Frame Count Reserve

Martin G. Stoel, MD; Felix Zijlstra, MD, PhD; Cees A. Visser, MD, PhD

Background—The Doppler wire–derived (relative) coronary flow velocity reserve (CVR) that is used to evaluate functional significance of a coronary stenosis is a method performed only by interventional cardiologists. An angiographic method would be useful in the diagnostic catheterization laboratory. For this purpose, we investigated the relation between TIMI frame count reserve (FCR) and CVR.

Methods and Results—In 38 patients, (relative) FCR of left anterior descending (LAD) and left circumflex coronary artery (LCx) was calculated by using manual, synchronized contrast agent injections and compared with (relative) CVR. In addition, vessel length was measured with an intracoronary guidewire and frame count flow velocity was calculated and compared with average peak velocity. There was a strong correlation between FCR and CVR ($r=0.62$, $P<0.001$) and between relative FCR and relative CVR ($r=0.84$, $P<0.001$). The LAD was significantly longer than the LCx (mean, 14.3±1.6 cm versus 11.4±1.8 cm, $P<0.001$), and, therefore, TIMI frame count of LAD was significantly higher than of LCx (mean basal 32.5±15.1 versus 23.6±9.1 and hyperemic 12.1±6.6 versus 8.7±3.2, both $P<0.02$). However, all flow velocity measurements and estimations of volume flow were not different for LAD compared with LCx. There were also no differences between mean FCR and CVR of LAD or LCx, of both vessels compared with each other and between relative FCR and relative CVR.

Conclusion—The (relative) frame count reserve can be used to estimate (relative) coronary flow velocity reserve.

(Circulation. 2003;107:3034-3039.)

Key Words: coronary disease ■ blood flow ■ angiography
hospital of the Free University Amsterdam, the Netherlands, approved the protocol. All patients gave written informed consent.

**Procedure**

One operator (M.S.), using 7F guiding catheters without side holes (Guidant) and ionic contrast agent (Hexabrix, Guerbet), performed all procedures. At the beginning of the procedure, an intravenous bolus of heparin (5000 IU) was given. In all but 1 case of PCI, a stent was implanted; there were no residual stenoses >30%. More than 5 minutes before angiography (Philips Integril 3000, 25 frames/s) and Doppler measurements (Cardiomedics), 0.2 to 0.4 mg intracoronary nitroglycerine was given. Angiography (right anterior oblique with caudal angulation without magnification) was performed by manual injection through the contrast-filled guiding catheter, synchronized to an acoustic heart beat signal. It was performed at least 10 minutes after last balloon inflation and 2 minutes after last contrast injection to prevent reactive hyperemia attributable to ischemia or contrast agent.

**Protocol and Calculations**

After positioning the Doppler wire in a normal segment of LAD or LCx, as proximal as possible but >2 cm distal to the culprit lesion if present, basal TFC of both vessels was measured. Basal APV was measured using the contrast-filled catheter as reference diameter/2. Coronary volume flow was estimated by the following equation: flow (mL/min) = FCV (cm/s) × 60 × π × (diameter/2)^2.

A coronary vascular resistance index (mm Hg per mL/min) was calculated by dividing mean arterial blood pressure by coronary flow, assuming right atrium pressure was zero.

**Statistical Analysis**

For statistical analysis, Student’s unpaired t-test and linear regression analysis (SPSS 9.0) were used. All continuous variables are expressed as mean±1 SD with their range. P<0.05 was considered statistically significant.

**Results**

In 9 patients, both LAD and LCx were normal; in 11 patients, there was visually no significant (<50%) stenosis in LAD and LCx; and in 13 patients, either the proximal LAD (8...
patients) or proximal LCx (5 patients) had significant stenosis for which angioplasty was thought appropriate. In 5 patients with intermediate (50% to 70%) lesions, PCI was deferred because of CVR >2.0 and rCVR >0.65. In 2 patients, the study protocol was terminated early, 1 because of advanced atrioventricular block during adenosine infusion and 1 because of damping of the pressure signal of the guiding catheter during hyperemia. Final analysis consisted of 96 flow velocity reserve measurements performed in 38 patients.

**Characteristics**

Baseline and procedure characteristics are listed in Table 1. In 4 patients, the length of LAD (3 patients) or LCx (3 patients) was not measured, mainly because of severe tortuosity. Most patients used β-blockers. The LAD was significant longer by a factor of 1.3 compared with the LCx (mean, 14.3±1.6 cm versus 11.4±1.8 cm, P<0.001), whereas there were no differences in diameter of proximal segments (mean 3.2±0.6 mm versus 3.3±0.6 mm) and percentage stenosis of the target lesion. During hyperemia, there was significant decrease in blood pressure (mean 100.7±10.8 to 93.4±10.4 mm Hg, P<0.005) and significant increase in heart rate (mean 67.4±9.0 to 76.3±9.9/min, P<0.005). The mean time interval between last QRS complex and first frame included in the TFC was 370±9 ms. The mean difference between basal and hyperemic injection in relation to the cardiac cycle was 0.07±0.06 seconds.

**Measurements**

The results of 48 paired (both LAD and LCx) measurements are displayed in Table 2, consisting of 38 patients with repeated protocol after PCI in 10 cases. The values of FCV, volume flow, and resistance index were derived from 44 paired measurements. In 3 vessels, CVR was not measured because the Doppler wire was not repositioned in the nontarget vessel after PCI. TFC of LAD was significantly higher than TFC of LCx (basal 32.5±15.1 versus 23.6±0.1 and hyperemic 12.1±6.6 versus 8.7±3.2, both P<0.02), but there were no significant differences in mean basal and hyperemic flow velocity, flow velocity reserve, volume flow, and resistance index between the vessels. Mean FCR and rFCR did not differ significantly from mean CVR and rCVR.

The results of 30 paired (both LAD and LCx) measurements concerning only coronary arteries without visually significant (<50%) stenosis are listed in Table 3, consisting of 20 patients without significant stenosis at baseline and 10 paired measurements after PCI. Again, TFC of LAD was significant higher than TFC of LCx (basal 35.1±17.0 versus 25.1±9.5 and hyperemic 10.3±3.6 versus 8.3±2.7, both P<0.02), without significant differences in mean basal and hyperemic flow velocity, flow velocity reserve, volume flow, and resistance index between the 2 vessels. As in the total group, mean FCR and rFCR did not differ significantly from mean CVR and rCVR.

Discussion

In this study, the FCR, an angiographic method using TIMI frame count to estimate coronary blood flow velocity reserve, was compared with Doppler wire--derived CVR. The results demonstrate strong correlation between (r)FCR and (r)CVR.
There were no significant differences between mean (r)FCR and mean (r)CVR.

In contrast to normal basal flow velocity, when the coronary artery is usually filled with contrast in 1 complete cycle of the heart (including systole with relative low flow velocity), high coronary flow velocity during hyperemia can cause contrast filling within 1 diastole (with relative high flow velocity). This will result in an augmented FCR compared with CVR in which peak flow velocity is averaged during diastole as well as systole. This can explain the fact that the correlation of FCR and CVR is not so good in the range of high (>3.0) flow velocity reserve compared with low (<3.0) flow velocity reserve, as shown in Figure 1. Low heart rate with relatively more influence from diastole can contribute to this effect, but in this study population, heart rate during hyperemia was higher compared with basal heart rate. In addition, the influence of the moment of contrast injection in relation to the cardiac cycle is more important in case of low TFC (high flow velocity or relative short vessels) compared with high TFC. Because CVR of 2.0 is used as cutoff value, the weaker correlation of values >3.0 has few clinical implications.

The correlation of rFCR and rCVR is stronger also in high values, as is shown in Figure 2, because differences in methods of flow velocity assessment are partially normalized, just like influence of microvascular resistance.

Comparison With Previous Studies
The findings are in accordance with the study by Manginas et al., which is the only other study comparing the TIMI frame count method to CVR. In that study, contrast agent was also

![Figure 1](image1.png)  
**Figure 1.** Relation between FCR and CVR, n=96 measurements.

![Figure 2](image2.png)  
**Figure 2.** Relation between rFCR and rCVR, n=45 measurements.
enough to show diffuse lumen narrowing causing flow completely normal because angiography is often not sensitive which Doppler measurements are performed are not always correction should not be necessary. However, segments in differences in proximal and distal flow velocity, additional Because in normal coronary arteries there are no significant APV by a factor of 0.518 or by using the velocity integral. A comparison between FCV and APV, n=174 measurements.

injected manually, but adenosine was given by intracoronary injection. However, because of the short half-life time of adenosine, it is difficult to inject the agent consistently in the maximal hyperemic phase. With intravenous adenosine, a steady state of hyperemia can be obtained, making it possible to inject contrast during maximal hyperemia and easier to synchronize injection to the cardiac cycle, resulting in a more accurate hyperemic TFC. As pointed out by Abaci et al., the phase of the cardiac cycle in which the contrast agent is injected has important influence on TFC. In the present study, there were only small differences in the timing of contrast injections, beginning at or near the end of the T wave, just before diastole.

The FCR using intracoronary adenosine was measured in a trial evaluating eptifibatide, and it correlated highly with digital subtraction angiographic reserve (r=0.76, P<0.001). All TFC (but not the ratios) found in the present European study can only be compared with US studies after being multiplied by a factor of 1.2 to convert to a frame rate of 30 per second. To the best of our knowledge, this is the first study to measure relative FCR and compare it with relative CVR.

Flow Velocity Measurements
A comparison between FCV and APV is complex. With the Doppler wire, peak blood flow velocity is measured locally, averaged during 2 cycles of the heart. It has to be converted to a mean velocity, compensating for lower blood flow velocity near the vessel wall. This can be done by multiplying APV by a factor of 0.518 or by using the velocity integral. Because in normal coronary arteries there are no significant differences in proximal and distal flow velocity, additional correction should not be necessary. However, segments in which Doppler measurements are performed are not always completely normal because angiography is often not sensitive enough to show diffuse lumen narrowing causing flow velocity acceleration or a positive remodeled vessel segment with possible influence on flow velocity assessment. In addition, in stenosed arteries, flow velocity can be higher proximal to the lesion compared with distal because of proximal side branches. This will influence FCV but not distal APV. Finally, length of the coronary artery measured with the guidewire and thus FCV can be underestimated because the wire takes the shortest way along the curves of the vessel. As discussed above, FCV can be overestimated when flow velocity is so high that contrast filling of the coronary artery takes place only in diastole. Figure 3 shows the good correlation between FCV and APV (r=0.75, P<0.001). In this population the ratio of mean APV and FCV was 0.63.

Comparison Between LAD and LCx
Basal and hyperemic TFCs of LAD were significantly higher compared with LCx (basal 32.5±15.1 versus 23.6±9.1 and hyperemic 12.1±6.6 versus 8.7±3.2, both P<0.02). The ratio of TFC of LAD and LCx is 1.4, whereas the ratio of length of both vessels is 1.3. This is less than the factor of 1.7 used to adjust TFC of LAD to derive the corrected TFC because the latter was corrected to mean TFC of both LCx and right coronary artery. In the present study, after adjusting TFC to the specific length of the artery, all basal and hyperemic mean blood flow velocity measurements were equal in both vessels. In addition, there were no significant differences in FCR and CVR of LAD compared with LCX. Because the proximal vessel diameter of both vessels was the same, there were also no differences in mean volume flow and resistance index.

Measurements in Nonsignificant Diseased Vessels
Table 3 shows the results of measurements in coronary arteries with visually no stenosis >50%. Mean normal basal FCV of LCA is 12.6±4.5 cm/s and hyperemic 38.0±10.5 cm/s, without differences between LAD and LCx. With this method, estimated volume flow of the LCA is basal 137.5±69.6 and 423.4±198.2 mL/min during hyperemia. However, above-mentioned considerations concerning FCV also apply here. In addition, these results cannot be interpreted as completely normal values because some of these patients had possible microvascular dysfunction (hypertension, dyslipidemia), causing lower hyperemic mean flow velocity with lower flow velocity reserve. Moreover, in 10 patients, measurements were also performed after PCI. Mean basal FCV after angioplasty was borderline significantly higher compared with the total group (15.8±5.2 versus 12.6±4.5 cm/s, P=0.032), causing a (not significant) lower FCR (2.7±1.1 versus 3.3±1.1). This is in accordance with previous studies in which high basal flow velocity after angioplasty and stenting sometimes persisted for longer than 10 minutes after the procedure because of persistent low microvascular resistance. Finally, a visual stenosis of <50% can sometimes unexpectedly prove to be functionally significant, and nonsignificant but diffuse epicardial stenosis can cause so much resistance that it impairs flow velocity reserve.
Limitations
All procedures were done by a single operator using manual contrast agent injections. Because timing of injection in relation to the phase of the heart cycle is important, it was synchronized to an acoustic heart beat signal. To do this, a basic sense of rhythm is needed. An alternative is the use of an ECG-triggered mechanical injector, but that was not done in this study because diagnostic coronary angiography is usually performed with manual injections. In addition, it has been shown that the impact of the injection rate on the TFC is only minor.

During adenosine infusion, there was a limited but significant drop in blood pressure with an increase in heart rate, as has been described by others. Therefore, hyperemic APV and FCV and thus flow velocity reserve were possibly underestimated.

All measurements were done in LAD and LCx. It is likely but not certain that these results are applicable to the right coronary artery.

The study population consisted of patients who were asymptomatic or had stable angina. Therefore, results may not be applicable to patients with acute coronary syndromes, for example, because flow in normal reference vessels can be impaired.

Conclusion
This study shows that the FCR and rFCR can provide a good estimate of CVR and rCVR. This relative simple, fast, and inexpensive angiographic method can be used during diagnostic catheterization to assess functional significance of a coronary stenosis and, in absence of coronary stenosis, to evaluate microvascular function.

References
Frame Count Reserve
Martin G. Stoel, Felix Zijlstra and Cees A. Visser

Circulation. 2003;107:3034-3039; originally published online June 9, 2003;
doi: 10.1161/01.CIR.0000074279.44131.DE
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2003 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://circ.ahajournals.org/content/107/24/3034

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published
in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial
Office. Once the online version of the published article for which permission is being requested is located,
click Request Permissions in the middle column of the Web page under Services. Further information about
this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/