Aortic Input Impedance in Man: Acute Response to Vasodilator Drugs

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SUMMARY In 18 patients who underwent coronary arteriography, aortic velocity and pressure data were obtained during a control state and during either isoproterenol infusion at 1, 2 and 3 μg/min or graded nitroprusside infusion (average peak dose 60 μg/min). Impedance moduli and phase angles were derived to 10 Hz for control states, isoproterenol at 2 μg/min, and at peak nitroprusside effect. Averaged control data included a mean resistance of 1460 dyn-sec-cm⁻⁵ and a characteristic impedance of 88 dyn-sec-cm⁻⁵. The characteristic impedance did not correlate with age (r = 0.21), coronary artery disease score (r = 0.17) or mean aortic pressure (r = −0.01). In 11 patients, isoproterenol induced a 38% reduction in mean resistance and a 10% reduction in mean aortic pressure. There was slight reduction in characteristic impedance and phase angles became less negative, to 2 Hz. In seven patients, nitroprusside induced a 38% reduction in mean resistance and a 22% reduction in mean aortic pressure. Impedance moduli decreased to 1.8 Hz and phase angles became less negative, to 3 Hz. Based on the different cardiovascular actions of these two drugs, the data suggest that vasodilators do not induce significant changes in the aortic impedance spectrum when not associated with a decrease in mean aortic pressure.

THE IMPEDANCE SPECTRUM of the proximal aorta is the most rigorous description of the hemodynamic properties of the arterial tree. It contributes importantly to the systolic wall stress and energy requirements of the left ventricle. Milnor¹ emphasized the role of proximal aortic impedance as ventricular afterload. His summary of the physiologic importance of aortic impedance also defines the complex analysis underlying this characterization of the systemic circulation. The construction of an aortic impedance spectrum requires high-fidelity pressure and flow signals, mathematical resolution of these signals into pure harmonic (frequency) constituents, and computation of an impedance modulus and pressure-flow angle for each harmonic term. Aortic impedance determinations have generally been the domain of experimental physiologists; few studies have described impedance measurements in man.

Vasodilator therapy in the treatment of congestive heart failure has focused clinical attention on the concept of vascular impedance. Representative articles, in describing the therapeutic principles, have referred to “decrease in impedance to left ventricular ejection,”¹" reducing left ventricular ejection impedance,”¹" and “pharmacologic manipulation of impedance.”¹’ Pharmacologically induced changes in the proximal aortic impedance spectrum are implied, but derivations are presented only for the mean resistive term (0th harmonic of the impedance spectrum). As customarily defined in physics and electrical engineering, impedance refers to “oscillatory motions or alternating current.”¹⁶ The capacitive component of aortic impedance has been emphasized,”¹⁶ but in clinical settings, impedance has become synonymous with peripheral vascular resistance.

The effects of pharmacologic agents on the proximal aortic impedance spectrum have been studied experimentally,²⁻⁵ but there are only a few clinical reports.⁶⁻¹³ In this study we provide additional data defining the proximal aortic impedance spectrum in man and describe the changes in impedance associated with the administration of two potent vasodilators, isoproterenol and sodium nitroprusside.

Methods

Patient Selection
All patients in this study had angina pectoris that was refractory to medical treatment and were thus candidates for coronary artery bypass grafting. Cardioactive drugs were discontinued at least 72 hours before catheterization. Informed consent was obtained from all patients for their participation in a long-term, prospective study of the effects of coronary artery bypass grafting on left ventricular (LV) function. The impedance data of a portion of the study group are the subject of this report.

Catheterization Technique
All patients received 10 mg of papaveretum and 0.4 mg of scopolamine by intramuscular injection 1 hour before catheterization. A right antecubital cutdown was performed for routine right-heart catheterization and insertion of a fine cannula into the right brachial artery for dye-dilution cardiac output determinations. The patients were heparinized and routine coronary arteriography was performed using the Judkins technique via the right femoral artery. A Judkins coronary catheter was replaced with a #8F pigtail catheter (Cordis Corp.) in a polyethylene sleeve, using a modification of the technique described by Brooksby et al.¹⁶ After LV cineangiography, the polyethylene sleeve was advanced along the catheter to a stable
position in the left ventricle. The pigtail catheter was removed and replaced with a #8F Velocimeter-Manometer catheter. The sleeve was then retracted so that its tip was at midthoracic level. The catheter was manipulated to achieve an optimal velocity signal, with the tip of the catheter usually remaining in the left ventricle and the plane of the velocity transducer 4–6 cm above the aortic valve. An interval of approximately 20 minutes preceded the beginning of experimental measurements.

Drug Administration

Infusion of sodium nitroprusside or isoproterenol by calibrated Watson-Marlow pump followed a period of baseline hemodynamic measurements. Nitroprusside was administered in a concentration of 7.5 µg/ml at an initial rate of 15 µg/min, which was increased by 10–20 µg/min every 2 minutes until the aortic systolic pressure decreased by approximately 20 mm Hg. The average dose at the time of discontinuation was 60 µg/min.

The safety of administering isoproterenol was ascertained during noninvasive studies on the day before catheterization. Isoproterenol was infused in graded increments of 1, 2 and 3 µg/min for 5 minutes at each level. No significant complications or adverse drug reactions occurred in any patient.

Measurements

Proximal aortic blood velocity was measured with a modified Mills\textsuperscript{17, 18} electromagnetic velocity transducer (fabricated locally) and flowmeter (model 275, S.E. Laboratories). The zero drift of the system in saline at a temperature of 37.5°C was 4–5% of flowmeter full-scale deflection over 2 hours, after a warm-up of 15 minutes. The frequency response of the flowmeter at the filter setting of 20 Hz used in these studies indicated no amplitude distortion (± 5%) from 0–20 Hz and a phase shift that was relatively linear and equal to a delay of 12 msec.\textsuperscript{19} The velocity transducer was calibrated with variable flow rates of saline from a constant head source, using the principle described by Bennett and co-workers.\textsuperscript{20} Velocity calibration factors were derived from full-scale (100%) flowmeter deflection at several gain settings. The dye-dilution technique was used to obtain an average control stroke volume from three determinations. If the velocity profile in the ascending aorta is considered flat and systolic changes in aortic cross-sectional area are assumed negligible, the velocity profile equals a flow profile. The integrated area under the velocity curve (cm/sec × sec = cm) was divided into stroke volume (cm\textsuperscript{3}) determined by the dye-dilution to give an effective aortic cross-sectional area (cm\textsuperscript{2}). This area, in the plane of the velocity electrodes, was used to convert velocity signals into flow signals. A close correlation (48 determinations) has been shown in this laboratory\textsuperscript{21} between outputs determined by the dye-dilution technique (x) and by the product of effective aortic cross-sectional area times the integrated velocity profile (y):

\[ y = 0.97x + 0.17, \ r = 0.97 \]

Aortic and LV pressures were measured through a fluid-filled catheter attached to a pressure transducer (S.E. 4-82). The frequency responses of the pressure recording systems were characterized immediately after removal of the catheter by application of a 5-Hz square wave. The range of natural frequencies was 28–46 Hz and the range of damping factors was 0.17–0.28, and their combination in each case yielded distortion-free (± 5%) amplitude to 10 Hz.

The pressure and velocity signals were recorded on magnetic tape (Ampex SP-300). The analog signals were digitized in a PDP 11/45 A/D system at intervals of 2 msec and stored on disc. Ten aortic pressure and velocity signals were selected from an interval of 30 seconds as displayed on a Tektronix screen. Individual velocity cycles were in some cases corrected for high-frequency artifacts by a least-squares polynomial fit covering up to 40 msec. The average value of the velocity signal during the last one-third of diastole was defined as zero flow. The 10 aortic pressure and velocity cycles were averaged and resolved into Fourier harmonics. The phase angle of the pressure Fourier terms was corrected for the dynamic response of the catheter and for a 1.1-cm difference between the location of the velocity electrodes and the aortic pressure port.\textsuperscript{22} The phase angle of the velocity terms was corrected for the phase shift introduced by the flowmeter. Impedance moduli for each Fourier harmonic term were derived by the following expression:

\[
\text{Impedance modulus (Z, in dyn-sec-cm}^{-4}) = \frac{\text{Pressure modulus (mm Hg)}}{\text{Velocity modulus (cm/sec)} \times \text{aortic area(cm}^{-2}) \times 1333 \text{ dyn}} \times \frac{\text{cm}^{-2}}{\text{mm Hg}}
\]

Impedance phase angles were obtained by subtracting the phase angle of flow from the phase angle of pressure. Velocity moduli ≤ 0.5 cm/sec and pressure moduli ≤ 0.5 mm Hg were at noise level and data were not derived when either of these thresholds was present, usually at frequencies greater than 9 Hz. Observing the definitions employed by Nichols et al.,\textsuperscript{23} the ratio of mean pressure to mean flow (R) is the input resistance of the system (0th harmonic term); and the characteristic impedance (Zo) is approximated by the average of impedance moduli between 2 and 12 Hz. Left ventricular power output was derived from the following relationships:

\[
\text{Total power} = \text{steady power} + \text{oscillatory power}
\]

where steady power = mean flow, oscillatory power = \(1/2 \sum Q_n^2 Z_n \cos \phi_n\), \(Q_n\) = Fourier flow modulus of term n, \(Z_n\) = impedance modulus of term
n, and \( \phi_n \) = pressure-flow phase angle of term \( n \).

The coronary arteriograms were scored according to the severity of disease by the system of Friesinger et al.\(^\text{14}\)

**Statistical Methods**

Data are expressed as the mean \( \pm \) SD. Correlation coefficients were obtained using standard regression equations. The moduli and phase angles on all patients were linearly interpolated to common frequencies so that groups of data from control and drug-induced changes could be compared by the paired \( t \) test. A \( p \) value \( \leq 0.05 \) was considered significant.

**Results**

Examples of unaveraged pressure and velocity signals for control and drug infusion states are shown in figures 1A and 1B. The hemodynamic data for the 11 patients who received isoproterenol are presented in table 1 and for the seven patients who received nitroprusside in table 2. Pooled control data for all 18 patients include an average peak aortic flow rate of 416 \( \pm \) 68 ml/sec and an average peak blood velocity of 43 \( \pm \) 9.5 cm/sec. For the six patients with LV ejection fractions \( \leq 0.55 \), the control average peak flow rate (413 \( \pm \) 67 ml/sec) and average peak velocity (40.1 \( \pm \) 9.5 cm/sec) did not differ significantly from those measurements in the 12 patients with LV ejection fractions \( \geq 0.55 \) (average peak flow rate 417 \( \pm \) 71 ml/sec; average peak velocity 44.5 \( \pm \) 9.6 cm/sec).

Pooled control impedance data from all 18 patients are displayed in figure 2. The mean input resistance was 1490 dyn-sec-cm\(^{-5}\). The mean value for the characteristic impedance was 88 \( \pm \) 35 dyn-sec-cm\(^{-5}\). This value, obtained mathematically, was confirmed by obtaining an identical value through graphic analysis of individual impedance spectra. Linear regression analysis did not demonstrate a correlation between characteristic impedance and age (\( r = 0.21 \)), mean aortic pressure (\( r = -0.01 \)) or coronary artery disease score (\( r = 0.17 \)). Relatively large standard deviations were noted in the impedance phase measurements. The general shape of the mean curve shows a phase angle most negative at the mean fundamental frequency, becoming more positive beyond 3 Hz and maximally positive at points where the impedance moduli appear closest to the characteristic impedance. Analysis of individual impedance plots permitted relatively discrete assignment of minima and maxima in the variation of modulus for 12 of the patients, a finding obscured by the pooled data of figure 1. The first minimum and maximum were at 4.2 \( \pm \) 0.5 Hz and 5.7 \( \pm \) 0.5 Hz. The second minimum and maximum were of lower amplitudes; deriving average frequencies for them was not appropriate.

The effects of isoproterenol and nitroprusside on the low-frequency band of the aortic impedance spectrum, both characteristic impedance and phase angle, are summarized in table 3.

**Figure 1.** (A) Representative unaveraged pressure (\( Pr \)) and velocity (\( Vel \)) signals from patient 7 in the control state and during isoproterenol (\( ISO \)) infusion. (B) Representative unaveraged pressure and velocity signals from patient 13 in the control state and during nitroprusside (\( NP \)) infusion. \( LV = \) left ventricular; \( Ao = \) aortic.
The administration of isoproterenol, 2.0 µg/min, was associated with a 38% decrease in mean input resistance, a 10% decrease in mean aortic pressure and a 40% increase in heart rate (HR). A sequential infusion of isoproterenol, 1.0 µg/min, induced a 23% decrease in mean input resistance and a 13% increase in HR; 3.0 µg/min induced a 38% decrease in mean input resistance and a 62% increase in HR. In the nine patients with a normal LV ejection fraction, peak aortic blood velocity at 2.0 µg/min increased from 45 ± 11 to 69 ± 22 cm/sec (mean increase 52%). The averaged impedance data during isoproterenol infusion are shown in figure 3. Isoproterenol induced a change in input modulus of borderline significance only at 2 Hz, where it also induced a more positive phase angle. Characteristic impedance did not change significantly. There was no evidence that isoproterenol induced changes in the frequencies at which minima and maxima occurred in impedance moduli; but it seemed qualitatively to damp out oscillations in impedance moduli at higher frequencies (fig. 3). Impedance data obtained during isoproterenol infusion at a new fundamental frequency seemed to “fit in” to the impedance spectra obtained during the control state.

Table 4 summarizes the average power measurements for both isoproterenol and nitroprusside patients. Isoproterenol increased both the steady and oscillatory constituents of total power and slightly increased the ratio of oscillatory power to total power. The increases in both steady and oscillatory power were related to increases in mean and harmonic flow terms.

The infusion of nitroprusside induced a 22% decrease in mean aortic pressure, a 13% increase in HR, and a 38% decrease in input resistance. The fact that both isoproterenol and nitroprusside caused a 38% decrease in input resistance was fortuitous. The averaged impedance data for the nitroprusside patients are presented in figure 4. Low-frequency
moduli were decreased significantly to 2 Hz; and the phase angle was less negative between 1 and 4 Hz. Mean Fourier flow moduli increased significantly ($p < 0.05$) for the mean term (24%) and for the first three harmonics (29%, 22% and 9%, respectively). There was no significant change in characteristic impedance. Individual impedance plots did not indicate a change in the location of impedance modulus minima and maxima related to nitroprusside. But four of the seven patients who received this agent seemed to show a damping out of impedance modulus oscillations, a qualitative observation exemplified in the impedance data of patient 15 in figure 5. The averaged power data for the nitroprusside patients in table 4 are expanded in table 5 to expose the variation of individual responses. The mean pressure modulus and mean in-

![Figure 3](http://circ.ahajournals.org/)

**Figure 3.** Aortic input impedance spectrum from pooled data of 11 patients for control state and during isoproterenol, 2.0 μg/min.

![Figure 4](http://circ.ahajournals.org/)

**Figure 4.** Aortic input impedance spectrum from pooled data of seven patients in the control state and during nitroprusside infusion.
with a significant rise in stroke volume. Steady power increased moderately and there was a large rise in oscillatory power, with an overall increase in power distributed to the aorta.

Patient 16, who also had advanced congestive heart failure, had a decrease in LVEDP and mean input resistance, but no change in stroke volume. Steady power decreased with no change in oscillatory power. There was a net decrease in LV power transmitted to the aorta.

Patient 18, who had a normal left ventricle, had a large increase in stroke volume after modest decreases in mean input resistance and LVEDP. Total power was increased by a change in steady power, but oscillatory power remained constant.

**Discussion**

**Sources of Error**

A principal limitation of this study is the relatively small number of points on the impedance spectrum of each patient, related to obtaining data at only one fundamental frequency. Aortic input impedance has been shown experimentally and clinically to be independent of heart rate. The impedance spectra could have been defined in much greater detail by pacing patients at multiple HRs or by studying patients with atrial fibrillation and a wide range of RR intervals, the latter permitting spectral analysis. This would have reduced the need for linear interpolation between contiguous impedance points. This technique was used to

**Table 2. Clinical and Hemodynamic Data in Nitroprusside Patients**

<table>
<thead>
<tr>
<th>Pt</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Dx</th>
<th>NP dose (µg/min)</th>
<th>LVEF (cm)</th>
<th>AoD (C)</th>
<th>NP HR (beats/min)</th>
<th>C NP</th>
<th>AoBP (mm Hg) C NP</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>52</td>
<td>M</td>
<td>3V CAD</td>
<td>60</td>
<td>0.53</td>
<td>3.8</td>
<td>55</td>
<td>54</td>
<td>157/74</td>
</tr>
<tr>
<td>13</td>
<td>58</td>
<td>M</td>
<td>CAID, CHF</td>
<td>100</td>
<td>0.29</td>
<td>3.7</td>
<td>80</td>
<td>82</td>
<td>121/75</td>
</tr>
<tr>
<td>14</td>
<td>56</td>
<td>M</td>
<td>3V CAD</td>
<td>60</td>
<td>0.53</td>
<td>3.8</td>
<td>47</td>
<td>66</td>
<td>151/73</td>
</tr>
<tr>
<td>15</td>
<td>47</td>
<td>M</td>
<td>Normal</td>
<td>40</td>
<td>0.76</td>
<td>3.3</td>
<td>45</td>
<td>54</td>
<td>140/65</td>
</tr>
<tr>
<td>16</td>
<td>53</td>
<td>M</td>
<td>CAID, CHF</td>
<td>60</td>
<td>0.22</td>
<td>3.8</td>
<td>98</td>
<td>98</td>
<td>116/73</td>
</tr>
<tr>
<td>17</td>
<td>50</td>
<td>M</td>
<td>3V CAD</td>
<td>60</td>
<td>0.68</td>
<td>3.5</td>
<td>75</td>
<td>96</td>
<td>119/76</td>
</tr>
<tr>
<td>18</td>
<td>53</td>
<td>M</td>
<td>2V CAD</td>
<td>40</td>
<td>0.64</td>
<td>3.9</td>
<td>53</td>
<td>76</td>
<td>134/65</td>
</tr>
</tbody>
</table>

Mean 53 60 0.52 3.7 65 74 134/72 102/54 ± 80 ±4 ±20 ±0.20 ±0.21 ±20 ±20 ±16/5 ±13/8

**Abbreviations**: NP = nitroprusside. See Table 1 for other abbreviations.

**Table 3. Effects of Isoproterenol and Nitroprusside on Impedance at Mean Frequencies**

<table>
<thead>
<tr>
<th>Hz</th>
<th>Zc</th>
<th>Zl</th>
<th>p</th>
<th>÷c</th>
<th>÷l</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1441</td>
<td>882</td>
<td>0.003</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>1.98</td>
<td>131</td>
<td>112</td>
<td>0.05</td>
<td>—49</td>
<td>—41</td>
<td>0.04</td>
</tr>
<tr>
<td>3.21</td>
<td>97</td>
<td>91</td>
<td>0.26</td>
<td>—37</td>
<td>—29</td>
<td>0.08</td>
</tr>
<tr>
<td>5.05</td>
<td>87</td>
<td>82</td>
<td>0.39</td>
<td>—18</td>
<td>—14</td>
<td>0.37</td>
</tr>
</tbody>
</table>

**Nitroprusside**

<table>
<thead>
<tr>
<th>Znp</th>
<th>÷np</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1667</td>
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<tr>
<td>1.04</td>
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<tr>
<td>1.85</td>
<td>164</td>
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<tr>
<td>2.92</td>
<td>117</td>
</tr>
<tr>
<td>3.94</td>
<td>62</td>
</tr>
<tr>
<td>5.19</td>
<td>73</td>
</tr>
</tbody>
</table>

**Abbreviations**: Z = mean impedance modulus (dyn·sec·cm⁻¹); Zc and Zl during the control (C) state and during isoproterenol (I) and nitroprusside (NP) infusion; ÷ = mean impedance phase angle (degrees).

put resistance decreased, while the mean and harmonic flow moduli increased with a tendency to small power changes.

In patient 13, who had severe LV dysfunction, a decrease in left ventricular end-diastolic pressure (LVEDP) and mean input resistance was associated with a significant rise in stroke volume. Steady power increased moderately and there was a large rise in oscillatory power, with an overall increase in power distributed to the aorta.

Patient 16, who also had advanced congestive heart failure, had a decrease in LVEDP and mean input resistance, but no change in stroke volume. Steady power decreased with no change in oscillatory power. There was a net decrease in LV power transmitted to the aorta.

Patient 18, who had a normal left ventricle, had a large increase in stroke volume after modest decreases in mean input resistance and LVEDP. Total power was increased by a change in steady power, but oscillatory power remained constant.

**Table 4. Power Measurements**

<table>
<thead>
<tr>
<th>Control1</th>
<th>Isoproterenol</th>
<th>Control2</th>
<th>Nitroprusside</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean AoBP (mm Hg)</td>
<td>97 ± 10</td>
<td>87 ± 9.0</td>
<td>98 ± 4.9</td>
</tr>
<tr>
<td>Oscillatory power (W)</td>
<td>0.18 ± 0.04</td>
<td>0.31 ± 0.17</td>
<td>0.16 ± 0.05</td>
</tr>
<tr>
<td>Total power (W)</td>
<td>1.27 ± 0.27</td>
<td>1.79 ± 0.51</td>
<td>1.21 ± 0.19</td>
</tr>
<tr>
<td>OP/TP</td>
<td>0.14</td>
<td>0.17</td>
<td>0.14</td>
</tr>
</tbody>
</table>

**Abbreviations**: OP/TP = ratio of oscillatory power to total power; AoBP = aortic pressure; I = isoproterenol; NP = nitroprusside.
obtain values in impedance modulus and phase angle at the same frequency for averaging and evaluating drug effects. However, the duration of the combined clinical and experimental study and the increased HR induced by isoproterenol did not permit more extended acquisition of impedance data.

A limited definition of the impedance spectrum is particularly disadvantageous in the lower frequency range (&lt; 4 Hz), where a major proportion of oscillatory energy is delivered to the vascular circuit and where there are several points of inflection in the modulus curve. This is exemplified in figure 3, where the interpolated impedance spectrum during isoproterenol gives a misleadingly high impedance modulus at the control fundamental frequency. Impedance data based upon a single fundamental frequency may be used to estimate steady and oscillatory energy distribution and the effects of interventions that effect a limited change in HR; but accurate estimation of all maxima and minima and application of the impedance spectrum over a range of HRs require more complete data.

Examination of the variation in individual impedance spectra and some of the relatively large standard deviations in the pooled impedance presentations raises doubt about the validity of averaging this complex physiologic measurement. However heterogeneous the patients were for defining average control values, directional changes in impedance in response to the two pharmacologic agents were uniform and justify a paired statistical analysis.

Any decrease in proximal aortic diameter induced by a decrease in aortic pressure with drug infusion was not determined. The control aortic dimensions were used with drug-induced changes in aortic velocity, so that derived flow measurements may be falsely elevated. The data of Greenfield and Patel may be used to estimate pressure-related changes in aortic dimensions. Their aortic compliance data were determined from the external ascending aorta in man above the pericardial reflection, and seem applicable to this study with respect to the estimated location of the velocity electrodes. With a correction for aortic wall thickness, a decrease in mean aortic pressure of 21 mm Hg with nitroprusside may have been associated with a 1-mm decrease in effective aortic diameter and a 5.8% decrease in cross-sectional area.

Control Data

The average input resistance during the control state (1490 dyn-sec-cm⁻²) is slightly higher than that in
the patients studied by Nichols et al.\textsuperscript{23} but the difference is probably not significant. Mean venous pressure was not subtracted from the mean arterial pressure term in deriving mean input resistance, so its value is approximately 5–10% higher than comparable mean resistance determinations in clinical studies.

The finding of two apparent sets of minimal and maximal impedance moduli in most patients is consistent with the asymmetric T hypothesis\textsuperscript{6, 10} to explain intravascular reflections. The short arm of the T represents a single, net terminal reflection from the arterioles of the head and arms; the long arm of the T is the net reflecting effect from the abdomen and legs. Significant variation among the patients in the location of impedance modulus maxima and minima would be expected from differences in pulse wave velocity and bodily dimensions. This consideration, associated with the limited data in each patient, precludes a more quantitative analysis of these impedance oscillations.

The average value of characteristic impedance in our patients (88 ± 35 dyn-sec-cm\textsuperscript{-4}) is in agreement with the derivation\textsuperscript{23} from the data of Patel et al.\textsuperscript{29} in three patients (82 dyn-sec-cm\textsuperscript{-4}), but somewhat lower than the pooled average value for the data of Nichols et al.\textsuperscript{23} in 16 patients (105 ± 63 dyn-sec-cm\textsuperscript{-4}). Our value agrees with the latter’s average for a subset of patients with normal mean aortic pressure and coronary disease (95 ± 12 dyn-sec-cm\textsuperscript{-4}) and with the average (89 ± 24 dyn-sec-cm\textsuperscript{-4}) for 10 patients not in heart failure reported by Pepine et al.\textsuperscript{30} The limited number of patients in this study and their relative homogeneity with respect to age and mean aortic pressure may explain the absence of correlations between characteristic impedance and age, mean aortic pressure or coronary artery disease score. The latter correlations seem evident in the data of Nichols et al.\textsuperscript{23} Our patients were comparable to theirs in age, although their normal patients were younger than the four normal patients in this study. Their study population included a subset with a mean aortic pressure somewhat higher than that of the patients reported here, so that any association between characteristic impedance and control mean aortic pressure would be more evident from their data. Our study included only three patients with advanced LV dysfunction, and although none had an elevated characteristic impedance, their number is too small to assess the correlation between this variable and congestive heart failure.\textsuperscript{30} This study shares with the three major clinical aortic impedance studies to date\textsuperscript{23, 23, 30} a limited data range (2–9 Hz, approximately six points per patient) from which to derive characteristic impedance. Characteristic impedance is more closely approximated by impedance moduli at frequencies greater than the noise threshold (9–10 Hz) in these studies.

The control measurements of the phase angle seem comparable to those of Nichols et al.\textsuperscript{23} when the latter are converted from radians to degrees. Pooling their estimated range of phase angle data seems to produce comparable variability, especially at higher frequencies, where accurate determination of phase angle is difficult.

### Isoproterenol and Nitroprusside Effects

The hemodynamic effects of isoproterenol have been well characterized.\textsuperscript{31, 32} In our study, full vasodilation occurred at lower doses of isoproterenol than either peak heart rate or maximal aortic blood velocity. This suggests a difference in specificity or availability of isoproterenol for the $\beta_1$ vascular receptors and the $\beta_1$ receptors of the heart.

The three patients with normal left ventricles who received nitroprusside had a 13% increase in peak aortic blood velocity; the nine patients with normal left ventricles who received isoproterenol increased peak velocity by 52%. Nitroprusside has not been found to have a significant inotropic effect on the left ventricle.\textsuperscript{15, 30} These observations reconfirm that vasodilation per se may modify ejection phase indexes of LV performance (e.g., peak aortic blood velocity). Variables derived from LV ejection will not permit unambiguous separation of changes in LV performance related to vasodilation from those induced by an inotropic effect. This is significant where a drug that possesses both properties (e.g., isoproterenol, salbutamol and pirbuterol) is administered.

Limited experimental and clinical data are available describing aortic input impedance changes with vasoactive drugs. O’Rourke and Taylor\textsuperscript{10} assessed aortic

### Table 5. Power Measurements for Nitroprusside Patients

<table>
<thead>
<tr>
<th>Pt</th>
<th>Pressure (mm Hg)</th>
<th>Flow (ml/sec)</th>
<th>Steady power (W)</th>
<th>Oscillatory power (W)</th>
<th>Total power (W)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>C</td>
<td>NP</td>
<td>C</td>
<td>NP</td>
<td>C</td>
</tr>
<tr>
<td>12</td>
<td>106</td>
<td>88</td>
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<tr>
<td>13*</td>
<td>95</td>
<td>67</td>
<td>69</td>
<td>105</td>
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<td>89</td>
<td>129</td>
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</table>

*Severe congestive heart failure.

Abbreviations: C = control; NP = nitroprusside.
impedance changes with pharmacologic agents, including norepinephrine and isoproterenol, in dogs. Relating impedance changes to alterations in pulse wave velocity induced by changes in blood pressure, they concluded that an increase in aortic pressure displaces the modulus curve to the right; decrease in aortic pressure moves it to the left. Their example of an impedance spectrum obtained during norepinephrine infusion suggests that a rise in aortic pressure may displace the phase curve in a negative direction. No consistent pattern of change in characteristic impedance was noted with changes in aortic pressure. Gersh et al., using phenylephrine and trimetaphan in dogs, found expected changes in mean input resistance but no changes in impedance moduli with phenylephrine. During trimetaphan infusion an increase in impedance moduli was noted between 4 and 16 Hz and characteristic impedance increased. Adams et al. assessed the effect of nitroprusside in a canine preparation with variable anesthesia and observed a decrease in mean input resistance and an increase in characteristic impedance and oscillatory energy requirements during nitroprusside.

The limited clinical study of three patients from Gabe et al. included evaluation of aortic impedance during norepinephrine infusion. With an increase in aortic pressure from 91 to 126 mm Hg, mean input resistance increased, characteristic impedance increased at low frequencies but decreased from 6 and 8 Hz, and phase angle seemed slightly more negative at low frequencies. Pepine et al. studied 12 patients with congestive heart failure to examine the effects of nitroprusside infusion on aortic input impedance. Their range of nitroprusside dosing and sequential data acquisition differed from ours, but many conclusions were similar. They also found reduced impedance moduli and less negative phase angles in the lower frequency harmonics during nitroprusside infusion. They quantitated a reduction in impedance oscillations, a qualitative finding in this study. In contradistinction to their results, we did not confirm a statistically significant change in characteristic impedance with nitroprusside. This may be partially related to the presence of heart failure and greater homogeneity of their patient population.

In this study, neither isoproterenol nor nitroprusside induced a significant change in mean characteristic impedance, although variation in small directional changes occurred. Characteristic impedance is inversely proportional to the cross-sectional aortic area at the recording site and directly proportional to the pulse wave velocity. Pulse wave velocity is directly proportional to \( \sqrt{E} \), where \( E \) is the effective dynamic elastic modulus of the aortic wall, which is in turn a function of mean aortic pressure. Examination of the static determinations of \( E \) for canine aortic preparations at variable mean pressures suggests the likelihood that over the range of pressure changes in this study, only moderate changes would be noted in \( \sqrt{E} \). With parallel changes in aortic area, characteristic impedance would not be predicted to change significantly.

This study provides a comparison of the effects of isoproterenol and nitroprusside on aortic impedance in two sets of patients. Both drugs effected an identical change in mean resistance and a qualitative diminution in impedance oscillations related to this effect on vascular reflections, but nitroprusside had a more significant effect upon impedance moduli and phase angles. We do not believe that the direct cardiac effects of isoproterenol account for the differences. The inotropic state of the left ventricle should not influence its vascular load, and the impedance spectrum has been shown to be independent of heart rate. However, the cardiac effects of isoproterenol, through an increase in heart rate and slight increase in stroke volume, did mediate a support of aortic pressure not available with nitroprusside. Mean aortic pressure decreased 10% with isoproterenol and 22% with nitroprusside. This difference in mean aortic pressure with its effect on pulse wave velocity is the most plausible basis for the different effects in the impedance spectra. The change in pressure-flow phase relations associated with nitroprusside infusion indicates changes in pulse wave propagation. It seems less tenable that a difference in pharmacologic site of action in regional arteriolar networks or smooth muscle in capacitance arteries would explain the impedance differences with the two drugs. In three of the 12 patients reported by Pepine et al., phenylephrine was simultaneously infused with nitroprusside to restore a decrease in aortic pressure. Their data suggest a nitroprusside-induced change in the impedance spectrum and an improvement in LV performance that persist after the restoration of aortic pressure. Mean and harmonic flow moduli are not available to determine if residual LV improvement is specifically related to pulsatile flow. The published impedance spectrum under these circumstances seems to approximate control at frequencies less than 6 Hz. Their suggestion that it might be possible to alter the pulsatile (capacitive) load while preserving mean aortic pressure, perhaps by selectively relaxing the smooth muscle of capacitance arteries, might explain some of the differences between isoproterenol and nitroprusside. Where vascular wall stress is supported by active smooth muscle tone, as opposed to collagen fibers, its reduction might be expected to facilitate pulsatile flow.

Implications in Congestive Heart Failure

The usual response to vasodilator therapy in congestive heart failure includes a decrease in mean input resistance and LV end-diastolic volume, an increase in stroke volume, and relatively small changes in heart rate or mean aortic pressure. Lowered mean LV filling pressure and increased cardiac output, especially if sustained during exercise, are of unequivocal benefit to patients. In the setting of limited myocardial oxygen availability in coronary artery disease, the reduction of LV systolic wall tension may reduce myocardial oxygen requirements. Many of these advantages have been related to pharmacologic alteration of the arterial system. Changes in mean arteriolar resistance and in the impedance spectrum are of particular clinical value in congestive heart
failure when they are associated with an increase in mean and harmonic flow moduli and a limited increase in LV energy requirements. During vasodilatation changes in mean resistance may parallel changes in characteristic impedance or impedance moduli.\(^{14}\) Flow moduli are needed to indicate selective changes in mean or pulsatile flow and total LV energy distributed to the vascular circuit. For example, during nitroprusside infusion in this study, the mean and first three harmonic flow moduli increased significantly with relatively constant LV energy requirements. Where vasodilator therapy is not associated with a decrease in aortic pressure, we would expect no significant change in the impedance spectrum and flow increases related chiefly to changes in the mean term.

Changes in steady and oscillatory power requirements for the left ventricle in association with vasodilatation were variable. Total power consumption in the arterial circuit remained relatively constant during nitroprusside administration. The mean pressure modulus, as a determinant of steady power, decreased in all patients with nitroprusside, so that a change in steady power was determined by the degree to which the mean flow modulus increased. Oscillatory power is related to the sum of the harmonic terms: \((\Omega_n)^2 Z_n \cos \phi_n\). The value of in-phase impedance, \(Z_n \cos \phi_n\), is buffered, and any decline in a given harmonic modulus \((Z_n)\) is offset by a parallel increase in the value of \(\cos \phi_n\). Oscillatory power will thus be determined principally by the squares of the harmonic flow moduli \((\Omega_n)^2\).

In conclusion, the comparative effects of isoproterenol and nitroprusside on proximal aortic impedance indicate that significant alterations in the impedance spectrum are related to changes in mean aortic pressure. The technically demanding characterization of the aortic impedance spectrum is of limited clinical value and appropriate principally for physiologic studies. The continued determination of mean input resistance remains a convenient and practical derived variable in the evaluation of vasodilator therapy.

**Acknowledgment**

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