented in table 1.

Patients whose atrial mechanism is normal sinus rhythm and who have CHB (patients 1 to 4) have fluctuating ventricular mechanics depending upon the relation of the atrial contraction to ventricular systole, which would not pertain to patients with atrial fibrillation and CHB (patients 5 to 9). Patient 8 was studied while in CHB with sinus atrial mechanism and when atrial fibrillation was induced by pacing the right atrium at a rate of 300/min (table 2). There was little difference in the mean values obtained in these two resting studies in patient 8 at the idioventricular rhythms. Analyses indicated no significant difference in the mean value of hemodynamic variables measured when patients were selected according to their atrial mechanism.

With the exception of patients 5 and 9, there was a decrease in the LVEDP in all
Table 2

<table>
<thead>
<tr>
<th>Hemodynamic Data in Patient 4</th>
<th>Sinoatrial and idioventricular rhythm</th>
<th>Atrial fibrillation* and idioventricular rhythm</th>
<th>Atrial fibrillation and ventricular pacing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac index (liters/min/m²)</td>
<td>1.6</td>
<td>1.9</td>
<td>2.0</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>24</td>
<td>33</td>
<td>81</td>
</tr>
<tr>
<td>Stroke index (ml/beat/m²)</td>
<td>67</td>
<td>58</td>
<td>25</td>
</tr>
<tr>
<td>Aortic systolic pressure (mm Hg)</td>
<td>172</td>
<td>167</td>
<td>135</td>
</tr>
<tr>
<td>Aortic diastolic pressure (mm Hg)</td>
<td>54</td>
<td>58</td>
<td>87</td>
</tr>
<tr>
<td>Aortic mean pressure (mm Hg)</td>
<td>85</td>
<td>84</td>
<td>105</td>
</tr>
<tr>
<td>LVED pressure (mm Hg)</td>
<td>14</td>
<td>12</td>
<td>10</td>
</tr>
<tr>
<td>LA mean pressure (mm Hg)</td>
<td>10</td>
<td>8</td>
<td>13</td>
</tr>
<tr>
<td>PA mean pressure (mm Hg)</td>
<td>22</td>
<td>13</td>
<td>23</td>
</tr>
<tr>
<td>Ejection time/beat (sec)</td>
<td>0.41</td>
<td>0.37</td>
<td>0.24</td>
</tr>
<tr>
<td>Ejection time/min (sec)</td>
<td>9.8</td>
<td>12.0</td>
<td>19.4</td>
</tr>
<tr>
<td>LVSWI (g-m/m²)</td>
<td>125</td>
<td>109</td>
<td>41</td>
</tr>
<tr>
<td>LVMWI (kg-m/m²)</td>
<td>3.0</td>
<td>3.6</td>
<td>3.4</td>
</tr>
<tr>
<td>TTI/min (mm Hg-sec)</td>
<td>1300</td>
<td>1500</td>
<td>2300</td>
</tr>
</tbody>
</table>

See text for abbreviations.

*Atrial fibrillation was induced by atrial pacing at a rate greater than 350/min.

patients (table 3). The increase in LVEDP in patient 5 may have been a response to a 15% increase in afterload. Patients 1 and 4, both with mild aortic insufficiency, had the greatest fall in LVEDP of 27 and 20 mm Hg, respectively.

The LA mean pressure followed the LVEDP and, with the exception of patient 5, it fell during pacing in all patients in whom it was elevated above normal values.

EDV, as measured by the dye-dilution technique, decreased in all patients from a mean control value of 242 to 180 ml during ventricular pacing (fig. 2) \( P < 0.001 \). EDV also decreased in response to pacing in the three patients in whom it was measured by the angiographic technique (table 3). There was good separation of values in each patient between the control and study determination and, with the exception of patient 9, there was no overlap of values between individual dye-dilution curves. The presence of aortic insufficiency likely interferes with the determination of EDV by the dye-dilution method. In spite of this, EDV decreased in response to pacing when measured both by the dye-dilution and by the angiographic method in patient 4 who had mild AI (2+) and a striking fall in LVEDP. Comparisons between the dye-dilution method and the angiographic method were made in patients 3, 4, and 9 (table 3). In all three patients there was a proportionately similar decrease in EDV by both methods. In patients 3 and 4 the dye-dilution EDV and ESV were larger than values determined...
Table 3

Individual Hemodynamic Data for Ten Studies in Patients with Complete Heart Block

<table>
<thead>
<tr>
<th>Patient</th>
<th>LVEDP (mm Hg)</th>
<th>EDV, by dye dilution (ml)</th>
<th>EDV, by angiography (ml)</th>
<th>LV dp/dt (mg Hg/sec)</th>
<th>LV dp/dt/CP/IP EDV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>C ± SD</td>
<td>S ± SD</td>
<td>% ↓</td>
<td>C ± SD</td>
<td>S ± SD</td>
</tr>
<tr>
<td>1</td>
<td>40 ± 13</td>
<td>241 ± 20</td>
<td>155 ± 14</td>
<td>36</td>
<td>2400 ± 3000</td>
</tr>
<tr>
<td>2</td>
<td>15 ± 7</td>
<td>178 ± 5</td>
<td>150 ± 22</td>
<td>16</td>
<td>1990 ± 1773</td>
</tr>
<tr>
<td>b</td>
<td>12 ± 10</td>
<td>181 ± 8</td>
<td>146 ± 20</td>
<td>19</td>
<td>1836 ± 1938</td>
</tr>
<tr>
<td>3</td>
<td>15 ± 6</td>
<td>192 ± 6</td>
<td>128 ± 9</td>
<td>33</td>
<td>130 ± 94</td>
</tr>
<tr>
<td>4</td>
<td>25 ± 5</td>
<td>355 ± 27</td>
<td>217 ± 30</td>
<td>39</td>
<td>178 ± 122</td>
</tr>
<tr>
<td>5</td>
<td>13 ± 17</td>
<td>281 ± 10</td>
<td>240 ± 8</td>
<td>15</td>
<td>2265 ± 2356</td>
</tr>
<tr>
<td>6</td>
<td>18 ± 12</td>
<td>267 ± 46</td>
<td>193 ± 16</td>
<td>28</td>
<td>1649 ± 2101</td>
</tr>
<tr>
<td>7</td>
<td>12 ± 7</td>
<td>181 ± 24</td>
<td>143 ± 4</td>
<td>21</td>
<td>1332 ± 1615</td>
</tr>
<tr>
<td>8</td>
<td>12 ± 10</td>
<td>242 ± 9</td>
<td>184 ± 4</td>
<td>24</td>
<td>1780 ± 1310</td>
</tr>
<tr>
<td>9</td>
<td>8 ± 10</td>
<td>301 ± 42</td>
<td>250 ± 41</td>
<td>17</td>
<td>333 ± 268</td>
</tr>
</tbody>
</table>

Abbreviations: C = control value; S = study value; SD = standard deviation of the mean; % ↓ = percent decrease; for others see text.

Angiographically. In patient 9 the reverse was true.

The dye-dilution ejection fraction decreased slightly from a control value of 40 ± 10% to 33 ± 10% following ventricular pacing.

The aortic systolic and mean pressure did not change significantly, but the aortic diastolic pressure increased in all 10 studies, the mean increasing from the control value of 60.5 to 82.8 mm Hg during ventricular pacing (P < 0.005). This may in part be due to a decrease in diastole during ventricular pacing. The average peak LV dp/dt did not change significantly during ventricular pacing, increasing in six studies and decreasing in four studies. When corrected for the change in aortic diastolic pressure by calculating (dp/dt)/CP/IP there was still no significant change.
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Since preload had also changed significantly, this expression for contractility was corrected for preload by dividing by EDV, and there was an increase in the resultant contractility expression in all patients, the mean increasing significantly from the control value of 0.120 to 0.160 (P < 0.005).

The cumulative measurements such as CI, ejection time per minute, LVMWI, and TTI/min all increased significantly in response to pacing. The same factors per beat, however, such as SV, ejection time, SWI (fig. 3), and TTI, all decreased significantly when the ventricular rate was increased by pacing. Thus, pressure volume work per minute increases but pressure volume work per beat decreases in response to increasing the ventricular rate by pacing. No significant change was noted in the mean pulmonary artery pressure or systemic or pulmonary resistance in response to pacing.

Discussion

Theoretical and practical criticisms of the dye-dilution technique for determining EDV have centered around (1) the method of injection of the indicator, (2) the dynamic response of the sampling system, and (3) adequate mixing of the indicator in the ventricle.\(^9\)\(^,\)\(^13\)-\(^17\) Injecting into the apex of the left ventricle in mid-diastole, ignoring the initial step or steps of the time concentration curve, and waiting until the residual fraction has become constant have been felt to aid in assuring good mixing of dye in the left ventricle,\(^9\) although others have felt this to be unnecessary.\(^18\) Model studies have indicated that when the above criteria are met adequate mixing ensues.\(^9\) The slow heart rates obtained in this study would also aid in adequate mixing.\(^13\) The reproducibility of the method is demonstrated by the similarity of the ejection fraction in numerous dye curves in the same

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individual during each study and by the similar EDV in studies 2a and 2b.

Theoretically, aortic insufficiency would interfere with the determination of EDV by the indicator-dilution technique because (1) aortic valve flow would be underestimated by the Fick determination of stroke volume (which measures net forward flow) and lead to an underestimation of EDV, and (2) the residual fraction will be influenced by regurgitant indicator and lead to an overestimate of the EDV. In aortic insufficiency the ascending aorta may also serve as a second mixing chamber. In spite of these theoretical differences, good agreement between the angiographic and fiberoptic indicator-dilution methods has been reported in humans. Our indicator-dilution time concentration curves did not have a downslope to each step as has been reported in some patients with aortic insufficiency, perhaps indicating a milder degree of regurgitation in our patients.

Angiographic determinations of EDV by the biplane technique have been reported and compared with single-plane angiography and indicator-dilution curves. EDV as measured by single-plane cineangiography has been shown to be representative of EDV as determined by the biplane technique and barium-filled human hearts. Differences in the EDV as determined by the angiographic and the indicator-dilution technique in this study could be due to inadequate sampling during the angiographic determination, as only 5 to 6 beats were recorded, and the fact that measurements were not made at exactly the same time. Additional error might be introduced by including the trabeculae carnae of these large ventricles, since volume increases as the cube of the factors measured. EDV calculated from single-plane cineangiograms has been shown to progressively overestimate EDV from barium-injected hearts as the heart size is increased. In patients 3 and 4 EDV measured by the dye-dilution technique was larger than the angiographically determined volume as reported by others. In any respect, ventricular volume decreased acutely in response to pacing as measured both by the angiographic and by the indicator-dilution techniques. The relative reduction in end-diastolic volume with pacing varied less than 10% between the indicator-dilution and the angiographic techniques (table 3).

The mean control EDV (134 ml/m²) as measured in this study by the indicator-dilution technique is somewhat higher than mean values found by others (96–124 ml/m²) by indicator-dilution techniques at normal heart rates in patients with normal or near-normal left ventricles. The EDV during ventricular pacing of 100 ml/m² is more nearly normal.

The effect on ventricular size of increasing the heart rate has been studied in dogs. Increasing the heart rate by atrial pacing produces a decrease in end-diastolic diameter as measured by a modified sonar technique in conscious reclining dogs, a decrease in EDV as measured by the thermodilution technique in anesthetized dogs, and a decrease in EDV as measured by biplane cineangiography in conscious sitting dogs. In addition, it has been shown that dogs with chronic heart block, studied when anesthetized, develop over several months time an increase in EDV as measured by the thermodilution method, and that ventricular pacing decreases EDV as measured by a cineangiographic technique.

There are very little data on human subjects available regarding the effect of pacing on ventricular volume. A single patient reported by Hugenholtz et al. had a decrease in EDV when paced at increasing ventricular rates. During tachycardia induced by mild exercise a reduction in EDV and ESV has been reported using thermodilution, fiberoptic indicator-dilution curves, and metallic myocardial clips. This may represent an increase in the sympathetic tone induced by exercise. The present study indicates that EDV also decreases in humans when the ventricular rate is increased in patients with CHB.

When the ventricular rate was increased in this study of patients with CHB, there was no change in the left ventricular peak derivative. A significant elevation of the aortic diastolic

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pressure alone results in an increase in ventricular afterload which has been shown in man to result in an increase in peak LV dp/dt. When we corrected for this increase in afterload by determining the left ventricular derivative at a common peak isovolumic pressure, there was still no significant change in this contractility index from the control to the paced study. Changes in preload (LVEDP and EDV) were consistent and significant from the control to the paced study and are also known to affect some contractility measurements. When the first derivative was corrected for changes in afterload and preload, there was a consistent and significant increase in this contractility index.

Because of the differences in experimental conditions it is difficult to correlate the numerous studies which pertain to the influence of the frequency of contractions on the strength of myocardial contraction as described by Bowditch in 1871. Increased contractility has been demonstrated with an increase in rate of contraction in isolated muscle preparations, in intact-heart animal experiments, and in conscious resting humans. In conscious resting humans it has been suggested that atrial pacing at rates greater than the normal resting rate merely shifts performance to a lower position on the same ventricular function curve, but others have shown that this maneuver displaces the force-velocity relationship upward and increases (dp/dt)/CPIP. Our data obtained at lower heart rates suggest a significant increase in contractility with ventricular pacing in patients with CHB.

The major determinants of myocardial oxygen consumption are the cumulative myocardial tension, i.e., the product of heart rate and myocardial tension per beat, and the state of myocardial contractility. In our study there was a 98% increase in mean heart rate and a 33.3% increase in the contractility index which would increase myocardial oxygen demand. There were, however, decreases in ventricular volume and pressure which would serve to decrease myocardial oxygen consumption and place the ventricle at a greater mechanical advantage. A rough calculation based on a spherical model indicates that ventricular tension per beat decreased by about 14% and cumulative myocardial tension increased by about 67% per minute. This increase in contractility and cumulative tension explains the recent observations that coronary blood flow per minute and myocardial oxygen consumption per minute increase progressively and in a linear fashion when the heart rate is increased by ventricular pacing in patients with CHB. The decreased myocardial oxygen demand would also explain the clinical observation that angina pectoris is rare in patients with CHB, even if present before the onset of heart block, but that increasing the ventricular rate in patients with CHB and severe coronary artery disease might result in the onset of angina pectoris.

The absolute values for coronary blood flow per minute reported in the above studies vary by as much as a factor of two at comparable heart rates, but the calculation of stroke coronary flow from their data indicates a decrease at higher heart rates in both studies. This is in accord with the observation in unanesthetized dogs with CHB that coronary blood flow per minute increases progressively during pacing while stroke coronary flow decreases progressively due to a decrease in diastolic stroke coronary flow with stroke systolic coronary flow being relatively well maintained. It seems reasonable to suggest that the proportion of total coronary blood flow occurring during systole may actually increase when patients with CHB are paced at faster ventricular rates.

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