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Quantitative Coronary Arteriography and Its Assessment of Atherosclerosis

Part II. Calculating Stenosis Flow Reserve from Percent Diameter Stenosis

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ABSTRACT

Background. Assessment of coronary artery disease by quantitative coronary arteriography (QCA), while highly accurate, is more expensive than visual estimates of disease and involves the measurement of numerous variables requiring specialized equipment and personnel, thereby reducing its clinical applicability. In part 1 of this paper, the independent variables that influence flow of 1040 coronary artery segments were analyzed.

Methods and Results. Using the information previously reported in part 1 of this paper, we set out to determine the importance of each of the independent variables (percent diameter and area stenosis, length, absolute diameter, entry and exit angles) in the prediction of stenosis flow reserve (SFR). Analysis of variance (ANOVA) was used to determine the importance of each of these variables, as well as their interactions, on the determination of SFR. Only percent diameter stenosis (%DS) demonstrated statistical significance ($P < 0.001$) in determining stenosis flow reserve. When the results of SFR were plotted against %DS, a quadratic relationship was demonstrated with an R^2 value of 0.903 ($r = 0.95$). To verify the quadratic equation, the %DS of 100 different arterial stenoses was measured and used to calculate an SFR by the quadratic formula. The QCA and quadratic (calculated) determined SFRs compared favorably, with a correlation of 0.97.

(continued on next page)

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(Abstract continued)

Conclusions. The ability to calculate SFR directly from measured %DS allows the incorporation of calculated SFR into the clinical setting, where cardiologists can interpret lesion severity both anatomically and hemodynamically. This incorporation can be done without additional cost to the physician, hospital, patient, or third-party payers.

ABSTRACT

Contemporary quantitative coronary arteriography (QCA) methods accurately measure stenosis flow reserve (SFR) under conditions of coronary artery disease but are too expensive for practical clinical use. A simple laminar flow (Poiseuille) model was fitted to 1040 stenotic lesions and cross-validated on an independent sample of 100 lesions. This simple model was found adequate for practical use with a cross-validated correlation of 0.97 with QCA measurement. Turbulence and other known complexities had no practical effect.

Introduction

In 1840 Jean Leonard Marie Poiseuille established a basic model for the physics of blood flow with his work¹ describing the effects of various parameters (eq 1) on fluid flow in cylindrical tubes.

$$Q = \frac{\pi (P_i - P_o) d^4}{128 \eta l} \quad (1)$$

where Q is flow, π is the constant 3.14, $P_i - P_o$ is the input/output pressure difference, d is the diameter of the tube, η is viscosity of fluid and l is the length of the tube.

Though it is known that the complex biological factors affecting fluid flow in the cardiovascular system go far beyond the simple physics of Poiseuille's laboratory, the fact remains that the simple physical characteristics are at least among the elements of the complex biological system. This study is an indirect empirical test of the adequacy of Poiseuille's model for the prediction of stenosis flow reserve (SFR).

SFR is defined as follows^{2,3}:

$$SFR = 5 \frac{Q_{\text{stenosed}}}{Q_{\text{unstenosed}}} \quad (2)$$

where Q is flow. This can be reexpressed as:

$$SFR = 5k \frac{(d-s)^4}{d^4} \quad (3)$$

where s is reduction in diameter due to stenosis; k is the factor representing effects of any difference in length, input/output pressures, or viscosity between the stenosed and normal condition; and d is the arterial diameter.

If the model is appropriate, then the expected value of k equals 1 since the length of the artery, the aortic and vascular bed pressures, and the viscosity are the same. Expanding equation 3,

$$SFR = k \times f(s/d) \quad (4)$$

where $f(s/d)$ is a fourth-order polynomial. All terms are nonzero.

As presented, equation 3 assumes the stenosis is distributed over the entire length of the artery. The stenotic lesion may, however, occupy only a relatively short segment of the artery. Thus, over its length, the functional diameter of an artery relative to normal varies from s/d to 1. Accordingly, the effective relative diameter of an artery over its entire length will be greater than $(d-s)/d$, ($0 < s/d < 1$). In this case the coefficients of the polynomial will differ from those obtained by simple expansion of equation 3. The question of effective diameter rests in biological, not model, properties. A test of the utility of the simple Poiseuille model can be satisfied by empirical fitting of a fourth-order (quadratic) polynomial in s/d and was investigated in this study.

In order to determine the effect of each of the independent variables and their ability to adequately predict SFR, the results of 1040 coronary

arterial stenoses (as reported in Part I)⁴ were analyzed by quantitative coronary arteriography (QCA). These independent variables were analyzed for their independent and combined effects for predictability of SFR. Applicability of the derived (quadratic) model was cross-validated on an independent sample of 100 arterial stenoses and compared with results obtained by QCA.

Methods

Coronary Arteriograms and Automated Quantitative Coronary Arteriography

From 241 coronary arteriograms, 1040 coronary arterial stenoses were taken and analyzed by QCA for percent diameter stenosis (%DS), percent area stenosis (%AS), length, absolute diameter, entry and exit angle, as well as SFR, as previously reported.⁴

Statistical Methods

Each of the 1040 coronary artery stenoses were analyzed for SFR, %DS, %AS, absolute diameter in mm, length in mm, and entry angle (alpha) and exit angle (omega) in degrees. Correlation of SFR to each of the variables was then determined. Analysis of variance (ANOVA) was performed on %DS, %AS, length and absolute diameter, as well as their interactions, to determine their significance to SFR. With the knowledge obtained from ANOVA, SFR was plotted against %DS and a quadratic function described. Finally, 100 independent arteries were analyzed by QCA for %DS. The SFR was calculated from the measured %DS by the quadratic equation and compared with the SFR derived by QCA.

Results

Excluding the 39 totally occluded arteries, the results of the 1040 coronary artery stenosis ranging from no disease to subtotal occlusion of the coronary artery were analyzed and are described elsewhere.⁴

Prior to ANOVA, each of the independent variables was correlated with SFR to determine whether there was any significant relationship. The entry angle demonstrated a minimal relationship to SFR with an R^2 value of 0.133, while the exit angle demonstrated another minimal relationship with an R^2 value of 0.139.

With the four remaining independent variables (1) %DS, (2) %AS, (3) length, and (4) absolute diameter, an ANOVA was performed for SFR. These results are displayed in Table I for each of the variables as well as their interactions. Percent diameter stenosis was the only single variable to demonstrate a statistically significant ($P \leq 0.001$) association with SFR. There were four two-way interactions and one three-way interaction that were statistically significantly associated with SFR. All but one of these multiple interactions involved %DS, and this (area $\times$ length) is the least significant ($P \leq 0.031$) of the multiple interactions.

The independent variables of length and absolute diameter were reanalyzed to determine whether variability in SFR could be reduced by looking at smaller ranges of these variables. There were no statistical differences detected by subgrouping the absolute diameters into 0.5 mm increments, ranging from 0.5 to 2.0 mm, proving that the variability of SFR was not dependent on certain ranges of absolute diameter. However, the subgrouping of stenoses revealed that when a stenosis had an absolute arterial lumen diameter of less than 1.0 mm, it had a greater than 30 %DS.

Similarly, the lengths of stenoses were broken down into 5 mm increments, ranging from 5 to 25 mm. No statistical differences were detectable in the variability of SFR over the different ranges of the subgrouped results. Like absolute diameter, stenosis length could not be sub-grouped to produce statistical significance in predicting SFR.

When SFR was compared with %AS, there was no significant decrease in SFR until %AS reached at least 60% to 70% reduction. Prior to this point there is no observable effect upon SFR.

In Figure 1, SFR is plotted against %DS. There is a decrease in SFR once %DS reaches a 40–45% reduction. This inverse curvilinear relationship between SFR and %DS is best described by the following quadratic equation:

$$SFR = (A) - (B \times \%DS) + (C \times \%DS^2) - (D \times \%DS^3) + (E \times \%DS^4) \quad (5)$$

where SFR is stenosis flow reserve and %DS is percent diameter stenosis divided by 100 (%DS/100) expressed as a value from 0–1. A, B, C, D, and E represent absolute values not listed here.

An independent cross-validation sample of 100 stenoses were analyzed for %DS and a cal-

Table I.
Results of General Linear Model of Analysis of Variance for Stenosis Flow Reserve

Source	F Ratio	t Value	P (Statistical Significance)
Dia	32.08	5.66	0.001***
Area	0.30	0.54	0.587 ns
Length	0.97	-0.99	0.324 ns
Abs	3.72	1.93	0.054 ns
Dia × area	166.92	-12.92	0.001***
Dia × length	5.56	2.36	0.019***
Dia × abs	13.32	-3.65	0.001***
Area × length	4.69	-2.16	0.031***
Area × abs	0.89	0.94	0.346 ns
Length × abs	0.63	0.79	0.427 ns
Dia × area × length	0.68	-0.82	0.410 ns
Dia × area × abs	31.11	5.58	0.001***
Dia × length × abs	0.03	-0.16	0.874 ns
Area × length × abs	0.91	0.96	0.340 ns
Dia × area × length × abs	1.08	-1.04	0.299 ns

***Equals statistical significance, ns = not significant.
Abs = absolute diameter, Dia = diameter.

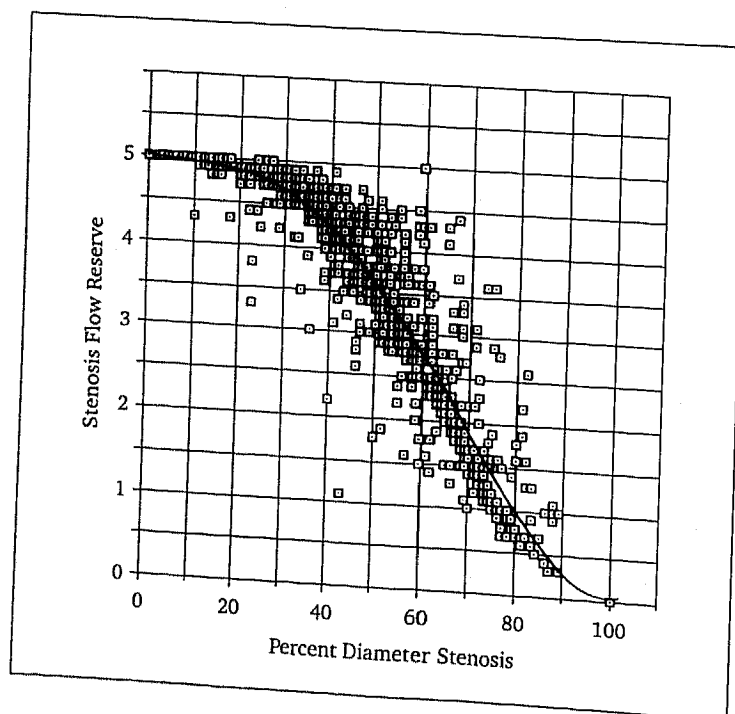


Figure 1. Comparison of percent diameter stenosis with SFR. When SFR of 1040 lesions was plotted against percent diameter stenosis, the results revealed a quadratic relationship. No apparent decrease in SFR was observed until a 15–20% reduction in diameter was reported. SFR then progressively decreased until %DS reached 80%, after which SFR was less than 1.

culated SFR was obtained for each of the arteries by use of equation 5. This calculated SFR was then correlated with the QCA-determined SFR, demonstrating an excellent agreement ($r = 0.97$) between the two methods as graphically depicted in Figure 2.

Discussion

The use of relative SFR to compare maximum flow through a stenosis with maximum flow through a nonstenosed artery is a useful tool for comparing stenosis with stenosis. It makes certain assumptions, such as: no collateral flow, an aortic pressure of 100 mm Hg, a maximum coronary blood flow of 8 times the resting flow, and a resting coronary flow velocity of 15 cm/second. While this method allows accurate determination of SFR and the independent variables of coronary artery stenoses, it requires considerable equipment, time, and experienced personnel to derive this information and is impractical in the clinical day-to-day setting of patient care.

When the major independent variables of SFR were examined, no significant relationship between SFR and entry and exit angles to and from a stenosis could be detected. Little additional in-

formation was supplied by density data, which looked similar to %AS data, although the number of stenoses with density data was only 15.7% of the 1040 arteries. Percent area stenosis did not reflect significant changes in SFR until 60% to 70% stenosis was reached. This may be the result of %AS' being a calculated value, derived from %DS measured from simultaneously imaged orthogonal views. Of the remaining variables only %DS was statistically significant in predicting SFR. When multiple interactions were compared, all but one included the variable of %DS. When absolute diameter and length were subgrouped, there was no difference in the association between these variables and SFR.

The relationship between SFR and %DS is best described by a quadratic equation (eq 5). While newly described here, this equation is consistent with the original work by Poiseuille, wherein he demonstrated that radius to the fourth power had the most significant impact on flow. It is also in agreement with the effects of predicted kinetic energy loss⁵ of blood flow through a stenosis, which is associated with a fourth-order (quadratic) magnitude of the radius. The correlation of 0.97 between %DS-predicted (eq 5) and QCA-obtained SFR more than satisfies

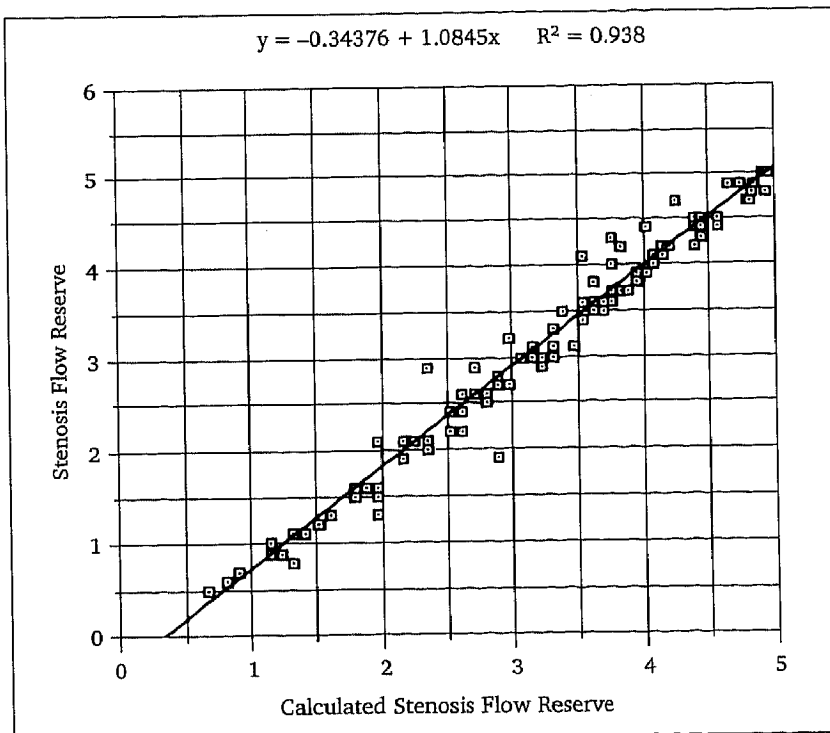


Figure 2. Comparison of measured and calculated SFR. When the results of QCA-determined SFR are plotted against the results obtained from equation 5 there is an excellent agreement ($r = 0.97$) between the two methods.

the standard rule-of-thumb goal of 0.94 for consistency for procedures to be used for individual diagnosis.⁶ The use of this quadratic equation derived from the SFR and %DS data allows the determination of SFR (a physiologic variable) from %DS (an anatomic variable) and vice-versa.

Conclusion

While the coefficients have been empirically derived to account for biological variation in effective %DS throughout the length of a vessel, the underlying model is quite similar to that of Poiseuille's law for laminar flow. Though the biological system is undoubtedly far more complex than this simple physical model, the combined

effect of all the complexities appears to be minimal, perhaps because a large number of small effects will tend to average out. Whatever the reason, the simple classical physical model proves to be adequate for practical application. The practical significance is substantial because diagnosis by the simple model is far more cost effective in time, equipment, and personnel in this major disease area.

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