Special Article

Hemodynamic Resistance as a Measure of Functional Impairment in Aortic Valvular Stenosis

Lincoln E. Ford, Ted Feldman, Y. Christopher Chiu, and John D. Carroll

Calculated valve area depicts anatomical stenosis but does not quantify hemodynamic impairment. We propose that hemodynamic resistance, defined as the mean pressure gradient across the valve divided by mean flow rate during systolic ejection, gives a better indication of hemodynamic obstruction. This index was compared with Gorlin valve area in 40 patients with aortic stenosis. Calculated area ranged from 0.22 to 1.26 cm², and mean transvalvular resistance ranged from 117 to 1,244 dyne · sec · cm⁻³. In general, resistance varied inversely with calculated area, but there was substantial variation about the mean relation. All of the variation could be accounted for by variations in the pressure gradients at each value of calculated area. Resistance was higher in proportion to area when flow and pressure gradient were high. Analysis of five published studies of a total of 83 valves showed that calculated area changed at least three times more than resistance when pressure gradient was varied. The utility of resistance as an index of stenosis is demonstrated by example calculations that show how during exercise a stenotic valve increases the ventricular work rate out of proportion to the work done on the peripheral resistance. These calculations are possible because hemodynamic resistance defines functional impairment in units commonly used for quantification of opposition to flow. Furthermore, resistance appears to be less dependent than area on conditions of measurement and does not require an empirical constant. (Circulation Research 1990;66:1-7)

Shortly before the Gorlins¹ developed their formula for valve area, several other authors suggested that hemodynamic resistance be used as a "stenotic index."²,³ This index was rejected by the Gorlins¹ and by others⁴ on the theoretical grounds that it was unlikely to remain constant at different flow rates. The Gorlin formula is based on the Torricelli model of nonturbulent fluid flow through a planar orifice. In this model, flow (F) is proportional to the square root of the pressure gradient (ΔP) across the orifice (F=√ΔP). The resistance index proposed by others was presumed to be simply the flow divided by the pressure gradient (R=F/ΔP). If this index were to remain constant, flow would have to be proportional to the first power of the pressure gradient (F=ΔP). The Torricelli and resistance models could not both be correct because the relation between flow and pressure gradient is different in the two models. The early workers argued that the Torricelli model was more appropriate because pulmonary capillary pressure rose out of proportion to flow during exercise in patients with mitral stenosis.¹,⁴ They made the reasonable argument that the pressure gradient across the valve was probably increased more than flow, even though they did not measure the mitral valve pressure gradient, or even the atrial pressure. This conclusion suggested that the resistance model was invalid in mitral stenosis and that, by default, the Torricelli model gave a more reliable indication of stenosis. At the time, anatomic valve area seemed to be the most desirable index of stenosis. This index, expressed in the familiar dimensions of square centimeters, conveys a picture of the stenotic valve that has been used as a clinical guide for nearly four decades.

Although calculated area is expressed in familiar anatomic terms, these terms are ill suited for dynamic calculations. As hemodynamics are becoming more widely understood, the dimensions of resistance are becoming better known. A major advantage of resistance as a stenotic index is that it does not require any assumptions, as do the calculations of valve area. The Gorlin formula requires an empirical constant to account for blood viscosity, density, turbulence, and

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³ Received April 18, 1989; accepted July 21, 1989.
the ratio of the valve area to the vena contracta, the area of the narrowest part of the stream that passes through the orifice.\textsuperscript{1} Evidence suggests that this value does not remain constant at different flow rates.\textsuperscript{5-9} Clearly, if the "constant" is variable, the areas calculated according to the Gorlin formula may not be regarded as reliable anatomic measures, even though the numbers derived could be useful indexes of hemodynamic impairment.

To compare resistance with calculated area, we examined both indexes in a group of 40 patients with aortic stenosis. We also compared changes in these indexes under different conditions of pressure and flow in a total of 82 patients with aortic or mitral stenosis and in one in vitro valve, taken from studies in the literature.

\textbf{Patients and Methods}

Hemodynamic measurements were made in 40 patients with aortic stenosis. Simultaneous left ventricular and aortic pressures were recorded during a 3-minute period used for determination of cardiac output by the Fick principle. Pressures were recorded with a double-transducer, high-fidelity micromanometer-tip catheter (Millar Instruments, Houston, Texas) in 15 patients, a left ventricular fluid-filled catheter and femoral arterial sheath in 22 patients, and a left ventricular and central aortic fluid-filled catheter in three patients. Valve area was calculated according to the Gorlin formula,\textsuperscript{1} using the constant 44.3 (=1×√2gh) as described by Carabello and Grossman.\textsuperscript{10} Valve resistance (R) was calculated as

\[ R = \frac{\Delta P}{F} \]  

where \( \Delta P \) is the mean systolic pressure gradient in dynes per square centimeter and \( F \) is the mean systolic flow determined as cardiac output divided by the fraction of the cardiac cycle spent in systole (FET). If \( \Delta P \) is expressed in dynes per square centimeter and \( F \) in cubic centimeters per second, then \( R \) will be given in dyne · sec · cm\(^{-5} \). If \( \Delta P \) is expressed in millimeters of mercury and \( F \) in liters per minute, then the ratio must be multiplied by 80 to obtain the same dimensions.

\textbf{Results}

\textbf{Patient Studies}

Valve resistance is plotted against calculated valve area in Figure 1. There is an inverse relation between resistance and area, with substantial variation around the mean relation. For each value of calculated area, there is a 20–50% variation in resistance. The patients with higher pressure gradients had higher resistances for a given calculated area than patients with the same calculated areas and lower pressure gradients (Table 1). This finding is expected because resistance and area are calculated from the same data and the exact relation between the two parameters would predict it.

\begin{figure}
\centering
\includegraphics[width=0.8\textwidth]{figure1.png}
\caption{Hemodynamic resistance versus calculated area in 40 patients with aortic stenosis. Mean valve resistance is 421±254 dyne · sec · cm\(^{-5} \). Mean calculated valve area is 0.62±0.26 cm\(^2 \).}
\end{figure}

The relation between pressure and area is calculated as follows: The formula for area (\( A = F/\sqrt[k]{\Delta P} \)) is combined with the formula for resistance (\( R = \Delta P/F \)) to give

\[ R = \frac{\Delta P}{k \times A} \]  

where \( k \) is the empirical constant for the Gorlin formula, taken as 44.3.\textsuperscript{10} This equation shows that resistance is inversely proportional to area and directly proportional to the square root of pressure gradient. Therefore, all of the variation in the relation between resistance and calculated area can be accounted for by variations in pressure gradient.

The variation in the relation shown in Figure 1 could be due to variations in calculated area, variations in resistance, or some combination of the two. This variation in one or the other index would be due to the incorrect assumption of the relation between pressure gradient and flow. For examination of this relation, it is necessary to vary flow under conditions where valve area does not change. We have examined published data for this purpose.

\textbf{Effect of Changing Hemodynamics on Indexes of Stenosis (Literature Survey)}

Five studies in which there were sufficient data for calculation of both area and resistance at two flow rates are summarized in Table 2. In all cases, the changes in flow were slightly greater than the changes in pressure gradient so that calculated valve area increased and resistance decreased. In addition, the changes in calculated area are at least three times larger than the changes in resistance when flow is varied. This is explained by flow being more nearly proportional to the first power of the pressure gradient than to the square root of the pressure gradient.

Two of these studies deserve special comment. The results of Cannon et al\textsuperscript{15} in Table 2 were from an extensive study of a single in vitro synthetic valve whose area could be set with a nondistensible snare. This study is especially important because flow
could be varied over a very wide range and because physical valve area was held constant. In spite of the constant physical area, the area calculated according to the Gorlin formula was found to change with flow. These changes in calculated area could not be attributed to dilation of the stenotic valves with an actual increase in physical area, as has been suggested as a possible mechanism to account for differences in calculated areas at different pressure gradients in native aortic valves.4,6,7 Cannon et al5 used these data to derive a new function to describe the variation of the empirical constant, k, in the Gorlin formula. They found that k was proportional to the square root of the pressure gradient. When the new relation was substituted in the Gorlin formula, calculated area was very nearly proportional to flow divided by the first power of pressure gradient, suggesting that flow is proportional to the first power of the pressure gradient. In 19 patients with porcine valves of known sizes, this new formula predicted valve area very much better than the Gorlin formula.

<table>
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<tr>
<th>Patient number</th>
<th>Mean gradient (mm Hg)</th>
<th>Systolic flow (cc/sec)</th>
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<th>Valve area (cm²)</th>
<th>Valve resistance (dyne · sec · cm⁻⁵)</th>
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</table>

Mean±SD 50±20 182±60 0.409±0.046 0.62±0.26 421±257
The study by Ubago et al was also done on porcine prosthetic valves and was undertaken because the valve sizes were known almost exactly. In this case, flows were not varied but hemodynamic data were collected for three different periods in diastole: early, middle, and late. Pressure gradients and flow varied considerably among the three periods, as did calculated valve areas. Resistance varied by less than one third as much as calculated area when the highest flow (early diastolic) period was compared with the lowest flow (late diastolic) period.

The remaining studies were performed on diseased, native valves in situ, where changes in flow were not as great as in the first two studies. These studies differ mainly in the intervention used to alter flow. The conclusions are nearly identical; calculated area varies at least three times as much as resistance when flow is altered.

Discussion

It would be difficult to overstate the importance of the Gorlin formula to cardiology. Valve area calculation by the Gorlin formula has been in wide use throughout much of the history of clinical cardiac catheterization. There are probably two reasons for this popularity: 1) The calculation is simple, and 2) it gives a picture of the valve in familiar anatomic units. Even though the calculated areas may not be exact in anatomic terms, they can be taken as numerical representations of stenosis that are easily compared among different patients with stenosis. The term “area” is easily understood, even when it is not exact.

Area Versus Resistance

No theoretical model is likely to give a good prediction of flow through a stenotic valve because the flow is turbulent and the viscous properties of blood are highly nonlinear. It seems reasonable to expect that the turbulence caused by stenosis will increase resistance as flow increases. Therefore, it is surprising that the pressure gradient across the valve is most closely proportional to the first power rather than some higher power of flow rate. A possible explanation suggested by several investigators is that the valve area increases with higher flow rates.\(^4,6,7,11-13\) There is conflicting evidence about the extent to which area changes with flow. Two aspects of the study of Cannon et al\(^5\) suggest that it does not change much: 1) Pressure gradient varied with the first power of flow rate in a synthetic valve with a rigidly fixed area, and 2) video analysis of a single diseased valve in vitro showed very little change in area over a 2.5-fold range of flow rates (Figure 3 of Reference 5).

The conclusions of the study are that in this case, the Gorlin formula is a reasonable approximation of pressure gradient. However, it is not an exact calculation, and it is not a substitute for a direct pressure measurement. It is a useful simplification, but it is not a precise predictor of pressure gradient. Therefore, it is important to understand the limitations of the Gorlin formula and to use it with caution. When it is used, it should be validated by direct pressure measurements when possible.

Discussion

It would be difficult to overstate the importance of the Gorlin formula to cardiology. Valve area calculation by the Gorlin formula has been in wide use throughout much of the history of clinical cardiac catheterization. There are probably two reasons for this popularity: 1) The calculation is simple, and 2) it gives a picture of the valve in familiar anatomic units. Even though the calculated areas may not be exact in anatomic terms, they can be taken as numerical representations of stenosis that are easily compared among different patients with stenosis. The term “area” is easily understood, even when it is not exact.

Table 2. Change in Calculated Valve Area and Resistance With Changes in Flow

<table>
<thead>
<tr>
<th>Reference</th>
<th>Number of valves</th>
<th>Kind of intervention</th>
<th>Change (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cannon et al(^*)</td>
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<td>Controlled flow</td>
<td>Systolic flow: 76, Pressure gradient: 69, Valve area: 35, Valve resistance: -4</td>
</tr>
<tr>
<td>Ubago et al(^6)</td>
<td>40</td>
<td>Early versus late diastole</td>
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<tr>
<td>Bache et al(^7)</td>
<td>20</td>
<td>Exercise</td>
<td>30, 25, 16, -4</td>
</tr>
<tr>
<td>Casale et al(^8)†</td>
<td>10</td>
<td>Dobutamine</td>
<td>36, 27, 21, -7</td>
</tr>
<tr>
<td>McCraskin et al(^9)†</td>
<td>12</td>
<td>Isoproterenol</td>
<td>48, 38, 27, -7</td>
</tr>
</tbody>
</table>

\(^*\)Study is of a single valve in vitro whose area was set with a nondistensible snare to 1.75 cm².

†These data are from tables in abstracts. Resistances could not be calculated separately for each patient, but ratio of mean value was calculated from mean values of pressure gradient and area.

Area Versus Resistance

No theoretical model is likely to give a good prediction of flow through a stenotic valve because the flow is turbulent and the viscous properties of blood are highly nonlinear. It seems reasonable to expect that the turbulence caused by stenosis will increase resistance as flow increases. Therefore, it is surprising that the pressure gradient across the valve is most closely proportional to the first power rather than some higher power of flow rate. A possible explanation suggested by several investigators is that the valve area increases with higher flow rates.\(^4,6,7,11-13\) There is conflicting evidence about the extent to which area changes with flow. Two aspects of the study of Cannon et al\(^5\) suggest that it does not change much: 1) Pressure gradient varied with the first power of flow rate in a synthetic valve with a rigidly fixed area, and 2) video analysis of a single diseased valve in vitro showed very little change in area over a 2.5-fold range of flow rates (Figure 3 of Reference 5).

On the other hand, additional evidence both from the same laboratory\(^11,12\) and from others\(^13\) indicates that some valves do increase in area with higher flow rates. Another possible explanation for the linear relation between pressure and flow is that the viscosity of blood decreases during turbulence. The main point to be made from these observations is that it is difficult to predict the hemodynamics of a diseased valve on purely theoretical grounds. The effects of an obstructed orifice are sufficiently complex that the choice of an index of stenosis will depend largely on empirical findings and the utility of the index. The results reviewed here suggest that the Gorlin's original reason for discounting resistance as a stenotic index was incorrect. They asserted that resistance was less likely than calculated area to remain constant at different flow rates. The results show that the opposite is true: resistance is more constant than calculated area. In this sense, resistance may be a more useful index because it is less subject to variations associated with differences in the conditions of measurement.

The decision to use one or the other index will depend on the way the measurement is used. As a simple descriptive term, area has the advantage of simplicity and familiarity. Resistance has a considerable advantage when used in conjunction with other measurements. It is defined in dimensions that can be used directly in hemodynamic calculations in much the same way that electrical resistance is used in electronic calculations. The following calculations of the relative loads imposed on the ventricle by valvular and peripheral resistance are presented for illustration of how valvular resistance can be used in quantitative calculations.

Work Required to Perfuse Valvular and Peripheral Resistances

Hemodynamic resistance is defined in the same manner as electrical resistance is defined by Ohm's law: voltage (pressure) gradient=current (blood)
flow \times \text{resistance}. In both electrical and hemodynamic circuits, it is frequently useful to calculate the power loss (work rate, \( W = \text{flow} \times \text{gradient} \)) across a resistance where the voltage or pressure gradient is not known. This is done by substituting Ohm's law equation for gradient into the equation for power loss to yield

\[
W = F^2 \times R
\]

(3)

The work rate \( W \) (defined as dynes \times \text{centimeters/second}) includes all the energy dissipated in forcing blood across the stenotic valve, including the energy of creating turbulence and of producing the extra acceleration required to move blood through the smaller orifice. Strictly speaking, Equation 3 defines the instantaneous work rate, but it can also be used for estimation of the average work rate where the work is performed continuously, as in perfusion of the periphery. Thus, cardiac output (CO) can be substituted for flow (F) in Equation 3 for calculation of the average work rate required to perfuse the periphery (\( W_p \)) as

\[
W_p = (CO^2 \times R_p)
\]

(4)

During intermittent flow, as occurs across the valve, the mean systolic flow rate varies inversely with the fraction of the cardiac cycle spent in systole (\( F = CO/FET \)), but since blood is only ejected during systole, the work rate averaged over the entire cardiac cycle varies directly with the systolic ejection period (\( W_e = W \times FET \)), so that

\[
W_e = \frac{(CO^2 \times R)}{FET}
\]

(5)

The average valve resistance in the patients studied here (about 400 dyn \cdot \text{sec} \cdot \text{cm}^{-5}) was about one third the normal peripheral resistance in resting humans (about 1,200 dyn \cdot \text{sec} \cdot \text{cm}^{-5}). While these valve resistances do not seem large, the average work load imposed by them is approximately equal to the average work rate required for perfusion of the periphery. The approximate equality is achieved because systolic ejection occurs during one third of the cardiac cycle. This causes the mean flow rate across the valve during systole to be about three times higher than the mean flow rate in the periphery, such that the mean pressure gradient across the valve is approximately equal to the mean pressure gradient across the periphery. Thus, both the average flow rate and the average pressure gradient during flow are the same.

Comparison of Valvular and Peripheral Resistances

It is useful to compare the work done on a stenotic valve with the work required for perfusion of the periphery. This comparison can be made easily when valvular resistance is related directly to the peripheral resistance. Since peripheral resistance can vary substantially, especially during exercise, it is necessary to specify the state in which the peripheral resistance is measured. The reference value to be used here is the peripheral resistance expected at rest (\( R_{p, rest} \)). The relative valvular resistance will be defined by the dimensionless ratio (\( r \)) of the effectiveness of the two resistances in absorbing hemodynamic work. This ratio is obtained by division of Equation 4 into Equation 5 as

\[
r = \frac{W_e}{W_p} = \frac{R_p}{(R_{p, rest} \times FET)}
\]

(6)

This ratio has the value 1 when the work rate across the valve equals the peripheral work rate at rest (i.e., when valvular resistance is about one third of peripheral resistance), and it varies in direct proportion to valvular resistance. It will equal the inverse of the FET when the valvular resistance equals the resting peripheral resistance. The most severely stenotic valve studied here (patient 22, Table 1, with a calculated area of 0.22 cm²) had a valve resistance of 1,244 dyn \cdot \text{sec} \cdot \text{cm}^{-5}, approximately the value expected for the peripheral resistance at rest. If the patient’s FET had been normal at 0.33, the value of \( r \) would have been 3; however, the patient had a prolonged FET of 0.467, such that the value of \( r \) was about 2.14. This observation emphasizes the important point that the value of \( r \) will not be absolutely constant in the same patient but will vary with the inverse of the fractional ejection time.

Effects of Exercise

During exercise the work load imposed by the valve resistance increases much more than the work load imposed by the periphery because peripheral resistance decreases while valve resistance remains constant. If blood pressure remains constant, peripheral resistance must fall in proportion to the increased cardiac output. The stroke work required for perfusion of the periphery will then vary in proportion to the first power of cardiac output. The value of \( R_p \) then becomes

\[
R_p = R_{p, rest} \times \frac{CO_{rest}}{CO}
\]

(7)

The expression for peripheral work rate (Equation 4) becomes

\[
W_p = R_{p, rest} \times CO_{rest} \times CO
\]

(8)

Since valve resistance changes very little with exercise, the stroke work required for perfusion of the valve varies with the square of cardiac output, as described by Equation 5, while that imposed by the periphery varies with the first power of cardiac output, as described by Equation 8. This disproportionate increase in the work load imposed by the stenotic valve can severely limit circulatory reserve, as shown in Figure 2.

Changes in Ventricular Work During Exercise

Figure 2 shows how the total work rate varies with changes in cardiac output. For elimination of the individual variation among patients that will be caused by differences in body size, the total work rate is normalized to different values of peripheral work rate. For the same reason, cardiac output is plotted relative to the value at rest, as defined by the ratio
of a hypertrophied ventricle. Because hypertrophy can compensate partially for the increased load, a better indication of the limitation imposed by the stenotic valve is shown in Figure 2B, which plots the total work rate normalized to the total work rate at rest. These plots show the relative increase in work rate required as cardiac output increases and illustrate how the ability of the ventricle to meet the demands of the circulation depends on the degree of ventricular hypertrophy and compensation.

A normal ventricle can increase its cardiac output and work rate about twofold to threefold, depending on the age and athletic conditioning of the individual. Figure 2B shows that an individual with a valvular resistance that doubles the work of the ventricle at rest (i.e., r = 1, equivalent to the average patient studied here) will require a threefold to sixfold increase in work rate for production of the same increase in cardiac output. Conversely, a twofold to threefold increase in ventricular work rate will increase cardiac output only 1.5-fold to twofold. These twofold and threefold limits are indicated by the dashed and dotted lines, respectively, in Figure 2. As shown, a fully compensated ventricle able to produce a threefold increase in cardiac work will only be able to double cardiac output, whereas the same degree of reserve will triple cardiac output in the absence of a stenotic valve. Unfortunately, the nature of the work load imposed by the stenotic ventricle makes it unlikely that a ventricle hypertrophied to match a stenotic valve will have the same reserve as a normal ventricle. The higher ventricular pressure with concomitantly higher wall stresses makes it unlikely that the speed of ventricular contraction could be increased sufficiently to raise cardiac work to the same extent as occurs in the normal heart.

The calculations presented here are intended mainly to illustrate the usefulness of hemodynamic resistance as an index of valvular stenosis. Such calculations are a natural outcome when stenosis is expressed in terms of resistance and are not possible when stenosis is defined in terms of area. Another advantage of resistance is that it appears, on empirical grounds, to remain more constant than area. Finally, measurements of resistance do not require an empirical constant, as do calculations of area.

**Appendix**

**Calculation of Ventricular Work**

Total ventricular work rate \( W_t \) can be defined by summing the work terms in Equations 4 and 5 as

\[
W_t = W_v + W_r = [R_p \cdot CO_{rest} \cdot CO] + [(R \cdot CO) / \text{FET}] = [R_p \cdot CO] [CO_{rest} + (r \times CO)]
\]

**Normalization of Work Rate**

The absolute units of cardiac work can be eliminated by normalization of the work rate to a reference value and substitution of dimensionless ratios (Equations 7 and 10) for resistance and cardiac output.
For estimation of the absolute increase in work rate, the total work rate can be normalized to the work rate required for perfusion of the periphery at rest. This is done by dividing the total work rate (Equation 10) by the rate of work done in the periphery at rest (Equation 4) as 

$$ W/W_{p,\text{rest}} = \frac{[R_{p,\text{rest}} \times CO][CO_{\text{rest}} + (r \times CO)]}{[R_{p,\text{rest}} \times CO_{\text{rest}}^2 + (r \times CO_{\text{rest}}^2)]/(1+r)} $$

(11)

This ratio, which estimates the total increase in work rate, is plotted in Figure 2A.

The relation expressed by Equation 11 and shown in Figure 2A does not adequately represent the restriction imposed by a stenotic valve because it does not account for the compensatory hypertrophy that occurs with prolonged stenosis. This is better shown by relation of total ventricular work rate to the total work rate at rest, as

$$ W/W_{\text{rest}} = \frac{[R_{p,\text{rest}} \times CO][CO_{\text{rest}} + (r \times CO)]}{[R_{p,\text{rest}} \times CO_{\text{rest}}^2 + (r \times CO_{\text{rest}}^2)]/(1+r)} $$

(12)

The graphs of this function are shown in Figure 2B.

References


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