Corrected Coronary Flow Velocity Reserve: A New Concept for Assessing Coronary Perfusion

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OBJECTIVES

In order to limit the variability of coronary flow velocity reserve (CFVR), we analyzed which factors independently affect CFVR and established a new parameter integrating these factors.

BACKGROUND

Coronary flow velocity reserve (CFVR) is a frequently used parameter for evaluating the physiological significance of epicardial stenosis and microvascular function. Since CFVR measurements are done in substantially different hemodynamic and clinical situations, interpretation of CFVR requires correction for major influencing factors.

METHODS

In 141 patients with angina-like symptoms and angiographically unobstructed coronary arteries, intracoronary Doppler measurements were performed in at least two coronary vessels. Coronary flow velocity reserve was calculated as the ratio of hyperemic average peak velocity (hAPV), after intracoronary bolus of adenosine, to baseline average peak velocity (bAPV).

RESULTS

Analysis of covariance revealed that only bAPV ($p < 0.0001$) and age ($p < 0.0001$) were independent factors influencing CFVR. Based on a regression model for estimation of predicted CFVR values, individual CFVR values (CFVR$_{ind}$) obtained at different bAPV and age were transformed into corrected CFVR values (CFVR$_{corr}$) by relating them to a mean bAPV of 15 cm/s and a mean age of 55 years. The transformation from CFVR$_{ind}$ into CFVR$_{corr}$ for the left anterior descending artery can be done by using the following equation:

$$ CFVR_{corr} = 2.85 + CFVR_{ind} \times 10^{-0.0025 \times \log(bAPV) + 0.48 \times \log(age) + 1.16} $$

When applying this new parameter to conditions assumed to cause microvascular dysfunction, analysis showed that only patients with diabetes showed a significant decrease of traditional CFVR and CFVR$_{corr}$, whereas a history of hypertension and current smoking habit had no influence on CFVR$_{corr}$.

CONCLUSIONS

The concept of CFVR$_{corr}$ standardizes CFVR for bAPV and age as the major physiological determinants. Especially in patients with microvascular dysfunction, this approach may help to discriminate between conditions directly affecting vasodilator reserve and conditions primarily affecting bAPV. (J Am Coll Cardiol 2000;35:1713–20) © 2000 by the American College of Cardiology

Due to limitations of assessment of coronary perfusion by coronary angiography, physiological approaches have been suggested for assessing the severity of coronary stenosis. Based on the fundamental works by Gould et al. (1) who developed the concept of coronary flow reserve in general terms, Wilson and colleagues (2) introduced the concept of coronary flow velocity reserve (CFVR) as a surrogate for evaluating the physiological significance of luminal narrowing. Coronary flow velocity reserve was defined as the ratio of maximal to resting flow velocity, which represents the coronary vasodilator capacity. Although many studies have evaluated CFVR in clinical practice (3–5), the interpretation of CFVR values remains controversial. Normal values for CFVR were reported to range from 2.3 to 4.8 (6–9). Due to such variability of CFVR, it has been difficult to establish true normal values and to interpret CFVR in individual patients. It is known that factors affecting resting myocardial blood flow velocity, like heart rate (10) and blood pressure (11), can influence CFVR. Additionally, a decreased CFVR has been reported with increasing age (12) and in disorders causing an increased cardiac work load like aortic stenosis (13). Although it has been proposed to relate myocardial blood flow reserve to blood flow at rest and age (12) or to standardize for heart rate by atrial pacing (8), to our knowledge, no concept has been developed to integrate these parameters into interpretation of CFVR until now.
The goal of this study was: 1) to evaluate which factors influence CFVR in patients with angiographically unobstructed coronary arteries and to which extent these factors contribute to the variability of CFVR values, 2) to establish a model to correct CFVR for these factors, and 3) to evaluate this model in patients who meet the Doppler criteria of microvascular dysfunction as recently proposed by comparing coronary flow reserve and CFVR (14).

METHODS

Patients. The study was performed in 141 patients undergoing diagnostic coronary angiography for suspected coronary artery disease, who showed angiographically unobstructed coronary arteries (i.e., coronary arteries with an angiographically smooth silhouette). Patients with valvular heart disease, hypertrophic obstructive cardiomyopathy, dilative cardiomyopathy, endocarditis or myocarditis were excluded from the study. Doppler data were only included for further evaluation if there were no signs of myocardial bridging (15). Measurements were performed in at least two major coronary arteries, the left anterior descending artery (LAD), left circumflex artery (LCX) and right coronary artery (RCA). Patient characteristics are summarized in Table 1. All participating patients gave written, informed consent. The study was approved by the local ethical committee.

Measurement of intracoronary hemodynamic parameters. Intracoronary Doppler was performed with a 0.014 in. Doppler wire (FloWire, Cardiometrics, Corp., California), as previously validated and described by Doucette et al. (16). Electrocardiogram (ECG), coronary ostial pressure, instantaneous spectral peak velocity and time average spectral peak flow velocity were recorded on-line. Heart rate, obtained from the ECG, and blood pressure, obtained from the guiding catheter, were recorded simultaneously during Doppler flow analysis. Angiography and Doppler measurements were documented on compact disc and videotape, respectively, for off-line analysis. The position of the Doppler wire was documented by the Echomap-System (Siemens, Erlangen, Germany) in a picture—in picture mode and saved in the DICOM3 format (17).

Coronary flow velocity measurements were performed after routine coronary angiography. A 7F or 8F guiding catheter without side holes was inserted in the left or right coronary artery without damping of the aortic pressure signal. All patients received 5,000 I.E. heparin and 0.2 mg intracoronary nitroglycerine before angiography and an additional 3,000 I.E. heparin at the beginning of the intracoronary Doppler examination. The Doppler wire was advanced into the target segment of the vessel, and, after a stable and high quality baseline signal without significant artefacts was obtained, baseline parameters were recorded. Then an intracoronary bolus of 18 µg adenosine in the left or 12 µg adenosine in the right coronary artery was injected, and peak hyperemic conditions were recorded. Coronary flow velocity reserve was calculated as the ratio of hyperemic average peak velocity (hAPV) and baseline average peak velocity (bAPV) (18). All measurements were performed twice. In case of disagreement, the mean value was calculated from two consecutive measurements. Doppler measurements were performed in the LAD in segment 7 or 8, in the LCX in segment 13 and in the RCA in segment 3. All 141 angiographic catheterization procedures including Doppler measurements were performed without complications.

Statistics. As a first step, factors potentially influencing CFVR were separately explored for each vessel by univariate regression analysis. The following factors were examined: systolic blood pressure, diastolic blood pressure, heart rate, age, bAPV and body mass index (BMI). The potential influence of gender on CFVR was analyzed by unpaired t test. To normalize data CFVR values and bAPV values were

<table>
<thead>
<tr>
<th>Table 1. Patient Characteristics</th>
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<tr>
<td>Patients examined: (total No. of patients)</td>
</tr>
<tr>
<td>Women</td>
</tr>
<tr>
<td>Men</td>
</tr>
<tr>
<td>Age (yrs)</td>
</tr>
<tr>
<td>Body mass index (kg·m⁻²)</td>
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<tr>
<td>Hemodynamic parameters†:</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm Hg)</td>
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<tr>
<td>Exercise tests</td>
</tr>
<tr>
<td>Stress ECG</td>
</tr>
<tr>
<td>Number of patients</td>
</tr>
<tr>
<td>Adequate exercise end points</td>
</tr>
<tr>
<td>Positive</td>
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<tr>
<td>Negative</td>
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</table>

*Mean ± standard deviation; †during intracoronary Doppler examination. ECG = electrocardiogram.
velocity; CFVR
r values in Figure 1 indicate that only between bAPV a and 6.12). was performed using the SAS statistical package (version p values are two-sided. P values of less than 0.05 were than 2.24 (14). For evaluation of this cut-off value, only dysfunction in women was proposed when CFVR was less from female patients were included (n 135 patients). As recently proposed, microvascular results from female patients were included (n vessels. For details of descriptive statistics of intracoronary Descriptive statistics. A total of 141 patients participated log10-transformed before analysis (\( \log_{10} \))(CFVR a, bAPV a). In a second step, we performed a multiple covariance analysis to evaluate these factors simultaneously. Analysis of factors potentially affecting bAPV was also done by multiple covariance analysis. Factors included here were age, BMI, systolic blood pressure, diastolic blood pressure, heart, gender and coronary vessel. Finally, estimation of predicted values and 95% prognostic intervals for CFVR was done by regression analysis. Those factors were included that were found to be statistically significant in the second step after appropriate adjustment for multiple testing according to Bonferroni. To avoid bias by repetitive measurements in the same patient, the evaluation of CFVR and corrected coronary flow velocity reserve—CFVR a close correlation existed. A significant correlation was found between CFVR a and hAPV (\( r = 0.28; p = 0.0019 \)) in the LCX, which could not be demonstrated in the LAD (\( r = 0.05; p = 0.53 \)) and the RCA (\( r = 0.10; p = 0.28 \)). In the RCA, CFVR a was marginally but significantly related to diastolic blood pressure (\( r = 0.21; p = 0.033 \)), whereas no correlation existed between these parameters in each coronary vessel showed no statistically significant influence on CFVR a after adjustment for multiple testing (Table 3). Analysis of covariance was performed for bAPV in order to examine interactions between the variables tested. By this analysis, statistically significant associations between bAPV a and systolic blood pressure, heart rate, BMI and gender were detected, whereas age, diastolic blood pressure and the coronary vessel showed no effect. Regression model for predicting CFVR on the basis of bAPV and age. As only bAPV and age were found to be relevant predictors of CFVR, we developed a regression model by which predicted CFVR values (CFVR pred) could be estimated for a given bAPV and age. Since intracoronary Doppler measurements were performed in at least two coronary vessels in all patients, the equation was developed for each vessel separately. Based on the results in Table 4, predicted CFVR values can be calculated by the following equations:

LAD:

\[
\text{CFVR}_{\text{pred}} = 10^{1.16 - 0.48 \log(bAPV) - 0.0025 \times \text{age}} (r = 0.71, p < 0.0001).
\]

LCX:

\[
\text{CFVR}_{\text{pred}} = 10^{1.14 - 0.45 \log(bAPV) - 0.0031 \times \text{age}} (r = 0.63, p < 0.0001).
\]

RCA:

\[
\text{CFVR}_{\text{pred}} = 10^{1.15 - 0.50 \log(bAPV) - 0.0021 \times \text{age}} (r = 0.67, p < 0.0001).
\]

Table 5 summarizes predicted CFVR values and 95% prognostic intervals for the mean age of 55 years and mean bAPV of 15 cm/s. Results were corresponding in all three coronary vessels, and no relevant differences existed.

Method for standardization of CFVR values for bAPV and age. After adjusting for multiple testing according to Bonferroni, CFVR was related only to bAPV and age. We developed a method for correcting CFVR values for these two parameters. To provide comparability of individual CFVR values (CFVR ind) obtained at different bAPV and

Table 2. Descriptive Statistics of Intracoronary Doppler Measurements

<table>
<thead>
<tr>
<th></th>
<th>LAD Mean ± SD</th>
<th>LCX Mean ± SD</th>
<th>RCA Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of vessels</td>
<td>135</td>
<td>116</td>
<td>103</td>
</tr>
<tr>
<td>bAPV (cm/s)*</td>
<td>15.6 ± 6.4</td>
<td>15.6 ± 5.8</td>
<td>12.9 ± 5.3‡</td>
</tr>
<tr>
<td>hAPV (cm/s)</td>
<td>43.6 ± 13.0</td>
<td>42.6 ± 13.5</td>
<td>38.9 ± 10.7‡</td>
</tr>
<tr>
<td>CFVR a</td>
<td>3.0 ± 0.8</td>
<td>2.8 ± 0.8</td>
<td>3.2 ± 0.9</td>
</tr>
</tbody>
</table>
|                      | \( p < 0.05 \) as compared with LAD; \( p < 0.01 \) as compared with LAD; \( p < 0.05 \) as compared with LCX; \( p < 0.01 \) as compared with LCX. 
| \( ^* \) = \( \log_{10} \) transformed for statistical analysis; hAPV = baseline average peak velocity; CFVR = coronary flow velocity reserve; hAPV = hyperemic average peak velocity; LAD = left anterior descending artery; LCX = left circumflex artery; RCA = right coronary artery. |
ages, we standardized CFVR values on a bAPV of 15 cm/s and an age of 55 years. These values were used because they represent the mean values of these parameters in our study population. Corrected coronary flow velocity reserve values can be calculated using the following equations:

\[
\text{CFVR}_{\text{corr}} = 2.85 \cdot \text{CFVR}_{\text{ind}} / \text{CFVR}_{\text{pred}}
\]

\[
= 2.85 \cdot \text{CFVR}_{\text{ind}} \cdot 10^{0.48 \cdot \log_{10}(\text{bAPV}) + 0.025 \cdot \text{age} - 1.16}
\]

Figure 1. Univariate regression analysis between systolic pressure, diastolic pressure, heart rate, age, baseline average peak velocity (bAPV), hyperemic average peak velocity (hAPV), body mass index (BMI) and coronary flow velocity reserve (CFVR). Values are plotted against log\(_{10}\)-transformed CFVR values. Results are shown for the left anterior descending artery (LAD).
By standardizing CFVR values for both bAPV and age, the variability of CFVR values could be significantly reduced in all three vessels (Fig. 2).

Application of corrected CFVR to factors assumed to cause microvascular dysfunction. Univariate regression analysis showed that there was a significant correlation between CFVR and bAPV, systolic blood pressure, heart rate and age. The new parameter CFVR corr was independent of these factors.

Twelve of 65 women patients (31%) presented with a CFVR of less than 2.24 in the LAD, the cut-off value recently proposed for microvascular dysfunction in women (14). These women with suspected microvascular disease showed a significantly increased bAPV and systolic blood pressure as compared with patients with CFVR $\geq 2.24$ (Table 6).

Patients were categorized according to risk factors for microvascular dysfunction. Patients with a history of hypertension showed a significantly increased bAPV and significantly reduced CFVR, whereas the CFVR corr showed no difference. Patients with diabetes mellitus had a significantly reduced CFVR and CFVR corr. No difference with regard to bAPV was observed between patients with diabetes and without diabetes. Smokers had a significantly increased bAPV and a significantly reduced CFVR. No difference was observed for CFVR corr. Cholesterol levels neither affected traditional CFVR nor CFVR corr (Table 7).

**DISCUSSION**

The primary finding of this study is that baseline peak velocity and age are significant determinants of CFVR in patients with angiographically unobstructed coronary arteries. In a univariate regression model, heart rate, blood pressure, gender, age and bAPV correlate with CFVR. Analysis of covariance revealed that bAPV and age are the only two independent factors influencing CFVR. The results suggest that effects of gender, blood pressure and heart rate are mediated by bAPV. Additionally, our analysis showed that age, although significantly related to CFVR, contributes only a minor part to overall correlation. To improve the quality of interpreting individual CFVR values in the catheterization laboratory, we developed an equation for correcting CFVR values for the variables bAPV and age.

| Table 3. Analysis of Covariance of CFVR$^a$ |  |
|---|---|---|
| Variable | Beta (SE beta)$^b$ | p Value |
| Age | $-0.0020 (0.0005)$ | 0.0001* |
| Body mass index | $-0.0003 (0.0012)$ | 0.8155 |
| Systolic blood pressure | $-0.0005 (0.0003)$ | 0.0502 |
| Diastolic blood pressure | $0.0014 (0.0005)$ | 0.0034 |
| Heart rate | $-0.0009 (0.0004)$ | 0.0199 |
| Gender (male vs. female) | $0.0301 (0.0117)$ | 0.0106 |
| bAPV$^a$ | $-0.3835 (0.0371)$ | 0.0001* |
| Vessel |  |
| LAD vs. RCX | $-0.0106 (0.0247)$ |  |
| LAD vs. RCA | $0.0024 (0.0264)$ | 0.6650 |

$^a$After adjustment for multiple testing according to Bonferroni p $< 0.003$ was assumed as statistically significant. $^b$log10 transformed for statistical analysis; $^b$SE $\beta$, standard error of $\beta$ coefficient.

| Table 4. Multiple Regression Analysis of CFVR$^a$ Used for Prediction |  |
|---|---|---|
| Artery Variable | r | Intercept |
| LAD | 0.71 | 1.1591 |
| Age |  | $-0.0024 (0.0006)$ | 0.0002 |
| bAPV$^a$ |  | $-0.4841 (0.0439)$ | 0.0001 |
| LCX | 0.63 | 1.1393 |
| Age |  | $-0.0031 (0.0008)$ | 0.0001 |
| bAPV$^a$ |  | $-0.4516 (0.0588)$ | 0.0001 |
| RCA | 0.67 | 1.1461 |
| Age |  | $-0.0021 (0.0008)$ | 0.0001 |
| bAPV$^a$ |  | $-0.5006 (0.0565)$ | 0.0001 |

$^a$SE $\beta$ = standard error of beta coefficient; bAPV$^a$ = log 10 transformed baseline average peak velocity; LAD = left anterior descending artery; LCX = left circumflex artery; r = coefficient of correlation; RCA = right coronary artery.

| Table 5. Predicted Values of CFVR |  |
|---|---|---|
| Artery | Predicted Value of CFVR at bAPV $= 15$ and Age $= 55$ (95% Prognostic Interval) |
| LAD | 2.85 (1.91–4.25) |
| LCX | 2.73 (1.74–4.29) |
| RCA | 2.78 (1.83–4.22) |

CFVR = coronary flow velocity reserve; LAD = left anterior descending artery; LCX = left circumflex artery; RCA = right coronary artery.
Factors affecting CFVR. In humans under experimental settings, coronary flow reserve decreases progressively as
heart rate increases (8,10). The reduction in coronary flow reserve is almost entirely caused by an increase in coronary
flow velocity at rest, whereas hyperemic flow is unchanged. Furthermore, patients with aortic stenosis (13) and arterial
hypertension (11), disorders characterized by an increased cardiac work load and, thereby, an increased myocardial
resting blood flow, have been shown to have a reduced CFVR. These observations suggest that an increased base-
line coronary flow velocity may contribute to the reduced CFVR in these patients. This hypothesis is endorsed by the
close correlation between bAPV and CFVR in the current study. A potential explanation for this interaction might be
that even small differences in cardiac work load lead to an increased basal flow velocity in coronary arteries and,
thereby, exhaust parts of the coronary reserve to fulfill increased demands. Since bAPV was significantly related to
BMI, systolic blood pressure and gender in this study, the results suggest that changes of bAPV are the summed effect
of these factors. The new parameters, CFVRcorr, showed no

relation to these factors and offer the advantage of being independent from these hemodynamic parameters.

CFVR in microvascular disease. Apart from evaluating the physiological significance of epicardial stenoses, intra-
coronary Doppler has become an important tool in patients with suspected microvascular disease. Recent studies report
an impaired coronary flow reserve in patients with diabetes mellitus, hypertension and smoking (11,19–22). These
findings are attributed to abnormalities in coronary vaso-
motion. It has been proposed that a coronary flow reserve of
less than 2.5 (23) and a CFVR of less than 2.24 (14) in the
absence of significant epicardial stenosis is a sign of micro-
vascular dysfunction. Categorizing women in this study
according to the cut-off value for CFVR of 2.24 revealed
that women with suspected microvascular dysfunction have a significantly increased bAPV, and systolic blood pressure.
As these factors may, in part, contribute to the reduction of
CFVR, the use of traditional CFVR as an indicator of
microvascular dysfunction may not sufficiently discriminate
between factors affecting vasodilator reserve and baseline
flow velocity.

In our patients a reduced CFVR was observed for arterial
hypertension, diabetes mellitus and smoking, whereas only
patients with diabetes also had a decreased CFVRcorr.
However, hypertensive patients and smokers had a signific-
antly increased bAPV. As CFVRcorr corrects CFVR for
bAPV and age, our data suggest that the reduced CFVR in
hypertensive patients and smokers is, in part, caused by the
increased bAPV and not predominantly by abnormalities in
CFVR. On the other hand, patients with diabetes seem to
have a dysfunction of endothelium-independent vasomo-
tion, which cannot be attributed to changes in basal flow
velocity. Correcting CFVR for baseline flow velocity and
age may help to discriminate between conditions directly
affecting coronary vasodilation and conditions increasing
baseline flow velocity. This concept is supported by the
observation that histologically confirmed microvessel dis-
ease is often accompanied by slow flow phenomenon re-
flecting decreased resting flow velocity (24). In particular,
patients with decreased bAPV showed high traditional
CFVR values in this study.

Standardization of CFVR. Under experimental settings
McGinn et al. (8) could demonstrate that CFVR was

<table>
<thead>
<tr>
<th>Parameter</th>
<th>CFVR &lt; 2.24 (n = 20)</th>
<th>CFVR ≥ 2.24 (n = 45)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>bAPV</td>
<td>23.7 ± 5.8</td>
<td>16.4 ± 6.1</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td>171 ± 35.4</td>
<td>147 ± 27.5</td>
<td>0.0027</td>
</tr>
<tr>
<td>Heart rate</td>
<td>88 ± 15.1</td>
<td>81 ± 17.3</td>
<td>0.11</td>
</tr>
<tr>
<td>Age</td>
<td>57 ± 15.7</td>
<td>56 ± 10.5</td>
<td>0.67</td>
</tr>
</tbody>
</table>

bAPV = baseline average peak velocity; CFVR = coronary flow velocity reserve; LAD = left anterior descending artery.
significantly affected by heart rate and pulmonary capillary wedge pressure. The observed changes were mediated by alterations in resting coronary flow velocity, whereas hyperemic flow velocity remained unchanged. To obtain a proper interpretation of CFVR measurements, they proposed to standardize CFVR by measuring at a paced heart rate of 100 beats/min. Although McGinn’s approach and the concept of CFVRcorr reflects the same intention to eliminate hemodynamic factors affecting CFVR, maintaining a certain heart rate by pacing requires major effort in the catheterization laboratory and does not reflect the physiological stimulation of the heart. Thus, a direct correction of CFVR for bAPV and age may be more advantageous.

**CFVR in assessing the hemodynamic significance of coronary stenoses.** Angiography yields only a limited anatomic assessment of coronary vessels, which allows no reliable prediction as to whether a stenosis causes exercise-induced ischemia (25,26). Coronary flow velocity reserve measurements have become an important issue in establishing indications of coronary interventions and evaluating their results (27,28), in particular as exercise tests documenting ischemia are often not performed before angioplasty (29). The Functional Angiometric Correlation with Thallium Scans Study Group recently reported an 88% agreement between $^{201}$TI imaging and intracoronary Doppler measurements using a cut-off value of 1.7 for CFVR (30). In order to improve reliability of CFVR in evaluating the significance of a coronary stenosis, the concept of relative flow reserve has been reintroduced into clinical application (31). The objective of this approach was to eliminate factors influencing CFVR like blood pressure, heart rate and microvascular dysfunction, which affect all myocardial perfusion territories in a similar fashion. This leads to a marked improvement of specificity and sensitivity. Since correction is done intraindividually by comparing target-vessel CFVR values with values obtained in a reference vessel, relative flow reserve might be superior to the concept of CFVRcorr in the presence of an epicardial stenosis. A shortcoming of this concept is that it requires measurements in at least two coronary arteries, of which one has to be definitely unobstructed. Corrected coronary flow velocity reserve may increase quality of interpretation in patients who are not eligible for the concept of relative flow reserve and in patients without obstructed epicardial arteries.

**Study limitations.** This investigation was performed in patients with angiographically unobstructed coronary arteries. It has been demonstrated by intracoronary ultrasound that plaque formation can be found in up to 50% of patients with normal appearing coronary arteries (32). Although we think that these early signs of atherosclerosis do not affect the observed relation between resting blood flow, age and CFVR, further studies with simultaneous intravascular ultrasound and Doppler measurements will have to clarify this point.

A limitation of this study is that the investigated patients cannot be taken as truly normal. All presented with angina suspicious for obstructed coronary artery disease. Since patients with valvular heart disease or myocarditis did not participate in the study, microvascular disease must be assumed in a significant part of these patients. However, the aim of this study was to disclose factors affecting CFVR in a large population with unobstructed coronary arteries as found in daily practice in the catheterization laboratory. With respect to coronary interventions, the validity of the concept has to be examined in patients with coronary stenoses where a physiological assessment is mandatory for decision-making. Before proposing this concept for clinical practice, a clear-cut threshold must be established for determination of the functional relevance of coronary stenosis.

**Clinical implications.** The concept of CFVRcorr standardizes CFVR for bAPV and age as the main determinants. This approach significantly reduces the high variability of CFVR. The new equations offer a practical method for a
physiological assessment of CFVR measurements in the catheterization laboratory in individual patients. As some disorders suspected to cause microvascular dysfunction also affect baseline coronary flow velocity, CFVRcorr should be integrated in the evaluation of microvascular function. This concept may give additional information in the assessment of small vessel disease and may help to discriminate between changes of resting flow velocity and vasodilator reserve.

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REFERENCES