Diagnostic Accuracy of Combined Intracoronary Pressure and Flow Velocity Information During Baseline Conditions

Adenosine-Free Assessment of Functional Coronary Lesion Severity

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Background—The assessment of functional coronary lesion severity using intracoronary physiological parameters such as coronary flow velocity reserve and the more widely used fractional flow reserve relies critically on the establishment of maximal hyperemia. We evaluated the diagnostic accuracy of the stenosis resistance index during nonhyperemic conditions, baseline stenosis resistance index, compared with established hyperemic intracoronary hemodynamic parameters, because achievement of hyperemia can be cumbersome in daily clinical practice.

Methods and Results—A total of 228 patients, including 299 lesions (mean stenosis diameter 55%±11%), underwent myocardial perfusion scintigraphy for documentation of reversible perfusion defects. Distal coronary pressure and flow velocity were assessed with sensor-equipped guidewires during baseline and maximal hyperemia, induced by an intracoronary bolus of adenosine (20–40 μg). We determined stenosis resistance (SR) during baseline and hyperemic conditions as well as fractional flow reserve and coronary flow velocity reserve. The discriminative value for myocardial ischemia on myocardial perfusion scintigraphy of all parameters was compared using receiver-operating-characteristic curves. Baseline SR showed good agreement with myocardial perfusion scintigraphy of all parameters was compared using receiver-operating-characteristic curves. Baseline SR showed good agreement with myocardial perfusion scintigraphy. The diagnostic performance of baseline SR (area under the curve, 0.77; 95% CI, 0.71–0.83) was as accurate as fractional flow reserve and coronary flow velocity reserve (area under the curve, 0.77; 95% CI, 0.71–0.83 and area under the curve, 0.75; 95% CI, 0.68–0.81 respectively; P<0.05 compared with baseline SR for both). However, hyperemic SR, combining both pressure and flow velocity information during hyperemia, was superior to all other parameters (area under the curve, 0.81; 95% CI, 0.76–0.87; P<0.05 compared with all other parameters).

Conclusions—Combined pressure and flow velocity measurements during baseline conditions may provide a useful tool for functional lesion severity assessment without the need for potent vasodilators. (Circ Cardiovasc Interv. 2012;5:508-514.)

Key Words: coronary artery disease ◼ coronary flow reserve ◼ fractional flow reserve ◼ hemodynamics ◼ physiology

Adequate patient selection for percutaneous coronary intervention is of utmost importance to avoid unnecessary complications. Consequently, objective evidence for myocardial ischemia is mandatory for optimal management of patients with coronary artery disease, in particular in patients with coronary lesions of intermediate severity (40%–70% diameter stenosis on coronary angiography). The use of sensor-equipped guidewires for the assessment of functional coronary lesion severity has emerged as a standard diagnostic modality to provide objective evidence of myocardial ischemia during catheterization. The indices derived from pressure or flow velocity measurements, fractional flow reserve (FFR) and coronary flow velocity reserve (CFVR), respectively, show a high agreement with noninvasive stress testing. Interpretation in individual cases may, however, be cumbersome. Because these indices are based on either intracoronary pressure or flow velocity, they do not differentiate between hemodynamic properties of the epicardial stenosis and the distal microvasculature, potentially leading to unfounded treatment when a single parameter is determined or to ambiguous observations when both are assessed. Combining pressure and flow velocity information, summarized by the hyperemic stenosis resistance index (HSR), was previously shown to improve diagnostic accuracy of intracoronary
hemodynamic parameters, especially in these discordant lesions.\textsuperscript{11} Importantly, where FFR and CFVR rely critically on the establishment of a maximal hyperemic state, accurate assessment of HSR is less dependent on maximal hyperemia.\textsuperscript{11}

\textbf{Editorial see p 456}

The use of intracoronary hyperemic agents in the cardiac catheterization laboratory, per definition required for assessment of FFR, CFVR, or HSR, can however be cumbersome in daily clinical practice due to their unavailability, time-consumingness, contraindications, or side effects.\textsuperscript{12,13} Furthermore, there is an ongoing debate with respect to the dose of agent needed to achieve maximal hyperemia and the site of administration to be used.\textsuperscript{14–21} Parameters requiring only baseline conditions could therefore be considered preferable to facilitate universal use of functional lesion severity assessment before coronary intervention.

Considering the previously documented high diagnostic accuracy of HSR for myocardial ischemia as well as the relative independence of HSR on maximal hyperemia, we hypothesized that the stenosis resistance index determined during baseline conditions has adequate diagnostic accuracy for functional coronary lesion severity assessment. Therefore, we compared the diagnostic accuracy of stenosis resistance index during baseline (BSR) and hyperemic conditions (HSR), as well as FFR and CFVR for myocardial ischemia assessed by myocardial perfusion scintigraphy (MPS).

\begin{table}
\centering
\begin{tabular}{|l|}
\hline
\textbf{Table 1. Definitions of the Parameters Used} \\
\hline
CFVR = hAPV/bAPV \\
FFR = mean Pdistal/mean Paorta (during hyperemia) \\
BSR = (Paorta – Pdistal)/bAPV \\
HSR = (Paorta – Pdistal)/hAPV \\
\hline
\end{tabular}
\end{table}

\textbf{WHAT IS KNOWN}

- The use of intracoronary physiology is important for guidance of percutaneous coronary intervention.
- FFR, CFVR, or HSR may be used for this purpose, but they rely critically on a maximal hyperemic state.
- The use of potent vasodilators to achieve a maximal hyperemic state can be cumbersome in daily clinical practice.

\textbf{WHAT THE STUDY ADDS}

- The BSR, a vasodilator-free parameter, results in similar diagnostic accuracy for myocardial ischemia as compared with FFR and CFVR.
- The use of potent vasodilators is cumbersome in daily clinical practice, BSR may provide a useful tool for stenosis severity assessment.

\section*{Methods}

Between April 1997 and September 2006, a total of 228 consecutive patients undergoing elective percutaneous coronary intervention for stable anginal complaints were included in the study. Patients were referred for single- or double-vessel coronary artery disease with at least one intermediate coronary lesion (40%–70% diameter stenosis on visual assessment). Exclusion criteria consisted of: ostial lesions, \textgreek{s} stenoses in the same coronary artery, severe renal function impairment (sMDRD calculated glomerular filtration rate <30 mL/min/1.73m\textsuperscript{2}), significant left main coronary artery stenosis, atrial fibrillation, recent myocardial infarction (<6 weeks before screening), left main coronary artery bypass graft surgery, or visible collateral development. The institutional ethics committee approved the study protocol and all patients gave written informed consent.

\textbf{Myocardial Perfusion Scintigraphy}

MPS was performed in all patients with the use of either \textsuperscript{99m}Tc TECHNETIUM-Labeled methoxyisobutylisonitrile or tetrofosmin (Myoview) according to a standard 2-day stress–rest protocol. Defect reversibility and localization were semiquantitatively determined by a panel of experienced nuclear medicine physicians, who were blinded to the angiographic data. Improvement at rest of more than one grade was considered to be a reversible perfusion defect. The result was considered positive when a reversible defect was allocated to the perfusion territory of the coronary artery of interest.\textsuperscript{22}

\textbf{Cardiac Catheterization and Hemodynamic Measurements}

All patients underwent cardiac catheterization within 1 week after MPS. Quantitative coronary angiography was performed offline to determine stenosis severity. Percent diameter stenosis was obtained with the use of a validated automated contour detection algorithm (QCA-CMS Version 3.32; MEDIS, Leiden, The Netherlands). Distal coronary pressure and blood flow velocity were assessed with sensor-equipped guidewires during baseline conditions and maximal hyperemia, which was induced by an intracoronary bolus of adenosine (20 \mu g for the right coronary artery and 40 \mu g for the left coronary artery). Intracoronary pressure was measured distal to the target lesion with a 0.014-inch pressure-monitoring guidewire (Volcano Corp, San Diego, CA). Coronary blood flow velocity measurements were performed directly after pressure measurements using a Doppler-tipped guidewire (Volcano Corp). Pressure- and flow velocity-derived parameters of functional coronary lesion severity were: BSR, HSR, FFR, and CFVR. The definitions of the evaluated parameters are shown in Table 1.

\section*{Statistical Analysis}

Receiver operating characteristic curves were used to compare the discriminative value of FFR, CFVR, HSR, and BSR for the presence of reversible perfusion defects by the area under the curve. Agreement with MPS outcomes was determined for HSR, FFR, and CFVR based on their respective cutoff values: 0.75 for FFR, 2.0 for CFVR, and 0.80 mm Hg · cm\textsuperscript{2} · sec for HSR. In absence of a clinically adopted cutoff value, the best cutoff value for BSR was defined as the highest sum of sensitivity and specificity. This value was subsequently used to determine agreement with MPS. False-positive and false-negative outcomes, positive and negative predictive value, and sensitivity and specificity for all parameters were defined according to the MPS outcomes using the previously mentioned cutoff values. Additionally, these were evaluated for the more recently adopted cutoff value for FFR of 0.80. Accuracy for agreement with MPS of all parameters was compared using the McNemar test. All analyses were performed at the lesion level. We additionally performed a patient-level analysis by randomly selecting one lesion per patient. Continuous variables were expressed as mean (±SD) or median (interquartile range) and comparison was performed using the Student t test or Mann-Whitney U test where appropriate. Categorical variables were presented as frequencies.
Results

Patients

A total of 228 patients (mean age, 60±11 years), including 299 coronary lesions, underwent MPS to determine the presence of reversible perfusion defects. Results for HSR have been reported previously for 151 patients, including 181 lesions.11 Baseline characteristics of all patients are shown in Table 2. Quantitative coronary angiography of the 299 lesions involved yielded a mean diameter stenosis of 55%±11%. MPS of reversible perfusion defects are listed in Table 3.

Discriminative Value

The receiver operating characteristic curves for FFR, CFVR, HSR, and BSR are visualized in the Figure. Receiver operating characteristic curve analysis yielded the highest diagnostic accuracy for myocardial ischemia when compared with CFVR.24 Pressure-derived parameters that have been investigated previously include the transstenotic pressure gradient during baseline conditions,25 resting distal pressure to aortic pressure ratio,26 the diastolic to systolic velocity ratio and the transstenotic pressure gradient during baseline conditions25 as the most frequently used method for coronary stenosis severity evaluation, FFR. Notably, accuracy of BSR was significantly higher compared with FFR with the use of 0.80 as a cutoff value. This novel approach to intracoronary pressure and flow velocity measurements may provide a useful tool for vasodilator-free stenosis severity evaluation when the use of potent vasodilators is cumbersome or contraindicated in daily clinical practice.

Evaluation of Functional Lesion Severity Without Hyperemia

Several intracoronary hemodynamic parameters for functional lesion severity assessment during baseline conditions have been investigated previously. Coronary flow-derived parameters include the diastolic to systolic velocity ratio and proximal to distal velocity ratio.23 Both parameters were, however, shown to have limited diagnostic accuracy for myocardial ischemia when compared with CFVR.24 Pressure-derived parameters that have been investigated previously include the transstenotic pressure gradient during baseline conditions,25 resting distal pressure to aortic pressure ratio,26 compared with FFR with a cutoff value of 0.80 (P=0.001; Table 6).

Discussion

The use of a parameter based on both intracoronary pressure and blood flow velocity measurements during baseline conditions, BSR, has a similar diagnostic accuracy for reversible perfusion defects on MPS as compared with the most frequently used method for coronary stenosis severity evaluation, FFR. Notably, accuracy of BSR was significantly higher compared with FFR with the use of 0.80 as a cutoff value. This novel approach to intracoronary pressure and flow velocity measurements may provide a useful tool for vasodilator-free stenosis severity evaluation when the use of potent vasodilators is cumbersome or contraindicated in daily clinical practice.

Table 2. Baseline Patient Characteristics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>N=228</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>60±11</td>
</tr>
<tr>
<td>Male sex</td>
<td>157 (69)</td>
</tr>
<tr>
<td>Coronary risk factors</td>
<td></td>
</tr>
<tr>
<td>Cigarette smoking</td>
<td>68 (30)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>85 (37)</td>
</tr>
<tr>
<td>Positive family history</td>
<td>101 (44)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>135 (59)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>33 (14)</td>
</tr>
<tr>
<td>Prior myocardial infarction</td>
<td>83 (36)</td>
</tr>
<tr>
<td>Prior coronary intervention</td>
<td>45 (20)</td>
</tr>
</tbody>
</table>

Data is presented as mean±SD or frequency (%). ACE indicates angiotensin-converting enzyme.

Table 3. Angiographic and Hemodynamic Lesion Characteristics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Reversible Defect</th>
<th>No Reversible Defect</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diameter stenosis, %</td>
<td>61±11</td>
<td>52±9</td>
<td>0.0001</td>
</tr>
<tr>
<td>Minimal lumen diameter, mm</td>
<td>1.10±0.42</td>
<td>1.39±0.40</td>
<td>0.0001</td>
</tr>
<tr>
<td>Reference vessel diameter, mm</td>
<td>2.90±0.64</td>
<td>2.92±0.67</td>
<td>0.96</td>
</tr>
<tr>
<td>CFVR</td>
<td>1.85±0.73</td>
<td>2.47±0.74</td>
<td>0.0001</td>
</tr>
<tr>
<td>bAPV, cm/sec</td>
<td>15.5±8.9</td>
<td>18.1±7.6</td>
<td>0.0001</td>
</tr>
<tr>
<td>hAPV, cm/sec</td>
<td>28.1±17.1</td>
<td>42.4±16.0</td>
<td>0.0001</td>
</tr>
<tr>
<td>FFR</td>
<td>0.65±0.19</td>
<td>0.81±0.12</td>
<td>0.0001</td>
</tr>
<tr>
<td>hPa, mm Hg</td>
<td>96.6±12.6</td>
<td>95.0±12.3</td>
<td>0.24</td>
</tr>
<tr>
<td>hPd, mm Hg</td>
<td>63.0±20.5</td>
<td>77.3±15.5</td>
<td>0.0001</td>
</tr>
<tr>
<td>HSR, mm Hg/cm/sec</td>
<td>2.07±2.44</td>
<td>0.60±1.26</td>
<td>0.0001</td>
</tr>
<tr>
<td>hDelta P, mm Hg</td>
<td>30.0 (18.5–46.5)</td>
<td>15.0 (10.0–23.0)</td>
<td>0.0001</td>
</tr>
<tr>
<td>BSR, mm Hg/cm/sec</td>
<td>1.84±2.43</td>
<td>0.54±1.10</td>
<td>0.0001</td>
</tr>
<tr>
<td>bDelta P, mm Hg</td>
<td>99.2±12.8</td>
<td>98.8±12.0</td>
<td>0.75</td>
</tr>
<tr>
<td>hPd, mm Hg</td>
<td>79.2±21.4</td>
<td>91.3±13.8</td>
<td>0.0001</td>
</tr>
<tr>
<td>bDelta P, mm Hg</td>
<td>13.0 (6.0–31.0)</td>
<td>5.0 (2.0–9.0)</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

Data are presented as mean±SD or median (interquartile range).

CFVR indicates coronary flow velocity reserve; APV, average peak flow velocity; h, hyperemia; b, baseline; FFR, fractional flow reserve; Pa, mean aortic pressure; Pd, mean distal pressure; HSR, hyperemic stenosis resistance index; delP, pressure gradient across the stenosis; BSR, baseline stenosis resistance; DS, diameter stenosis.
and the pulse transmission coefficient.\textsuperscript{27,28} None of the previously investigated nonhyperemic parameters have been implemented in clinical practice so far because of limited diagnostic accuracy or a lack of supportive data.

Most recently, Sen et al\textsuperscript{29} introduced the instantaneous wave-free ratio as a vasodilator-free pressure-derived parameter for evaluation of functional lesion severity. This novel parameter is defined as the distal pressure to aortic pressure ratio in middiastole during baseline conditions. The authors postulate that coronary resistance is stable and minimal during a specific time window during middiastole, comparable to hyperemic microvascular resistance, and therefore the distal pressure to aortic pressure ratio during this time window is expected to be similar to FFR. However, the concept of FFR is based on an assumed linear relationship between pressure and flow when microvascular resistance is expected to be minimal, during maximal vasodilation. During baseline conditions, coronary flow is autoregulated, that is, vascular tone is present, and coronary flow is relatively pressure-independent within the physiological range of pressures.\textsuperscript{7} Additionally, it has been shown at several occasions that diastolic resistance is not stable.\textsuperscript{30,31} Hence, the finding that beat-averaged hyperemic resistance equals diastolic resistance in the presence of tone lacks a theoretical basis, and one may wonder whether instantaneous wave-free ratio has a solid physiological fundament. The authors report that, overall, instantaneous wave-free ratio correlated well with FFR, but the reported correlation is predominated by patients with a highly normal FFR, and correlation within the diagnostically relevant range of FFR is notably less accurate. Although an interesting novel parameter, that may well facilitate universal use of coronary physiology in daily clinical practice, instantaneous wave-free ratio is still under investigation, and further prospective studies are needed to define its accuracy for detection of myocardial ischemia.

### Ambiguities in FFR and CFVR

As mentioned previously, assessment of both FFR and CFVR depends critically on the achievement of maximal hyperemia,\textsuperscript{8,32} which is, at times, not taken into account in daily clinical practice. Furthermore, FFR is per definition determined when microvascular resistance is lowest and constant, during maximal vasodilation. However, when microvascular disease is present or maximal hyperemia is not achieved, microvascular resistance is increased and consequently coronary

### Table 4. Diagnostic Accuracy by Area Under the Receiver Operating Characteristic curves (AUCs)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>AUC</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>BSR</td>
<td>0.77</td>
<td>0.71–0.83</td>
</tr>
<tr>
<td>HSR</td>
<td>0.81</td>
<td>0.76–0.87</td>
</tr>
<tr>
<td>CFVR</td>
<td>0.75</td>
<td>0.68–0.81</td>
</tr>
<tr>
<td>FFR</td>
<td>0.77</td>
<td>0.71–0.83</td>
</tr>
</tbody>
</table>

BSR indicates baseline stenosis resistance index; HSR, hyperemic stenosis resistance index; CFVR, coronary flow velocity reserve; FFR, fractional flow reserve.

### Table 5. Differences in Area Under the Receiver Operating Characteristic Curves (AUCs)

<table>
<thead>
<tr>
<th>Contrast</th>
<th>Difference in AUC</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BSR versus FFR</td>
<td>0.00</td>
<td>0.88</td>
</tr>
<tr>
<td>BSR versus CFVR</td>
<td>0.02</td>
<td>0.52</td>
</tr>
<tr>
<td>HSR versus FFR</td>
<td>0.04</td>
<td>0.005</td>
</tr>
<tr>
<td>HSR versus CFVR</td>
<td>0.07</td>
<td>0.02</td>
</tr>
<tr>
<td>HSR versus BSR</td>
<td>0.05</td>
<td>0.007</td>
</tr>
<tr>
<td>FFR versus CFVR</td>
<td>0.02</td>
<td>0.44</td>
</tr>
</tbody>
</table>

*HSR indicates hyperemic stenosis resistance index; FFR, fractional flow reserve; CFVR, coronary flow velocity reserve; BSR, baseline stenosis resistance index.*
flow may be reduced. This results in a decrease in maximal flow across the stenosis and an increase in distal pressure, which may result in a negative FFR even in the presence of a functionally significant stenosis.9,32,33 Conversely, a low microvascular resistance causing a high flow rate through an epicardial vessel may in the presence of a stenosis give rise to a positive FFR by increasing the stenosis pressure gradient although flow through the stenosis is normal.9,33,34 In assessment of CFVR, in addition to its sensitivity to alterations in microvascular resistance, the absolute value obtained is influenced to a large extent by variations in baseline and maximal flow velocity, which can be caused by factors not related to stenosis severity.8 Furthermore, assessment of an optimal flow velocity signal, necessary for an objective CFVR value, is more difficult than pressure measurements. Both FFR and CFVR therefore have their ambiguities when representing the only physiological parameter assessed. Although previously assumed that the combination of FFR and CFVR would improve diagnostic and prognostic value,32 it has already been shown that discordance between FFR and CFVR is present in 27% of cases,9 hampering clinical decision-making.

Indices of Stenosis Resistance
The advantage of either index of stenosis resistance is inherited by the simultaneous use of both pressure and flow velocity information, which results in the ability to assess the relative influence of microvascular and stenosis resistances (SRs). Although the previously introduced HSR11 also depends on the presence of maximal hyperemia, the pressure drop across the stenosis and flow velocity are affected similarly when the hyperemic state is suboptimal. Therefore, the effect of submaximal hyperemic flow on HSR is rather limited. Obviously, the major advantage of BSR is that it does not require a hyperemic state at all.

Overall, the assessment of indices of SR inherits the same technical difficulties accompanying Doppler flow velocity measurements in the assessment of CFVR. Importantly, because of the low pressure gradient and flow velocity during baseline conditions, small errors in pressure and flow velocity measurements may result in relatively large errors in stenosis resistance values, and therefore the use of a hyperemic agent is expected to result in an improvement of diagnostic accuracy, as is supported by the findings in the present study.

False-Positive and False-Negative Results
False-positive or false-negative results for FFR have been reported to occur in 7% to 25% of cases,11,32 and in 8% to 25% of cases11,32 for CFVR. In our study, false-positive or -negative outcomes for FFR or CFVR were present in 26% and 29% of cases, respectively (Table 6). Importantly, the shift in the cutoff value for FFR from 0.75 to 0.80, which is implemented in recent revascularization guidelines,3 would have resulted in a significant increase in nonischemic lesions that receive percutaneous coronary intervention from 16% to 27%, whereas the decrease in ischemic lesions left untreated is only minor from 10% to 8%. However, the cutoff value of 0.80 is based on studies assessing the prognostic value of FFR, which explains the lower diagnostic accuracy.36 Notwithstanding the superior diagnostic accuracy of HSR, the use of BSR notably results in a similar amount of false-positive and false-negative outcomes when compared with both FFR and CFVR and in a significant decrease in the number of inaccurately treated lesions when compared with FFR with a cutoff value of 0.80 (P=0.001).

Study Limitations
Whereas developments in wire technology have resulted in the availability of a double sensor-equipped guidewire,37 pressure and flow velocity measurements were performed subsequently with separate sensor-equipped guidewires in the present study, which could inherit a bias due to a possible location shift between simultaneous measurement. Although the technique for simultaneous measurement of coronary pressure and flow velocity is readily available, the technique is currently only minimally adopted in daily clinical practice due to the perception of clinical cardiologists and industrial partners that coronary pressure alone is sufficient for diagnostic purposes in daily coronary interventional practice. Because there is an important underdevelopment in comparison with systems measuring only intracoronary pressure, assessment of optimal intracoronary hemodynamic signals is dependent on operator experience with this specific armamentarium, and universal adoption will depend on currently ongoing technical improvements that are expected to improve the feasibility of simultaneous measurements of coronary pressure and flow in the near future.

Furthermore, as mentioned previously, there still exists debate regarding the magnitude of the adenosine dose to be used to induce maximal hyperemia. The dosage used in this study (20 μg for the right coronary artery and 40 μg for the left coronary artery) is, however, considered adequate to induce maximal hyperemia.14,15,20 Importantly, an insufficient amount of adenosine induces limited maximal flow, but stenosis pressure drop and flow velocity are affected in the same direction, limiting the effect of insufficient hyperemia on HSR.

### Table 6. Outcomes Compared With Myocardial Perfusion Scintigraphy

<table>
<thead>
<tr>
<th></th>
<th>FFR Cutoff 0.75</th>
<th>FFR Cutoff 0.80</th>
<th>CFVR</th>
<th>BSR</th>
<th>HSR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>58 (19)</td>
<td>66 (22)</td>
<td>54 (18)</td>
<td>55 (18)</td>
<td>60 (20)</td>
</tr>
<tr>
<td>False-positive</td>
<td>48 (16)</td>
<td>81 (27)</td>
<td>52 (17)</td>
<td>42 (14)</td>
<td>26 (9)</td>
</tr>
<tr>
<td>False-negative</td>
<td>31 (10)</td>
<td>23 (8)</td>
<td>35 (12)</td>
<td>32 (11)</td>
<td>29 (10)</td>
</tr>
<tr>
<td>Total inaccurate</td>
<td>79 (26)*</td>
<td>104 (35)* †</td>
<td>87 (29)*</td>
<td>74 (25)*</td>
<td>55 (18)</td>
</tr>
<tr>
<td>PPV</td>
<td>0.55</td>
<td>0.45</td>
<td>0.51</td>
<td>0.57</td>
<td>0.70</td>
</tr>
<tr>
<td>NPV</td>
<td>0.84</td>
<td>0.85</td>
<td>0.82</td>
<td>0.86</td>
<td>0.86</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>0.65</td>
<td>0.74</td>
<td>0.61</td>
<td>0.64</td>
<td>0.67</td>
</tr>
<tr>
<td>Specificity</td>
<td>0.77</td>
<td>0.61</td>
<td>0.75</td>
<td>0.80</td>
<td>0.88</td>
</tr>
</tbody>
</table>

Data are presented as frequency (%). FFR indicates fractional flow reserve; CFVR, coronary flow velocity reserve; BSR, baseline stenosis resistance index; HSR, hyperemic stenosis resistance index; PPV, positive predictive value; NPV, negative predictive value.

*P<0.005 compared with HSR.
†P<0.001 compared with BSR.
Additionally, it is important to note that the cutoff value for BSR was derived from the current data set, which provides some advantage over the other parameters for which we used prespecified cutoff values. However, the best cutoff values derived from this data set would have been 0.76 for FFR, 1.80 for CFV, and 0.81 mm Hg · cm⁻¹ · sec for HSR. The use of data-derived cutoff values would therefore not have influenced the conclusions of the present article.

Finally, the use of MPS as a gold standard for detection of myocardial ischemia has its limitations, because MPS is known to be limited in detecting true ischemia, especially in patients with multivessel disease or previous myocardial infarction, as were included in this study.

Conclusion
The use of a parameter based on both intracoronary pressure and blood flow velocity measurements during baseline conditions, BSR, has an equal diagnostic accuracy for reversible perfusion defects on MPS as compared with the most frequently used method for coronary stenosis severity evaluation, FFR. When the use of hyperemic agents is cumbersome, BSR may therefore provide a novel tool for vasodilator-free functional stenosis severity assessment. Further prospective studies are however needed to confirm these findings in the setting of contemporary physiologically guided percutaneous coronary intervention.

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Disclosures
None.

References


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In the article by van de Hoef et al, “Diagnostic Accuracy of Combined Intracoronary Pressure and Flow Velocity Information During Baseline Conditions: Adenosine-Free Assessment of Functional Coronary Lesion Severity,” which published online July 10, 2012, and appeared in the August 2012 issue of the journal (Circ Cardiovasc Interv. 2012;5:508–514), a correction was needed.

The authors discovered an inadvertent error in the baseline patient characteristics described in Table 2 and the corresponding text.

The final version of Table 2 and the corresponding text have been corrected in the online version of the article.

The authors regret this error.
Comparaison entre intervention coronaire percutanée et traitement médical optimal dans la maladie coronaire stable
Revue systématique et méta-analyse des essais cliniques randomisés

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Contexte—L’intérêt d’une intervention coronaire percutanée (ICP) dans la prise en charge des coronaropathies stables demeure controversé. Compte tenu des progrès accomplis dans les traitements médicaux et l’arrivée des stents au cours des dix dernières années, nous avons voulu savoir si le fait de pratiquer une ICP en complément du traitement médical contribuait ou non à améliorer le pronostic comparativement au traitement médical institué isolément.

Méthodes et résultats—En interrogeant les bases de données PubMed, EMBASE et CENTRAL, nous avons effectué une revue systématique et une méta-analyse des essais cliniques randomisés publiés jusqu’en janvier 2012 et qui avaient comparé la revascularisation par ICP au traitement médical optimal (TMO) chez des patients coronariens stables. Le critère de jugement principal a été la mortalité liée à une quelconque cause tandis que les critères de jugement secondaires comprenaient le décès de cause cardiovasculaire, l’infarctus du myocarde non fatal, la réalisation d’une nouvelle revascularisation et l’absence d’angor. Les analyses principales ont porté sur la plus longue durée de suivi disponible et les analyses secondaires ont été stratifiées en fonction de la durée des essais en distinguant suivis à court terme (n’ayant pas excédé 1 an), de durée intermédiaire (1 à 5 ans) et de longue durée (5 ans ou plus). Nous avons identifié 12 essais cliniques randomisés ayant porté sur un total de 7 812 patients qui satisfaisaient à nos critères de sélection. Les analyses principales ont montré que, comparativement au TMO, la réalisation d’une ICP n’avait pas significativement amélioré la mortalité globale (risque relatif [RR] : 0,85 ; intervalle de confiance [IC] à 95 % : 0,71–1,01) ni les taux de décès de cause cardioïaque (RR : 0,71 ; IC à 95 % : 0,47–1,06), d’infarctus du myocarde non fataux (RR : 0,93 ; IC à 95 % : 0,70–1,24) et de nouvelles revascularisations (RR : 0,93 ; IC à 95 % : 0,76–1,14), les résultats ayant été similaires quelle qu’eût été la durée de suivi. L’analyse de sensibilité réalisée en retenant uniquement les essais dans lesquels l’utilisation de stents avait dépassé 50 % a objectivé un aménissement de la taille de l’effet exercé par l’ICP sur la mortalité liée à toute cause (RR : 0,93 ; IC à 95 % : 0,78–1,11). En revanche, s’agissant de l’absence d’angor, la réalisation d’une ICP a significativement amélioré le pronostic comparativement au TMO (RR : 1,20 ; IC à 95 % : 1,06–1,37) et ce, à tous les temps d’évaluation.

Conclusions—Cette analyse exhaustive et extrêmement rigoureuse des essais menés chez des patients atteints de maladie coronaire stable a montré que, comparativement au TMO, la réalisation d’une ICP n’avait pas diminué les risques de mortalité, de décès de cause cardiovasculaire, d’infarctus du myocarde non fatal ou de nouvelle revascularisation. L’ICP ayant toutefois plus fortement amélioré les symptômes angineux que le TMO instauré seul, des études plus vastes et offrant davantage de puissance sont nécessaires pour confirmer cette observation. (Traduit de l’anglais : Percutaneous Coronary Intervention Versus Optimal Medical Therapy in Stable Coronary Artery Disease; A Systematic Review and Meta-Analysis of Randomized Clinical Trials. Circ Cardiovasc Interv. 2012;5:476–490.)

Mots clés : angor ■ maladie coronaire ■ traitement médical optimal ■ intervention coronaire percutanée

Valeur diagnostique des mesures combinées de la pression intracoronaire et de la vitesse du flux sanguin en conditions basales
Evaluation de la sévérité des lésions fonctionnelles coronaires sans recours à l’adénosine

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Contexte—L’appréciation de la sévérité des lésions fonctionnelles coronaires à partir des paramètres physiologiques intracoronaire tels que la réserve de vitesse du flux coronaire et la fraction de flux de réserve, d’utilisation plus courante, est hautement conditionnée par l’induction d’une hypérmédiation maximale. Nous avons évalué la valeur diagnostique de l’indice de résistance sténotique en l’absence d’hypérmétrie, c’est-à-dire dans les conditions basales, comparativement aux paramètres hémodynamiques intracoronaire ordinairement mesurés en phase hypérmérique, car l’obtention d’une telle hypérmétrie peut être malaisée en pratique clinique courante.
L’index de résistance microcirculatoire est prédic和平 du risque d’infarctus du myocarde secondaire à une intervention coronaire percutanée

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**Contexte**—Un pourcentage non négligeable de patients ayant fait l’objet d’une intervention coronaire percutanée (ICP) développent un infarctus du myocarde (IDM) périopéraatoire ayant un impact péjoratif sur le pronostic. À l’heure actuelle, aucun moyen clinique ne permet de prédire l’éventuelle survenue d’un tel événement en salle de cathétérisme cardiaque. Nous avons formé l’hypothèse que l’existence initiale d’une altération de la réserve microcirculatoire coronaire, ayant pour effet de diminuer la tolérance du patient à l’égard des agressions ischémiques, était susceptible de favoriser la survenue d’un IDM périopéraatoire et que celle-ci pouvait être anticipée en mesurant l’index de résistance microcirculatoire (IRm) pendant la réalisation de l’ICP.

**Méthodes et résultats**—L’étude a porté sur des patients consécutifs chez lesquels une lésion unique siègeant sur l’artère interventriculaire antérieure avait été traitée par ICP réglée. Une sonde munie d’un capteur de pression et de température a été employée pour mesurer l’IRm préalablement à l’intervention. Sur les 50 patients étudiés, 10 ont présenté un IDM périopéraatoire. Les analyses par régression logistique binaire effectuées sur l’ensemble des paramètres cliniques, opératoires et physiologiques ont révélé que les facteurs univariés prédictifs de la survenue d’un IDM périopéraatoire étaient l’IRm préopéraatoire (p = 0,003) et le nombre de stents utilisés (p = 0,039). L’IRm préopéraatoire a été le seul facteur prédic和平 indépendant mis en évidence par les analyses par régression bivariée pratiquées en ajustant les données en fonction de chaque covariable disponible une par une (p ≤0,02 pour toutes les analyses). L’existence d’un IRm préopéraatoire égal ou supérieur à 27 U a été prédic和平 du risque de survenue d’un IDM périopéraatoire avec une sensibilité de 80,0 % et une spécificité de 85,0 % (statistique C = 0,80 ; p = 0,003). Elle est, de fait, apparue comme un facteur indépendant à l’origine d’un risque 23 fois supérieur de survenue d’un IDM périopéraatoire (odds ratio : 22,7 ; IC à 95 % : 3,8–133,9).

**Conclusions**—Ces données portent à penser que l’état de la microcirculation coronaire joue un rôle déterminant dans la propension à développer un IDM périopéraatoire à l’occasion d’une ICP programmée. La mesure de l’IRm peut être mise à profit pour anticiper le risque de nécrose myocardique et pour décider des stratégies préventives adéquates. (Traduit de l’anglais : *The Index of Microcirculatory Resistance Predicts Myocardial Infarction Related to Percutaneous Coronary Intervention. Circ Cardiovasc Inter. 2012;5:515–522.*)

Mots clés : angioplastie ■ microvaisseaux ■ microcirculation ■ infarctus du myocarde