Ejection Load Changes in Aortic Stenosis
Observations Made After Balloon Aortic Valvuloplasty

Youngtack Shim, Thomas G. Hampton, Craig A. Straley, J. Kevin Harrison, Laurence A. Spero, Thomas M. Bashore, and Ares D. Pasipoularides

To investigate complementarity and competitiveness between the intrinsic and extrinsic components of the total left ventricular systolic load, hemodynamic data from 18 elderly subjects with severe aortic stenosis were analyzed before and after balloon dilation of the stenosed aortic valve. Multisensor micromanometric pressure measurements allowed calculation (simplified Bernoulli equation) of the ejection velocity and aortic input impedance spectra. Despite a 32% increase in the aortic valve area (from 0.56±0.04 to 0.74±0.05 cm² [mean±SEM], p<0.01), the peak left ventricular systolic pressure fell by only 12% (from 189±10 to 167±8 mm Hg, p<0.01). This was accompanied by an increase in the impedance at the same cardiac output. In a subset of patients (n=9) in whom the peak aortic systolic pressure rose after valvuloplasty (from 115±10 to 128±12 mm Hg, p<0.01), a 40% increase in the aortic valve area was accompanied by a marked increase in the aortic input impedance. In this subset, the steady component of the aortic input impedance increased by 24% (from 960±96 to 1,188±134 dyne·sec/ml, p<0.05), and the characteristic impedance increased by 25% (from 106±13 to 132±19 dyne·sec/ml, p<0.05). Because of an increased aortic impedance acutely following the procedure, the total left ventricular systolic load after balloon dilation of the stenotic valve was only slightly decreased despite a significant increase in aortic valve area. This represents an example of complementarity and competitiveness between the intrinsic and extrinsic components of the total systolic ventricular load. It may explain why improvement in left ventricular performance may be modest acutely following balloon aortic valvuloplasty. (Circulation Research 1992;71:1174–1184)

Key Words • left ventricular loading in aortic stenosis • left ventricular systolic dynamics • aortic input impedance • complementarity • competitiveness

The hemodynamic impact of pressure overload in aortic stenosis is directly related to ventricular wall stress and the associated hypertrophic response.1–7 Hemodynamic changes after balloon dilation of the aortic valve in elderly subjects have indicated that left ventricular function is improved, but the extent of the improvement has turned out to be substantially lower than anticipated.8–11 Although data exist regarding acute hemodynamic changes after valvuloplasty,1,8–11 no quantitative analyses have been performed to investigate the resultant changes in the total systolic load of the left ventricle after the procedure. The instantaneous total left ventricular systolic load can be separated into an intrinsic component, associated with intraventricular pressure gradients, and an extrinsic component, represented by the aortic root ejection pressure waveform produced by the interaction of the aortic input impedance with the ejection flow pulse delivered by the ventricle. The objectives of the present study were to investigate, in the context of the recently proposed12,13 concept of complementarity and competitiveness between the two components of the total systolic load, the acute changes in total left ventricular ejection load associated with balloon dilation of the aortic valve in the elderly and to identify underlying hemodynamic factors responsible for these changes.

Materials and Methods

Study Subjects

The study group comprised twenty-two consecutive patients with hemodynamically significant aortic stenosis. Included were five men and 17 women, and their mean age was 76±2 years. None had prior myocardial infarction or cardiac surgery. Table 1 shows baseline clinical patient characteristics before valvuloplasty. The four subjects (patients 2, 8, 9, and 17 in Table 1) with aortic regurgitation (AR) >1+ (on a visual grading scale of 0–4+)14,15 were eliminated from further study. All patients had been seen by a cardiothoracic surgeon and were felt to be at high risk for aortic valve replacement because of associated and often severe illnesses, such as chronic lung disease and neoplasm. All patients signed informed consent for the study, which had been previously approved by the investigational review board of our institution.

This manuscript was sent to Dr. Matthew N. Levy, Consulting Editor, for review by expert referees, editorial decision, and final disposition.

From the Departments of Biomedical Engineering and Medicine, Duke University and Medical Center, Durham, N.C.

Supported in part by SCOR grant HL–17670 from the National Heart, Lung, and Blood Institute, Bethesda, Md.

Address for correspondence: Ares D. Pasipoularides, MD, PhD, FACC, Departments of Biomedical Engineering and Medicine, Room 136, Engineering Building, Duke University, Durham, NC 27706.

Received March 3, 1992; accepted June 23, 1992.
Table 1. Baseline Clinical Patient Characteristics

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (years)</th>
<th>Sex</th>
<th>CHF</th>
<th>Ang</th>
<th>Syn</th>
<th>AR</th>
<th>Other diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>81</td>
<td>F</td>
<td>3</td>
<td>3</td>
<td>0</td>
<td>1</td>
<td>None</td>
</tr>
<tr>
<td>2*</td>
<td>84</td>
<td>F</td>
<td>4</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td>MR</td>
</tr>
<tr>
<td>3</td>
<td>67</td>
<td>F</td>
<td>3</td>
<td>3</td>
<td>Pre</td>
<td>1</td>
<td>MR</td>
</tr>
<tr>
<td>4</td>
<td>67</td>
<td>F</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>MR</td>
</tr>
<tr>
<td>5</td>
<td>67</td>
<td>F</td>
<td>4</td>
<td>4</td>
<td>0</td>
<td>1</td>
<td>MR</td>
</tr>
<tr>
<td>6</td>
<td>83</td>
<td>F</td>
<td>4</td>
<td>3</td>
<td>0</td>
<td>1</td>
<td>None</td>
</tr>
<tr>
<td>7</td>
<td>73</td>
<td>F</td>
<td>4</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>None</td>
</tr>
<tr>
<td>8*</td>
<td>67</td>
<td>M</td>
<td>3</td>
<td>3</td>
<td>0</td>
<td>2</td>
<td>None</td>
</tr>
<tr>
<td>9*</td>
<td>66</td>
<td>F</td>
<td>4</td>
<td>4</td>
<td>0</td>
<td>2</td>
<td>None</td>
</tr>
<tr>
<td>10</td>
<td>77</td>
<td>F</td>
<td>2</td>
<td>3</td>
<td>0</td>
<td>1</td>
<td>MR</td>
</tr>
<tr>
<td>11</td>
<td>73</td>
<td>F</td>
<td>...</td>
<td>...</td>
<td>0</td>
<td>1+</td>
<td>None</td>
</tr>
<tr>
<td>12</td>
<td>84</td>
<td>M</td>
<td>4</td>
<td>4</td>
<td>0</td>
<td>1</td>
<td>None</td>
</tr>
<tr>
<td>13</td>
<td>80</td>
<td>F</td>
<td>4</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>None</td>
</tr>
<tr>
<td>14</td>
<td>69</td>
<td>M</td>
<td>3</td>
<td>2</td>
<td>Pre</td>
<td>1</td>
<td>None</td>
</tr>
<tr>
<td>15</td>
<td>84</td>
<td>M</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>MR</td>
</tr>
<tr>
<td>16</td>
<td>85</td>
<td>F</td>
<td>4</td>
<td>3</td>
<td>0</td>
<td>Tr</td>
<td>None</td>
</tr>
<tr>
<td>17*</td>
<td>78</td>
<td>F</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>MR</td>
</tr>
<tr>
<td>18</td>
<td>82</td>
<td>M</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>Tr</td>
<td>None</td>
</tr>
<tr>
<td>19</td>
<td>85</td>
<td>F</td>
<td>...</td>
<td>...</td>
<td>Pre</td>
<td>1+</td>
<td>MR</td>
</tr>
<tr>
<td>20</td>
<td>85</td>
<td>F</td>
<td>2</td>
<td>3</td>
<td>0</td>
<td>1</td>
<td>MR</td>
</tr>
<tr>
<td>21</td>
<td>84</td>
<td>F</td>
<td>...</td>
<td>...</td>
<td>0</td>
<td>1+</td>
<td>MR</td>
</tr>
<tr>
<td>22</td>
<td>86</td>
<td>F</td>
<td>...</td>
<td>...</td>
<td>0</td>
<td>1+</td>
<td>MR</td>
</tr>
</tbody>
</table>

CHF, congestive heart failure; Ang, angina; Syn, syncope; AR, aortic regurgitation (0–4+ visual grading scale\(^{14,15}\)); MR, mitral regurgitation; Pre, presyncope; Tr, trivial.

*Patients with AR >1+, who were excluded from analysis according to the study protocol.

Cardiac Catheterization and Angiography

Hemodynamic parameters were measured using an 8F dual-sensor micromanometric pigtail catheter (Micro-Tip model SPC-474A, Millar Instrument, Inc., Houston, Tex.) inserted through the femoral artery via a 10F or 14F sheath. Catheter placement is illustrated in Figure 1. Right-sided heart pressures were measured with a fluid-filled 7F Criticon catheter (Arrow International Inc., Reading, Pa.) connected to a strain gauge (Hewlett-Packard Co., Andover, Mass.). A temporary pacemaker was positioned in the right ventricle before the procedure. Immediately before valvuloplasty, a digital ventriculogram was performed in the 30° right anterior oblique projection. Forty-five milliliters of nonionic contrast agent (Isovue [iopamidol], E.R. Squibb and Sons, Inc., Princeton, N.J., or Omnipaque [iohexol], Winthrop Pharmaceuticals Lab., Des Plaines, Ill.) was injected at 12–15 ml/sec directly into the left ventricle using a pump (Medrad, Pittsburgh, Pa.). The x-ray unit (model MLX L/U, GE Co., Cincinnati, Ohio) was coupled to a computer (model ADAC 4100-C, ADAC Laboratories, Milpitas, Calif.) for image processing. The ventriculogram was recorded at end inspiration on a 256×256×8-bit matrix at 30 frames per second. Expired gas was analyzed (MMC Horizon System, Sensor Medics Corp., Anaheim, Calif.), and blood oxygen content and saturation were measured (282 CO-oximeter, Instrument Laboratories Corp., Palatine, Ill.) for calculation of the Fick cardiac output. Aortic regurgitation was graded visually using the standard 0–4+ visual grading scale.\(^{14,15}\) Details have been reported previously.\(^{8–11,16}\)

![Diagram showing catheter placement. The high fidelity dual-sensor micromanometric catheter is inserted through the femoral artery. Simultaneous left ventricular pressure and aortic root pressure are measured by two laterally mounted solid-state micromanometers (small arrows) located 5 cm apart along the catheter.](http://circres.ahajournals.org/content/1175)
### Table 2. Hemodynamic and Angiographic Data Before and After Valvuloplasty

<table>
<thead>
<tr>
<th>Patient</th>
<th>HR (bpm)</th>
<th>LVSP (mm Hg)</th>
<th>AoSP (mm Hg)</th>
<th>PK-to-pk (mm Hg)</th>
<th>Mean (mm Hg)</th>
<th>AVA (cm²)</th>
<th>LVEF (%)</th>
<th>Mean PA (mm Hg)</th>
<th>PCWP (mm Hg)</th>
<th>CO (l/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>64</td>
<td>210</td>
<td>188</td>
<td>134</td>
<td>150</td>
<td>76</td>
<td>38</td>
<td>58</td>
<td>33</td>
<td>0.5</td>
</tr>
<tr>
<td>2</td>
<td>89</td>
<td>192</td>
<td>147</td>
<td>135</td>
<td>110</td>
<td>57</td>
<td>37</td>
<td>50</td>
<td>32</td>
<td>0.7</td>
</tr>
<tr>
<td>3</td>
<td>107</td>
<td>150</td>
<td>132</td>
<td>110</td>
<td>100</td>
<td>40</td>
<td>32</td>
<td>37</td>
<td>21</td>
<td>0.4</td>
</tr>
<tr>
<td>4</td>
<td>83</td>
<td>154</td>
<td>145</td>
<td>110</td>
<td>120</td>
<td>44</td>
<td>25</td>
<td>38</td>
<td>22</td>
<td>0.6</td>
</tr>
<tr>
<td>5</td>
<td>87</td>
<td>235</td>
<td>225</td>
<td>150</td>
<td>150</td>
<td>85</td>
<td>75</td>
<td>52</td>
<td>47</td>
<td>0.9</td>
</tr>
<tr>
<td>6</td>
<td>70</td>
<td>240</td>
<td>175</td>
<td>186</td>
<td>127</td>
<td>54</td>
<td>48</td>
<td>52</td>
<td>36</td>
<td>0.6</td>
</tr>
<tr>
<td>7</td>
<td>94</td>
<td>120</td>
<td>110</td>
<td>85</td>
<td>90</td>
<td>35</td>
<td>20</td>
<td>27</td>
<td>17</td>
<td>0.3</td>
</tr>
<tr>
<td>8</td>
<td>71</td>
<td>226</td>
<td>185</td>
<td>171</td>
<td>156</td>
<td>59</td>
<td>30</td>
<td>57</td>
<td>29</td>
<td>0.6</td>
</tr>
<tr>
<td>9</td>
<td>62</td>
<td>190</td>
<td>200</td>
<td>140</td>
<td>160</td>
<td>51</td>
<td>38</td>
<td>45</td>
<td>38</td>
<td>0.8</td>
</tr>
<tr>
<td>10</td>
<td>93</td>
<td>137</td>
<td>115</td>
<td>120</td>
<td>107</td>
<td>19</td>
<td>10</td>
<td>16</td>
<td>11</td>
<td>0.6</td>
</tr>
<tr>
<td>11</td>
<td>73</td>
<td>210</td>
<td>175</td>
<td>140</td>
<td>115</td>
<td>71</td>
<td>62</td>
<td>61</td>
<td>54</td>
<td>0.6</td>
</tr>
<tr>
<td>12</td>
<td>85</td>
<td>193</td>
<td>192</td>
<td>130</td>
<td>150</td>
<td>66</td>
<td>39</td>
<td>59</td>
<td>35</td>
<td>0.6</td>
</tr>
<tr>
<td>13</td>
<td>70</td>
<td>218</td>
<td>188</td>
<td>132</td>
<td>128</td>
<td>96</td>
<td>64</td>
<td>66</td>
<td>43</td>
<td>0.4</td>
</tr>
<tr>
<td>14</td>
<td>93</td>
<td>130</td>
<td>117</td>
<td>76</td>
<td>80</td>
<td>54</td>
<td>37</td>
<td>35</td>
<td>26</td>
<td>0.4</td>
</tr>
<tr>
<td>15</td>
<td>83</td>
<td>146</td>
<td>149</td>
<td>86</td>
<td>103</td>
<td>65</td>
<td>38</td>
<td>51</td>
<td>29</td>
<td>0.6</td>
</tr>
<tr>
<td>16</td>
<td>89</td>
<td>210</td>
<td>210</td>
<td>160</td>
<td>180</td>
<td>50</td>
<td>30</td>
<td>47</td>
<td>23</td>
<td>0.6</td>
</tr>
<tr>
<td>17</td>
<td>72</td>
<td>126</td>
<td>262</td>
<td>175</td>
<td>176</td>
<td>85</td>
<td>64</td>
<td>78</td>
<td>59</td>
<td>0.4</td>
</tr>
<tr>
<td>18</td>
<td>91</td>
<td>177</td>
<td>110</td>
<td>173</td>
<td>115</td>
<td>68</td>
<td>49</td>
<td>48</td>
<td>41</td>
<td>0.4</td>
</tr>
</tbody>
</table>

Mean 82 ± 3 SEM 4

HR, heart rate; bpm, beats per minute; Pre, before valvuloplasty; Post, after valvuloplasty; LVSP, peak left ventricular systolic pressure; AoSP, peak aortic systolic pressure; LV/Ao, ejection gradient; PK-to-pk, peak-to-peak; AVA, aortic valve area; LVEF, left ventricular ejection fraction; PA, pulmonary arterial pressure; PCWP, pulmonary capillary wedge pressure; CO, cardiac output; NA, not applicable.

### Pressure Measurements

Simultaneous left ventricular pressure and aortic root pressure were measured with the dual sensor Millar catheter, which has two laterally mounted solid-state micromanometers, one located at the catheter tip and the second located 5 cm proximal to the first, as shown in Figure 1. The catheter was manipulated such that the proximal and distal sensors were positioned along the outflow axis defined by the left ventricular chamber and the proximal aorta. Micromanometric pressures were balanced externally and calibrated against the fluid-filled catheter-manometer pressures. Analog pressure signals were digitized at 200 Hz using the ADAC 4100-C system.

### Valvuloplasty Procedure

A 20-mm-diameter aortic valvuloplasty balloon (Mansfield Scientific Corp., Mansfield, Mass.) was used in all cases. The balloon was positioned retrogradely across the aortic valve from the femoral artery, and it was hand inflated with a mixture of contrast and saline until the waist in the balloon was seen to disappear. The balloon was inflated two to five times at 3–8 atm. The dual-sensor micromanometric left heart catheter was reintroduced 10 minutes after valvuloplasty, and left ventricular and aortic root pressures were again measured simultaneously. In addition, left ventriculography was repeated, and right-sided heart data were reacquired according to the procedure used before the valvuloplasty. A summary of hemodynamic and angiographic data before and after valvuloplasty is given in Table 2.

### Aortic Valve Area

The Gorlin formula\(^7\) was used to determine the aortic valve area (AVA, in square centimeters):

\[ \text{AVA} = \frac{\bar{Q}}{44.3\sqrt{\Delta P(t)}} \]

where \(\Delta P(t)\) is the mean systolic pressure gradient (in millimeters of mercury). This formula is based on the Torricelli model of quasi–steady flow through an orifice. The Gorlin formula was applied to obtain nominal estimates of the aortic valve area, before and after valvuloplasty.

### Ensemble Averaging

Because of physiological beat-to-beat variation, analyses were performed on a series of beats rather than on a single beat. The pressure signals were digitized and split into individual left ventricular and companion aortic waveforms. Multiple-beat ensemble averages of the aortic and left ventricular pressure pulses were generated by a Lotus123 spreadsheet (Lotus Development Corp., Cambridge, Mass.) to obtain accurate representative waveforms, with the shortest signal as a reference. Longer tracings were truncated, but in no

---

\(^{7}\) Gorlin R: J Clin Invest 22, 471, 1943.
case was any individual tracing longer than 5% of the reference.

Ejection Velocity

The ejection velocity at the aortic root was calculated, point-by-point from the simultaneous pressure pulses, by an adaptation of the simplified Bernoulli formula, which accounts for the predominant convective acceleration but omits the negligible local acceleration and viscous effects:

\[ V_{A0}(t) = \sqrt{\Delta P(t)/2} \]  

where \( V_{A0}(t) \) is the aortic root velocity (in meters per second) and \( \Delta P(t) \) is the pressure drop (in millimeters of mercury) between the two micromanometers. Since no patient had significant aortic regurgitation (see “Study Subjects” and Table 1), ejection velocity was assumed to be zero throughout the cardiac cycle, except during ejection.19,20

Fourier Analysis

The pressure and velocity signals from the aortic root, before and after balloon aortic valvuloplasty, were ensemble-averaged and analyzed by standard Fourier analysis methods21,22 with software developed by the authors. The Fourier coefficients of the harmonics of the compound waveforms were calculated by a Simpson numerical integration routine incorporated into a custom-made FORTRAN 77 program run on a Sun SPARC 1+ workstation (Sun Microsystems, Inc., Mountain View, Calif.).

Impedance Analysis

The input impedance of the ascending aorta was obtained from the aortic root pressure and the ejection velocity waveform calculated by Equation 2. The modulus of the input impedance for the jth harmonic, \( Z_{in}(\omega_j) \), is the ratio of the amplitude of the jth pressure harmonic, \( P_{A0}(\omega_j) \), to that of the jth harmonic of the ejection velocity, \( V_{A0}(\omega_j) \). The phase angle of the jth harmonic of input impedance, \( \theta_{in}(\omega_j) \), is the difference between the phase angles of pressure, \( \theta_{p}(\omega_j) \), and flow velocity, \( \theta_{v}(\omega_j) \):

\[ |Z_{in}(\omega_j)| = |P_{A0}(\omega_j)|/|V_{A0}(\omega_j)| \]  
\[ \theta_{in}(\omega_j) = \theta_{p}(\omega_j) - \theta_{v}(\omega_j) \]

The modulus of the zeroth harmonic of the aortic input impedance is defined as the steady component of the impedance (\( Z_{s0} \)) spectrum and approximates total systemic peripheral vascular resistance. The average of the aortic input impedance moduli from the first to eighth harmonic was obtained as an approximation to the ascending aortic characteristic impedance (\( Z_{ch} \)):

\[ Z_{ch} = \frac{1}{8} \sum_{j=1}^{8} |Z_{in}(\omega_j)| \]  

This represents the input impedance of a uniform tube in the absence of reflections (matching terminal impedance).21-25 A pulsatility index (PI), an empirical indicator of the intensity of reflections, was defined as the ratio of the maximum to minimum modulus of the harmonic components of the aortic input impedance spectrum. The maximum and minimum moduli were taken over the range from the first to fifth harmonic, since values of moduli at higher harmonic frequencies are calculated from values of pressure and flow that are characterized by relatively low signal-to-noise ratios. Thus,

\[ PI = \frac{|Z_{in}(\omega_j)|_{max}}{|Z_{in}(\omega_j)|_{min}}, \quad j=1-5 \]  

Statistical Analysis

The observed changes before and after valvuloplasty were analyzed for statistical significance using Student’s paired t test. Statistical significance was defined at \( p<0.05 \) and \( p<0.01 \). The data are summarized as mean±SEM.

Results

Aortic Valve Area Increase and Ensuing Hemodynamics

Tables 2 and 3 epitomize the hemodynamic changes associated with balloon aortic valvuloplasty in the overall study group. The procedure increased the calculated area of the stenotic aortic valve by 32% (from 0.56±0.04 to 0.74±0.05 cm², \( p<0.01 \)), but peak measured left ventricular systolic pressure decreased by only 12% (from 189±10 to 167±8 mm Hg, \( p<0.01 \)). Peak measured aortic systolic pressure and cardiac output did not change after the procedure (from 131±8 to 126±7 mm Hg, \( p>0.05 \), and from 4.1±0.3 to 4.3±0.3 l/min, \( p>0.05 \), respectively).

Pressure Waveforms

Figure 2 illustrates left ventricular and aortic pressure waveforms and the transaortic ejection pressure gradient before valvuloplasty. As is typical for aortic stenosis,
the left ventricular pressure is greatly increased. The systolic part of the left ventricular pressure waveform is symmetric and bell-shaped. The systolic peak of the aortic root pressure is attained in the latter part of ejection. The greatly augmented transvalvular systolic pressure gradient, point-by-point difference between the digitized left ventricular and aortic ejection pressure waveforms, is quite symmetric and rounded. Compared with normal values, the time to peak instantaneous pressure gradient is prolonged, and the systolic time interval of positive pressure gradient is extended.

Ejection Pressure Gradient and Velocity

Figure 3 displays the calculated ejection velocity waveform with the corresponding ensemble-averaged signals of the left ventricular and aortic pressures before valvuloplasty. Since ejection velocity was calculated from the ejection pressure gradient, the shape of the ejection velocity waveform tracks that of the pressure gradient and is therefore symmetric and rounded. Additionally, the duration of ejection is prolonged (Figures 2 and 3).

Changes in ejection pressure gradient and velocity after valvuloplasty in the overall study group are summarized in Table 3. The peak transvalvular pressure gradient decreased by 30% (from 83±6 to 58±4 mm Hg). The peak ejection velocity across the stenotic aortic valve also decreased, by 14% (from 4.3±0.2 to 3.7±0.2 m/sec). The decreases in peak ejection pressure gradient and velocity, which reflect the increase in aortic valve area, were accompanied by only a modest (12%) decrease in peak left ventricular systolic pressure.

Representative pressure and velocity waveforms, before and after valvuloplasty, are displayed in Figure 4. The peak as well as the mean values of the ejection pressure gradient and velocity tracings decreased after the intervention. Note that, in addition to the decrease in their magnitudes, their shapes tended to become less symmetric, with steeper upstrokes than downstrokes. Comparison of the top and bottom panels demonstrates that the time to peak ejection gradient and peak ejection velocity are decreased after valvuloplasty. Interestingly, the left ventricular pressure is decreased only slightly, whereas the aortic pressure is clearly increased in the pattern commonly observed after the procedure and illustrated in Figure 4.

Aortic Input Impedance

Representative aortic input impedance spectra or frequency plots, before and after valvuloplasty, are shown in Figure 5. The spectra of the modulus of aortic input impedance, before and after valvuloplasty, are displayed in the top panels; the spectra of the phase angle are shown in the bottom panels. Within the first several harmonics, the impedance moduli decrease from the relatively high level of the zeroth harmonic to substantially lower values, which approximate the characteristic impedance of the ascending aorta. The phase angles are initially negative and, as illustrated in Figure 5, both before and after valvuloplasty tend to cross the zero line at approximately the same frequency values at which the broad minimum of the impedance modulus is attained.

As shown in Table 3, the steady term of the impedance modulus was elevated after valvuloplasty (from 989±63 to 1,229±104 dyne·sec/ml), whereas the characteristic impedance did not change significantly (from 116±17 to 128±17 dyne·sec/ml). The pulsatility index did not change significantly after valvuloplasty.

Subgroup Hemodynamics

An elevated peak systolic aortic pressure was observed after valvuloplasty in nine subjects (subgroup EAP). Pressure waveforms of a typical patient in this group, before and after valvuloplasty, are displayed in Figure 6. This figure illustrates the pattern characteristic of this subgroup, in which, although the ejection pressure gradient was greatly reduced, there was a complementary increase in systolic aortic pressure and in which left ventricular pressure remained practically unchanged. The increase in aortic pressure is accompanied by a significant increase in ascending aortic characteristic impedance in this subgroup. Hemodynamic changes in subgroup EAP, as well as in the remaining nine subjects who exhibited a decreased peak systolic aortic pressure after valvuloplasty (subgroup DAP), are summarized in Table 4. Alterations of the moduli of the first three harmonics of the input impedance after valvuloplasty in the two subgroups are shown in Figure.
The most dramatic finding after valvuloplasty was the large and significant increase in subgroup EAP of the ascending aortic impedance associated with the first three harmonics of the flow waveform. This upward shift is important for ventricular function after valvuloplasty since, as is also shown in Figure 7, the first three harmonics account for over two thirds of the variance of the ejection velocity waveform and thus contain most of the pulsatile power of the wave.

Discussion

Degenerative aortic stenosis is characterized by immobilization of the aortic valve due to chronic fibrocalcific changes. To compensate for the greatly augmented pressure gradient across the stenotic valve, the left ventricular musculature hypertrophies, and this may lead to eventual failure of the left ventricle and development of pulmonary edema.4-7 Hemodynamic changes
anticipated to ensue immediately after balloon dilation of a stenotic aortic valve include a decrease in the transvalvular pressure gradient, a decline in linear ejection velocity for the same cardiac output, a decrease in peak left ventricular systolic pressure, and a reduction in stroke work of the left ventricle.8-11

Previous studies have not addressed the impact of aortic valvuloplasty on the total systolic left ventricular load. The present study clearly demonstrates that adverse changes in aortic impedance occur acutely after balloon aortic valvuloplasty and that these changes lessen the magnitude of the decrease in left ventricular systolic load. Recognition that such changes can ensue has obvious implications for clinical management immediately after valvuloplasty. Moreover, such changes are a manifestation of complementarity and competitiveness between the intrinsic and extrinsic components of the total systolic left ventricular load, a concept recently introduced by Pasipoularides.12,13 Complementarity means the two components are additive, and competitiveness means that a decrease (increase) in one is compensated by an increase (fall) in the other for any given set of preload and contractility levels.

**Predominance of Convective Acceleration During Ejection**

An important hemodynamic characteristic of the ejection process associated with aortic stenosis is the substantial augmentation of convective acceleration effects throughout the entire ejection period as a result of the constrictive tapering of the subvalvular region.12,19,20 In step with this, both subvalvular and transvalvular gradients and thus the intrinsic component of left ventricular systolic load increase. Moreover, the subvalvular and transvalvular pressure gradient waveforms tend to become symmetric and rounded and more in phase with the ejection flow waveform.12,19,20

When the aortic valve is successfully dilated as a result of balloon aortic valvuloplasty, reverse hemodynamic changes are expected because of the somewhat increased contribution of local acceleration effects to the intrinsic component. Comparison of the transvalvular gradients, before and after valvuloplasty, clearly illustrates the aforementioned quantitative as well as qualitative changes. The decreased transvalvular pressure gradient after valvuloplasty reflects the increase in aortic valve area. Ejection pressure gradient and velocity assume more of the distinctive asymmetry, with sharper upstroke and much less declivitous downstroke, that is seen in normal individuals.12,19,20

The aortic valve area was less than 1.1 cm² for all subjects studied in this work, both before and after valvuloplasty. As demonstrated in another article from this laboratory,26 this value ensures that more than 90% of the total instantaneous pressure gradient, even at peak outflow acceleration, is due to convective acceleration forces. Therefore, ejection velocity at the aortic root was calculated from the ejection gradient using the simplified Bernoulli equation, where only convective acceleration is taken into account and local acceleration is neglected. The large values of the peak ejection velocity (Table 3) compared with normal (1 m/sec) support the theory that convective acceleration is the dominant gradient-producing mechanism during ejection, not only before but also after valvuloplasty.12,19,20

**Total Left Ventricular Systolic Load**

The intrinsic component of the total left ventricular systolic load is associated with intraventricular blood flow up to and through the aortic orifice. In aortic stenosis, this component of the ejection load is greatly

---

**Figure 5.** Graphs showing aortic input impedance spectra from a representative patient (subgroup EAP, with elevated peak systolic aortic pressure after valvuloplasty). After valvuloplasty, both the steady component of the impedance modulus and the characteristic impedance increase. Frequencies of the first harmonic before and after valvuloplasty are 1.37 and 1.39 Hz, respectively.
increased because of the strong convective acceleration of the intraventricular flow. The extrinsic component of the ejection load is represented by the aortic root ejection pressure waveform, which is produced by the interaction of the aortic input impedance with the ejection flow pulse that is delivered by the ventricle. Because of the dilation of the aortic valve, the intrinsic component (ejection pressure gradient) decreased after valvuloplasty. However, the extrinsic component was as likely, or more, to increase acutely after the procedure as to decrease, so that in the overall study group the extrinsic component did not change. Thus, in many subjects a complementary augmentation of the extrinsic component tended to counteract acutely the beneficial decrease of the intrinsic component. In the overall study group, left ventricular systolic pressure and total load decreased only modestly immediately after valvuloplasty. This suggests that the total left ventricular systolic load was relieved disproportionately less than might be anticipated in view of the increase in the aortic valve area and the ensuing decrease of the intrinsic component of the load.

Table 4. Summary of Hemodynamic Changes in Subgroups With Increased and With Decreased Peak Systolic Aortic Pressure After Balloon Aortic Valvuloplasty

<table>
<thead>
<tr>
<th></th>
<th>LVSP (mm Hg)</th>
<th>AoSP (mm Hg)</th>
<th>Z&lt; (dyne·sec/ml)</th>
<th>ZCh (dyne·sec/ml)</th>
<th>AVA (cm²)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>EAP subgroup</strong> (n=9)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre</td>
<td>170</td>
<td>115</td>
<td>960</td>
<td>106</td>
<td>0.53</td>
</tr>
<tr>
<td>Post</td>
<td>165</td>
<td>128</td>
<td>1,188</td>
<td>132</td>
<td>0.74</td>
</tr>
<tr>
<td>p</td>
<td>NS</td>
<td>&lt;0.01</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td></td>
</tr>
<tr>
<td><strong>DAP subgroup</strong> (n=9)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre</td>
<td>208</td>
<td>147</td>
<td>1,017</td>
<td>125</td>
<td>0.58</td>
</tr>
<tr>
<td>Post</td>
<td>169</td>
<td>123</td>
<td>1,269</td>
<td>124</td>
<td>0.74</td>
</tr>
<tr>
<td>p</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>NS</td>
<td>NS</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

LVSP, peak left ventricular systolic pressure; AoSP, peak aortic systolic pressure; Z<, steady component of the input impedance; ZCh, characteristic impedance; AVA, aortic valve area; EAP, subjects with elevated AoSP after valvuloplasty; Pre, before valvuloplasty; Post, after valvuloplasty; DAP, subjects with decreased AoSP after valvuloplasty; NS, not significant.
Aortic Input Impedance

The extrinsic component of the total left ventricular systolic load is represented by the aortic root ejection pressure waveform produced by the interaction of the aortic input impedance with the ejection flow pulse delivered by the ventricle. The aortic input impedance is therefore a strong determinant of the extrinsic component. In the present study, the aortic input impedance was defined in terms of linear ejection velocity at the aortic root, as shown in Equation 3. Precise knowledge of aortic valve area would have allowed calculation of the aortic input impedance in terms of volumetric flow rate. However, inherent errors in the Gorlin formula preclude accurate estimation of aortic valve area. By using linear ejection velocity at the aortic root calculated directly from the high-fidelity micromanometric pressures rather than volumetric flow rate, which requires, in addition, use of the Gorlin approximation for aortic valve area, the reliability of the impedance values is enhanced.

An interesting observation, exemplified in Figure 5, is that the impedance spectra were shifted strongly to the right, with an increase in the frequency of the modulus minimum and phase crossover. The latter took place at 8–10 Hz, or about twice the frequency found in most human studies. However, virtually all published data21–24,30 have been from humans in the 40–60-year age bracket, whereas the range for the present study group was 67–86 years. The high pulse wave velocity in our elderly group explains, in part, the relatively high frequency values of phase crossover. As derived from characteristic impedance (see below), aortic pulse wave velocity levels in our group were about 12 m/sec. By use of the quarter-wavelength relation,25,26 a major effective reflecting site can be calculated at a distance of approximately 35 cm from the aortic root. This is much closer to the aortic valve than expected from published human data for younger (40–60-year-old) subjects,31–34,36 namely 40–55 cm.

The major effective reflection site for our elderly population seems to be at the level of the renal arteries. An important reflecting site at this level was determined in the elegant human catheterization studies of Latham et al,31 who used a catheter with six micromanometers. Such a discrete reflection site in adult humans is confirmed by the autopsy series of Langewouters;32 it may develop as a result of greater aortic dilatation above and less dilatation below the renal arteries, which accrues with age. Not only the advanced age of our group but also the aortic stenosis (poststenotic dilatation) would render the aorta proximal to the renal branches particularly prone to degeneration and aneurysmal dilatation.

In the absence of reflected wave components, input impedance becomes identical with characteristic impedance. The characteristic impedance of the ascending aorta based on linear ejection velocity, $Z_{ch}^{(V)}$, is defined by Equation 7a

$$Z_{ch}^{(V)} = Z_{ch} = \rho c_{s}$$

(7a)

where $\rho$ is blood density and $c_{s}$ is ascending aortic pulse wave velocity. In contrast, the characteristic impedance based on volumetric flow rate ($Z_{ch}^{(Q)}$) is defined by Equation 7b

$$Z_{ch}^{(Q)} = \frac{\rho c_{s}}{A}$$

(7b)

where $A$ is flow cross-sectional area.22,23 Note that the two characteristic impedance expressions differ only by the area factor. However, when it is expressed in terms of linear velocity as in the present study, the characteristic impedance increases to a similar degree as pulse wave velocity when arterial pressure is increased. When pulse wave velocity is expressed in centimeters per second and $Z_{ch}$ is expressed in dynes times seconds per cubic centimeter (Equation 7a), their values are practically identical, since the blood density is close to unity (1.06 g/cm³). Since pulse wave velocity is proportional to the square root of the effective circumferential elastic modulus of the wall, $Z_{ch}^{(V)}$ is directly useful as an index of arterial stiffness. When the entire study group was examined, the characteristic impedance did not change after valvuloplasty, whereas the steady component of the input impedance at the aortic root increased. This increase in the zeroth harmonic indicates peripheral vasoconstriction.

EAP and DAP Subgroup Hemodynamics

In subgroup EAP, the peripheral vasoconstriction after valvuloplasty was associated with an upward shift of the
impedance moduli for the lowest three harmonics of the pulse, which account for over two thirds of the variance of the velocity waveform and thus contain most of the pulsatile power of the wave. This shift is illustrated in Figure 7. It suggests a reflexly mediated deterioration of ventriculoarterial coordination and may indicate a place for vasodilator therapy. In this subgroup, although the peak transvalvular gradient fell substantially after valvuloplasty, there was no significant reduction in peak left ventricular systolic pressure; rather, the peak aortic systolic pressure was actually increased (Figure 6).

The aortic root pressure represents the extrinsic component of the total systolic left ventricular load and is affected by the magnitude of the characteristic impedance of the ascending aorta. The elevated systolic aortic root pressure in subgroup EAP was associated with an increased characteristic impedance. On the other hand, in subgroup DAP there was no significant change in ascending aortic characteristic impedance after valvuloplasty and no evidence of any deterioration in ventriculoarterial coupling. Both left ventricular and aortic systolic pressures were found to decrease significantly and substantially after the procedure in subgroup DAP. Thus, in the overall study group undergoing balloon aortic valvuloplasty, the decrease in left ventricular pressure (total systolic load) was quite small compared with what one would have predicted from the increase in the Gorlin-derived valve areas.

Conclusions and Implications

Balloon aortic valvuloplasty increases moderately the aortic valve area of elderly patients with degenerative calcific aortic stenosis. This results in a significant decrease in the intrinsic component of the total left ventricular systolic load. However, our results show that increases in both the systemic peripheral resistance and the characteristic impedance of the ascending aorta may lead to a rise in the extrinsic load (aortic root pressure) complementary to the decrease in the intrinsic component (transaortic ejection pressure gradient) after successful valvuloplasty. Thus, there is complementarity between the intrinsic and extrinsic components of the total left ventricular systolic load. This explains why changes in aortic valve area after balloon aortic valvuloplasty have not correlated with clinical outcome. In half of the subjects studied, the peak systolic aortic pressure increased after the procedure, along with aortic characteristic impedance, pulse wave velocity, and stiffness. Complex reciprocal influences exist between aortic stiffness and pressure that affect left ventricular systolic loading and ventriculoarterial coupling after the procedure. The present findings point to the need for further studies to detail mechanisms that underlie the complementarity and competitiveness of the intrinsic and extrinsic components of left ventricular load in the setting of interventions aimed at the relief of aortic stenosis in the elderly.

References


Ejection load changes in aortic stenosis. Observations made after balloon aortic valvuloplasty.
Y Shim, T G Hampton, C A Straley, J K Harrison, L A Spero, T M Bashore and A D Pasipoularides

*Circ Res.* 1992;71:1174-1184
doi: 10.1161/01.RES.71.5.1174

*Circulation Research* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1992 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7330. Online ISSN: 1524-4571

The online version of this article, along with updated information and services, is located on the World Wide Web at:

http://circres.ahajournals.org/content/71/5/1174