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FUNCTIONAL AND ANATOMICAL DIAGNOSIS OF CORONARY ARTERY STENOSES: A RETROSPECTIVE STUDY IN HUMANS

Kranthi K Kolli[1], Mohamed Effat[2,3], Imran Arif[2,3], Tarek Helmy[2,3], Massoud Leesar[2,3], Lloyd H Back[4], Srikara V Peelukhana[1], Rupak K Banerjee[1,3]

[1]School of Dynamic Systems,
Mechanical Engineering Program,
University of Cincinnati,
Cincinnati,OH.

[2]Department of Internal Medicine,
Division of Cardiology,
University of Cincinnati,
Cincinnati, OH.

[3]Cincinnati Veteran Affairs Medical Center,
Cincinnati, OH.

[4]Jet Propulsion Laboratory,
California Institute of Technology,
Pasadena,CA.

ABSTRACT

Fractional flow reserve (FFR: ratio of distal to proximal *pressure* of a stenotic section) is used to evaluate hemodynamic significance of epicardial stenosis. However, FFR and coronary flow reserve (CFR: ratio of hyperemic blood *velocity* to that of resting condition) are used in conjunction to evaluate combination of both epicardial and microvascular disease. It has been proposed that optimization of cut-off values for diagnostic parameters in determining stenosis severity depends on coupling functional (pressure and velocity) and anatomical data (% area stenosis). We *hypothesize* that, pressure drop coefficient (CDP: the ratio of trans-stenotic pressure drop to distal dynamic pressure) which has the functional information of pressure and velocity in its formulation correlates significantly with FFR and CFR, and lesion flow coefficient (LFC: ratio of %area stenoses to CDP at throat region) which combines both functional and anatomical (% area stenoses) information in its formulation correlates significantly with FFR, CFR and % area stenosis. We retrospectively analyzed the hemodynamic information from Meuwissen et al [3] to test this hypothesis. It was observed that, CDP, a functional index based on pressure drop and velocity, correlated linearly and significantly with FFR and CFR. And, LFC (combined functional and anatomic parameter) also correlated significantly with FFR, CFR (both hemodynamic endpoints) and %area stenosis (anatomic endpoint).

INTRODUCTION

Both *pressure-derived* myocardial fractional flow reserve (FFR: the ratio of mean pressure distal to the stenosis [P_d] to the mean aortic pressure [P_a]; Fig 1) and *velocity-derived* coronary flow reserve (CFR: the ratio of hyperemic to basal coronary velocity across an epicardial lesion) are currently used to evaluate hemodynamic severity of coronary lesions. It should be noted that, FFR is a specific index for evaluating epicardial stenosis. And, CFR in conjunction with FFR could assess both epicardial and microvascular diseases. In order to better delineate between these two diseases and improve diagnostic accuracy, it was anticipated that the functional (*pressure* and *velocity*) and anatomical *(% area stenosis*) information should be combined into a single diagnostic index. Recently, our group has proposed two new diagnostic parameters based on fundamental fluid dynamic principles, namely: (i) pressure drop coefficient (CDP: ratio of translesional pressure drop to distal dynamic pressure), a functional parameter and (ii) lesion flow coefficient (LFC: ratio of %area stenoses to CDP at throat region), a combined anatomical and functional parameter [1, 2]. In our recent studies [1, 2] using a pig model, we showed that both CDP and LFC can delineate between epicardial disease and microvascular dysfunction.

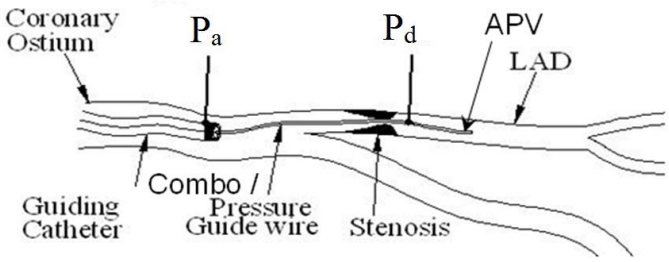

Figure 1: Pressure – Flow measurements in coronary arteries

In this study, we further extend our analysis of CDP and LFC to human data, based on the hemodynamic information from Meuwissen et al. [3]. We *hypothesize* that, CDP which has the functional information of pressure and velocity in its formulation correlates significantly with FFR and CFR, and LFC which has both functional

and anatomical (% area stenoses) information in its formulation correlates significantly with FFR, CFR and % area stenosis.

METHODS

Patient Group. The study population consisted of 19 patients [3]. Data from three patients with pressure drop across stenosis being equal to distal pressure was excluded from the analysis. Thus, 16 patients with stable chest pain scheduled for cardiac catheterization were included in the study. Exclusion criteria were diffuse or 3-vessel disease, significant left main coronary artery stenosis, or a subtotal lesion in the target vessel; recent myocardial infarction (< 6 weeks); prior cardiac surgery; or hypertrophic cardiomyopathy. All patients gave written informed consent.

Hemodynamic Measurements. Aortic pressure (P_a) was measured using guiding catheter. Distal to stenosis in target vessel, intra coronary pressure measurements (P_d) were monitored with a 0.014-inch-diameter pressure guidewire (Volcano Corporation, CA or RADI medical systems, Sweden) at baseline and during maximal hyperemia induced by intracoronary adenosine. Average peak flow velocity (APV) readings at baseline and at hyperemia (induced by adenosine) were recorded. Percent diameter stenosis, reference diameter, and minimal lumen diameter were obtained by quantitative analysis of coronary angiograms, with the use of a validated automated contour detection algorithm.

Data Analysis. Percent area stenosis (1-k) is calculated from the diameter measurements. The mean internal vessel diameter (used to calculate area stenosis) was 2.99± 0.63 mm and minimum lumen diameter was 1.45±0.45 mm. Individual hemodynamic information (P_a, P_d, APV_b and APV_h) for all the 16 patients was evaluated using the data from Table III of Meuwissen et al. [3] and mean proximal aortic pressure (P_a) at hyperemia (90.4 ± 12.4 mmHg) [3]. The functional hemodynamic index based on fundamental fluid dynamic principles, pressure drop coefficient (CDP) was calculated as the ratio of mean pressure drop ($\Delta P=P_a-P_d$) and distal dynamic pressure ($0.5x\rho xAPV^2$), where ρ is the density of blood (1.05 gm/cm^3) and APV is the average peak flow velocity.

$$CDP = \frac{\Delta P}{(0.5\times \rho \times APV^2)} \qquad (1)$$

The combined functional and anatomical index, LFC, was calculated from area stenosis and CDP measured at the throat.

$$LFC = \frac{(1-k)}{\sqrt{CDP_m}} \qquad (2)$$

Statistical Analysis: Analysis of variance was used to analyze the data and assess any significant linear correlations among CDP, LFC, FFR and CFR. A probability value of $p<0.05$ was considered statistically significant.

RESULTS

The mean values of CFR, FFR, (1-k), CDP and LFC for all the 16 patients are reported in Table 1.

Table 1: Mean values of CFR, FFR, 1-k, CDP and LFC

	Mean	Range
CFR	2.30±0.16	1.42 – 3.7
FFR	0.79±0.02	0.69 - 0.95
1-k	0.78±0.02	0.64 - 0.88
CDP	46.44±5.94	11.86 – 88.24
LFC	0.29±0.03	0.12 - 0.48

The functional index, CDP, when correlated simultaneously with FFR and CFR was found to have a significant correlation ($r=0.66;p<0.05$). This is consistent with the definition of CDP, which is a functional parameter that includes both pressure (FFR) and flow (CFR) information. Similarly, when LFC was correlated simultaneously with CFR and FFR, the correlation was found to be marginally significant ($r=0.58$; $p=0.069$). Further when area obstruction was included as a parameter for the correlation along with FFR and CFR, the correlation was significant and improved to a value of 0.82 with $p<0.05$.

Table 2: Correlation of CDP, LFC with FFR, CFR and (1-κ)

Dependent vs. Independent variable	Regression equation	Correlation coefficient	p-value
CDP vs CFR and FFR	CDP= -21.98x(CFR)-213.58x(FFR)+266.58	r=0.66	***p<0.05***
LFC vs CFR and FFR	LFC=0.12x(CFR)+ 0.70x(FFR)-0.53	r=0.58	p=0.069
LFC vs CFR, FFR and (1-κ)	LFC=0.06x(CFR)-0.87x(FFR)+1.11x (1-κ)-1.40	r=0.82	***p<0.05***

CONCLUSION AND DISCUSSION

We showed that: (i) CDP (functional parameter) correlated linearly and significantly with FFR and CFR; (ii) LFC (combined functional and anatomic parameter) correlated with FFR, CFR (both functional endpoints) and % area stenosis (anatomic endpoint). This retrospective data analysis based on 16 patient human data from Meuwissen et al. [3] has validated the concept of combined assessment of pressure drop and flow for diagnostic assessment of coronary stenoses. Abnormal results of FFR and CFR are frequently encountered in patients with intermediate coronary lesions. Lesions characterized by discordant results between FFR and CFR can only be identified when both pressure and flow are measured. Since CDP and LFC have both pressure and flow information in its formulation, it may be more practical to report a single value of CDP or LFC over the combined measurements of FFR and CFR. In future, it is of interest to evaluate the diagnostic cutoff values for functional index CDP and the combined functional and anatomical diagnostic parameter LFC.

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