Abnormal Left Ventricular Contraction in Patients with Mitral Stenosis

By Stanley J. Heller, M.D., and Richard A. Carleton, M.D.

SUMMARY
Twenty-five patients with pure mitral stenosis and nine normal subjects were studied by selective left ventricular cineangiography. Left ventricular volumes were measured at end systole, throughout diastole, and at end diastole. Although filling curves showed that the left ventricles filled slowly in patients with mitral stenosis, normal end-diastolic volumes were attained provided diastole lasted 400 msec. Despite normal end-diastolic volumes, end-systolic volumes were significantly larger (P < 0.0005) in the patients with mitral stenosis (av = 64.6 ml) than in normal subjects (30.8 ml). Correspondingly, left ventricular ejection fractions were significantly lower (P < 0.0005) in the patients with mitral stenosis (55.7%) than in the normal subjects (76.7%).

Qualitative analysis of the cineangiograms demonstrated that 20 patients with mitral stenosis had distortion, immobility, and rigidity of the posterobasal area of the left ventricle. It is hypothesized that a rigid “mitral complex” immobilizes the posterobasal area of the left ventricle in patients with mitral stenosis, thereby impairing left ventricular contraction, and that this impairment is an important factor in the reduced cardiac output of these patients.

Additional Indexing Words:
Cineangiography Cardiac output Left ventricular function
Ejection fraction

CARDIAC output is low in most patients with symptomatic mitral stenosis.\(^1,2\) The traditional view is that this low output is a direct result of the narrowed mitral orifice.\(^3\) However, this concept of a purely mechanical obstruction to left ventricular filling cannot account for the failure of cardiac output to rise in many patients after demonstrably adequate (though not necessarily optimal) mitral commissurotomy.\(^4,5\) The fact that this low output persists after surgery has led many investigators to suspect that some sort of left ventricular dysfunction exists in such patients.\(^2,5,6\) Attempts to demonstrate such an abnormality, however, have not been notably successful.

We have employed selective left ventricular cineangiography to demonstrate both quantitative and qualitative abnormalities of left ventricular function in patients with mitral stenosis.

Methods
Twenty-five patients with pure mitral stenosis were studied (table 1). All patients had experienced symptoms of pulmonary congestion. The average age of the patients with mitral stenosis was 46.1 years; 60% were female. Seventy-two per cent were in atrial fibrillation; the remainder were in sinus rhythm. Four patients had previously undergone closed mitral commissurotomy. Patients with mitral stenosis with clinical, electrocardiographic, or angiocar-
### Table 1

Summary of Data from 25 Patients with Mitral Stenosis (A) and from Nine Normal Subjects (B)

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age (yr) &amp; sex</th>
<th>Mitral valve area (cm²)</th>
<th>Heart rate* (beats/min) rhythm</th>
<th>BSA (m²)</th>
<th>Left ventricular</th>
<th>Mean pulmonary arterial wedge</th>
<th>Mean pulmonary arterial</th>
<th>Cardiac output (L/min/m²)</th>
<th>End-diastolic vol (ml)</th>
<th>End-systolic vol (ml)</th>
<th>Ejection fraction (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>69-340</td>
<td>66 F</td>
<td>0.4</td>
<td>60, 65 AF</td>
<td>1.36</td>
<td>133/14</td>
<td>35</td>
<td>67</td>
<td>1.51</td>
<td>137</td>
<td>67</td>
<td>51.1</td>
</tr>
<tr>
<td>69-467</td>
<td>67 M</td>
<td>0.4</td>
<td>108,100 AF</td>
<td>1.56</td>
<td>147/13</td>
<td>31</td>
<td>80</td>
<td>1.33</td>
<td>132</td>
<td>54</td>
<td>59.1</td>
</tr>
<tr>
<td>69-190</td>
<td>50 M</td>
<td>0.5</td>
<td>75, 72 AF</td>
<td>1.68</td>
<td>100/ 2</td>
<td>29</td>
<td>49</td>
<td>1.38</td>
<td>200</td>
<td>115</td>
<td>42.5</td>
</tr>
<tr>
<td>69-149</td>
<td>48 M</td>
<td>0.6</td>
<td>127,118 AF</td>
<td>†</td>
<td>122/7</td>
<td>34</td>
<td>73</td>
<td>2.40‡</td>
<td>210</td>
<td>101</td>
<td>51.9</td>
</tr>
<tr>
<td>69-038</td>
<td>27 F</td>
<td>0.6</td>
<td>117, 78 S</td>
<td>1.41</td>
<td>118/7</td>
<td>32</td>
<td>70</td>
<td>2.12</td>
<td>143</td>
<td>67</td>
<td>53.1</td>
</tr>
<tr>
<td>69-036</td>
<td>36 F</td>
<td>0.6</td>
<td>56, 54 AF</td>
<td>1.59</td>
<td>104/12</td>
<td>20</td>
<td>24</td>
<td>1.35</td>
<td>113</td>
<td>40</td>
<td>64.6</td>
</tr>
<tr>
<td>69-186</td>
<td>57 F</td>
<td>0.7</td>
<td>78, 80 AF</td>
<td>1.78</td>
<td>146/12</td>
<td>27</td>
<td>54</td>
<td>1.95</td>
<td>132</td>
<td>61</td>
<td>53.8</td>
</tr>
<tr>
<td>68-168</td>
<td>38 F</td>
<td>0.8</td>
<td>78, 80 S</td>
<td>1.73</td>
<td>121/6</td>
<td>18</td>
<td>54</td>
<td>1.43</td>
<td>123</td>
<td>59</td>
<td>52.0</td>
</tr>
<tr>
<td>69-311</td>
<td>59 M</td>
<td>0.8</td>
<td>68, 60 AF</td>
<td>1.95</td>
<td>136/8</td>
<td>18</td>
<td>27</td>
<td>1.19</td>
<td>154</td>
<td>52</td>
<td>66.2</td>
</tr>
<tr>
<td>69-221</td>
<td>51 F</td>
<td>0.8</td>
<td>90, 90 AF</td>
<td>1.60</td>
<td>126/9</td>
<td>24</td>
<td>33</td>
<td>1.94</td>
<td>133</td>
<td>78</td>
<td>41.4</td>
</tr>
<tr>
<td>69-338</td>
<td>54 F</td>
<td>0.8</td>
<td>88, 80 AF</td>
<td>1.77</td>
<td>137/11</td>
<td>24</td>
<td>44</td>
<td>1.60</td>
<td>150</td>
<td>59</td>
<td>60.7</td>
</tr>
<tr>
<td>69-277</td>
<td>49 M</td>
<td>0.9</td>
<td>69, 71 AF</td>
<td>1.72</td>
<td>129/6</td>
<td>21</td>
<td>38</td>
<td>1.74</td>
<td>166</td>
<td>69</td>
<td>58.4</td>
</tr>
<tr>
<td>69-253</td>
<td>55 M</td>
<td>1.0</td>
<td>80, 80 AF</td>
<td>1.95</td>
<td>112/12</td>
<td>31</td>
<td>73</td>
<td>2.47</td>
<td>190</td>
<td>79</td>
<td>58.4</td>
</tr>
<tr>
<td>69-402</td>
<td>43 M</td>
<td>1.0</td>
<td>68, 66 AF</td>
<td>1.77</td>
<td>105/7</td>
<td>18</td>
<td>25</td>
<td>2.14</td>
<td>157</td>
<td>99</td>
<td>36.9</td>
</tr>
<tr>
<td>69-094</td>
<td>41 F</td>
<td>1.0</td>
<td>78, 82 AF</td>
<td>1.61</td>
<td>86/9</td>
<td>28</td>
<td>34</td>
<td>2.76</td>
<td>118</td>
<td>57</td>
<td>51.7</td>
</tr>
<tr>
<td>69-167</td>
<td>60 M</td>
<td>1.0</td>
<td>72, 75 AF</td>
<td>2.04</td>
<td>123/11</td>
<td>25</td>
<td>39</td>
<td>1.91</td>
<td>147</td>
<td>65</td>
<td>55.8</td>
</tr>
<tr>
<td>69-107</td>
<td>54 F</td>
<td>1.2</td>
<td>100, 90 AF</td>
<td>1.57</td>
<td>97/7</td>
<td>20</td>
<td>22</td>
<td>1.92</td>
<td>144</td>
<td>61</td>
<td>57.6</td>
</tr>
<tr>
<td>69-108</td>
<td>40 F</td>
<td>1.3</td>
<td>81, 82 S</td>
<td>1.44</td>
<td>114/10</td>
<td>28</td>
<td>39</td>
<td>2.65</td>
<td>104</td>
<td>47</td>
<td>54.8</td>
</tr>
<tr>
<td>69-153</td>
<td>24 F</td>
<td>1.4</td>
<td>85, 92 S</td>
<td>1.59</td>
<td>113/10</td>
<td>30</td>
<td>41</td>
<td>4.08</td>
<td>98</td>
<td>41</td>
<td>58.2</td>
</tr>
<tr>
<td>69-063</td>
<td>44 M</td>
<td>1.4</td>
<td>80, 80 AF</td>
<td>1.83</td>
<td>110/10</td>
<td>22</td>
<td>31</td>
<td>2.92</td>
<td>112</td>
<td>37</td>
<td>67.0</td>
</tr>
<tr>
<td>69-393</td>
<td>28 M</td>
<td>1.5</td>
<td>60, 56 AF</td>
<td>2.10</td>
<td>110/11</td>
<td>22</td>
<td>27</td>
<td>2.69</td>
<td>221</td>
<td>107</td>
<td>51.6</td>
</tr>
<tr>
<td>69-165</td>
<td>34 F</td>
<td>1.8</td>
<td>54, 56 AF</td>
<td>1.68</td>
<td>120/10</td>
<td>14</td>
<td>20</td>
<td>2.72</td>
<td>132</td>
<td>58</td>
<td>56.1</td>
</tr>
<tr>
<td>69-026</td>
<td>41 F</td>
<td>1.9</td>
<td>86, 84 S</td>
<td>1.76</td>
<td>118/10</td>
<td>25</td>
<td>29</td>
<td>3.05</td>
<td>176</td>
<td>88</td>
<td>50.0</td>
</tr>
<tr>
<td>69-390</td>
<td>48 F</td>
<td>2.1</td>
<td>62, 63 S</td>
<td>1.69</td>
<td>137/17</td>
<td>15</td>
<td>26</td>
<td>2.12</td>
<td>104</td>
<td>26</td>
<td>75.0</td>
</tr>
<tr>
<td>69-101</td>
<td>35 F</td>
<td>2.1</td>
<td>77, 79 S</td>
<td>1.55</td>
<td>122/11</td>
<td>21</td>
<td>22</td>
<td>2.84</td>
<td>99</td>
<td>35</td>
<td>64.6</td>
</tr>
<tr>
<td>Average</td>
<td>46.1</td>
<td>1.06</td>
<td>79.9, 77.7</td>
<td>1.70</td>
<td>119.4/9.7</td>
<td>24.5</td>
<td>41.6</td>
<td>2.16</td>
<td>143.8</td>
<td>64.6</td>
<td>55.7</td>
</tr>
</tbody>
</table>

* SEM
mitral stenosis

<table>
<thead>
<tr>
<th>Method</th>
<th>Normal subjects</th>
<th>AF (stenosis)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central</td>
<td>3.60</td>
<td>3.89</td>
</tr>
<tr>
<td>Systemic</td>
<td>4.75</td>
<td>4.98</td>
</tr>
<tr>
<td>Statham</td>
<td>3.18</td>
<td>3.38</td>
</tr>
<tr>
<td>General</td>
<td>7.71</td>
<td>8.02</td>
</tr>
</tbody>
</table>

The results obtained in these patients with mitral stenosis are compared with those in nine normal subjects. A Normal subjects had an average age of 40.8 years; 56% were female. All were in sinus rhythm except for one subject who developed atrial fibrillation during cardiac catheterization and was studied in that rhythm. Spontaneous reversion to sinus rhythm occurred 6 hours later.

**General Methods**

Each patient with mitral stenosis and four of the normal subjects underwent routine right and retrograde left heart catheterization. Cardiac output was determined by the direct Fick method, using technics previously described from this laboratory. Pressure was recorded with a Statham P23Db strain gauge and optical galvanometers on photographic paper at a speed of 75 mm/sec. This system was critically damped at 22 Hz. Mean pressures and the mitral valvular gradients were measured by planimetric integration. The mitral valve area was calculated by the Gorlin's formula, using the pulmonary arterial wedge-left ventricular pressure differential as the mitral valve gradient and an empirical constant of 0.7.

Five of the nine normal subjects were studied by selective coronary arteriography and left ventricular cineangiocardiography only and did not have cardiac outputs determined by the Fick method. All patients were lightly sedated with 50 to 100 mg of sodium secobarbital and 50 to 75 mg of meperidine hydrochloride.

**Angiocardiographic Methods**

A catheter with six side holes in the distal 1.5 cm was passed retrograde across the aortic valve into the left ventricle. Left ventricular injections were chosen for this study because the base of the ventricle and the region of the mitral valve are often obscured when contrast agents are injected into the left atrium or pulmonary artery, particularly when left atrial enlargement exists.

Each angiocardiogram was recorded on 35-mm film at 50 to 60 frames/sec. Kilovoltage and milliamperage were automatically regulated to provide optimal exposure. Each patient was positioned with the right shoulder elevated toward the image intensifier to produce an approximately 35° right anterior oblique projec-
tion of the left ventricle. This projection permits calculations of left ventricular volume,\textsuperscript{10} displays the plane of the mitral valve well,\textsuperscript{11} and avoids superimposition of the descending aorta and the mitral valve area. Forty-five to 60 ml of 50\% Hypaque (sodium diatrizoate) was injected into the left ventricle over 2 to 3 sec with an automatic injection device.\textsuperscript{*} The electrocardiogram was recorded during and after each injection. The beginning and end of the injections were recorded automatically on the same paper.

Radiopaque rulers, placed above and below each patient perpendicular to the central x-ray beam, were filmed before each study and served to correct for image magnification.

Twenty-one subjects had simultaneous right anterior oblique and right posterior oblique biplane cineangiocardiograms. The other 13 had only single-plane cineangiocardiograms in the right anterior oblique position.

The right posterior oblique views were employed to assess the validity of the procedure for correcting for the magnification of the image recorded in the right anterior oblique view. Analysis of the 21 right posterior oblique cineangiocardiograms showed that the left ventricular cavity was consistently approximately equidistant from the thoracic wall in that position. Therefore, correction for image magnification in the right anterior oblique position was made by correcting each left ventricular dimension by the average of the magnification of the previously filmed radiopaque rulers.

The first cycle following injection of the contrast material was generally not measured because the aortic valve plane was often not readily discernible. Ventricular extrasystoles and postextrasystolic beats were not analyzed. Left ventricular outlines were traced from individual cine frames projected on the screen of a viewer. Left ventricular volumes were calculated by the area-length method of Dodge and associates.\textsuperscript{12} The area of the projected image was measured planimetrically and corrected for magnification. The midpoint of the aortic valve plane and the visible apex of the cavity defined the major semiaxis (a) of the assumed ellipsoid of revolution. The minor semiaxis (b) was calculated from the major semiaxis and the area. Left ventricular volume was then calculated from the formula:

\[
V = \frac{4}{3} \pi a \cdot b^2
\]

Volumes were calculated at end systole (defined as the frame with the smallest calculable volume), throughout diastole, and at end diastole (defined as the frame with the largest volume). Left ventricular filling curves were constructed from these volume measurements. Three to five successive cardiac cycles were available for analysis in each patient. Left ventricular ejection fractions were calculated for all patients from the equation:

\[\text{Ejection fraction} = \frac{\text{end-diastolic volume} - \text{end-systolic volume}}{\text{end-diastolic volume}}\]

The presence of atrial fibrillation in the majority of the patients with mitral stenosis necessitated consideration of the effects of the irregular rhythm on the volume measurement. We found that end-diastolic volume increased as the R-R interval lengthened, the rate of increase being, of course, the slope of the left ventricular filling curve. The relationship between end-systolic volume and the preceding end-diastolic volume was not entirely predictable from patient to patient. In some patients the left ventricles reached the same end-systolic volume regardless of the preceding end-diastolic volume, while in other patients the larger the end-diastolic volume, the smaller the subsequent end-systolic volume. Thus the smallest end-systolic volume could always be found following the largest end-diastolic volume. In any case, to avoid biasing the important end-systolic volume data, we chose as our values for analysis the end-systolic volumes corresponding to the largest end-diastolic volumes. These two values were used to calculate the ejection fraction. The values tabulated represent, therefore, minimal end-systolic volumes, maximal end-diastolic volumes, and maximal ejection fractions.

The left ventricular cineangiocardiograms were also assessed qualitatively for diffuse and focal abnormalities in contraction patterns.

One patient (69-467) with mitral stenosis died after an effort at mitral commissurotomy. The heart was sectioned to reveal the mitral valve region approximately as it had been seen during cineangiocardiography.

Comparisons between the data obtained in normal subjects and in patients with mitral stenosis were analyzed for significance using the two-tailed Student's t-test.\textsuperscript{13}

**Results**

The data are presented in table 1. The severity of mitral stenosis ranged from mild

---

(calculated mitral valve area of 2.1 cm²) to severe (0.4 cm²). The heart rates of the two groups were similar. Cardiac outputs by the Fick method averaged 2.16 L/min/m² in the patients with mitral stenosis and 3.82 L/min/m² in those control patients in whom it was measured. Mean pulmonary arterial wedge pressures were appropriately elevated in the patients with mitral stenosis. Left ventricular end-diastolic pressures were normal in every patient except for a value of 17 mm Hg in patient 69-390.

Representative left ventricular filling curves obtained in three normal subjects and in five patients with mitral stenosis of varying severity are shown in figure 1. Left ventricular volume is plotted at intervals of 100 msec from the beginning of diastole. The left ventricular filling curves of the normal subjects demonstrate rapid filling during the initial 200 msec of diastole. A slower filling phase occupies the next 200 msec, followed by a plateau period comprising the rest of diastole, during which relatively little additional filling occurs until the onset of atrial systole. In contrast to the normal, the left ventricles of the patients with mitral stenosis fill more slowly. Nevertheless, the left ventricle fills to a normal volume when the duration of diastole exceeds 400 msec, even when the mitral valve area is as small as 0.4 cm².

The end-diastolic volumes, the end-systolic volumes, and the ejection fractions for all patients are presented in table 1. The end-diastolic volumes are slightly larger in the patients with mitral stenosis than in the normal subjects, with average values of 143.8 (98 to 221) and 124.2 (75 to 215) ml, respectively. The larger value in the patients with mitral stenosis appears to reflect the process, described previously, by which cardiac cycles were selected for analysis. This bias did not exist in the seven patients with mitral stenosis who were in sinus rhythm. The average end-diastolic volume was 121.0 ml in these seven. These data demonstrate that the end-diastolic volume is not subnormal in resting patients with mitral stenosis.

The end-systolic volumes in the patients with mitral stenosis averaged 64.6 (26 to 115) ml compared to 30.8 (14 to 77) ml in the normal subjects, a difference which is significant at a level of P < 0.0005. These values for end-systolic volume, as discussed previously, are the smallest values obtained in each patient. The values obtained in the seven patients with sinus rhythm were also significantly above the normal value, with an average of 51.9 ml. The two patients with the mildest mitral stenosis had the smallest end-systolic volumes of the entire mitral stenosis group, values which fall into the normal range. Apart from these two cases, no correlation between end-systolic volume and mitral valve area is evident. Calculation of left ventricular end-systolic volume per square meter of BSA slightly decreases the variances of both the mitral stenosis and the normal groups, but does not otherwise affect the data.

The left ventricular ejection fraction averaged 55.7% (36.9 to 75.0) in the patients with mitral stenosis and 76.7% (64.2 to 84.0) in the
normal subjects, a difference which is significant at a level of $P < 0.0005$. If the two patients with the mildest mitral stenosis are excluded, there exists no correlation between ejection fraction and mitral valve area.

Left ventricular contraction patterns were analyzed qualitatively in an attempt to characterize the observed abnormality of left ventricular ejection. A typical normal left ventricle is shown at end diastole (fig. 2A) and at end systole (fig. 2B). The aortic valve (AV) and mitral valve (MV) are indicated, as is the posterobasal area (PBA) of the left ventricle adjacent to the mitral valve. The normal left ventricle, including this posterobasal area, contracts symmetrically and synchronously. In contrast, the left ventricles of 20 of the 25 patients with mitral stenosis had clearly

**Figure 2**
Right anterior oblique cineangiocardiographic frames from a normal subject (69-1591) at end diastole (A) and at end systole (B). The aortic (AV) and mitral (MV) valve planes are indicated. The posterobasal area (PBA) of the left ventricle adjacent to the mitral valve is also indicated. A catheter in the right ventricle overlies the left ventricular silhouette.

**Figure 3**
Right anterior oblique cineangiocardiographic frames from a patient with mitral stenosis (69-340) at end diastole (A) and at end systole (B). The irregularity and distortion of the posterobasal area are indicated (brackets).
abnormal contraction patterns. A decrease in left ventricular wall motion was visible in 20 patients with ejection fractions under 65%. Of these 20 patients all but one (69-149) had a focal abnormality of the posterobasal area adjacent to the mitral valve. This area was distorted, rigid, and immobile compared to the rest of the left ventricle. This focal abnormality was more easily visible when the cineangiograms were viewed in motion, but was discernible even from single frames, as illustrated in figures 3 and 4. In these figures the distortion of the posterobasal area is evidenced by surface irregularities (brackets); the rigidity and immobility of this posterobasal area is demonstrated by the presence of the same surface irregularities at end diastole and at end systole.

The salient pathologic features of the one patient (69-467) who died are shown in figure 5. The mitral commissures are fused; the leaflets are grossly thickened. The chordae tendineae of the posterior mitral leaflet are fused into a single rigid columnar structure 8 mm in diameter. The apex of the papillary muscle is fibrotic. The entire posterobasal portion of the ventricle has been drawn...
Single-plane (anteroposterior) angiocardiograms by Dodge and associates,12,14 Greene and co-workers10 have demonstrated that left ventricular volumes can also be derived from single-plane cineangiocardiograms using the right anterior oblique position.

Data from the literature concerning angiocardiographic determination of normal left ventricular volumes is limited15-22 (table 2). Miller and Swan17 in 1964, Graham and co-workers21 in 1968, and Hugenholtz and associates22 in 1968 gave data for children. The classic paper of Arvidsson15 does not give values for normal subjects, but rather for subjects without volume overload of the left ventricle, including patients with valvular stenosis. The latter have been excluded from the entry in table 2. Sanmarco and Bartle16 in 1964, Bunnell and associates19 in 1965, and Björk and Lodin18 in 1965 have each reported a few cases. A larger series of 16 cases, reported by Kennedy and associates20 in 1966, permits more meaningful comparison with the present series. The principal difference is that our end-systolic volumes tend to be lower, resulting in somewhat higher ejection fractions. We believe that this discrepancy reflects, at least in part, different angiocardiographic filming technic. Kennedy and associates20 exposed only six films per second, and averaged the smallest volume from each of several cycles. This technic must overestimate end-systolic volume. Greene and associates10 compared observations made at cineangiography with those of 6 sec angiocardiography and generally found that end-systolic volumes obtained by the former technic were lower. They felt that this occurred because the 6 sec technic frequently missed end systole.

Angiography systematically overestimates left ventricular volume,10,12,14 and even when this is corrected by a regression equation, angiographically determined stroke volumes generally exceed Fick stroke volumes.23,24 The reasons for this stroke volume disparity are not clear, but the overestimations appear systematic23,24 and should not affect comparisons between subjects studied by the same angiographic technic.

Discussion
The ability to calculate left ventricular volumes has been demonstrated from biplane (anteroposterior and lateral) and later from single-plane (anteroposterior) angiocardiograms by Dodge and associates,12,14 Greene and co-workers10 have demonstrated that left ventricular volumes can also be derived from single-plane cineangiocardiograms using the right anterior oblique position.

Data from the literature concerning angiocardiographic determination of normal left ventricular volumes is limited15-22 (table 2). Miller and Swan17 in 1964, Graham and co-workers21 in 1968, and Hugenholtz and associates22 in 1968 gave data for children. The classic paper of Arvidsson15 does not give values for normal subjects, but rather for subjects without volume overload of the left ventricle, including patients with valvular stenosis. The latter have been excluded from the entry in table 2. Sanmarco and Bartle16 in 1964, Bunnell and associates19 in 1965, and Björk and Lodin18 in 1965 have each reported a few cases. A larger series of 16 cases, reported by Kennedy and associates20 in 1966, permits more meaningful comparison with the present series. The principal difference is that our end-systolic volumes tend to be lower, resulting in somewhat higher ejection fractions. We believe that this discrepancy reflects, at least in part, different angiocardiographic filming technic. Kennedy and associates20 exposed only six films per second, and averaged the smallest volume from each of several cycles. This technic must overestimate end-systolic volume. Greene and associates10 compared observations made at cineangiography with those of 6 sec angiocardiography and generally found that end-systolic volumes obtained by the former technic were lower. They felt that this occurred because the 6 sec technic frequently missed end systole.

Angiography systematically overestimates left ventricular volume,10,12,14 and even when this is corrected by a regression equation, angiographically determined stroke volumes generally exceed Fick stroke volumes.23,24 The reasons for this stroke volume disparity are not clear, but the overestimations appear systematic23,24 and should not affect comparisons between subjects studied by the same angiographic technic.

Circulation, Volume XLII, December 1970
The possible effect of the angiographic medium on left ventricular function was considered. In the subjects and patients with sustained sinus rhythm, slight increases in end-diastolic volume and end-systolic volume, and slight decreases in ejection fractions were seen by the fourth beat following the injection of dye into the left ventricle. Since these changes were rather small and of equal magnitude in both the patients with mitral stenosis and the normal subjects, the injection of the dye was not considered to have any effect on the comparisons made between the two groups.

The concept of left ventricular dysfunction in patients with pure mitral stenosis was apparently first raised in 1929 by Kirch, who pointed out that in most hearts studied at autopsy from patients with mitral stenosis the posterior wall of the left ventricle was markedly shortened.

Twenty-three years later, Grant studied several hearts at autopsy from patients with pure mitral stenosis and substantiated Kirch's findings. He concluded that this shortening was due to selective atrophy of the myocardium of the posterior wall of the left ventricle. Grant hypothesized that in mitral stenosis the thickening of the valve leaflets and fibrosis of the chordae tendineae convert the valve into a rigid cylinder of dense scar tissue, immobilizing the posterior wall of the left ventricle, with secondary atrophy of the immobilized muscle.

The only hemodynamic data purporting to show a left ventricular abnormality in patients with mitral stenosis are those of Feigenbaum and associates in 1966 and of Kasalický and associates in 1968. These investigators showed higher left ventricular end-diastolic pressures, particularly with exercise, in patients with mitral stenosis than in normals. Feigenbaum's group observed abnormal rises in ventricular diastolic pressure for a given increase in diastolic volume and suggested that this implied reduced left ventricular compliance in patients with mitral stenosis. However, interpretation of these data as indicative of left ventricular abnormality is based on the a priori assumption that left ventricular volume is normal or decreased in patients with mitral stenosis; our data show this assumption to be incorrect.

Angiocardiographic data concerning left ventricular function in patients with mitral stenosis is quite limited (table 3). Criley and Ross in 1961 observed that poor left ventricular emptying is often seen in patients with mild mitral stenosis "whose symptoms are out of proportion to the degree of mitral

---

Table 2

<table>
<thead>
<tr>
<th>Author</th>
<th>No.</th>
<th>End-diastolic (ml)</th>
<th>End-systolic (ml)</th>
<th>End-diastolic (ml/m² BSA)</th>
<th>End-systolic (ml/m² BSA)</th>
<th>Ejection fraction (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arvidsson, 1961</td>
<td>8</td>
<td>87</td>
<td>22</td>
<td></td>
<td></td>
<td>74</td>
</tr>
<tr>
<td>Sanmarco &amp; Bartle, 1964</td>
<td>2</td>
<td>80</td>
<td></td>
<td></td>
<td></td>
<td>60-70</td>
</tr>
<tr>
<td>Miller &amp; Swan, 1964</td>
<td>14</td>
<td>85</td>
<td>28</td>
<td></td>
<td></td>
<td>68</td>
</tr>
<tr>
<td>Björk &amp; Lodin, 1965</td>
<td>4</td>
<td>152</td>
<td>21</td>
<td></td>
<td></td>
<td>86</td>
</tr>
<tr>
<td>Bunnell et al., 1965</td>
<td>3</td>
<td>160</td>
<td>60</td>
<td>95</td>
<td>36</td>
<td>63</td>
</tr>
<tr>
<td>Kennedy et al., 1966</td>
<td>16</td>
<td>125</td>
<td>42</td>
<td>70</td>
<td>24</td>
<td>67</td>
</tr>
<tr>
<td>Graham et al., 1968</td>
<td>16</td>
<td>71</td>
<td>27</td>
<td></td>
<td></td>
<td>63</td>
</tr>
<tr>
<td>Hugenhotz et al., 1968</td>
<td>5</td>
<td>52</td>
<td>13</td>
<td></td>
<td></td>
<td>75</td>
</tr>
<tr>
<td>Heller &amp; Carleton, 1970</td>
<td>9</td>
<td>124</td>
<td>31</td>
<td>71</td>
<td>18</td>
<td>77</td>
</tr>
</tbody>
</table>

*Data recalculated to exclude patients with mitral or aortic stenosis.
†Abstract.
‡Data from children—recalculated to exclude those under 2 years of age.
§Children (over 2 years of age).
**Children—one normal and four with pure pulmonic stenosis, selected from a larger group with various types of congenital heart disease.
††Present study.
valve obstruction." However, no quantitative data were given. Jones and associates in 1964 reported 12 cases of mitral stenosis and mild (averaging 7 ml/beat) mitral regurgitation. These 12 patients had higher end-systolic volumes and lower ejection fractions than the 16 normal subjects subsequently reported from the same laboratory (Kennedy and associates 1966; see table 2). Bunnell and associates in 1965 reported six cases with left ventricular volumes nearly identical to their three normals. However, neither the normals nor the patients with mitral stenosis were characterized, except that four of the six patients were in sinus rhythm. Miller and associates in 1965 reported two cases of mitral stenosis; these had lower ejection fractions and higher end-systolic volumes than their normal controls, but the controls were children. Arvidsson in 1961 reported six cases (five in females) of pure mitral stenosis with apparently normal left ventricular volume parameters. However, these patients had an average mean pulmonary arterial pressure of only 23 mm Hg and an average Fick cardiac output of 6.8 L/min, making it unlikely that they had significant mitral stenosis.

It is generally assumed that left ventricular filling is impaired in patients with mitral stenosis and that this impairment is the cause of the observed low cardiac outputs. The data presented in the present study stand in sharp contrast to this traditional view. Our analyses of left ventricular filling curves confirm that left ventricular filling is, indeed, impaired in patients with mitral stenosis. However, the fact that even with severe stenosis the filling is largely complete by 400 msec implies that at slow or moderate rates the impairment of left ventricular filling, though present, is not severe enough to decrease cardiac output significantly.

It can be seen from the left ventricular filling curves of the patients with mitral stenosis that significant shortening of the diastolic filling period would limit stroke volume; this is consistent with the observed deleterious effects of tachycardia in patients with mitral stenosis. The data suggest that at rest, even in severe mitral stenosis, the left ventricle is able to fill adequately, though the requisite mitral valve gradient necessarily elevates pulmonary venous pressure, often to symptomatic levels.

The qualitative analysis of left ventricular contraction patterns is, as far as we are aware, the first attempt to employ, in patients with mitral stenosis, the technic of segmental left ventricular cineangiocardiographic analysis used by Herman and associates in the study of coronary artery disease. The distinctive abnormalities we have found in the posterobasal area of the left ventricle are, in our experience, quite specific for mitral stenosis. The cause of this abnormality is not clear. The focal character speaks against a diffuse lesion such as old rheumatic myocarditis. The age of the patients and the focal nature of the abnormality raise the question of coronary occlusive disease as a possible cause. However, patients with any history or electrocardiographic evidence of this were excluded from the study and in most of the patients the coronary arteries were visible on the cineangiograms and appeared normal. Finally, the posterobasal abnormalities are, as noted

### Table 3

Angiocardiographic Data from the Literature on Left Ventricular Volume of Patients with Mitral Stenosis

<table>
<thead>
<tr>
<th>Author</th>
<th>No.</th>
<th>End-diastolic Volume (ml)</th>
<th>End-systolic Volume (ml)</th>
<th>End-diastolic Volume (ml/m² BSA)</th>
<th>End-systolic Volume (ml/m² BSA)</th>
<th>Ejection Fraction (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jones et al., 1964†</td>
<td>12</td>
<td>121</td>
<td>58</td>
<td>92</td>
<td>36</td>
<td>55</td>
</tr>
<tr>
<td>Bunnell et al., 1965</td>
<td>6</td>
<td>144</td>
<td>57</td>
<td>92</td>
<td>36</td>
<td>61</td>
</tr>
<tr>
<td>Miller et al., 1965</td>
<td>2</td>
<td>144</td>
<td>65</td>
<td>97</td>
<td>55</td>
<td>45</td>
</tr>
<tr>
<td>Heller &amp; Carleton, 1970ją</td>
<td>25</td>
<td>144</td>
<td>65</td>
<td>85</td>
<td>38</td>
<td>56</td>
</tr>
</tbody>
</table>

*Slight mitral insufficiency.
†Present study.
MITRAL STENOSIS

above, quite distinctive and have not been seen in any patient with coronary disease studied in our laboratory.

Our qualitative cineangiographic findings support the hypothesis of Grant that the mitral valve ring, mitral leaflets, chordae tendineae, and papillary muscles form a rigid complex which restricts the mobility of the adjacent left ventricle, and that fibrosis of this area results. The pathologic information obtained in patient 69-467 provides additional support for this hypothesis. Our quantitative measurements suggest that this abnormality significantly impairs left ventricular function and that this impairment is a major factor in the reduction of cardiac output seen in patients with mitral stenosis.

Acknowledgment

We are grateful to many of our colleagues who participated in the study of these patients and to Mr. Dennis Page, Miss Barbara Goldstein, Miss Margaret McStocker, and Mrs. Linda Campbell who provided invaluable technical assistance.

References


Circulation, Volume XLIII, December 1970

100 Years Ago
Dickens as Diagnostician

What a gain it would have been to physic if one so keen to observe and so facile to describe had devoted his powers to the medical art.
Abnormal Left Ventricular Contraction in Patients with Mitral Stenosis
STANLEY J. HELLER and RICHARD A. CARLETON

Circulation. 1970;42:1099-1110
doi: 10.1161/01.CIR.42.6.1099

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1970 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

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/42/6/1099

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/