Abnormal Coronary Flow Velocity Reserve After Coronary Artery Stenting in Patients
Role of Relative Coronary Reserve to Assess Potential Mechanisms

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Background—Absolute coronary flow velocity reserve (CVR) after stenting may remain abnormal as a result of several different mechanisms. Relative CVR (rCVR = CVR_{target} / CVR_{reference}) theoretically normalizes for global microcirculatory disturbances and facilitates interpretation of abnormal CVR.

Methods and Results—To characterize potential mechanisms of poststent physiology, CVR was measured using a Doppler-tipped angioplasty guidewire in 55 patients before and after angioplasty, after stenting, and in an angiographically normal reference vessel. For the group, the percent diameter stenosis decreased from 75 ± 13% to 40 ± 18% after angioplasty and to 10 ± 9% (all P < 0.05) after stent placement. After angioplasty, CVR increased from 1.63 ± 0.71 to 1.89 ± 0.55 (P < 0.05) and after stent placement, to 2.48 ± 0.75 (P < 0.05 versus pre- and postangioplasty). After angioplasty, rCVR increased from 0.64 ± 0.26 to 0.75 ± 0.23 and after stent placement to 1.00 ± 0.34. In 17 patients with CVR_{stent} ≥ 2.0, increased basal coronary flow, rather than attenuated hyperemia, was responsible in large part for the lower CVR_{stent} compared with patients having CVR_{stent} > 2.0. In 8 patients with CVR_{stent} < 2.0, a normal rCVR supported global microvascular disease. The subgroup of 9 patients with CVR_{stent} < 2.0 and abnormal rCVR (16% of the studied patients) may require a pressure-derived fractional flow reserve to differentiate persistent obstruction from diffuse atherosclerotic disease or microvascular stunning.

Conclusions—Although a majority of patients after stenting normalize CVR for the individual circulation (ie, normal CVR or normal rCVR), in those with impaired CVR_{stent}, the analysis of coronary flow dynamics suggests several different physiological mechanisms. Additional assessment may be required to fully characterize the physiological result for such patients to exclude remediable luminal abnormalities. (Circulation. 1999;100:2491-2498.)

Key Words: coronary disease ▪ blood flow ▪ stents ▪ stenosis

Coronary balloon angioplasty and stent implantation enlarge luminal cross-sectional area and improve blood flow.1−4 Compared with balloon angioplasty, coronary stenting produces larger luminal areas and minimal residual stenoses.3,4 Due largely to symmetrical conduit morphological results, the scaffolding of the arterial segments after stenting provides better local flow conditions, a factor which is in large part responsible for the normalization of coronary vasodilatory reserve (CVR) in most patients after stenting.3 However, even after substantial conduit area enlargement with stenting, postprocedural CVR remains abnormal in some patients. Several potential mechanisms of the flow impairment have been suggested. These mechanisms include persistently elevated basal flow after transient ischemia, microvascular stunning due to particulate embolization, acute or chronic impairment of the microvascular circulatory response, an inadequate lumen at or adjacent to stent sites not recognized by conventional angiography due to residual stenosis or unappreciated thrombus, or diffuse epicardial atherosclerosis.

In patients with clinical conditions often associated with microvascular abnormalities (eg, diabetes mellitus, left ventricular hypertrophy, or myocardial ischemia/infarction), poststent CVR may be expected to be reduced even in the absence of any residual coronary artery stenoses.5−8 Assuming a relatively homogeneous distribution of global microcirculatory abnormalities,9,10 relative coronary flow velocity reserve ratio (rCVR), the ratio of CVR in the target vessel to CVR in an angiographically normal reference vessel, theoretically would normalize for the common microcirculatory
abnormality and would be a more specific index of persistent conduit flow limitation.11–13

The purpose of this study was to examine absolute and relative CVR after balloon angioplasty and stenting to categorize the potential mechanisms of individual patient responses. We tested the hypothesis that rCVR would be normalized in most patients after stenting, but that patient subgroups with abnormal CVR and rCVR responses would identify several coexistent pathophysiologic alterations. An appreciation of different mechanisms would support the use of adjunctive techniques [eg, pressure-derived fractional flow reserve (FFR) and/or intravascular ultrasound] to establish the active process and direct further intervention, as indicated, in patients with impaired post-stent CVR.

Figure 1. A, Absolute and relative coronary flow velocity data obtained during coronary stenting. Left, Pre-PTCA angiogram of left anterior descending artery (LAD) with a 60% proximal stenosis. Right, Flow velocity data obtained in LAD. Coronary flow reserve was 1.9. Basal average peak velocity (BAPV) was 16, peak hyperemic average velocity (PAPV) was 30. Velocity panel demonstrates continuous flow velocity signal (top) with the ECG and arterial pressure tracings. S and D demarcate systolic and diastolic periods based on the ECG. Heart rate (53 beats/min) and blood pressure (104/48 mm Hg) are noted in the top left corner. The velocity scale is 0 to 90 cm/s. The lower section is split into the basal panel (left) and peak hyperemic panel (right). Numerical format as in the top panel. A reference vessel (ref, circumflex artery) coronary vasodilatory reserve was 2.9. rCVR was 1.9/2.9 = 0.66. DSVR indicates diastolic/systolic velocity ratio; MPV, maximal peak velocity; DPVi, diastolic peak velocity index. B, left, Angiographic frames demonstrating post-PTCA and poststent cineangiographic appearance. Right, Coronary flow reserve is 1.5 (rCVR = 0.52) after balloon angioplasty and 3.0 after stenting (rCVR = 1.0). Note that the BAPV remained relatively unchanged between 12 and 14 cm/s. Format for flow velocity data as in A.
Methods

Study Patients
Fifty-five patients undergoing routine coronary angioplasty and elective stent placement were studied. Results in 19 of these patients were reported previously. Patients with recent (<4 weeks) myocardial infarction in the target or reference vessel territory or severe diffuse multivessel disease were excluded. Patients with clinical conditions of hypertension, diabetes mellitus, or myocardial infarction (remote in time from the study, >4 weeks) associated with impaired CVR were not excluded from the study. Oral and written consent was obtained from each patient before the study. The study protocol was approved by the Human Subjects Committee of the Institutional Review Board. No patient had a complication due to the study protocol. Anti-ischemic and antiplatelet medications were continued over the study period as clinically indicated.

Angioplasty and Stent Procedures
All patients received routine precatheterization medications of diphenhydramine (25 mg orally) and diazepam (2 to 4 mg intravenously) before the procedure. Vascular access was obtained using the femoral approach with Seldinger technique. Heparin (10 000 U intravenous bolus with 1 000 U/h intravenous infusion) was administered before beginning angioplasty. Angioplasty was performed in a routine manner using 6 or 8F guiding catheters and standard angioplasty balloon catheters. The angioplasty guidewire was 0.014-inch Doppler-tipped guidewire (FloWire™, EndoSonics, Inc). All stents placed in this study were the Johnson & Johnson Palmaz-Schatz sheathed stents varying in size from 3.0 to 4.0 mm.

Coronary Flow Velocity Technique
Coronary flow velocity was measured using the Doppler-tipped guidewire 3 to 5 minutes after intracoronary nitroglycerin (100 to 200 μg). The average peak velocity (APV, cm/s) was obtained from the spectral velocity signals averaged over 2 cardiac cycles. Coronary hyperemia was induced with bolus administration of intracoronary adenosine (8 to 12 μg for right coronary artery and 18 to 24 μg for the left coronary artery) as previously reported. CVR was computed as the ratio of hyperemic to basal average peak velocity. CVR measurements were made in duplicate with previously reported variation of 15 ± 9%. The CVR was measured in the reference vessel (CVRreference), followed by the target vessel at least 2 cm distal to the stenosis before angioplasty. CVR was measured after angioplasty and again after stenting (CVRstent). Data were obtained before and at least 5 to 10 minutes after coronary angioplasty and stent placement. rCVR was computed for each portion of the study as the ratio of CVRreference/CVRstent and normal cut-off values (CVR > 2.0, rCVR > 0.8) were determined from previous thresholds and receiver operating curves related to myocardial perfusion imaging. An example of absolute and relative coronary flow velocity data during stenting is shown on Figure 1.

Quantitative Coronary Angiographic Technique
Quantitative coronary angiography (QCA) was performed using the Phillips DCI-ACA or ADA imaging system. The percent diameter, area stenosis, and minimal lumen diameter were computed in a standard manner using the proximal normal reference vessel segments in single plane, worst view angulation. The contrast-filled guiding catheter was used as calibration for vessel dimension calculation. The reproducibility of QCA from this laboratory has been previously reported with inter- and intraobserver variability of 8% and 12%, respectively. In patients with 3-vessel coronary artery disease, a reference vessel was accepted as the vessel with <40% narrowing by QCA.

Statistical Analysis
All data were expressed as mean±SD. ANOVA was used to compare baseline, postangioplasty and poststent hemodynamic data, Doppler flow, and angiographic variables. Scheffe’s test was used to compare mean values when significant differences among the study periods were identified by ANOVA. *P<0.05 was considered statistically significant.

Results
Patient Characteristics
The study included 55 patients (37 male, 18 female, mean age 58±12 years) with predominantly 1- or 2-vessel coronary disease (Table 1). Hypertension was present in 56% of patients, diabetes mellitus in 24%, and smoking in 63%. A prior history of remote myocardial infarction was noted in 46% of the patients. The target vessel was the left anterior descending artery in 21, circumflex in 10, and right coronary artery in 24. Six patients had segmental left ventricular hypokinesis in the distribution of the target stenosis (3 inferior-posterior, 2 anterior, 1 apical). The angiographically normal reference vessels supplying regions of normal left ventricular wall motion were the left anterior descending in...
24, circumflex in 26, obtuse marginal in 2, and diagonal branch in 3 patients.

**Quantitative Coronary Angiographic and Hemodynamic Data**
Balloon angioplasty decreased the diameter stenosis from 75±13% (minimal luminal diameter 0.76±0.45 mm) to 40±18% (minimal luminal diameter 1.77±0.61 mm, \(P<0.05\)). Stent implantation further decreased the percent diameter stenosis to 10±9% (minimal luminal diameter 2.91±0.52 mm, \(P<0.05\) versus both before and after angioplasty). The reference vessel segment mean diameter was similar, 2.94±0.52 mm (Table 2). There was no significant change in heart rate or mean arterial pressure over the study period.

**Coronary Flow Velocity Data**
For the entire group before angioplasty, basal poststenotic APV increased from 14±6 to 23±12 cm/s at peak hyperemia with a resulting CVR of 1.63±0.71. After angioplasty, basal APV increased to 19±8 cm/s \((P<0.05)\). Hyperemic APV increased to 35±15 cm/s \((P<0.05\) versus preangioplasty) with CVR increasing to 1.89±0.55 \((P=NS\) versus preangioplasty). After stent placement, resting APV was unchanged \((19±7\) cm/s), hyperemic APV increased to 44±12 cm/s and CVR increased to 2.48±0.75 \((P<0.05\) versus before and after angioplasty) (Table 3). The reference vessel basal APV was 22±8 cm/s which increased to 51±15 cm/s with hyperemia yielding CVR\textsubscript{reference} of 2.55±0.49, similar to the poststenot result. Before angioplasty, rCVR was 0.64±0.26. After angioplasty, rCVR increased to 0.75±0.23 \((P<0.05)\) and after stent implantation to 1.00±0.34 \((P<0.05\) versus pre- and postangioplasty). When examined by individual target vessel, CVR and rCVR were similar among the left anterior descending, circumflex, and right coronary arteries. Figure 2 shows CVR and rCVR and corresponding percent diameter stenosis for the 3 study periods.

**Stratification of CVR After Stenting**
The results were also stratified by CVR\textsubscript{stent} >2.0 or ≤2.0. There were 38 patients with CVR\textsubscript{stent} >2.0. There were no significant angiographic differences between the 2 groups.

In the CVR\textsubscript{stent} >2.0 group, the resting APV was similar among pre- and postangioplasty, and poststen period \((15±5, 19±8, 17±6\) cm/s, respectively, \(P=NS\)) (Figure 3). The CVR increased from 1.79±0.78 to 2.03±0.58 after angioplasty \((P=NS)\) and to 2.82±0.61 after stenting \((P<0.05\) versus pre- and postangioplasty). rCVR increased from 0.69±0.28 before to 0.78±0.25 after angioplasty and to 1.11±0.35 after stenting \((P<0.05\) versus pre- and postangioplasty).

In the 17 patients with CVR\textsubscript{stent} =2.0 (8 left anterior descending, 5 right coronary artery, and 4 circumflex target vessels), resting APV was similar before \((12±8\) cm/s) and after angioplasty \((19±7\) cm/s), but was higher after stenting \((23±5\) cm/s, \(P<0.05\) versus pre- and postangioplasty) and higher than basal flow in CVR\textsubscript{stent} >2.0 patients \((P<0.05)\). Hyperemic APV increased from 17±14 to 31±13 cm/s after angioplasty, values lower than CVR\textsubscript{stent} >2.0 patients \((P<0.05)\). After stent implantation, hyperemic APV increased to 40±10 cm/s \((P<0.05\) versus pre- and postangioplasty). Figure 3 summarizes the changes in basal and hyperemic velocity in the CVR\textsubscript{stent} subgroups.

After angioplasty in the group with CVR\textsubscript{stent} <2.0, CVR increased from 1.27±0.31 to 1.57±0.28 \((P<0.05)\) and to 1.73±0.14 after stent implantation \((P<0.05\) versus preangioplasty; \(P<0.05\) versus CVR\textsubscript{stent} >2.0). In this group, CVR\textsubscript{stent} was less than CVR\textsubscript{reference} \((1.73±0.14\) versus 2.38±0.39, \(P<0.05)\). rCVR increased from 0.54±0.15 at baseline to 0.68±0.25 after angioplasty and further increased after stent implantation to 0.75±0.13 \((P<0.05\) versus preangioplasty and CVR\textsubscript{stent} >2.0). Figure 4 summarized the changes in CVR and rCVR for the CVR\textsubscript{stent} subgroups.

### TABLE 3. Coronary Flow Velocity Data

<table>
<thead>
<tr>
<th></th>
<th>APV (cm/s)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Rest</td>
</tr>
<tr>
<td>Preangioplasty</td>
<td>14.0±6.1</td>
</tr>
<tr>
<td>Postangioplasty</td>
<td>19.1±7.5*</td>
</tr>
<tr>
<td>Poststent</td>
<td>18.7±6.5†</td>
</tr>
<tr>
<td>Reference</td>
<td>21.6±8.4†</td>
</tr>
</tbody>
</table>

\*\(P<0.05\) vs preangioplasty.

†\(P<0.05\) vs pre- and postangioplasty.
Microvascular Disease, Multivessel Coronary Artery Disease, and CVR

Microvascular disease was based on CVR reference < 2.0 and was present in 9 patients (Table 4, Figure 5). Compared with patients with CVR reference > 2.0, patients with CVR reference ≤ 2.0 had higher reference vessel basal APV (31 ± 7 versus 20 ± 7 cm/s, P < 0.05) and higher postangioplasty basal APV (P < 0.05). In addition, after stenting, the hyperemic APV was lower than hyperemic reference APV (40 ± 12 versus 56 ± 9 cm/s, P < 0.05) compared with patients without microvascular disease (44 ± 12 versus 50 ± 16 cm/s, P = NS). However, these variations in flow velocity did not result in the mean CVR stent being significantly different than patients with CVR reference > 2.0. All patients with CVR reference < 2.0, including 5 patients with CVR stent < 2.0, had normalized rCVR after stenting (Figure 6). There was no significant difference between CVR stent and rCVR for patients with single- and multivessel coronary artery disease (Figure 6).

Coronary Flow Velocity Responses After Stenting and Potential Mechanisms

Using previously established thresholds of CVR stent (> 2.0) and rCVR (> 0.8), 4 subgroups of patients were identified that have potentially different mechanisms accounting for the physiological end result (Figure 6). Four patients had normal CVR stent with abnormal rCVR (group I: CVR 2.25 ± 0.17, rCVR 0.72 ± 0.03); 34 patients had normal CVR stent with normal (or supranormal) rCVR (group II: CVR 2.89 ± 0.66, rCVR 1.16 ± 0.34); 8 patients had abnormal CVR stent with normal rCVR (group III: CVR 1.76 ± 0.15, rCVR 0.86 ± 0.6); and 9 patients had abnormal CVR stent and abnormal rCVR (group IV: CVR 1.70 ± 0.14, rCVR 0.65 ± 0.09). The mean values for CVR stent and rCVR for each group are shown in Figure 6 (right panel). The potential mechanisms by subgroup are discussed below.

Discussion

This study demonstrates that although impaired CVR (< 2.0) after stenting was observed in some patients (30%), rCVR could be normalized in most patients. In the examination of these results, CVR stent and the associated rCVR suggest several potential different mechanisms for the resultant physiology which include, individually or combined, 1) increased baseline flow after stenting, 2) residual conduit obstruction, 3) microvascular stunning or small vessel disease, or 4) diffuse epicardial atherosclerosis. Dissection of specific flow velocity parameters can aid in differentiating these mechanisms.

Abnormal CVR After Stenting

An augmentation of basal flow velocity, more than a significant attenuation of maximal hyperemic flow velocity appears to account for the failure to achieve an CVR stent > 2.0 in most patients. The current data reproduces the findings of van Liebergen et al, wherein patients with impaired CVR after stenting had a mean baseline APV that was nearly double the APV after balloon angioplasty and after stenting in patients with CVR stent > 2.5. As in the current study, the hyperemic APV stent was similar for both groups immediately after the procedure. The exact mechanism of an increased basal APV stent in these patients is unclear but may be due to atherosclerotic plaque compression during stent implantation.

Figure 3. Basal (left) and hyperemic (right) APV for the 3 study periods.

Figure 4. CVR (left) and rCVR (right) for the 3 study periods.
and release of factors and/or particulates that produce a sustained hyperemic stimulus or transiently alter coronary autoregulation or vasomotion.19–21

**Abnormal rCVR After Stenting**

In the 2 groups with normal CVR_{stent} (I, II), the abnormal rCVR in group I suggests that although the CVR exceeds 2.0, this value does not achieve 80% of the reference flow potential resulting from either continued unappreciated epicardial stenosis or regional microvascular abnormalities. Conversely, in group II the reference vessel flow in some patients (eg, those with rCVR<1.2) fails to equal or exceed poststent flow. This response suggests potential regional reference vessel microvascular disease, diffuse atherosclerosis of the reference vessel, or unappreciated reference vessel obstruction. Our laboratory has recently demonstrated significant spatial heterogeneity of the coronary circulation in some cardiac transplant recipients,10 a factor which confounds the usefulness of rCVR in some circumstances. Transcoronary guidewire pressure-derived FFR would discriminate between impaired flow due to diffuse disease in the reference vessel (FFR_{normal}) or occult reference or target vessel obstruction (FFR_{abnormal}).22,23

In the 2 groups with abnormal CVR_{stent} (III, IV), rCVR suggests other mechanisms. In group III, the normal rCVR suggests that impaired CVR_{stent} is sufficient for globally reduced microcirculatory function. CVR may be reduced by comorbid conditions such as diabetes mellitus, hypertension, or hypercholesterolemia, conditions associated with abnormal microcirculatory responses.5–8 It is interesting to note that the 9 patients with CVR_{reference}<2.0 had normal rCVR poststenting, with 5 having an abnormal CVR_{stent}. The 4 patients with normal CVR_{stent} had supranormal rCVR (>1.4), suggesting that an alternative mechanism may also be present. Although van Liebergen et al4 had no patients immediately after angioplasty or stenting with a CVR_{reference}>2.0, a supranormal rCVR was also demonstrated, occurring exclusively in stent patients at the 6-month follow-up evaluation. Although the reference vessel appeared angiographically normal, diffuse atherosclerosis, unappreciated by angiography, may have again reduced CVR_{reference} (akin to group II) in the absence of focal epicardial narrowing.24 Mintz et al25 indicated that intravascular ultrasound imaging commonly identifies diffuse atherosclerosis in angiographically normal vessels, a factor confounding any evaluation when angiography represents the imaging modality used.24

In group IV, the abnormal rCVR suggests 2 mechanisms: either residual conduit obstruction (eg, occult stenosis or thrombus) or regional microvascular stunning. Impaired CVR_{stent} may be due to an acute attenuation of the microvascular vasomotor responses by distal embolization and microvascular stunning following balloon angioplasty or stent deployment. In this case, both CVR_{stent} and rCVR would

**TABLE 4. Coronary Flow Velocity Data Stratified by Microvascular Disease (CVR_{ref} ≤2.0)**

<table>
<thead>
<tr>
<th>Groups</th>
<th>APV (cm/s)</th>
<th>CVR rest</th>
<th>Hyperemic</th>
<th>rCVR</th>
</tr>
</thead>
<tbody>
<tr>
<td>CVR_{ref}&gt;2.0 (n=36)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preangioplasty</td>
<td>13.9±6.4</td>
<td>23.3±12.5</td>
<td>1.69±0.74</td>
<td>0.63±0.27</td>
</tr>
<tr>
<td>Postangioplasty</td>
<td>18.3±7.0*†</td>
<td>34.1±15.0*</td>
<td>1.91±0.54</td>
<td>0.72±0.2‡</td>
</tr>
<tr>
<td>Poststent</td>
<td>18.7±6.1†</td>
<td>44.3±11.9†</td>
<td>2.50±0.74†</td>
<td>0.93±0.27†</td>
</tr>
<tr>
<td>Reference</td>
<td>19.6±7.2†</td>
<td>50.4±16.0†</td>
<td>2.69±0.40†</td>
<td>...</td>
</tr>
<tr>
<td>CVR_{ref}=2.0 (n=9)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preangioplasty</td>
<td>14.3±4.8</td>
<td>17.8±7.3</td>
<td>1.24±0.36</td>
<td>0.69±0.19</td>
</tr>
<tr>
<td>Postangioplasty</td>
<td>23.6±8.9</td>
<td>38.6±11.2*</td>
<td>1.79±0.63</td>
<td>0.94±0.31</td>
</tr>
<tr>
<td>Poststent</td>
<td>18.6±8.7</td>
<td>40.0±11.6*</td>
<td>2.41±0.86*</td>
<td>1.32±0.49</td>
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<tr>
<td>Reference</td>
<td>31.3±7.0</td>
<td>56.3±9.4†</td>
<td>1.84±0.17</td>
<td>...</td>
</tr>
</tbody>
</table>

*P<0.05 vs preangioplasty.
†P<0.05 vs postangioplasty.
‡P<0.05 vs CVR<2.0.
§P<0.05 vs post-stent.

![Figure 5](image-url)

Figure 5. Correlation between coronary vasodilatory reserve after stenting (CVR_{stent}) and the reference vessel (CVR_{ref}). Nine patients (see numbered circles) had CVR_{ref} ≤2.0.
initially be abnormal and normalize at follow-up. Persistent microvascular vasoconstriction may also be a contributing factor, one that should be minimized by postprocedure nitrates. An alternative mechanism is unappreciated luminal obstruction. Although stent implantation nearly always leads to a significant increase in cross-sectional area with generally concentric and cylindrical conduits, inapparent stent edge dissections, and new accumulation of focally extruded plaque into the nonstented vessel segments may occur. In this circumstance, both CVR\textsubscript{target} and rCVR would also be abnormal. In this subgroup, FFR would be particularly useful to differentiate conduit obstruction (FFR\textsubscript{abnormal}) from microvascular stunning (FFR\textsubscript{normal}).

**Durability of Improved Physiology After Angioplasty and Stenting**

Haude et al,\textsuperscript{2} using densitometric angiographic methods, as well as van Liebergen et al,\textsuperscript{4} demonstrated that improved myocardial perfusion reserve and CVR immediately after stenting is associated with normalized maximal blood flow ratios, an effect that was generally sustained for 6 months. A durable normalized anatomy coupled with physiology for both balloon angioplasty, and most recently stenting, has also translated to enhanced clinical outcomes.\textsuperscript{27,28} A prospective multicenter trial reported that an optimized coronary lumen area produced by conventional balloon angioplasty, sufficient to increase CVR\textsubscript{PPTCA} >2.5, produced stent-like outcomes with 6-month target lesion revascularization and angiographic restenosis rates of 16%.\textsuperscript{28}

**Limitations**

The technical limitations of Doppler CVR have been described in detail elsewhere.\textsuperscript{29} It is recognized that the current study population is small, a factor limiting the strength of conclusions regarding mechanisms of impaired poststenose CVR. However, the role of rCVR, especially in patients with microvascular disease, appears promising to identify potential mechanisms and, when coupled with FFR, can fully define the proposed mechanisms of impaired flow and direct further intervention.

FFR was not routinely used in the current study due to the limited availability of pressure sensor wires during the study period. FFR is theoretically more specific for conduit obstruction than CVR in that the effect of the microcirculation is nullified in the derived calculations. Baumgart et al\textsuperscript{13} demonstrated that rCVR, but not CVR\textsubscript{target}, had a significant correlation to FFR ($r=0.95, P<0.001$; CVR\textsubscript{target} versus FFR, $r=0.45, P=0.09$), an expected result considering the confounding influence of the microcirculation on CVR. The mechanisms postulated in group IV patients with abnormal CVR and rCVR can be further defined using FFR.

The selection of normal CVR and rCVR values has been derived from studies of angioplasty outcomes and myocardial perfusion imaging.\textsuperscript{4,13,16-18,30} The validity of the rCVR concept assumes that there is a uniform microcirculation across the target and reference vessel regions. Previous studies\textsuperscript{9,10} support a relatively uniform CVR distribution in patients without coronary artery disease, but this finding may not apply in patients with active ischemia or moderate multivessel coronary artery disease.\textsuperscript{31,32}

Intravascular ultrasound was also not routinely used in this study but would have confirmed both diffuse atherosclerotic disease or focal obstructions. Ziada et al\textsuperscript{26} demonstrated persistent haziness in 15% of patients after high-pressure coronary stent implantation, which was associated with angiographically occult but intravascular ultrasound-identified coronary dissections.

**Clinical Implications**

In most patients, stent implantation significantly augments coronary blood flow with improvement in both absolute CVR and normalization of rCVR. Failure to normalize CVR after stenting, observed in a minority of patients, may be due to multiple mechanisms which may be investigated using coronary flow velocity. The rCVR can assist in identifying a need for further examination by pressure-derived FFR, additional angiographic views, or possibly intravascular ultrasound imaging to exclude remediable luminal abnormalities. Identifying the mechanism of persistently abnormal coronary blood flow after stenting will assist in decisions for additional interventions with the potential to reduce stent restenosis or limit adverse clinical outcomes.

**Acknowledgment**

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