Functional Diagnosis of Coronary Stenoses Using Pressure Drop Coefficient: A Pilot Study in Humans

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Objectives and Background: Myocardial fractional flow reserve (FFR) in conjunction with coronary flow reserve (CFR) is used to evaluate the hemodynamic severity of coronary lesions. However, discordant results between FFR and CFR have been observed in intermediate coronary lesions. A functional parameter, pressure drop coefficient (CDP; ratio of pressure drop to distal dynamic pressure), was assessed using intracoronary pressure drop (dp) and average peak velocity (APV). The CDP is a nondimensional ratio, derived from fundamental fluid dynamic principles. We sought to evaluate the correlation of CDP with FFR, CFR, and hyperemic stenosis resistance (HSR: ratio of pressure drop to APV) in human subjects.

Methods: Twenty-seven patients with reversible perfusion defects based on SPECT were consented for the study before cardiac catheterization. Distal coronary pressure and APV were measured simultaneously for each coronary lesion using a Combowire during cardiac catheterization. Reference diameter, minimal lumen diameter, and %AS were obtained by quantitative coronary angiography. Maximum hyperemia was induced by IV adenosine (140 µg/kg/min). CDP was calculated as, $CDP = \frac{\Delta p}{0.5 \times \rho \times APV^2}$. The density of blood ($\rho$) was assumed to be 1.05 gm/cm³. Results: The functional index, CDP, when correlated simultaneously with FFR and CFR, was found to have a significant correlation ($r = 0.61; P < 0.05$). Similarly a significant correlation was achieved when CDP was correlated with HSR ($r = 0.91; P < 0.001$). This is consistent with the definition of CDP, which is a functional parameter that includes both pressure and flow information. Conclusions: CDP, a nondimensional parameter combining simultaneous measurements of pressure drop and velocity data, can accurately define the severity of coronary stenoses and could prove advantageous clinically.

Key words: coronary disease; stenosis; cardiac hemodynamics; catheterization

INTRODUCTION

Intermediate coronary stenosis represents an ongoing challenge for interventional cardiologists. Although coronary angiography is considered the current standard for the diagnosis of coronary artery disease, it has significant limitations in the accurate assessment of intermediate coronary lesions, owing to multiple factors...
including lesion eccentricity, image overlap, angulations, and diffuse coronary disease without a clear healthy reference segment.

Invasive assessments of the hemodynamic significance of coronary stenosis have evolved over the past 15 years and have been shown in multiple studies to correlate well with reversible ischemia on noninvasive stress test. Furthermore, the use of functional assessment of lesions to guide revascularization decisions has been shown to improve patient outcomes as compared to the use of angiography alone.

Multiple parameters are available for the functional evaluation of coronary lesions including coronary flow reserve (CFR) and fractional flow reserve (FFR), and hyperemic stenosis resistance index (HSR). FFR is currently the most widely used, and in fact is considered by many to be the current gold standard for the evaluation of hemodynamic significance of coronary stenosis, and hence the presence of myocardial ischemia [1–4].

A recent meta-analysis of 31 studies comparing the results of FFR with noninvasive stress imaging and/or quantitative coronary angiography revealed only modest concordance of FFR with noninvasive stress imaging [5]. Accordingly, hemodynamic evaluation of intermediate coronary stenosis has achieved class 2a, level of evidence A, recommendation in the focused update to the ACC/AHA guidelines [6], and is also recommended by the Appropriate Use Criteria for coronary revascularization focused update [7]. Despite these recommendations, FFR is currently used to guide only 6% of interventions performed in the United States [8].

It should also be noted that some limitations of FFR include its assumption of zero central venous pressure and its dependence on achieving maximal hyperemia. Failure to achieve peak hyperemia may result in not achieving minimal constant microvascular resistance leading to under estimation of pressure drop and over estimation of FFR across a stenosis [9].

CFR can be measured using a Doppler-tipped sensor guide wire. CFR was found to have excellent agreement with noninvasive stress testing at cutoff value of 2.0. An abnormal CFR (<2.0) correlated with reversible myocardial perfusion defects with high sensitivity and specificity [10]. It should be noted that CFR can give the combined effect of epicardial stenosis and microvascular dysfunction but cannot delineate between the two. This uncertainty of the microcirculatory contribution to an abnormal CFR makes CFR alone less useful for epicardial lesion assessment. Further, CFR can be affected by changes in basal or hyperemic flow, which are influenced by hemodynamic variables like heart rate, left ventricular mass and volume, and rheological parameters [11].

To overcome these issues, simultaneous measurement of pressure drop and velocity is proposed for the diagnosis of epicardial coronary stenosis. Simultaneous assessment of pressure drop and flow was included in HSR index (HSR; ratio of pressure drop across the stenosis to the distal flow velocity during hyperemia) [12]. Although FFR and CFR are ratios and do not have any units, HSR has units of mm Hg/cm/sec.

Recently, we introduced the functional index, the pressure drop coefficient [13] (CDP; the ratio of trans-stenotic pressure drop [Δp] to distal dynamic pressure, [½ × blood density × APV²; where APV: average peak flow velocity] measured under maximal hyperemia). This parameter is a nondimensional ratio, derived from fundamental fluid dynamic principles that incorporate simultaneous assessment of pressure drop (Δp) and flow (APV) in its formulation. The functional measurements (Δp and APV) necessary for the evaluation of CDP can be readily obtained during routine cardiac catheterization procedures using a dual sensor tipped guidewire. The CDP was validated in in vitro [13,14] and in vivo animal studies [15,16] and shown to distinguish between stenosis severities. Further, CDP was also shown to be independent of heart rate [17] and contractility [18] in our recent in vivo animal study. The purpose of this study was to test the hypothesis that CDP, by incorporating both intracoronary pressure and flow measurements, correlates significantly with traditional hemodynamic parameters derived from either pressure or flow velocity alone. Consequently, we report herein the preliminary data from our clinical study examining the correlations of nondimensional parameter CDP with currently used indices (FFR, CFR, and HSR). This clinical study is a single center, prospective, and nonrandomized study.

METHODS

Study Patients

The study population consisted of 27 clinically stable patients with single- or two-vessel coronary artery disease (de novo lesion) and without hypertrophic cardiomyopathy or other obvious comorbidity associated with microvascular dysfunction. 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% by
visual examination) in a major coronary artery; (c) left ventricular ejection fraction >25%; and (e) uncertainty about whether the chest pain was related to reversible ischemia (as detected by abnormal SPECT scan) caused by the moderate stenosis. The exclusion criteria include: (a) left ventricular ejection fraction <25%; (b) nondialysis-dependent chronic kidney disease with baseline serum creatinine greater than 2.5 gm/dL; (c) history of type-II heparin induced thrombocytopenia; (d) significant comorbid conditions that would make coronary angiography prohibitive and contraindicated; and (e) pregnant women. 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 and myocardial perfusion scans were consented based on the above inclusion and exclusion criteria. These patients were scheduled for cardiac catheterization.

Cardiac Catheterization and Hemodynamic Measurement

At the time of catheterization, vascular access was obtained in the usual fashion through the femoral approach; a 5-to-6-French coronary catheter was introduced into the femoral sheath and advanced into the ostium of the coronary artery. Unfractionated heparin was administered using a weight based protocol. Aortic pressure was measured through the guiding catheter. Intracoronary pressure and flow measurements were obtained across the lesions using a 0.014-in.-diameter guidewire (Combowire, Volcano Corporation, CA) that combines a standard Doppler sensor at the tip and a standard pressure sensor 1.5 cm proximal to the tip. The Combowire was set at zero, calibrated, advanced through the guiding catheter, introduced into the coronary artery, and positioned distal to the stenosis in the target vessel, with the pressure transducer at least 5 mm distal to lesion. The position of the Doppler sensor was manipulated until an optimal and stable blood velocity signal was obtained distal to the lesion. Adenosine was then infused intravenously (140 μg/kg/min) to induce maximal coronary blood flow, corresponding with minimal distal coronary resistance. Aortic pressure (p<sub>a</sub>), coronary pressure (p<sub>d</sub>), and average peak velocity (APV) distal to the stenosis were recorded. All signals were continuously recorded at rest and throughout induction and decline of maximum hyperemia.

Study Protocol

Intracoronary-pressure, flow measurements, and the calculation of FFR were performed in all patients, according to the current standard of care procedure. The clinical decision to perform myocardial revascularization (percutaneous transluminal coronary angioplasty or bypass surgery) was made when the FFR was less than 0.8, and at the discretion of the operator. If the lesion was suitable for percutaneous coronary intervention, hemodynamic measurements of pressure and velocity were measured before and after the intervention. The FFR value (greater than 0.90) measured after PCI was used to assess the success of intervention.

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 (Centricity Cardiology, GE Healthcare). The calculation of diagnostic parameters is as described below:

Calculation of FFR

FFR is defined as the ratio of maximal myocardial blood flow distal to a stenotic artery (Q) to the theoretical maximal flow in the absence of the stenosis (Q<sub>N</sub>). Clinically, maximal flow is achieved by administering intracoronary Papaverine or intracoronary Adenosine. Under this maximum flow (hyperemia), the resistance (R) imposed by the microvascular bed is minimal and blood flow is proportional to driving pressure. FFR can thus be expressed as:

\[
\text{FFR} = \frac{Q}{Q_N} = \frac{(p_d-p_v)/R_1}{(p_a-p_v)/R_2} \tag{1}
\]

where \(p_a\), \(p_d\), and \(p_v\) represent the mean aortic, distal coronary, and central venous pressures obtained at hyperemia.

During maximum hyperemia, because the resistances \(R_1\) and \(R_2\) are very low, they will be similar and cancel out. In addition, \(p_v\) is usually very low and does not contribute significantly. Using these simplifications, the formula is simplified as:

\[
\text{FFR} = \frac{(p_d-p_v)}{(p_a-p_v)} \cdot \frac{p_d}{p_a} \tag{2}
\]

Calculation of CDP

CDP has been previously described in detail in literature [13,15,16,19]. Briefly, CDP is defined as the ratio of trans-stenotic pressure drop (\(\Delta p = p_a - p_d\), where \(p_a\) and \(p_d\) are average pressures measured proximal and distal to the stenosis at hyperemia, respectively) to distal dynamic pressure. Distal dynamic pressure is calcul-
of average peak flow velocity (APV) and a constant value of 0.5; \((0.5 \times \rho \times APV^2)\), measured at maximal hyperemia. Blood density, \(\rho\), does not change significantly at hyperemia and thus can be assumed to have a constant value \((1.05 \, \text{gm/cm}^3)\) [15,19].

\[
CDP = \frac{\Delta p}{0.5 \times \rho \times APV^2} \quad \text{(a dimensionless parameter)} \tag{3}
\]

where \(\Delta p = p_a - p_d\)

Statistical Analysis

Analysis of variance was used to analyze the data and assess any significant linear correlations among CDP, FFR, and CFR. Multiple linear regression analysis was also applied to compare the simultaneous correlations among hemodynamic parameters. Data analysis was performed using SAS version 9.1.3 (SAS Institute, NC). A probability value of \(P < 0.05\) was considered statistically significant. All functional measurements and hemodynamic parameters are represented as mean \(\pm\) SE.

RESULTS

Clinical and Angiographic Results

A total of 27 patients (mean age, 60 \(\pm\) 2 years), underwent coronary catheterization to determine the presence of obstructive epicardial coronary stenosis. A summary of 27 patients’ clinical profile is shown in Table I. The mean values of reference vessel and minimal luminal diameter are \(2.94 \pm 0.1\) mm and \(1.58 \pm 0.08\) mm, respectively. Figure 1 shows the representative coronary angiogram and coronary-pressure and flow tracings from a patient, used to calculate FFR and CFR, respectively. The mean value of proximal aortic pressure \((p_a)\), distal pressure \((p_d)\), and average peak flow velocity \((APV)\) of blood were 81.81 \(\pm\) 3.14 mm Hg, 65.74 \(\pm\) 3.05 mm Hg and 36.74 \(\pm\) 1.86 cm/sec, respectively. The angiographic (%AS: percentage area stenosis) and hemodynamic (CFR, FFR, HSR, and CDP) characteristics for lesions are listed in Table II.

In patients with FFR less than 0.80 percutaneous coronary intervention was performed and FFR was measured again after the revascularization. The FFR measured after successful intervention was found to have a value greater than 0.90.

CDP Correlations

Figure 2 shows the results of linear correlation of CDP with FFR and CFR. CDP when correlated with FFR showed a linear and significant correlation \((r = 0.57, P < 0.05)\) as shown in Fig. 2A. When

<table>
<thead>
<tr>
<th>Variable</th>
<th>Study group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (M/F)</td>
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</tr>
<tr>
<td>Age (years)</td>
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</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>60 (\pm) 1.9</td>
</tr>
<tr>
<td>Clinical history</td>
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<tr>
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<tr>
<td>Hypertension</td>
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<tr>
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<td>20 (74%)</td>
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<td>Smoker</td>
<td>19 (70%)</td>
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<tr>
<td>Family history of CAD</td>
<td>17 (63%)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>3 (11%)</td>
</tr>
<tr>
<td>LV hypertrophy</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>Affected artery</td>
<td></td>
</tr>
<tr>
<td>Left anterior descending</td>
<td>15</td>
</tr>
<tr>
<td>Left circumflex</td>
<td>3</td>
</tr>
<tr>
<td>Right coronary</td>
<td>8</td>
</tr>
<tr>
<td>Reference diameter (mm)</td>
<td>2.94 (\pm) 0.1</td>
</tr>
<tr>
<td>Percent area stenosis (%)</td>
<td>68 (\pm) 2</td>
</tr>
<tr>
<td>Minimal luminal diameter (mm)</td>
<td>1.58 (\pm) 0.08</td>
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TABLE I. Characteristics of Patients, Results of Noninvasive Tests, and Quantitative Coronary Angiographic Measurements

Fig. 1. (A) Coronary angiograms and (B) simultaneously obtained pressure and velocity recordings. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]
correlated with CFR, CDP showed linear correlation with moderate correlation ($r = 0.35$, $P = 0.07$) as shown in Fig. 2B. Further, as stenosis severity decreases, values of CDP were found to decrease, whereas values of FFR and CFR increased. This is consistent with the fluid dynamic behavior of coronary stenoses [15,16].

The functional index, CDP, when correlated simultaneously with FFR and CFR, was found to have a significant and improved correlation ($r = 0.61$, $P < 0.05$) and is shown in Fig. 3. This is consistent with the definition of CDP, which is a functional parameter that includes both pressure (FFR) and flow (CFR) information.

When CDP was correlated with the epicardial specific parameter HSR (Fig. 4), a linearly significant correlation ($r = 0.91$, $P < 0.001$) was observed. This is expected since both CDP and HSR are measures of stenosis resistances as they are functions of pressure and flow measurements.

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DISCUSSION

This is the first reported clinical study in human subjects validating the use of CDP as a parameter for invasive assessment of hemodynamic significance of intermediate coronary lesions. Invasive assessment of pressure drop and coronary flow can provide clinically useful information in patients with known or suspected ischemic heart disease. Recent advances have introduced a dual sensor pressure and flow wire, which will further simplify the simultaneous assessment of pressure drop and flow. This study has established a combined in vivo measurement of pressure drop and blood flow velocity for evaluating the fundamental fluid dynamic diagnostic parameter CDP in a clinical setting using a 0.014-in. ComboWire (with both pressure and Doppler sensors). This study showed that the fundamental fluid dynamics derived diagnostic parameter, CDP, which incorporates both pressure drop and flow velocity in its formulation correlated significantly with: (1) CFR and FFR, (2) HSR. This study was performed in a select group of clinically stable patients with single- or two-vessel coronary artery disease (de novo lesion) and without hypertrophic cardiomyopathy or other obvious comorbidity associated with microvascular dysfunction [20]. Despite the absence of such pathologic conditions, our results demonstrated a significant dependence of CDP on FFR, CFR (Fig. 3) and a significant dependence on HSR (Fig. 4). Thus, we believe that our findings may be even more pertinent in an extended clinical setting with concomitant microvascular impairment [20].

Traditional Methods for Stenosis Evaluation

Conventional methods of stenosis evaluation in the catheterization laboratory involve the assessment of pressure-derived FFR and flow-derived CFR. FFR represents the ratio of maximal flow through a stenosed vessel with that of maximal flow achieved if the vessel was disease free. FFR has been proposed and validated as being more specific to epicardial obstructions and independent of changes in external hemodynamic conditions. It should be noted that FFR presumes maximal hyperemia in the vascular bed being interrogated, which may not be reliably achieved in certain patients. Further, the effect of microvascular dysfunction on FFR measurements also remains an area of controversy [9]. In the presence of microvascular dysfunction, the maximal hyperemic flow may not be fully achieved and thus may indicate falsely higher FFR values; thus understimating the severity of stenosis.

CFR represents the ratio of maximal-to-baseline flow velocity distal to stenosis, regardless of the variation in either concomitant pressure drop or the absolute values of flow. Its value inherently depends on frequent variations in baseline or maximal flow that may be caused by factors unrelated to stenosis severity. Further, the determination of CFR also critically depends on the achievement of maximal vasodilation [11]. It should also be noted that in current clinical practice stenosis evaluation is done with either FFR (primary) or CFR but, not together. Hence, the limitation of assessing only one of the two interdependent signals, pressure for FFR or velocity for CFR, may be a source for potential inaccuracies in the assessment of functional stenosis severity.

Advantages of Combined Measurement of Pressure and Flow

Simultaneous measurements of coronary blood pressure and velocity (ideally with a dual-sensor guide wire) can provide complementary information in assessing coronary stenosis severity and microvascular abnormalities [12, 21]. The total pressure drop across a stenosis is the sum of viscous losses due to friction (outcome of Poiseuille equation in straight conduit) and momentum change losses caused by area reduction at the throat of the stenoses (modified Bernoulli equation under area reduction). The relationship between pressure drop (\(\Delta p\)) and flow (\(Q\)) can be described by, \(\Delta p = A_v Q + B_m Q^2\), where \(A_v\) and \(B_m\) are the viscous (friction) and momentum-change (area change) loss coefficients, respectively [19]. These coefficients depend on the properties of blood and on the geometry of the stenosis. It should be noted that the flow limiting behavior of coronary stenosis is mainly determined by the second term which increases with square of the flow [19]. Moreover, owing to the nonlinear nature of pressure drop-flow relationship, it is rather appropriate that the prediction of functional severity of a stenosis should account for these two interdependent loss components, as has been done in this study.

Recent advancements in sensor guidewire technology allow a more complete interrogation of the coronary circulation with a single wire (by pressure and velocity). With combined distal measurements, a clinician will have all the relevant hemodynamic information to make an informed decision about the physiological condition of the entire coronary circulation.

The dual sensor wire used to measure the intracoronary pressure and velocity simultaneously is similar in size (0.014 in. diameter) to the more widely used single sensor wire used to measure pressure or velocity. However, the utilization of alternative indices using dual sensor wires has not gained sufficient traction in cardiac catheterization laboratories partly because of the added technical and cognitive complexity of these
measurements. Nevertheless, it is our opinion that given the time and as the technology advances further in making the dual sensor wires more steerable, less expensive and easier to use, the employment of these sophisticated concepts will be more tenable for use and application in the cardiac catheterization laboratory. Further, as more information becomes available from additional studies and investigations, the evidence in favor of these combined pressure-flow parameters will become more established for practical use.

Advantages of CDP

In pressure drop calculations for fluid flowing through a piping network, it is engineering practice to use nondimensional numbers derived from fluid dynamic fundamentals. The CDP (the ratio of pressure drop $\Delta p$ to distal dynamic pressure, $\left(\frac{1}{2} \times \text{fluid density} \times \text{velocity}^2\right)$) is a dimensionless value commonly used for analyzing fluid flow dynamics problems where the pressure difference between two points is important [19]. Analogously, this nondimensional equation (with velocity squared term in the denominator) was used to assess the physiological significance of coronary stenosis on blood flow in a coronary artery. Thus, with more weight given to distal blood flow, we hypothesize that, we can effectively distinguish between epicardial and microvascular dysfunction [15].

We have recently proposed and tested CDP, a nondimensional diagnostic parameter formulated based on fundamental fluid dynamic principles as a measure of stenosis severity in an animal model [15–18,22]. CDP, by definition, combines both hyperemic pressure drop and velocity measurements. Moreover, in CDP, the normalization of pressure drop ($\Delta p$) with nonlinear dynamic pressure term $(0.5 \times \rho \times APV^2)$ is developed from fundamental fluid dynamic concepts as the pressure drop across a typical stenosis (>70% area stenosis) is predominantly due to momentum change loss caused by area reduction [19]. In our recent preclinical trials we have found that CDP is a promising clinical diagnostic parameter that can independently assess the severity of epicardial stenosis and microvascular impairment [15]. Further, it was also reported in our recent studies that CDP is independent of variable hemodynamic conditions such as heart rate and contractility under both epicardial and microvascular impairment [17,18,22].

As mentioned previously, assessment of FFR and CFR depends critically on the achievement of maximal hyperemia. Failure to achieve peak hyperemia can occur in situations where either the patient is unresponsive to adenosine or has been on drugs/caffeine which inhibit effect of adenosine. This may result in not achieving minimal constant microvascular resistance leading to under estimation of FFR across a stenosis [9]. To overcome these issues, recently, parameters based on basal measurements have been proposed [23,24].

Further, it should be noted that in the presence of microvascular dysfunction and submaximal hyperemia, pressure drop, and blood flow are affected in the same direction. Physiologically, the extent of reduction in maximal hyperemic flow due to microvascular dysfunction is higher than that due to epicardial stenosis [15]. In such circumstances, the square of maximal hyperemic flow in the denominator of CDP significantly accounts for this reduction, thus providing an increased resolving power for CDP for accurate evaluation of the status of epicardial and microcirculation dysfunction simultaneously. The values of CDP range from zero to infinity. Thus, we believe that, CDP, a diagnostic parameter based on combined pressure and velocity measurements can also evaluate stenosis severity under baseline conditions. Accordingly, to study the effect of hyperemia on CDP, we correlated CDP measured under hyperemic conditions with CDP measured at rest (basal) conditions (Fig. 5A). It can be seen that there is a significant correlation ($r = 0.78$, $P < 0.001$) between CDP measured at hyperemia and basal conditions. Additionally, the agreement between the basal and hyperemic CDP was also assessed using a Bland–Altman analysis (Fig. 5B). The mean differences between CDP (measured at hyperemia) and the CDP_b (CDP measured under basal or resting conditions) were $-10.94 \pm 23.60$ (95% limit of agreement = $-20.28$ to $-1.61$). The Bland–Altman analysis revealed neither trend nor bias between differences for the functional parameter, CDP. In the future, extending this analysis, we also plan to test the reproducibility and diagnostic accuracy of CDP measured under basal conditions in a larger patient pool.

We demonstrated in the study the significant correlation between CDP and FFR, CFR, and HSR, validating the use of CDP as a parameter for evaluation of physiologic significance of intermediate coronary lesions. Given the advantages CDP has over the other parameters it stands to have a significant role in clinical practice.

Limitations

The study was performed in a small group of patients undergoing cardiac catheterization with reversible defects detected on noninvasive cardiac evaluation. Hence, the results of our study may need to be expanded for larger patient group. Despite a good correlation with FFR, currently there is no cut-off value for CDP similar to FFR owing to the small number of patients.

Even though, the hemodynamic parameters (pressure and velocity) were measured before and after PCI. We could not study the performance of the diagnostic parameters post-PCI as the number of patients who...
underwent PCI was not large enough to make a statistical inference.

The Combowire used to measure the pressure and flow values currently is available in two models as listed below:

a. Model 9515: Doppler sensor at tip and pressure sensor at 1.5 cm offset and
b. Model 9500: both Doppler and pressure sensors at the tip.

Ideally, pressure and velocity should be measured at the same location to avoid time delays between the signals. Our clinical study was initiated with Combowire (Model 9515), which was more widely available when compared with the newer Combowire (Model 9500) at that time. To maintain consistency we chose to continue with the same sensor. Further, it should also be noted that the offset of sensors is not expected to introduce measurable error when time averaged mean values of pressure and velocity are evaluated [25].

Although no visible collaterals were present in these patients, we cannot exclude the effect of recruitable collateral flow, especially in areas supplied by the severely narrowed coronary arteries. The effect of collaterals needs to be further evaluated.

**Future Work**

We plan to increase our patient enrollment in this clinical study to evaluate the limiting value of CDP based on $\text{FFR} = 0.80$ and $\text{CFR} = 2$ [12,26] that can distinguish between patients with epicardial and microvascular dysfunction. Further, we would also like to compare the noninvasive measures of degree of ischemia in humans for specificity, sensitivity, and accuracy. In addition to the above, owing to the high magnifying power of CDP [15] we are planning to evaluate the diagnostic accuracy of CDP under nonhyperemic conditions.

**CONCLUSION**

In patients with scintigraphic evidence of ischemia, the combined pressure and flow diagnostic parameter (CDP) correlated significantly with the current traditional diagnostic parameters FFR, CFR, and epicardial specific parameter HSR. By combining velocity and pressure information, CDP can be more accurate than FFR or CFR in predicting ischemia. This pilot study also confirms the advantage of combined measurements with a dual-sensor wire for the evaluation of stenosis severity in the catheterization laboratory.

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