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**FUNCTIONAL DIAGNOSIS OF CORONARY ARTERY STENOSES USING PRESSURE
DROP COEFFICIENT: A PILOT STUDY IN HUMANS**

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ABSTRACT

Optimization of cut-off values for diagnostic parameters in determining stenosis severity depends on coupling functional (hemodynamic) and anatomical data. In this study, we sought to investigate the functional diagnostic parameter (CDP; the ratio of trans-stenotic pressure drop to distal dynamic pressure) by correlating with FFR (ratio of distal to proximal pressure of a stenotic section) and CFR (ratio of hyperemic blood flow velocity to that of resting condition). A 0.014-inch dual sensor (pressure and Doppler velocity) guidewire was used in 9 patients to obtain pressure drop and velocity at hyperemia. Functional index CDP was assessed from measured hyperemic pressure drop and velocity. CDP correlated linearly and significantly with FFR and CFR. Indicating that, measurements of CDP can provide a better assessment of stenosis severity.

INTRODUCTION

In patients with chest pain and stenosis of moderate severity as assessed by coronary angiography, evaluation and treatment of coronary artery disease are challenging. Both pressure-derived myocardial fractional flow reserve (FFR) and coronary flow reserve (CFR) have been found as predictors of inducible ischemia. However, as the underlying models of these traditional indices demonstrate, their values depend not only on stenosis resistance but also on microvascular resistance at full dilation, which may vary as a result of heart rate, contractility, or microvascular disease and which affects FFR and CFR. It was proposed that the combination of pressure and flow velocity into a functional diagnostic index based on fundamental fluid dynamic principles, pressure drop coefficient (CDP: ratio of translesional pressure drop to distal dynamic pressure) can significantly improve the diagnostic accuracy, especially in cases with discordant outcomes between the traditional parameters. Recently,

simultaneous measurement of distal pressure and velocity single dual sensor equipped guidewire has also been used for coronary diagnostics in a cath lab.

On the basis of simultaneous pressure–flow analysis of coronary stenoses during maximal flow, the concept of CDP [1, 2] has been developed as an invasively determined index for assessing the functional severity of coronary stenoses. This index is independent of changes in systemic blood pressure, contractility and heart rate [3]. In this initial pilot study, we aim to combine and correlate the functional diagnostic parameter CDP with FFR and CFR on the first group of human patients.

METHODS

Study Patients. The study population consisted of 9 consecutive patients. To be eligible for the study, each patient was required to have: a) chest pain; b) an angiographically detectable stenosis of moderate severity (defined as approximately 50 percent by visual examination) in the proximal part of one major coronary artery; c) left ventricular ejection fraction >25%; and e) uncertainty about whether the chest pain was related to reversible ischemia caused by the moderate stenosis. The study protocol was approved by the institutional review board at University of Cincinnati (UC) and Cincinnati Veteran Affairs Medical Center (CVAMC), and informed consent for all tests was obtained from all the participants. Patients who underwent bicycle exercise testing, thallium scintigraphy, stress echocardiography with dobutamine, and coronary arteriography were consented based on the above inclusion criteria. And these patients were scheduled for cardiac catheterization.

Hemodynamic Measurement. At the time of catheterization, a 4-to-6-French coronary catheter was introduced into femoral artery and

advanced into the ostium of the coronary artery. Aortic pressure was measured using this guiding catheter. In an angiographically normal reference vessel and distal to stenosis in target vessel, intra coronary pressure and flow measurements were measured with a 0.014-inch-diameter guidewire (Combwire, Volcano Corporation, California, USA) that combines a standard Doppler sensor at the tip and a standard pressure sensor 1.5 cm proximal to tip. The Combwire was set at zero, calibrated, advanced through the guiding catheter, introduced into the coronary artery, and positioned distal to the stenosis in target vessel. The position of Doppler sensor was manipulated until an optimal and stable blood velocity signal was obtained distal to lesion [4]. Adenosine was then infused intravenously (140 mg per kilogram per minute) to induce maximal coronary blood flow, corresponding with minimal distal coronary pressure. Aortic pressure (P_a), coronary pressure (P_d) and instantaneous peak velocity (APV) distal to the stenosis were recorded. All signals were continuously recorded at rest and throughout induction and decline of maximum hyperemia.

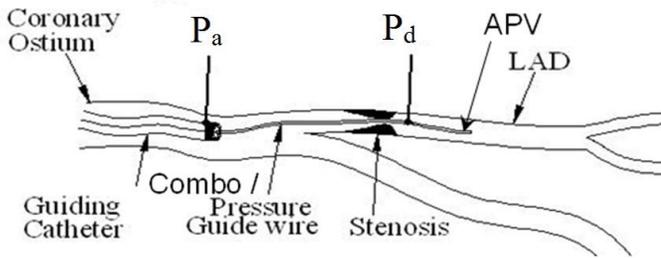


Figure 1: Physiological Pressure – Flow measurements in LAD

Study Protocol. As per standard of care, intracoronary-pressure, flow measurements and the calculation of FFR were performed in all patients. The clinical decision to perform myocardial revascularization (percutaneous transluminal coronary angioplasty or bypass surgery) was made when the FFR was less than 0.75, a value selected on the basis of the results of earlier studies. If the FFR was 0.75 or higher, no revascularization procedure was performed. If the lesion was suitable for coronary angioplasty, FFR measurement was performed before angioplasty, and again after successful angioplasty.

Data Analysis. 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. FFR was calculated as the ratio of mean distal to aortic pressure during maximal hyperemia ($FFR = P_d/P_a$). CFR was calculated as the ratio of hyperemic to baseline APV ($CFR = APV_h/APV_b$). 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, where ρ is the density of blood (1.05 gm/cm^3) and APV is the average peak flow velocity.

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

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

RESULTS

Figure 2 shows the linear correlation: (i) CDP versus FFR ($R^2 = 0.86$, $p < 0.05$); (ii) CDP versus CFR ($R^2 = 0.18$, $p < 0.05$). As stenosis severity decreases, CDP decreases, where as FFR and CFR increase. This is consistent with the fluid dynamic behavior of coronary stenoses. Further, when CDP was correlated simultaneously with FFR and CFR, the correlation coefficient was 0.74 ($CDP = -67.4CFR - 174.6FFR + 288.8$, $p < 0.05$). The correlations of CDP with FFR and CFR remained significant, since CDP is a functional parameter that includes both pressure and flow.

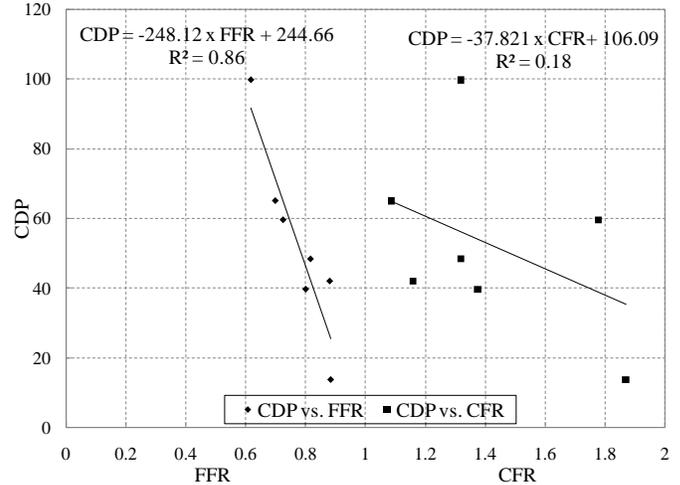


Figure 2: Regression analysis: (i) CDP vs FFR and (ii) CDP vs CFR

CONCLUSION AND DISCUSSION

This pilot human study has validated the concept of combined *in vivo* estimation of pressure drop and flow for diagnostic assessment of coronary stenoses. Since CDP has both pressure and flow information in its formulation, it may be more practical to report a single value of CDP over the separate assessment of FFR and CFR. In future, it is of interest to increase the enrolment and study the correlation of FFR, CFR with the futuristic diagnostic parameter lesion flow coefficient (LFC) which combines both functional and anatomical information such as area stenosis in its formulation.

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