Evaluation of Left Ventricular Contractile State in Childhood

Normal Values and Observations with a Pressure Overload

By Thomas P. Graham, Jr., M.D., Jay M. Jarmakani, M.D., Ramon V. Canent, Jr., M.D., and Page A. W. Anderson, M.D.

SUMMARY

Left ventricular contractile state was evaluated in 20 children ages 3 to 11 years with normal left hearts and in 15 children ages 2 to 16 years with a left ventricular pressure overload. All patients were studied during diagnostic cardiac catheterization with catheter-tip micromanometry. Pressure-velocity curves were obtained during isovolumic systole by plotting (dp/dt)/28 P versus developed or total pressure (P). Computer analysis of five cardiac cycles was used to yield one composite pressure-velocity curve for each patient with both linear and second-degree polynomial curve analysis. The developed pressure method yielded higher values for the calculated \( V_{\text{max}} \) index, (dp/dt)/28 P at zero P than the total-pressure method for all patients. Normal standards were defined for both methods. The \( V_{\text{max}} \) index calculated with total pressure as well as peak (dp/dt)/28 P was significantly less than normal for the hypertrophy group. The \( V_{\text{max}} \) index calculated with developed pressure was not significantly different from normal, except for the entire hypertrophy group, but four of the 15 patients showed a depression of contractile state defined as a value for the \( V_{\text{max}} \) index less than 2 sd of normal. These results indicate the potential importance of preoperative and postoperative estimation of contractile state in patients with a left ventricular pressure overload in evaluation of possible irreversible alterations of contractility that may accompany myocardial hypertrophy.

Additional Indexing Words:

\( \text{dp/dt} \) \hspace{1cm} \( V_{\text{max}} \) \hspace{1cm} Aortic stenosis \hspace{1cm} Coarctation

RECENT animal investigations have indicated that the production of myocardial hypertrophy by means of a pressure overload is associated with a depression of myocardial contractile state as determined by the force velocity relationship.\(^1\) Similar observations in adult patients have demonstrated a depression of myocardial contractility in the presence of chronic myocardial hypertrophy secondary to a pressure overload.\(^6\)\(^-\)\(^8\)

The relative rate of pressure rise in the left ventricle during isovolumic systole has been used to evaluate myocardial contractile state both in animal experiments and during patient investigations.\(^6\)\(^-\)\(^8\) This method has been shown to detect alterations in left ventricular contractility independent of changes in end-diastolic volume or aortic pressure,\(^11\)\(^,\)\(^14\)\(^,\)\(^17\)\(^,\)\(^19\) and thus is potentially useful for comparison of myocardial performance in patients with different hemodynamic alterations from normal.

Children with a left ventricular pressure overload secondary to aortic stenosis or coarctation of the aorta have an augmentation...
of left ventricular function when expressed in terms of the ejection fraction.\textsuperscript{20} These patients have a normal or increased ejection fraction despite large increases in afterload or resistance to ejection, a variable known to depress the ejection fraction when increased acutely.\textsuperscript{21, 22} Myocardial contractile state, however, has not been evaluated in children with severe hypertrophy secondary to a left ventricular pressure overload and compared with normal values.

The purpose of this investigation, therefore, was to develop normal standards for the evaluation of left ventricular contractile state in children and to utilize these standards for the assessment of contractile state in children with a chronic left ventricular pressure overload.

**Methods**

**Patient Population**

All data were obtained during routine diagnostic cardiac catheterization. Twenty patients with normal left hearts comprised group I. Diagnoses included: mild pulmonary stenosis with right ventricular pressure \( \leq 75 \) mm Hg \((n = 8)\), small atrial septal defect with left-to-right shunt \(<35\%\) \((n = 2)\), postoperative atrial septal defect 1½ to 3 years after surgery \((n = 3)\), small ventricular septal defect detectable only by hydrogen electrode \((n = 2)\), vascular anomaly \((n = 1)\), and patients whose precatheterization diagnosis was atrial septal defect but whose catheterization was entirely normal \((n = 4)\). Vital statistics, hemodynamic data, and left ventricular volume data are presented in table 1. Ages ranged from 3 to 11 years. All patients had left ventricular end-diastolic volumes, ejection fractions, cardiac outputs, and left ventricular wall mass values which were normal by previously derived standards.\textsuperscript{23}

Group II consisted of 15 patients with aortic stenosis \((n = 10)\) or coarctation of the aorta \((n = 5)\). Two patients had fixed subvalvular aortic stenosis, two patients had idiopathic hypertrophic subaortic stenosis, one patient had supravalvular aortic stenosis, and five patients had valvular aortic stenosis (table 2). Patients

### Table 1

**Vital Statistics, Hemodynamic Data, and Left Heart Volumes for Patients with Normal Left Hearts (Group I)**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (yr)</th>
<th>BSA (m(^2))</th>
<th>HR</th>
<th>LVP (mm Hg)</th>
<th>LVEDV (ml/m(^2))</th>
<th>LVEF (%)</th>
<th>LVSO (liters/min/m(^2))</th>
<th>LVM (g/m(^2))</th>
<th>Dx</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. R.M.</td>
<td>3.0</td>
<td>0.63</td>
<td>97</td>
<td>110/16</td>
<td>66</td>
<td>95</td>
<td>0.61</td>
<td>3.93</td>
<td>85</td>
</tr>
<tr>
<td>2. J.M.</td>
<td>4.0</td>
<td>0.68</td>
<td>97</td>
<td>85/12</td>
<td>63</td>
<td>91</td>
<td>0.57</td>
<td>3.47</td>
<td>74</td>
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<td>3. A.I.</td>
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<td>0.69</td>
<td>107</td>
<td>105/13</td>
<td>72</td>
<td>102</td>
<td>0.60</td>
<td>4.67</td>
<td>102</td>
</tr>
<tr>
<td>4. J.C.</td>
<td>5.0</td>
<td>0.72</td>
<td>100</td>
<td>94/16</td>
<td>81</td>
<td>114</td>
<td>0.53</td>
<td>4.29</td>
<td>95</td>
</tr>
<tr>
<td>5. T.T.</td>
<td>5.0</td>
<td>0.79</td>
<td>91</td>
<td>100/12</td>
<td>72</td>
<td>96</td>
<td>0.65</td>
<td>4.24</td>
<td>89</td>
</tr>
<tr>
<td>6. R.B.</td>
<td>6.0</td>
<td>0.88</td>
<td>94</td>
<td>94/16</td>
<td>88</td>
<td>118</td>
<td>0.63</td>
<td>5.41</td>
<td>117</td>
</tr>
<tr>
<td>7. F.M.</td>
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<td>0.67</td>
<td>90/8</td>
<td>85</td>
<td>36</td>
<td>58</td>
<td>0.58</td>
<td>4.03</td>
<td>91</td>
</tr>
<tr>
<td>8. P.S.</td>
<td>6.0</td>
<td>0.71</td>
<td>94</td>
<td>86/12</td>
<td>64</td>
<td>92</td>
<td>0.66</td>
<td>3.97</td>
<td>91</td>
</tr>
<tr>
<td>9. C.T.</td>
<td>6.0</td>
<td>0.83</td>
<td>125</td>
<td>89/6</td>
<td>71</td>
<td>94</td>
<td>0.74</td>
<td>6.53</td>
<td>142</td>
</tr>
<tr>
<td>10. C.F.</td>
<td>6.0</td>
<td>0.81</td>
<td>113</td>
<td>130/16</td>
<td>78</td>
<td>110</td>
<td>0.70</td>
<td>6.64</td>
<td>127</td>
</tr>
<tr>
<td>11. D.H.</td>
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<td>0.71</td>
<td>91</td>
<td>118/8</td>
<td>70</td>
<td>107</td>
<td>0.63</td>
<td>4.00</td>
<td>89</td>
</tr>
<tr>
<td>12. J.K.</td>
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<td>0.80</td>
<td>88</td>
<td>95/12</td>
<td>69</td>
<td>99</td>
<td>0.54</td>
<td>3.27</td>
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<tr>
<td>13. E.S.</td>
<td>7.0</td>
<td>1.05</td>
<td>65</td>
<td>85/5</td>
<td>89</td>
<td>116</td>
<td>0.59</td>
<td>3.45</td>
<td>78</td>
</tr>
<tr>
<td>14. W.B.</td>
<td>7.0</td>
<td>0.83</td>
<td>115</td>
<td>86/9</td>
<td>82</td>
<td>116</td>
<td>0.63</td>
<td>5.92</td>
<td>129</td>
</tr>
<tr>
<td>15. R.R.</td>
<td>7.0</td>
<td>0.91</td>
<td>86</td>
<td>92/14</td>
<td>75</td>
<td>100</td>
<td>0.72</td>
<td>4.61</td>
<td>103</td>
</tr>
<tr>
<td>16. W.S.</td>
<td>8.0</td>
<td>0.91</td>
<td>88</td>
<td>93/11</td>
<td>65</td>
<td>87</td>
<td>0.68</td>
<td>3.87</td>
<td>87</td>
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<tr>
<td>17. J.G.</td>
<td>8.0</td>
<td>0.98</td>
<td>107</td>
<td>105/5</td>
<td>74</td>
<td>98</td>
<td>0.62</td>
<td>4.94</td>
<td>113</td>
</tr>
<tr>
<td>18. B.G.</td>
<td>8.0</td>
<td>0.90</td>
<td>91</td>
<td>100/10</td>
<td>77</td>
<td>102</td>
<td>0.64</td>
<td>4.44</td>
<td>98</td>
</tr>
<tr>
<td>19. G.M.</td>
<td>9.0</td>
<td>0.92</td>
<td>88</td>
<td>118/16</td>
<td>77</td>
<td>100</td>
<td>0.67</td>
<td>4.33</td>
<td>98</td>
</tr>
<tr>
<td>20. R.C.</td>
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<td>1.25</td>
<td>100</td>
<td>90/11</td>
<td>95</td>
<td>126</td>
<td>0.63</td>
<td>5.99</td>
<td>135</td>
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<tr>
<td>Mean</td>
<td>6.4</td>
<td>0.84</td>
<td>99</td>
<td>116</td>
<td>74</td>
<td>102</td>
<td>0.64</td>
<td>4.67</td>
<td>101</td>
</tr>
<tr>
<td>sd</td>
<td>1.9</td>
<td>0.16</td>
<td>14</td>
<td>13/4</td>
<td>10</td>
<td>11</td>
<td>0.06</td>
<td>0.94</td>
<td>20</td>
</tr>
</tbody>
</table>

Abbreviations: HR = heart rate; LVP = left ventricular pressure; LVEDV = LV end-diastolic volume; LVEF = LV ejection fraction; LVSQ = LV systolic output; LVM = LV wall mass; Dx = diagnosis; NL = normal left heart; Vase = vascular anomaly; PS = pulmonary stenosis.
Table 2
Vital Statistics, Hemodynamic Data, and Left Heart Volume Variables for Patients with a Left Ventricular Pressure Overload (Group II)

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (yr)</th>
<th>BSA (m²)</th>
<th>HR</th>
<th>LVP (mm Hg)</th>
<th>LVEDV (ml/m²) (%)</th>
<th>LVEF (liters/min/m²) (%)</th>
<th>LVSO (g/m²) (%)</th>
<th>LVM (g/m²) (%)</th>
<th>Dx</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. J.H.</td>
<td>2.0</td>
<td>0.63</td>
<td>136</td>
<td>180/20</td>
<td>78 108</td>
<td>0.75 7.89</td>
<td>167</td>
<td>233</td>
<td>267</td>
</tr>
<tr>
<td>2. N.K.</td>
<td>4.0</td>
<td>0.66</td>
<td>120</td>
<td>194/17</td>
<td>65 91</td>
<td>0.65 5.12</td>
<td>107</td>
<td>141</td>
<td>161</td>
</tr>
<tr>
<td>3. P.F.</td>
<td>4.0</td>
<td>0.76</td>
<td>88</td>
<td>142/20</td>
<td>93 123</td>
<td>0.77 6.25</td>
<td>127</td>
<td>221</td>
<td>266</td>
</tr>
<tr>
<td>4. C.W.</td>
<td>5.0</td>
<td>0.72</td>
<td>103</td>
<td>126/20</td>
<td>67 93</td>
<td>0.75 5.13</td>
<td>115</td>
<td>173</td>
<td>207</td>
</tr>
<tr>
<td>5. G.L.</td>
<td>6.0</td>
<td>0.76</td>
<td>125</td>
<td>120/14</td>
<td>63 91</td>
<td>0.70 5.53</td>
<td>118</td>
<td>153</td>
<td>178</td>
</tr>
<tr>
<td>6. A.M.</td>
<td>6.0</td>
<td>0.94</td>
<td>111</td>
<td>167/30</td>
<td>75 98</td>
<td>0.57 4.61</td>
<td>104</td>
<td>170</td>
<td>189</td>
</tr>
<tr>
<td>7. T.N.</td>
<td>6.0</td>
<td>0.90</td>
<td>107</td>
<td>150/8</td>
<td>69 92</td>
<td>0.75 5.31</td>
<td>122</td>
<td>117</td>
<td>140</td>
</tr>
<tr>
<td>8. B.S.</td>
<td>6.0</td>
<td>0.92</td>
<td>90</td>
<td>133/16</td>
<td>87 113</td>
<td>0.70 5.51</td>
<td>122</td>
<td>145</td>
<td>173</td>
</tr>
<tr>
<td>9. T.C.</td>
<td>6.0</td>
<td>0.84</td>
<td>125</td>
<td>120/31</td>
<td>83 110</td>
<td>0.53 5.51</td>
<td>118</td>
<td>155</td>
<td>180</td>
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<tr>
<td>10. S.E.</td>
<td>8.0</td>
<td>0.94</td>
<td>111</td>
<td>115/12</td>
<td>86 87</td>
<td>0.51 4.82</td>
<td>106</td>
<td>135</td>
<td>158</td>
</tr>
<tr>
<td>11. D.A.</td>
<td>12.0</td>
<td>1.18</td>
<td>91</td>
<td>119/11</td>
<td>79 100</td>
<td>0.79 5.65</td>
<td>131</td>
<td>221</td>
<td>241</td>
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<tr>
<td>12. W.B.</td>
<td>12.0</td>
<td>1.40</td>
<td>91</td>
<td>135/15</td>
<td>98 128</td>
<td>0.72 4.85</td>
<td>119</td>
<td>206</td>
<td>237</td>
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<tr>
<td>13. T.B.</td>
<td>12.0</td>
<td>1.20</td>
<td>86</td>
<td>87/10</td>
<td>71 98</td>
<td>0.62 3.79</td>
<td>85</td>
<td>132</td>
<td>148</td>
</tr>
<tr>
<td>14. T.G.</td>
<td>12.5</td>
<td>1.21</td>
<td>88</td>
<td>146/20</td>
<td>85 116</td>
<td>0.55 4.08</td>
<td>95</td>
<td>130</td>
<td>153</td>
</tr>
<tr>
<td>15. J.T.</td>
<td>14.0</td>
<td>1.73</td>
<td>68</td>
<td>145/20</td>
<td>98 119</td>
<td>0.75 5.36</td>
<td>122</td>
<td>138</td>
<td>141</td>
</tr>
<tr>
<td>Mean</td>
<td>7.6</td>
<td>0.95</td>
<td>101</td>
<td>146/17</td>
<td>81 104</td>
<td>0.67 5.33</td>
<td>119</td>
<td>167</td>
<td>189</td>
</tr>
<tr>
<td>sd</td>
<td>3.8</td>
<td>0.29</td>
<td>17</td>
<td>35/7</td>
<td>14 13</td>
<td>0.10 0.86</td>
<td>21</td>
<td>42</td>
<td>44</td>
</tr>
</tbody>
</table>

P value:
Gr II vs Gr I

Abbreviations: VAS = valvar aortic stenosis; IHSS = idiopathic hypertrophic subaortic stenosis; SAS = subvalvar aortic stenosis; SVAS = supravalvar aortic stenosis; ns = not significant (P > 0.1). Other abbreviations as in table 1.

with mitral insufficiency during left ventricular cineangiography were excluded from this group. Peak left ventricular pressure averaged 146 mm Hg for these patients. All patients had normal left ventricular end-diastolic volumes, and normal or increased ejection fractions and cardiac outputs. Ages ranged from 2 to 16 years, and the average age (7.6 years) was not significantly different (P > 0.2) from that of the normal group (6.4 years). Heart rate averaged 101 beats/min in group II and again was not significantly different (P > 0.5) from the heart rate of the normal group (101 beats/min). All patients in group II had left ventricular wall mass values >140% of normal (mean 189% of normal).

Data Collection
All patients were studied during routine diagnostic cardiac catheterization under light general anesthesia with nitrous oxide and ≤ 0.5% halothane. Left ventricular pressure (LVP) was measured with a Statham SF1 micromanometer. Zero pressure was referenced to midchest with the patient supine by using the lumen of the micromanometer attached to a Statham P-23Gb transducer. The first derivative of LVP, dp/dt, was measured with an electronic differentiator.* The dynamic characteristics of this differentiator have been described previously.24

Prior to the first cineangiogram, the electrocardiogram, LVP from the lumen of the micromanometer for in vivo baseline and sensitivity, and LV dp/dt were recorded on analog magnetic tape† at 7% ips and on a photographic recorder‡ at 200 mm/sec for 10 or more consecutive cardiac cycles. In addition, these data were replayed from tape at 3% ips onto the photographic recorder at 200 mm/sec. This technique yields an effective paper speed of 400 mm/sec to facilitate data analysis (fig. 1).

A biplane cineangiogram was then performed with injection of 1 to 1.25 ml/kg of 75% Hypaque-M into the main pulmonary artery. Left ventricular volumes and wall mass were calculated from the levogram phase of these cine by the area-length method and were compared with previously derived normal values. The details of this method have been described elsewhere.25

Data Analysis
Left ventricular pressure (LVP) recorded with the micromanometer, and LV dp/dt were measured each 5 msec during isovolumic systole for five cardiac cycles in each patient. To insure...
The inclusion of data only during isovolumic systole, LVP and dp/dt were obtained only during the time interval from 5 msec after LV end-diastolic pressure up to and including maximal positive dp/dt. With this method, 8 to 14 points per beat were obtained during isovolumic contraction in each patient, and the data from five beats were analyzed together to yield one composite pressure-velocity curve as described below.

The LVP and dp/dt data were then punched on IBM cards and the following calculations performed with use of an IBM 360-75 computer system. An index of contractile element velocity, VCE, was calculated by the equation: 

\[ V_{CE} = \frac{(dp/dt)}{KP} + C, \]

where \( P \) = developed LVP (instantaneous LVP − LV end-diastolic pressure), \( K = 28 \), and the constant C omitted from the calculations as described below.

This variable, \((dp/dt)/KP\), will be termed the velocity index. In order to avoid the difficulties inherent in pressure analysis during fractionate contraction of the left ventricle early in isovolumic systole as well as to minimize the possible role of the constant C in the velocity equation, only developed pressures equal to or above 10 mm Hg were included in the following analysis. By means of a polynomial curve fitting routine of degree one and degree two, the velocity index, \((dp/dt)/KP\), was expressed as a function of developed pressure as illustrated: first-degree equation \( y = a + bx \), second-degree equation \( y = a + b_1(x) + b_2(x)^2 \) where \( y = (dp/dt)/KP \), \( x = \) developed pressure, \( a = \) the y intercept, and \( b_n = \) the respective coefficients. One linear and one exponential equation were derived with use of composite data from five heart beats in each patient. The individual data points from all five beats and the derived regression equations (linear and exponential) were then plotted with a Calcomp plotter to yield a composite “force-velocity” or more properly a pressure-velocity index curve. The y-intercept of the derived equations is analogous to the velocity of the unloaded muscle, \( V_{max} \), and therefore will be termed the \( V_{max} \) index.

The equations derived for each patient in the normal group were used to calculate values of the velocity index at 5, 10, 15, 20, 25, 30, 35, and 40 mm Hg developed pressure by substituting these values for \( x \) in the derived equations. Thus, each normal patient had a value calculated for the velocity index at each of these developed pressures, and average values for this group were obtained. A similar analysis was performed for the pressure-overload group. Comparisons between the two groups were made by Student’s t-test. In addition, a similar analysis was performed for each group by means of developed pressure \( \geq 5 \) mm Hg above end-diastolic pressure for the velocity calculations.

Finally, a similar analysis was performed, substituting instantaneous or total pressure for developed pressures in the velocity calculations. Only the points during isovolumic systole showing the inverse relationship between velocity index and pressure were used to derive regression equations for this method.

The results will include the following comparisons: (a) pressure-velocity index curves in normal subjects for developed pressure \( \geq 10 \) mm Hg, for developed pressure \( \geq 5 \) mm Hg, and for total pressure; (b) all three methods for assessment of contractile state in normal subjects versus patients with hypertrophy.

Results

Normal Group: Pressure-Velocity Indices

A representative composite pressure-velocity curve for one of the normal patients is shown in Figure 2. Exponential regression equations were calculated, and the resultant curves are shown for developed pressure \( \geq 5 \) mm Hg (broken line) as well as developed pressure \( \geq 10 \) mm Hg (solid line). The equations derived by developed pressure \( \geq 5 \) mm Hg yielded higher velocity intercepts (\( V_{max} \) index) in all patients as illustrated here.

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LV CONTRACTILE STATE

Left ventricular velocity index as a function of developed pressure during isovolumic systole. Pressure-velocity curves are shown for all data with LVP ≤ 5 mm Hg (broken line) and for data with LVP ≥ 10 mm Hg (solid line). Data points are derived from five cardiac cycles to give one composite curve.

The exponential equations in all cases demonstrated a better fit in terms of higher F values and higher r values than the linear equations.27 These differences in F and r values for the exponential versus the linear equations were less pronounced for the total-pressure method than for the developed-pressure methods.

In figure 3, the pressure-velocity curve derived with use of total pressure instead of developed pressure is shown for the same patient whose data are illustrated in figure 2. This method yields an initial positive slope to the relationship between velocity index and pressure before the inverse relationship is achieved. Only the data showing an inverse relationship between pressure and velocity index were used in the regression equation derivations for this method. This analysis yielded a lower $V_{\text{max}}$ index than the two developed-pressure methods as illustrated by this patient's data. In table 3, average values and ranges of normal ($\bar{x} \pm 2 \text{SD}$) are shown for the $V_{\text{max}}$ index for the normal group by the three methods described. The average $V_{\text{max}}$ index for the method with use of developed pressure ≥10 mm Hg is slightly greater than twice that for the instantaneous or total-pressure analysis.

The peak measured velocity index by the instantaneous-pressure method (fig. 3) has been defined as the highest velocity index value measured during isovolumic systole and has been termed the physiological maximal velocity ($V_{\text{pm}}$).17 This variable, $V_{\text{pm}}$, showed a weakly positive correlation with the $V_{\text{max}}$ index.

| Table 3 |

<table>
<thead>
<tr>
<th>Comparison of $V_{\text{max}}$ Index for Normal Group by Three Different Methods of Analysis ($n = 20$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Method</td>
</tr>
<tr>
<td>I. Developed pressure ≥ 10 mm Hg</td>
</tr>
<tr>
<td>II. Developed pressure ≥ 5 mm Hg</td>
</tr>
<tr>
<td>III. Instantaneous pressure</td>
</tr>
</tbody>
</table>

$P$ values: I vs II | <0.001 |
| I vs III | <0.001 |
| II vs III | <0.001 |

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derived by the developed-pressure $\approx 10$ mm Hg method, $r = 0.489$, $P < 0.05$.

In the following comparison of the normal and hypertrophy groups, the results were similar, unless otherwise indicated, whether or not the developed-pressure methods or the total-pressure method was used. In table IV, a comparison of the three methods for calculating the $V_{\text{max}}$ index for the hypertrophy group is shown. The $V_{\text{max}}$ index by means of developed-pressure $\approx 10$ mm Hg analysis is almost three times greater than that for the total-pressure analysis.

**Comparisons of Normal and Hypertrophy Groups**

A composite pressure-velocity curve for the normal group is shown in figure 4. This "average curve" was determined by deriving the exponential curves for $P \approx 10$ mg for all normal patients, calculating values for $(dp/dt)/kP$ from these equations for $P$ of 5, 10, 15, 20, 25, 30, 35, and 40 mm Hg, and averaging these values to form an average curve to serve as the basis for comparison with the hypertrophy group.

As a group, the hypertrophy patients did not show a significantly different $V_{\text{max}}$ index ($P > 0.10$) from the normal patients when the two developed-pressure methods were used. Four of the 15 hypertrophy patients, however, did show a significant decrease (> 2 sd below the mean) in the y intercept ($V_{\text{max}}$ index) as well as depressed values for $(dp/dt)/kP$ at $P$ of 5 to 15 mm Hg as shown in figure 5.

In contrast, when the $V_{\text{max}}$ index was calculated by total pressure, the hypertrophy group averaged $1.04 \pm 0.48$ versus a value for the normal group of $1.50 \pm 0.39$ ($P < 0.01$). In addition, the "physiological maximal velocity" or $V_{\text{pm}}$ also was decreased significantly in the hypertrophy group, averaging $0.97 \pm 0.22$ versus a normal value of $1.30 \pm 0.24$ ($P < 0.001$, fig. 6).

Only one of the hypertrophy patients showed a significant decrease ($\bar{x} \pm 2$ sd) in peak $dp/dt$, over significant increase in time from onset of pressure rise to peak $dp/dt$, or in time to $V_{\text{pm}}$. None of these variables was signifi-
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Figure 5
Pressure-velocity values for the hypertrophy group plotted against the normal "pressure-velocity curve." All data calculated with regression equations derived with use of developed pressure > 10 mm Hg.

significantly different from normal (P > 0.3) for the hypertrophy group.

Finally, an attempt was made to correlate the $V_{\max}$ index by all three methods and $V_{pm}$ with age and with wall mass/BSA in the hypertrophy group. There was no significant correlation between these variables (P > 0.05).

Discussion

The use of the relative rate of pressure rise in the left ventricle to estimate myocardial contractile state represents an attempt to apply principles of muscle mechanics to the intact heart. The quantity $[(dp/dt)/K \cdot P]$ provides an estimate of contractile element velocity if the following assumptions are made.

1. Only isovolumic contraction is studied since significant fiber shortening results in deviation from the basic force-velocity curve. This assumption is invalid in patients with significant mitral insufficiency or ventricular shunts in whom isovolumic systole is frequently abbreviated or nonexistent. In addition, there may be a minimal degree of overall fiber shortening associated with mitral valve closure in all patients. Such a minimal decrease in ventricular volume with mitral valve closure, however, should be similar in all patients in this study and thus not affect comparisons between groups.

2. Pressure (P) is substituted for wall stress in plotting force-velocity curves for each patient. Since isovolumic contraction is studied in which overall dimensions are unchanged, stress that is approximated by $(P \cdot radius)/(wall\ thickness)$ will be directly proportional to P.

3. Wall thickness is assumed to be constant during isovolumic contraction. This assumption is not true; Fiegl and Fry reported a 10% increase in wall thickness during isovolumic contraction in open-chest dogs and Cothran and co-workers found a 6% increase in unanesthetized horses. It is not known wheth-
er or not this increase in wall thickness during isovolumic contraction is similar in degree in patients with different anatomical lesions.

4. Velocity measurements can be performed from high-fidelity pressure and first-derivative measurements. During isovolumic contraction, contractile element velocity ($V_{CE}$) is directly proportional to the rate of force development (dF/dt) and inversely related to the stiffness of the functional series elastic component (dF/dl). Thus, $V_{CE} = (dF/dt)/(dF/dl)$ during isovolumic systole since dF/dt can be approximated by dp/dt during this period. The series elastic stiffness (dF/dl) can be approximated from the value 28P, which is derived from isolated heart muscle investigations. Series elastic stiffness in isolated muscle has been found to remain unchanged with inotropic interventions, hyperthyroidism, experimental hypertrophy, or congestive heart failure.

Both total pressure and developed pressure (instantaneous pressure minus end-diastolic pressure) have been used in the velocity calculations and in plotting pressure-velocity curves. Animal investigations in this area have shown somewhat conflicting results in regard to the practical use of developed pressure versus total pressure in $V_{max}$ estimations to assess contractile state independent of change in end-diastolic volume or aortic pressure. Urschel and associates found no change in $V_{max}$ when calculated by developed pressure ($V_{max}$DP) under conditions of volume loading but a small decrease in $V_{max}$ calculated by total pressure ($V_{max}$TP) and in peak measured velocity, $V_{pm}$. Peirce and co-workers found $V_{max}$DP to decrease with volume or pressure loading, but $V_{max}$TP to remain constant. These authors, however, did not comment on the control of heart rate, a variable known to influence contractile state. Nejad's group found $V_{max}$TP to decrease with severe volume loading, while $V_{pm}$ remained constant. Wolk and associates found $V_{max}$TP to remain unchanged with volume loading. $V_{max}$DP was not calculated in either of the last two investigations.

These investigations suggest that contractile state can be estimated by $V_{max}$DP, $V_{max}$TP, or $V_{pm}$ if large differences in volume loading are not present between groups to be compared. In the present study, both $V_{pm}$ and $V_{max}$TP showed a slightly greater sensitivity to detection of alterations in contractile state of hypertrophy patients from normal than did $V_{max}$DP. The presence of a slightly higher end-diastolic pressure in the hypertrophy group ($17 \pm 7$ vs $11 \pm 4$ mm Hg, $P < 0.01$) undoubtedly played a role in this difference. The results of this investigation do not clarify whether the use of developed pressure or total pressure to estimate $V_{max}$ provides a more sensitive means for assessment of contractile state under varying conditions of volume loading since end-diastolic volume was not different between the two groups. Current knowledge concerning muscle models suggests that developed pressure may be the more appropriate variable for use in velocity calculations.

With both developed-pressure and total-pressure methods, normal values for left ventricular contractile state have been derived from 20 patients with normal left hearts undergoing diagnostic cardiac catheterization. The composite developed pressure-velocity plot of the mean normal values ±2 SD (fig. 5) and the normal values for $V_{max}$ in table 3 provide a basis for comparison with patients with anatomical or physiological defects affecting the left ventricle.

Mehmel and Nejad and their associates in animals and Mirsky and co-workers in patients have suggested that the peak measured velocity of shortening, peak (dp/dt)/k • P or $V_{pm}$, can be used to assess contractile state. Our average value for $V_{pm}$ was $1.30 \pm 0.24$ (x ± sd), which was lower than the average value of $2.15 \pm 0.78$ found by Mirsky et al. However, largely because of the wide sd, there is considerable overlap of the values reported from the two studies. The higher mean value in the previous investigation may be related to the use of fluid-filled catheters in 26 of the 46 patients and the heterogeneity of the normal group. Falsetti and co-workers found a normal value for $V_{pm}$ of $1.29 \pm 0.37$ for 17 adult patients whom they studied with

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mitral stenosis, atrial septal defect, or normal left hearts.

The stimulus to study contractile state in children with left ventricular hypertrophy has been provided by several investigations, disclosing depressed contractility in experimental hypertrophy\textsuperscript{1-5} as well as in adult patients with hypertrophy.\textsuperscript{6-8} The group of children studied with a left ventricular pressure overload in this investigation had left ventricular mass values that average 189% of normal, but showed no alterations from the normal group in terms of LV end-diastolic volume, LV output, or heart rate. Despite the large increase in LV muscle mass, a depression of contractile state was not present in all patients. In addition, there was no correlation between contractile state indices and degree of hypertrophy or age.

Of the four patients with values for $V_{\text{max}}$ index less than 2 sd below normal, none was symptomatic or had ever required digitalis therapy. Three patients have undergone successful surgery for valvular aortic stenosis, supravalvular aortic stenosis, and coarctation and remain asymptomatic. The fourth patient, with hypertrophic subaortic stenosis, remains asymptomatic and has not undergone surgery. Long-term follow-up of these patients, as well as other patients with myocardial hypertrophy, will be required to assess the possible significance of these observed alterations in pressure-velocity indices of myocardial contractility. Simon and co-workers\textsuperscript{6} as well as Mason and co-workers\textsuperscript{8} have shown depressed contractile state in adults with pressure overload lesions, and Levine and associates\textsuperscript{7} found depressed contractile state in four of 12 adults with valvular aortic stenosis. Thus, there may well be an alteration in myocardial contractile state in the presence of hypertrophy related to age, duration, and severity of the hypertrophy.

These observations indicate the potential importance of further investigations in this field in an attempt to clarify the determinants of depressed contractile state with hypertrophy and the factors of potential importance in reversing the process.

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