Prediction of Restenosis After Coronary Angioplasty by Use of a New Index

TIMI Frame Count/Minimal Luminal Diameter Ratio

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Background—It has been shown recently that postangioplasty coronary flow reserve and the degree of residual stenosis have a modest predictive value for short- and long-term clinical outcomes after coronary angioplasty. Corrected TIMI frame count (CTFC) is a simple quantitative index of coronary blood flow. Its relationship with Doppler coronary flow velocity and clinical outcome after coronary angioplasty has not been fully clarified. The aim of this study was to identify clinical, angiographic, and functional predictors of clinical and angiographic restenosis after conventional coronary angioplasty.

Methods and Results—We studied 70 consecutive patients in whom intracoronary Doppler flow-velocity measurements were performed before and after angioplasty. Patients were evaluated for restenosis by clinical follow-up, exercise stress test/201 Tl scintigraphy, and follow-up angiography, which was performed at 10.5 ± 10.3 months in 63 patients. According to the results of univariate analysis, a new index, postangioplasty CTFC/minimal luminal diameter (MLD) ratio, was created. Multivariate analysis revealed that CTFC/MLD ratio was the only independent predictor of angiographic (OR 2.02; 95% CI 1.37 to 2.97; \( P \), 0.0004) and clinical (OR 1.60; 95% CI 1.15 to 2.21; \( P \), 0.005) restenosis. The receiver operating characteristic curve area of this index was 79% for angiographic and 73% for clinical restenosis. The optimal CTFC/MLD ratio cutoff values were 7.88 for angiographic and 7.94 for clinical restenosis, respectively.

Conclusions—Our data indicate that postangioplasty CTFC/MLD ratio, which incorporates both the angiographic and functional features of coronary lesions, is a reliable, objective, and inexpensive index for prediction of angiographic and clinical restenosis after conventional coronary angioplasty. (Circulation. 2000;101:962-968.)

Key Words: angioplasty • blood flow • restenosis • coronary disease

Restenosis remains the most important limitation of PTCA. A number of clinical, angiographic, and procedural factors3-7 have been reported to be related to increased risk of restenosis. It appears that the most important predictive factor is a small postprocedural luminal diameter, regardless of the device used.1,5 However, in large clinical studies, the predictive power of all these variables has been poor. The inability of angiography to accurately define the arterial lumen after angioplasty has prompted clinicians to search for alternative methods for the functional assessment of angioplasty results.8-13

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The recent advent of the Doppler-tipped angioplasty guidewire (FloWire) allows the continuous measurement of blood flow velocity during angioplasty.10,12,13 Normalization of flow-velocity parameters immediately after PTCA may indicate that an adequate lumen enlargement has been achieved and a normal vascular conductance restored.14 The DEBATE study (Doppler Endpoints Balloon Angioplasty Trial Europe)15 showed that measurements of distal coronary flow reserve (CFR) after PTCA, in conjunction with postprocedural diameter stenosis, had a modest predictive value for short- and long-term outcomes after PTCA. Importantly, FloWire is expensive, and it is not available in most laboratories.

On the other hand, the conventional TIMI (Thrombolysis In Myocardial Infarction) flow-grading system is widely used as a qualitative measure of coronary flow.16 However, the main limitation of the flow-grading system is its subjective and categorical nature. To standardize the assessment of coronary flow, a simple continuous index of coronary blood flow, the corrected TIMI frame count (CTFC) has been developed.17,18

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TABLE 1. Baseline Clinical and Angiographic Characteristics of Patients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age ± SD, y</td>
<td>57 ± 9</td>
</tr>
<tr>
<td>Sex, F/M</td>
<td>7/63</td>
</tr>
<tr>
<td>Family history of CAD, n (%)</td>
<td>15 (21.4)</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>27 (38.6)</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>7 (10.0)</td>
</tr>
<tr>
<td>Hyperlipidemia, n (%)</td>
<td>29 (41.4)</td>
</tr>
<tr>
<td>Cigarette smoking, n (%)</td>
<td>36 (51.4)</td>
</tr>
<tr>
<td>Unstable angina, n (%)</td>
<td>13 (18.6)</td>
</tr>
<tr>
<td>TIMI flow &lt; 3, n (%)</td>
<td>18 (25.7)</td>
</tr>
<tr>
<td>Treated vessel, n (%)</td>
<td></td>
</tr>
<tr>
<td>LAD</td>
<td>42 (60.0)</td>
</tr>
<tr>
<td>LCx</td>
<td>11 (15.7)</td>
</tr>
<tr>
<td>RCA</td>
<td>17 (24.3)</td>
</tr>
<tr>
<td>ACC/AHA type of lesion, n (%)</td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>33 (47.2)</td>
</tr>
<tr>
<td>B</td>
<td>29 (41.4)</td>
</tr>
<tr>
<td>C</td>
<td>8 (11.4)</td>
</tr>
</tbody>
</table>

ACC/AHA indicates American College of Cardiology/American Heart Association classification. n = 70.

This study sought to identify clinical, angiographic, and functional predictors of clinical and angiographic restenosis after conventional PTCA and to assess the predictive value of a new index, postangioplasty CTFC/MLD ratio.

Methods

Study Patients

We studied 70 consecutive patients undergoing conventional single-lesion balloon angioplasty in whom coronary flow parameters were recorded during the period from August 1993 through June 1994. All patients had a history of angina pectoris refractory to medical treatment and documented signs of myocardial ischemia (positive exercise stress test and/or reversible perfusion defect on 201 T1 scintigraphy). Exclusion criteria were as follows: use of other interventional treatments (eg, stent implantation or atherectomy), angioplasty of totally occluded target vessels, severe multivessel disease, previous transmural myocardial infarction in the target- vessel territory, thrombus in the target vessel, left bundle-branch block, second- and third-degree atrioventricular block, an open bypass graft to the target vessel, and evidence of primary myocardial or valvular heart disease. Patients with clinical conditions such as hypertension and diabetes mellitus that are associated with impaired CFR were not excluded from the study. Baseline characteristics of the patients are shown in Table 1. The study protocol was approved by the Ethics Committee and Institutional Review Board of the Onassis Cardiac Surgery Center, and all patients gave informed consent.

Coronary Balloon Angioplasty

Balloon angioplasty was performed in the usual manner with the femoral arterial technique, standard guiding and balloon catheters, and a 0.014-in Doppler-tipped angioplasty guidewire. An initial intravenous bolus of heparin (10 000 U) and additional doses of 2500 U during the procedure were given to maintain an activated clotting time >300 seconds. All patients were pretreated with aspirin 100 to 325 mg/d. Intracoronary nitrates (200 µg) were administered before flow measurements to preserve a state of maximum vasodilatation.

Angioplasty success was defined angiographically as <50% residual diameter stenosis. All angiograms were reviewed by 2 experienced interventional cardiologists. End-diastolic frames in the projection showing the maximal stenosis severity were chosen for luminal diameter measurements with electronic calipers. The contrast-filled guiding catheter was used as a scaling device to obtain absolute arterial dimensions. Intraobserver and interobserver variabilities for the measurement of diameter stenosis (DS) and MLD with this technique were 8 ±12% and 7 ±14% and 0.18 ±0.26 and 0.19 ±0.22 mm, respectively.

TIMI Frame Count

CTFC (the number of cine frames required for contrast to first reach standardized distal coronary landmarks) was measured with a cine projector equipped with a frame counter (Tagarno AS 35). The first frame used for TIMI frame counting was the first frame in which dye fully entered the artery, and the last frame was that when dye first entered the distal landmark branch. The distal landmarks included the apical "moustache" branch for the left anterior descending coronary artery (LAD), the most distal obtuse marginal branch for the left circumflex artery (LCx), and the most distal posterolateral branch or posterior descending artery for the right coronary artery (RCA). Cine film speed was 25 frames/s. The cine film reviewer was blinded to the Doppler coronary flow parameters. Intraobserver variability was 0.91 ±3.2 frames.

Coronary Flow–Velocity Measurements

Coronary blood flow velocity was measured with a 0.014-in Doppler-tipped angioplasty guidewire system (FloWire, Cardiometrics Inc). After online assessment of the baseline average peak velocity (APV), hyperemia was induced by administration of an intracoronary bolus of adenosine (18 µg in the LCx and 12 µg in the RCA), and CFR was defined as the ratio of the adenosine-induced hyperemic APV to the baseline APV. Distal velocity measurements were reacquired after PTCA. Flow-velocity signals were recorded continuously on standard 0.5-in videotape, and single-frame images were printed for offline analysis.

Follow-Up Procedures

Patients were evaluated for clinical and angiographic restenosis. Clinical definition of restenosis included history of recurrence of angina and/or positive exercise stress test or 201 T1 myocardial perfusion imaging. Follow-up coronary angiograms were performed after 10.5 ±10.3 months, with the same set of matched views obtained during angioplasty. Angiographic definition of restenosis was the presence of ≥50% DS at the follow-up angiogram. If symptoms recurred within 6 months after PTCA, control coronary angiography was performed sooner.

Statistical Analysis

Continuous variables were compared by t test or factorial ANOVA with the Scheffé test. Categorical data were compared with Fisher exact test or χ2 test. Univariate and multivariate logistic regression analyses were used to determine predictors of clinical and angiographic restenosis. Univariate predictors with a P value <0.2 were entered into the multivariate model. Independent predictors of restenosis and their 95% CIs were calculated.

Receiver operating characteristic (ROC) curves were constructed for selected significant predictors to evaluate their diagnostic power (represented by the area under the ROC curve, range 50% to 100%) and to determine the cutoff points as the threshold with the highest diagnostic accuracy, which divides the population into 2 categories.

Cox proportional hazards regression model was used to investigate the independent influence of different anatomic and functional parameters on clinical and angiographic restenosis.

Probability values of <0.05 were considered significant.
Results
Mean clinical follow-up was 10.5±10.3 months. Follow-up coronary angiograms were obtained in 63 (90%) of 70 patients. Follow-up angiograms were not obtained in 6 asymptomatic patients with negative stress tests. One asymptomatic patient with a positive stress test refused repeated coronary angiography. Clinical restenosis was detected in 25 (35.7%) of 70 patients, and angiographic restenosis was found in 26 (41.3%) of 63 patients.

Procedural Angiographic and Doppler Flow Parameters and TIMI Frame Counts
The angiographic and Doppler flow-velocity measurements and TIMI frame counts, before and after PTCA, are summarized in Table 2. All measured anatomic and functional descriptors of stenosis severity improved significantly after PTCA. The reference vessel diameter remained unchanged, whereas DS and CTFC decreased and MLD and distal CFR increased after PTCA. Distal baseline diastolic/systolic velocity ratio (DSVR) increased, and proximal/distal velocity ratio (P/D) decreased after the procedure.

Correlation of Doppler Flow Parameters and TIMI Frame Counts
Close linear correlations were found between CTFC and distal APV, as well as volumetric flow before PTCA (Figure 1, top). Weaker but also significant correlations persisted after PTCA (Figure 1, bottom). There was no relationship between CTFC and other Doppler flow parameters (CFR, P/D, and DSVR).

Prediction of Clinical and Angiographic Restenosis
Univariate predictors of clinical and angiographic restenosis are summarized in Tables 3 and 4. Other clinical variables (age, sex, family history of coronary artery disease, hypertension, hyperlipidemia, and smoking), lesion- and procedure-related variables (ostial, proximal, bifurcation, eccentric, angle >45°, tortuous, calcified, collaterals, TIMI flow <3, extent of dissection after PTCA), and Doppler flow variables (P/D, DSVR, and CFR before PTCA) tested were not significant univariate predictors of restenosis.

When MLD after PTCA was dichotomized by its median value (2.33 mm), adjusted relative risks (RRs) for postprocedure MLD <2.33 mm were 2.93 (95% CI 1.4 to 6.12; \( P=0.001 \)) for angiographic restenosis and 1.88 (95% CI 1.09 to 3.48; \( P=0.025 \)) for clinical restenosis.

In multivariate logistic regression analysis, only CTFC/MLD ratio after PTCA was significantly related to angiographic (OR 2.02; 95% CI 1.34 to 2.55; \( x^2=17.39; P=0.0002 \)) and clinical restenosis (OR 1.60; 95% CI 1.15 to 2.21; \( P=0.005 \)).

ROC analysis (Table 5) showed that the CTFC/MLD ratio after PTCA had a good prognostic value in predicting angiographic restenosis (ROC area=79%) and reasonable prognostic value in predicting clinical restenosis (ROC area=73%) (Figure 2). The “optimal” cutoff values of CTFC/MLD ratio for angiographic and clinical restenosis were 7.88 and 7.94, respectively (Figures 3 and 4). Patients with index values >7.88 for angiographic restenosis and >7.94 for clinical restenosis showed significantly higher restenosis rates (56% versus 15%, RR 3.94, 95% CI 1.36 to 11.37; \( P=0.001 \); and 51% versus 18%, RR 3.0, 95% CI 1.09 to 8.25; \( P=0.006 \), respectively).

Multivariate Cox regression analysis also showed that CTFC/MLD ratio after PTCA was the only independent predictor of both angiographic (hazard ratio 1.85; 95% CI 1.34 to 2.55; \( \chi^2=17.39; P=0.0002 \)) and clinical (hazard ratio 1.83; 95% CI 1.26 to 2.67; \( \chi^2=12.64; P=0.0016 \)) restenosis.

**TABLE 2.** Matched Variables for Angiographic, Doppler Flow and CTFC Measurements Before and After PTCA

<table>
<thead>
<tr>
<th>Variable</th>
<th>Before PTCA</th>
<th>After PTCA</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angiographic data</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reference vessel diameter, mm</td>
<td>3.05±0.4</td>
<td>3.07±0.4</td>
<td>0.099</td>
</tr>
<tr>
<td>DS, %</td>
<td>70.23±11.26</td>
<td>22.57±10.61</td>
<td>0.0001</td>
</tr>
<tr>
<td>MLD, mm</td>
<td>0.91±0.36</td>
<td>2.36±0.46</td>
<td>0.0001</td>
</tr>
<tr>
<td>Doppler flow data</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Distal CFR</td>
<td>1.54±0.49</td>
<td>2.49±0.73</td>
<td>0.0001</td>
</tr>
<tr>
<td>Distal DSVR (baseline)</td>
<td>1.49±0.67</td>
<td>1.93±0.86</td>
<td>0.001</td>
</tr>
<tr>
<td>P/D ratio (baseline)</td>
<td>2.41±1.88</td>
<td>1.44±0.8</td>
<td>0.002</td>
</tr>
<tr>
<td>CTFC data</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CTFC</td>
<td>39.17±18.43</td>
<td>17.99±4.63</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

Data presented are mean±SD.

Figure 1. Correlations of distal APV and volumetric coronary blood flow (mL/min) with CTFC before (top) and after (bottom) angioplasty.
TABLE 3. Univariate Predictors of Clinical Restenosis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total (n=70)</th>
<th>No Restenosis (n=45)</th>
<th>Restenosis (n=25)</th>
<th>OR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unstable angina, n (%)</td>
<td>13 (18.57)</td>
<td>6 (13.33)</td>
<td>7 (28.00)</td>
<td>1.22 (1.03–1.81)</td>
<td>0.042</td>
</tr>
<tr>
<td>LAD lesion location, n (%)</td>
<td>42 (60.00)</td>
<td>22 (48.89)</td>
<td>20 (80.00)</td>
<td>1.31 (1.11–1.82)</td>
<td>0.031</td>
</tr>
<tr>
<td>DS after PTCA, %</td>
<td>22.57±10.61</td>
<td>20.33±10.96</td>
<td>26.6±8.78</td>
<td>1.07 (1.01–1.14)</td>
<td>0.022</td>
</tr>
<tr>
<td>MLD after PTCA, mm</td>
<td>2.36±0.46</td>
<td>2.48±0.46</td>
<td>2.2±0.42</td>
<td>0.24 (0.06–0.94)</td>
<td>0.041</td>
</tr>
<tr>
<td>CTFC after PTCA</td>
<td>17.99±4.63</td>
<td>17.0±4.55</td>
<td>19.76±4.3</td>
<td>1.15 (1.02–1.29)</td>
<td>0.02</td>
</tr>
<tr>
<td>CTFC/MLD after PTCA</td>
<td>7.94±2.63</td>
<td>7.19±2.29</td>
<td>9.29±2.69</td>
<td>1.42 (1.13–1.79)</td>
<td>0.003</td>
</tr>
</tbody>
</table>

Data presented are mean±SD or number (%) of patients.
Other variables tested in the multivariate model were diabetes mellitus (P=0.081), lesion length ≥10 mm (P=0.066), and distal CFR after angioplasty (P=0.156).

Discussion

Several predictors of restenosis after conventional PTCA have been described, and postprocedural MLD was consistently identified as the most important factor, confirming that "bigger is better."\(^1,5\) In addition, the recently published DEBATE\(^15\) and RESTORE (Randomized Efficacy Study of Tirofiban for Outcomes and REstenosis) studies\(^27\) revealed the predictive power of coronary flow indices, expressed as CFR and CTFC, respectively.

In the present study, the univariate predictors of restenosis were similar to those found in previously published reports.\(^1,7\) The strongest univariate predictor was final MLD, which identified the importance of reference dimensions and residual DS may be reduced by maximizing final luminal dimensions. On the other hand, analysis of physiological parameters showed that Doppler flow-velocity indices were not significantly associated with clinical and angiographic restenosis. This was also reported in the DEBATE study,\(^15\) in which clinical recurrence of symptoms at 6 months and reintervention rate were not predicted by functional (CFR ≤2.5) or anatomic (DS >35%) parameters individually. However, their combination identified 44 of 224 patients with a low (16%) rate of angiographic restenosis at 6-month restudy.

We found that postprocedural CTFC was the only physiological parameter associated with restenosis. That result is consistent with RESTORE study results,\(^27\) in which the independent predictors for late loss in MLD were post-PTCA MLD and CTFC, with post-PTCA MLD the more powerful predictor. Importantly, our data revealed that CTFC correlated well with poststenotic APV and volumetric flow before as well as after PTCA (although less convincingly, as expected), which indicates its applicability in the assessment of coronary flow. Similar correlations were reported by Kern et al\(^22\) during primary PTCA.

To integrate anatomic and functional aspects of the postprocedure result, we introduced a new index, the CTFC/MLD ratio, which contains information on coronary flow after PTCA, normalized by the residual minimal vessel diameter. In the univariate model, this index showed the strongest individual predictive power for both clinical and angiographic restenosis. The most important finding of the present study was that the newly created index, the CTFC/MLD ratio, was the only independent predictor of both angiographic and clinical restenosis in a multivariate model. Our results point to the complexity of the relationship between anatomic and functional indices of stenosis severity after interventional procedures, indicating together with previous studies that lumen enlargement, although crucial, is not the sole parameter that should be determined. As previously reported by numerous investigators, focal dissections create a hazy lumen after angioplasty owing to contrast becoming interspersed around the dissection flaps, and the progressive release of thrombogenic and vasoactive factors produces disturbances of coronary flow\(^10,11,14,28\) that impair the ability of any anatomic measure to precisely assess the resulting lumen. The DEBATE study\(^15\) showed the great importance of CFR assessment in those cases of angiographic pseudosuccesses.

TABLE 4. Univariate Predictors of Angiographic Restenosis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total (n=63)</th>
<th>No Restenosis (n=37)</th>
<th>Restenosis (n=26)</th>
<th>OR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>7 (11.11)</td>
<td>2 (5.41)</td>
<td>5 (19.23)</td>
<td>1.33 (1.01–1.75)</td>
<td>0.04</td>
</tr>
<tr>
<td>LAD lesion location, n (%)</td>
<td>38 (60.31)</td>
<td>17 (45.95)</td>
<td>21 (80.76)</td>
<td>1.41 (1.19–1.83)</td>
<td>0.014</td>
</tr>
<tr>
<td>Stenosis length ≥10 mm, n (%)</td>
<td>37 (58.73)</td>
<td>19 (51.35)</td>
<td>18 (69.23)</td>
<td>1.05 (1.02–1.17)</td>
<td>0.026</td>
</tr>
<tr>
<td>Reference vessel diameter, mm</td>
<td>3.07±0.4</td>
<td>3.17±0.42</td>
<td>2.92±0.38</td>
<td>0.19 (0.05–0.79)</td>
<td>0.023</td>
</tr>
<tr>
<td>MLD before PTCA, mm</td>
<td>0.91±0.36</td>
<td>0.99±0.37</td>
<td>0.8±0.35</td>
<td>0.21 (0.05–0.97)</td>
<td>0.045</td>
</tr>
<tr>
<td>MLD after PTCA, mm</td>
<td>2.36±0.46</td>
<td>2.52±0.48</td>
<td>2.15±0.39</td>
<td>0.10 (0.02–0.51)</td>
<td>0.006</td>
</tr>
<tr>
<td>CTFC after PTCA</td>
<td>17.99±4.63</td>
<td>16.59±4.37</td>
<td>19.88±4.82</td>
<td>1.17 (1.04–1.32)</td>
<td>0.01</td>
</tr>
<tr>
<td>CTFC/MLD after PTCA</td>
<td>7.94±2.63</td>
<td>6.8±2.08</td>
<td>9.52±2.72</td>
<td>1.63 (1.24–2.14)</td>
<td>0.0005</td>
</tr>
</tbody>
</table>

Data presented are mean±SD or number (%) of patients.
Other variables tested in the multivariate model were unstable angina (P=0.066), distal CFR after PTCA (P=0.096), and residual DS (P=0.116).
and demonstrated that the risk for early recurrence of symptoms was doubled in patients with a postprocedural CFR <2.5 (24% versus 12%).

CTFC/MLD ratio represents an integrated approach to final result assessment. It is noteworthy that this simple index had a better prognostic value in ROC analysis than that achieved by DS and CFR in the DEBATE study. In addition, when the optimal prognostic cutoff values for CTFC/MLD ratio were applied, patients with a high risk for restenosis could be identified. Relative risk analysis showed that those patients had an $\approx 4$ times higher risk for angiographic and 3 times higher risk for clinical restenosis. Thus, the widely embraced strategy of angioplasty, namely, that “bigger is better,” should be modified to “bigger and faster is better.”

**Clinical Application**

Use of the CTFC/MLD ratio to provide early identification of patients prone to develop restenosis should be considered in view of preliminary results of 3 recently completed multicenter studies, DEBATE II, DESTINI (Doppler End-points STent INternational investigation), and FROST (FRench Optimal Stenting Trial), which compared efficacy of primary stenting and a strategy of “optimal PTCA.” The studies mentioned above used sophisticated techniques, quantitative coronary angiography and intracoronary Doppler, to “guide” balloon angioplasty and to identify patients with suboptimal angiographic or functional results. Both primary stenting and optimal PTCA followed by stenting for inadequate final result showed a low incidence of early complications and similar short- and long-term clinical outcomes.

The use of the CTFC/MLD ratio in determining who is most likely to benefit from additional stent implantation after conventional PTCA (provisional stenting) may be potentially an attractive option for many catheterization laboratories. Intracorony Doppler flow measurements necessary for CFR determination and quantitative coronary arteriography are sophisticated, expensive, and not always feasible tools. On the other hand, CTFC/MLD ratio is a simple quantitative index that can be calculated immediately after PTCA in all laboratories. It is easy to learn and to perform and can be measured by anyone with a frame counter, which is present on most of the cine-film viewers. Its consistency and continuous nature suggest that this index could be a reproducible and clinically applicable method for assessing early angioplasty results. However, to confirm the clinical applicability of CTFC/MLD ratio in this setting, it needs to be evaluated in a prospective, large-scale clinical trial.

**Study Limitations**

The relatively small number of patients eligible for the analysis in the present study may render it difficult to generalize the results and to apply them to other patient populations. However, inclusion and exclusion criteria were similar to those in the DEBATE study, allowing direct comparisons. Furthermore, the predictive power of the CTFC has already been tested and confirmed in the TIMI 4, 10A, 10B trials, in which higher CTFCs after thrombolytic administration were related to increased risk of adverse clinical outcomes.

The CTFC technique did not exist years ago when cine filming was performed, and proper panning is essential to identify both the initial and final cine frame during a single injection. A possible selection bias may have arisen by the necessary exclusion of cine films with insufficient panning in this retrospective analysis. However, some technical issues have already been addressed, and it was shown that

**TABLE 5. Predictive Values of the CTFC/MLD Ratio**

<table>
<thead>
<tr>
<th>Event</th>
<th>Cutoff Value</th>
<th>ROC Area (95% CI)</th>
<th>Univariate $P$ Value</th>
<th>Multivariate $P$ Value</th>
<th>Se, %</th>
<th>Sp, %</th>
<th>PPV, %</th>
<th>NPV, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angiographic restenosis</td>
<td>7.88</td>
<td>79 (67–88)</td>
<td>0.0005</td>
<td>0.012</td>
<td>77</td>
<td>68</td>
<td>62</td>
<td>81</td>
</tr>
<tr>
<td>Clinical restenosis</td>
<td>7.94</td>
<td>73 (61–83)</td>
<td>0.003</td>
<td>0.003</td>
<td>72</td>
<td>64</td>
<td>53</td>
<td>81</td>
</tr>
</tbody>
</table>

Se indicates sensitivity; Sp, specificity; PPV, positive predictive value; and NPV, negative predictive value. Se, Sp, PPV, and NPV correspond with chosen CTFC/MLD ratio cutoff values.
differential injection rates had a minor influence (<7%) on the mean CTFC. Also, it was shown that the CTFC ends early in an injection, before development of contrast-mediated hyperemia.

We used electronic calipers and not automated edge-detection systems to measure lumen diameter. Uehata et al validated electronic digital calipers against quantitative coronary angiography and showed that both methods produce similar relative changes in arterial diameters and percent stenosis in a broad range of stenosis severities (difference ±9%, r=0.89, range of stenosis severity 11% to 80%). After angioplasty and at follow-up, there were no systematic differences (±10%) between the mean stenosis severity measured by the 2 methods. Thus, digital calipers can be considered a convenient alternative to computerized quantitative angiography for assessing stenosis severity in clinical practice.

Conclusions

Our data indicate that a new index, the CTFC/MLD ratio, which incorporates both anatomic and physiological parameters obtained after successful PTCA, predicts clinical and angiographic restenosis. The predictive value of this index compares favorably with more sophisticated interventional devices. In addition, it is simple to obtain, inexpensive, and readily available in all catheterization laboratories.

References


Prediction of Restenosis After Coronary Angioplasty by Use of a New Index: TIMI Frame Count/Minimal Luminal Diameter Ratio
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