Simultaneous pressure and flow velocity measurements in diagnosis and treatment of coronary artery disease
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Influence of Percutaneous Coronary Intervention on Coronary Microvascular Resistance Index

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Background—Coronary microvascular resistance during maximal hyperemia is generally assumed to be unaffected by percutaneous coronary interventions (PCIs). We assessed a velocity-based index of hyperemic microvascular resistance (h-MR$_v$) by using prototypes of a novel, dual-sensor (Doppler velocity and pressure)–equipped guidewire before and after PCI to test this hypothesis.

Methods and Results—Aortic pressure, flow velocity (h-v), and pressure (h-P$_a$) distal to 24 coronary lesions were measured simultaneously during maximal hyperemia induced by intracoronary adenosine. Measurements were obtained in the reference vessel before PCI and in the target vessel before and after PCI, stenting, and ultrasound-guided, upsized stenting. h-P$_a$ increased from 57.9±17.0 to 85.5±15.6 mm Hg, and h-MR$_v$ (ie, h-P$_a$/h-v) decreased from 2.74±1.40 to 1.58±0.61 mm Hg · cm$^{-1}$ · s after stenting (both $P<0.001$). The reduction in h-MR$_v$ accounted for 34% of the decrease in total coronary resistance achieved by PCI. h-MR$_v$ of the target vessel after PCI was lower than that of the corresponding reference vessel despite a higher h-P$_a$ in the reference vessel ($P<0.01$). Post-PCI baseline MR$_v$ was correlated with baseline P$_a$ before PCI ($P<0.01$).

Conclusions—PCI-induced restoration of P$_a$ resulted in a reduction of h-MR$_v$ in accordance with the pressure dependence of h-MR$_v$. The decrease in h-MR$_v$ to a level below that of the corresponding reference vessel in the immediate post-PCI period and a lowered baseline MR$_v$ suggest microvascular remodeling induced by long-term exposure to a low-pressure environment.
Hyperemic coronary microvascular resistance is an important factor for maximal coronary blood flow in health and disease. Although experimental studies have demonstrated that it is nonuniformly distributed(4) and is furthermore pressure dependent,(10, 16) the concept of a minimal and constant microvascular resistance during distal vasodilation has evolved as a paradigm in clinical studies. However, the validity of this concept has been challenged by recent studies demonstrating regional differences in minimal coronary resistance distal to diseased and normal coronary arteries of the same patient(3) and the disparity in outcomes between the fractional flow reserve (FFR) and coronary flow velocity reserve (CFVR) in the same artery owing to variability in microvascular resistance.(20)

On the basis of the pressure dependence of resistance of the maximally vasodilated coronary bed as demonstrated in animal studies, we hypothesized that the pressure dependence of hyperemic coronary microvascular resistance in humans contributes to functional gain after percutaneous coronary interventions (PCIs). The aim of this study was to assess the effect of pressure restoration after stepwise-executed PCI on coronary microvascular resistance and to investigate the underlying potential mechanisms.

Methods

Patients

The study group consisted of 23 patients with stable angina (Canadian Cardiovascular Society classes 1 through 3) scheduled for elective PCI. All patients had a single de novo lesion in one coronary artery and at least one angiographically normal coronary artery. Patients with diffuse disease, serial lesions, ejection fraction <30%, serious valve abnormalities, hypertrophic cardiomyopathy, left main coronary artery stenosis, abnormal clotting profiles, subtotal lesions in the target vessel, or severe renal failure were excluded. All antianginal and antiplatelet medications were continued. All patients gave written, informed consent. The institutional review board approved the study, and all procedures were conducted in accordance with institutional guidelines.
Cardiac Catheterization and Angiography
Lorazepam (1 mg) was administered orally before the procedure. Cardiac catheterization was performed through a percutaneous femoral approach with a 5F or 6F guiding catheter. All patients received a bolus of heparin (7500 IU) before the procedure, and additional heparin was given if the procedure lasted >90 minutes. An intracoronary bolus of nitroglycerine (0.1 mg) was administered at the start of the procedure and repeated every 30 minutes.

Hemodynamic Measurements
Aortic pressure ($P_a$) was measured through the guiding catheter. Distal pressure ($P_d$) and flow velocity were measured simultaneously with prototypes of a 0.014-inch, dual-sensor (pressure and Doppler velocity) guidewire (Volcano Therapeutics). The Doppler crystal is located on the distal tip of the wire, and the pressure sensor is 3 cm proximal to the tip. The wire was positioned with the pressure sensor distal to the coronary lesion in the target vessel or in the distal part of an angiographically normal reference vessel and manipulated until a good velocity signal was obtained. The signals were processed with standard equipment (WaveMap and FloMap, Volcano Therapeutics). $P_a$, $P_d$, instantaneous peak velocity, and the ECG were digitally recorded on a personal computer after 12-bit, A/D conversion at 120 Hz for offline analysis. All signals were obtained at rest and after induction of maximal hyperemia with an intracoronary bolus of 20 to 40 μg adenosine to limit the procedure time and possible adverse systemic effects associated with continuous infusion of adenosine. (6)

Study Protocol
After baseline angiograms and hemodynamic measurements were obtained in the reference and target vessels, balloon angioplasty was performed, followed by placement of a single slotted-tube stent. Balloon size was determined by the angiographically determined dimension of the target vessel. In 11 patients, intravascular ultrasound–guided upsizing of the stent was performed according to CLOUT criteria. (31) After each treatment step, angiography and hemodynamic measurements were repeated.
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Data Analysis
Coronary angiograms were quantitatively analyzed (QCA-CMS 5.2, Medis). When possible, orthogonal views were used and the results averaged. Per-beat averages of the recorded instantaneous peak velocity, \( P_a \) and \( P_d \) were calculated (StudentLab Pro 3.6.2, Biopac Systems). Hyperemia was defined as the highest average of 3 consecutive per-beat velocity averages (h-v) after adenosine administration. Corresponding values of aortic (h-\( P_a \)) and distal (h-\( P_d \)) pressures were used to calculate hyperemic indices of velocity-based stenosis (h-SRv=\[h-P_a–h-P_d]\)/h-v) and h-MRv (h-MRv=h-\( P_d \)/h-v).(29) Microvascular resistance index under resting conditions (b-MRv) was determined from the respective baseline measurements. FFR, CFVR, and relative CFVR were determined as previously described.(29) Collateral index was calculated as the ratio of wedge pressure (\( P_w \)) to \( P_a \) at the end of balloon occlusion.

Statistical Analysis
Data are expressed as mean±SD, mean±SEm, or n (%). Hemodynamic measurements obtained after each PCI step were compared with the previous step and with the reference vessel by ANOVA with repeated measures, followed by contrast analysis (SPSS, version 11.5). Values of \( P<0.05 \) were considered statistically significant.

Results

Study Population
Clinical characteristics of all patients are listed in Table 1. Four patients suffered from angina pectoris Canadian Cardiovascular Society class I, 14 patients from class II, and 5 patients from class III. One patient had 2 lesions that were treated on separate occasions. The 24 target lesions were located in the left anterior descending coronary artery (n=12), left circumflex artery (n=3), obtuse marginal branch (n=3), or the right coronary artery (n=6). All but 2 lesions were in the proximal or mid-segment of the target vessel. All reference vessels were left coronary arteries. In 5 patients, direct stent implantation was performed without hemodynamic or angiographic recording after balloon predilatation. These were included in the balloon angioplasty group for comparison with pretreatment values.
Table 1: Clinical characteristics (n=23)

<table>
<thead>
<tr>
<th>Age</th>
<th>57.8 ± 7.3 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>17 (74%)</td>
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</table>

**Coronary risk factors**

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Count (Percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cigarette smoking</td>
<td>10 (43%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>7 (30%)</td>
</tr>
<tr>
<td>Positive family history</td>
<td>11 (48%)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>12 (52%)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>4 (17%)</td>
</tr>
<tr>
<td>Prior myocardial infarction &gt; 6 weeks</td>
<td>7 (30%)</td>
</tr>
<tr>
<td>Prior coronary angioplasty in other vessel</td>
<td>5 (22%)</td>
</tr>
</tbody>
</table>

**Medication**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Count (Percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta-blockers</td>
<td>21 (91%)</td>
</tr>
<tr>
<td>Nitrates</td>
<td>13 (57%)</td>
</tr>
<tr>
<td>Calcium-antagonists</td>
<td>9 (39%)</td>
</tr>
<tr>
<td>ACE-inhibitors</td>
<td>3 (13%)</td>
</tr>
<tr>
<td>Lipid lowering drugs</td>
<td>20 (87%)</td>
</tr>
<tr>
<td>Aspirin</td>
<td>23 (100%)</td>
</tr>
</tbody>
</table>

**Hemodynamic Outcomes**

Representative phasic recordings of pretreatment and posttreatment pressure and velocity signals during maximal hyperemia are shown in Figure 1 for 2 patients. The velocity waveform was damped before treatment (left), more so for the more severe lesion presented in the lower panels. The $P_d$ profile was dissociated from the $P_a$ signal and bore a stronger resemblance to a left ventricular pressure waveform. After treatment, hyperemic velocity and $P_d$ increased and hemodynamic waveforms were restored to a normal appearance, with $P_d$ resembling the $P_a$ waveform and the velocity signal exhibiting a typical biphasic shape. $h\text{-MR}_v$ progressively decreased with increasing distal perfusion pressure after sequential treatment steps (right). Note that $h\text{-MR}_v$ is lower in the upper panel than in the lower but that the relative decrease (by ≈41%) after PCI is quite similar.
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**Figure 1:** Hyperemic signals obtained in two patients. Stenosis diameter reduction was 42% and 57% for the top and bottom patient, respectively. Left: Phasic hyperemic signals before and after treatment. Both hyperemic flow velocity (h-v) and distal pressure (h-Pd) increased after treatment, while aortic pressure (h-Pa) remained constant. Right: Progressive decrease of the respective hyperemic microvascular resistance index (h-MRv) with increasing distal pressure (h-Pd) after stepwise PCI (balloon angioplasty, stent deployment, and upsized stent).

Heart rate and P a did not change throughout the procedure. Successful dilation of the stenosis as documented by quantitative coronary angiography was reflected in the hemodynamic results (Table 2). During hyperemia, distal pressure and flow velocity increased after PCI ($P<0.001$), whereas the stenosis pressure gradient decreased ($P<0.001$). Both h-SR, and h-MR, decreased significantly compared with pretreatment values ($P<0.001$), with an initial large decrease after balloon angioplasty followed by smaller decrements with subsequent treatment steps (Figure 2). Overall, h-MRv decreased by 32±31%, which accounted for 34±41% of the reduction in total coronary...
resistance at maximal vasodilation. Traditional measures of stenosis severity, such as FFR, CFVR, or relative CFVR, were all normalized after PCI (Table 2).

Table 2: Hemodynamic and angiographic characteristics of target and reference vessels

<table>
<thead>
<tr>
<th></th>
<th>Pre (n=24)</th>
<th>Balloon (n=19)</th>
<th>Stent (n=24)</th>
<th>Up-stent (n=11)</th>
<th>Reference (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>b-v (cm/s)</td>
<td>15.7±7.3‡</td>
<td>20.5±3.7†</td>
<td>21.4±7.7</td>
<td>24.0±10.9</td>
<td>21.9±8.2</td>
</tr>
<tr>
<td>h-v (cm/s)</td>
<td>27.2±15.7§</td>
<td>45.5±11.2*‡</td>
<td>58.5±16.9*</td>
<td>62.7±19.5</td>
<td>56.3±14.1</td>
</tr>
<tr>
<td>b-P_d (mmHg)</td>
<td>75.9±22.5§</td>
<td>92.0±17.0*‡</td>
<td>97.9±17.1‡</td>
<td>92.1±14.9</td>
<td>98.7±16.3</td>
</tr>
<tr>
<td>h-P_d (mmHg)</td>
<td>57.9±17.0§</td>
<td>74.3±14.6*‡</td>
<td>85.5±15.6*‡</td>
<td>76.9±13.7¶</td>
<td>93.2±14.9</td>
</tr>
<tr>
<td>b-P_a (mmHg)</td>
<td>99.1±14.9</td>
<td>94.3±15.0</td>
<td>96.4±14.3</td>
<td>90.1±15.4</td>
<td>97.2±14.5</td>
</tr>
<tr>
<td>h-P_a (mmHg)</td>
<td>41.2±17.2§</td>
<td>20.0±9.6*‡</td>
<td>10.9±10.3*‡</td>
<td>13.2±10.5¶</td>
<td>4.0±4.2</td>
</tr>
<tr>
<td>b-MR_r (CRU)</td>
<td>5.62±2.61</td>
<td>4.73±1.65</td>
<td>5.08±1.84</td>
<td>4.61±2.08</td>
<td>5.17±1.95</td>
</tr>
<tr>
<td>h-MR_r (CRU)</td>
<td>2.74±1.40¶</td>
<td>1.72±0.53‡</td>
<td>1.58±0.61‡</td>
<td>1.32±0.39¶</td>
<td>1.73±0.38</td>
</tr>
<tr>
<td>h-SR_r (CRU)</td>
<td>2.41±2.10¶</td>
<td>0.50±0.36*‡</td>
<td>0.21±0.21¶</td>
<td>0.24±0.25</td>
<td>0.08±0.08</td>
</tr>
<tr>
<td>FFR</td>
<td>0.59±0.16§</td>
<td>0.79±0.09*‡</td>
<td>0.89±0.10*‡</td>
<td>0.86±0.10*‡</td>
<td>0.96±0.04</td>
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<tr>
<td>CFVR</td>
<td>1.70±0.57§</td>
<td>2.27±0.64*‡</td>
<td>2.84±0.64*</td>
<td>2.83±0.66</td>
<td>2.76±0.73</td>
</tr>
<tr>
<td>Relative CFVR</td>
<td>0.59±0.19§</td>
<td>0.82±0.21*‡</td>
<td>1.03±0.25*</td>
<td>1.10±0.38</td>
<td>1.00±0.00</td>
</tr>
<tr>
<td>mLD (mm)</td>
<td>1.21±0.32‡</td>
<td>2.00±0.77*‡</td>
<td>3.11±0.59*‡</td>
<td>3.30±0.50‡</td>
<td>2.27±0.59</td>
</tr>
<tr>
<td>%DS</td>
<td>60.0±10.3§</td>
<td>44.1±15.7*‡</td>
<td>7.8±11.6*‡</td>
<td>1.2±8.7‡</td>
<td>16.5±9.4</td>
</tr>
</tbody>
</table>

Values are mean ± SD. b, baseline, h, hyperemia. P_d, distal pressure, P_a, aortic pressure, v, flow velocity, MR_r, microvascular resistance index, SR_r, stenosis resistance index, CRU, coronary resistance unit (mmHg/cm/sec), FFR, fractional flow reserve, CFVR, coronary flow velocity reserve, MLD, minimum lumen diameter, %DS, percent diameter stenosis. Target vessel geometry refers to treatment location. *p<0.001, †p<0.01, ‡p<0.05 compared to previous step. §p<0.01, ¶p<0.05 compared to reference vessel.

Figure 2: Decline of hyperemic stenosis (h-SR_r) and microvascular (h-MR_r) resistance index with PCI. Before treatment, h-MR_r and h-SR_r were not significantly different (p=0.3). Data are shown as mean ± SEM. *p<0.005, †p<0.02, h-MR_r compared to previous PCI-step. ‡p<0.05, h-MR_r compared to ‘Stent’ and ‘Up-stent’. 
Before treatment, h-MRV was significantly higher in the target vessel than in the reference vessel (P<0.05). h-MRV decreased progressively with restoration of distal perfusion pressure after stepwise PCI, as illustrated in Figure 3 for those lesions in which upsized stenting was performed (n=11). Incremental changes in h-MRV were significant after balloon angioplasty (P<0.01) and stenting (P<0.05) but not after upsizing of the stent. After treatment, h-MRV was lower in the target vessel compared with the corresponding reference vessel (P<0.03), although the perfusion pressure in the corresponding reference vessels was ≈11 mm Hg higher. This trend was similar for the whole group of patients after stent placement (P<0.01, Table 2). In addition, baseline P_d before PCI was correlated with h-MRV after balloon angioplasty (r=0.58, P<0.01) or stenting (r=0.68, P<0.001), as illustrated in Figure 4. The collateral index P_w/P_a was 0.23±0.07 and was unrelated to pretreatment h-MRV (r=0.28, P=0.19; Figure 5).

Figure 3: Changes of hyperemic microvascular resistance index (h-MRV) with increasing hyperemic distal pressure (h-P_d) for those lesions, where the stent was upsized (n=11). Data are shown as mean ± SEM. *p<0.01, †p<0.05 compared to previous PCI-step. ‡p<0.05 compared to ‘Stent’ and ‘Up-stent’. Aortic pressure was not different between reference and target vessels (p=0.21).
Discussion

This study clearly demonstrates a decrease in h-MR with an increase in coronary perfusion pressure in patients. The functional gain after successful PCI was thus due not only to epicardial revascularization but also to a substantial periprocedural reduction in h-MR (34% of total resistance decrease) resulting from the distal pressure...
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increase following the reduction in h-SR\textsubscript{v}. Low perfusion pressure before PCI was associated with a low postprocedural b-MR\textsubscript{v} suggesting an impaired autoregulatory capacity immediately after PCI. h-MR\textsubscript{v} in the target vessel after PCI was lower than in the reference vessel, pointing to structural vascular changes.

**Coronary Perfusion Pressure and Microvascular Resistance**

In clinical studies, it has become an accepted hypothesis that microvascular resistance during maximum hyperemia is minimal and constant.(25) However, in the experimental setting, the pressure dependence of hyperemic microvascular resistance is well established.(10) An increase in coronary pressure leads to an increase in diameter of the vasodilated vessels and hence, to a decrease in microvascular resistance.(16, 30) In patients with 2-vessel disease, we recently described regional differences in h-MR\textsubscript{v} depending on stenosis severity, and a diminished h-MR\textsubscript{v} after angioplasty. (3) It should be noted that revascularization in that study did not include stent placement, and P\textsubscript{a} was not measured in the reference vessel or after treatment, thus necessitating inclusion of possible residual epicardial vessel resistance by calculating h-MR\textsubscript{v} as P\textsubscript{a} divided by velocity. These experimental and clinical studies support the present finding that h-MR\textsubscript{v} is inversely related to distal perfusion pressure in humans. There are only a few reports by other groups about changes in hyperemic microvascular resistance after revascularization.(18, 26) Microvascular resistance in those studies was defined as the ratio of h-P\textsubscript{a} to volume flow, calculated from velocity measurements proximal to the stenosis, and vessel area, as determined by quantitative coronary angiography from angiograms obtained at baseline. Both studies reported a decrease in hyperemic microvascular resistance after PCI, which did not reach statistical significance. The methodological differences with the present study may in part explain their neutral findings.

**Alternative Mechanisms for Changes in Microvascular Resistance After PCI**

Diversification of blood flow away from the endocardium during adenosine-induced vasodilation, known as “coronary steal,” may occur before PCI, although intracoronary nitroglycerin minimizes the risk of developing coronary steal.(7, 11) Derecruitment of parallel vascular units at low perfusion pressure before PCI may also play a role.(27)
These mechanisms may coexist with pressure-induced diameter changes of dilated resistance vessels, which have been documented both in isolated hearts(10) and in vivo.(16, 19) Coronary microembolization has been implicated as a cause for decreased flow reserve due to augmented basal coronary blood flow elicited by an elevated release of endogenous adenosine.(15) An impaired absolute and relative CFVR after PCI was associated with microembolization, as indicated by elevated markers of myocardial injury.(12) α-Adrenergic receptor–mediated vasoconstriction after PCI, resulting in increased basal flow and reduced hyperemic flow, has also been cited in conjunction with a reduced flow reserve after PCI.(9) We did not determine cardiac markers of myocardial injury, but the normal values of both absolute and relative CFVR did not support the possibility of microembolization or myocardial stunning(2) as a possible cause for the observed decrease in h-MR_v or the lowered b-MR_v. The aforementioned mechanisms would furthermore tend to increase h-MR_v rather than decrease it, as observed in this study.

**Mechanism for h-MR_v Differences Between Target and Reference Vessels**

Initially, h-MR_v was higher in the stenosed target artery compared with the reference vessel, consistent with the pressure dependence of minimum microvascular resistance. In contrast, postprocedural h-MR_v of the target vessel was lower than that of the reference vessel despite a lower perfusion pressure in the target vessel, indicating structural adaptation of the arteriolar resistance vessels. A prolonged increase in tone results in inward remodeling.(1) However, when perfusion pressure is lowered, autoregulatory flow maintenance leads to reduced arteriolar tone,(5) with more dilation of subendocardial arterioles.(19) A long-term reduction in tone conceivably induces the opposite structural response, ie, outward remodeling. This would lead to a larger diameter of the dilated arterioles and a lower h-MR_v immediately after PCI-induced pressure restoration compared with the unremodeled microvasculature perfused by the reference vessel. The literature in this area is inconclusive. Inward remodeling was found in animal models distal to a severe stenosis causing chronic ischemia and myocardial hibernation.(14, 23) These exacerbated conditions were not present in our study. Outward remodeling with an increase in vessel diameter
and a decrease in basal vascular tone was found in response to hypotension.\(^{17, 34}\)

In case remodeling is the cause of a reduced h-MR\(_v\), a gradual normalization of h-MR\(_v\) can be expected at follow-up.

Remodeling of resistance vessels may also have consequences for the control of tone after PCI. b-MR\(_v\) after PCI was positively related to distal perfusion pressure before treatment. Autoregulatory adjustment of coronary resistance vessels requires a relatively higher level of tone when hyperemic diameters have increased because of outward remodeling. The remodeled resistance vessels may be unable to produce the necessary tone, and basal flow would be expected to be higher in that case, which is consistent with a 60% increase in basal flow velocity in our study group. This agrees with the findings of earlier studies, which demonstrated that elevated basal flow just after PCI decreased at follow-up, suggesting a gradual restoration of resistance vessel properties after perfusion pressure is restored.\(^{32, 33}\)

**Methodological Considerations**

PCI did not result in a complete reduction of epicardial coronary artery resistance. Additional vascular irregularities may be responsible for this result; however, this does not affect our findings regarding MR\(_v\). Resistance parameters derived from \(P_d\) and velocity measurements were shown to be highly reproducible.\(^{29}\) According to recent recommendations,\(^{6}\) the adenosine dosage was considered adequate to elicit maximal vasodilation while minimizing adverse systemic effects, as confirmed by unaltered outcomes after doubling the dosage in some patients (data not shown).

No patient had visible collaterals, and \(P_w/P_d\) was unrelated to the pre-PCI h-MR\(_v\), indicating that recruitable collateral flow was not an important confounding factor.\(^{25}\)

Although the normalization of relative flow reserve provides evidence for the absence of microembolization after PCI, the lack of creatine kinase-MB fraction measurements prevents us from definitively ruling out any influence of distal embolization on h-MR\(_v\)-measurements.

We determined a velocity-based index of microvascular resistance, which requires control of active epicardial vessel diameter with nitrates, as was done in this study. In contrast to volume flow, which depends on perfused myocardial tissue, flow velocity
is preserved from proximal to distal segments in normal coronary arteries, which indicates a relative independence of velocity from the perfused vascular volume. (24) A passive increase in distal epicardial vessel diameter after PCI-induced pressure restoration cannot be excluded and may have inversely affected flow velocity. However, this would imply a relative overestimation of posttreatment h-MR, which strengthens our conclusions. Although our findings were consistent, the selected group of patients in this study limits extension of the results to a more diverse population, in whom other mechanisms may come into play. Additional studies, including follow-up measurements, are needed to further investigate the mechanisms responsible for our findings.

Clinical Implications
This study established the feasibility of assessing the functional status of the coronary microcirculation in humans based on combined distal pressure and flow velocity measurements with use of a single, dual-sensor guidewire. This approach avoids ambiguities inherent in thermodilution-based methods regarding interpretation of the inverse of the mean indicator transit time as a surrogate for flow when the vascular tracer distribution volume is not known. (8) In addition, it allows simultaneous assessment of coronary stenosis and microvascular resistance index on a per-beat basis and the construction of stenosis pressure drop-velocity relations, (29) which is currently not possible with any other method. The pressure dependence of h-MR may provide an additional reason why h-SR is a better predictor of inducible ischemia (21) than are traditional pressure- or velocity-based functional parameters, which depend on both stenosis and microvascular resistance. (13, 20, 22) Our findings may also have implications for diagnostic methods that rely on the assumption of a constant minimal resistance across different vascular beds, such as FFR or relative CFVR, or imaging modalities based on comparison of regional myocardial perfusion. (3, 13, 22, 28) The possibility of assessing the status of the coronary microcirculation in humans by measuring the coronary microvascular resistance index opens areas of scientific inquiry into the pathogenesis, pathophysiology, and therapeutic strategies regarding coronary microvascular dysfunction that were previously restricted to experimental studies.
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Conclusions
PCI of a coronary narrowing led to a decrease not only of stenosis but also of coronary microvascular resistance index. Restoration of coronary driving pressure after PCI resulted in a reciprocal reduction in minimal microvascular resistance index during distal vasodilation, providing evidence for its pressure dependence in humans. The decrease in hyperemic MR, contributed considerably to the gain in myocardial perfusion after PCI. Low perfusion pressure before PCI was associated with a low postprocedural baseline MR, suggesting an impaired capacity for autoregulatory control possibly caused by outward microvascular remodeling.

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References
Chapter 3


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