OBJECTIVES
This study evaluated the acute physiological gain of adjunctive intravascular ultrasound (IVUS) guided balloon angioplasty and stent implantation.

BACKGROUND
Recent studies indicate safe coronary luminal enlargement and "stent-like" long-term outcomes using upsized balloons guided by IVUS.

METHODS
After angiographically guided balloon angioplasty in 20 patients with 1-vessel disease and normal left ventricular function, IVUS was performed to determine the size of the adjunctive balloon using the mean of the maximal luminal diameter and the maximal diameter of the external elastic membrane measured in the adjacent proximal and distal reference segments. Serial adenosine-induced hyperemic blood flow velocity measurements were performed using a 0.014" Doppler guide wire to determine the physiological lumen obstruction after standard balloon angioplasty, followed by IVUS-guided balloon angioplasty and stent implantation.

RESULTS
Upsized balloon angioplasty (increase balloon size: 0.98 ± 0.26 mm; balloon:artery ratio 1.35 ± 0.21) resulted in an additional increase of arterial dimensions: minimal lumen diameter (MLD) 2.18 ± 0.38 mm to 2.73 ± 0.51 mm; percent diameter stenosis (%DS) 34 ± 13% to 19 ± 22%; IVUS assessed minimal lumen area (MLA) 7.53 ± 1.55 mm² to 10.24 ± 2.22 mm² (all p < 0.0001). Major dissections (≥ type C) did not occur. Hyperemic blood flow velocity increased from 49.8 ± 20.1 cm/s to 59.1 ± 22.9 cm/s (p < 0.05) after IVUS-guided balloon angioplasty. Adjunctive stent implantation resulted in a further increase of MLD to 3.84 ± 0.51 mm, %DS to −9 ± 21% and MLA to 13.39 ± 1.80 mm² (all p < 0.0001), while hyperemic blood flow velocity remained unchanged (61.2 ± 24.7 cm/s, p = 0.7).

CONCLUSIONS
Upsized IVUS-guided balloon angioplasty increases arterial coronary dimensions and the distal hyperemic blood flow velocity. Adjunctive stent implantation does not yield a further gain in the hyperemic blood flow velocity, indicating the absence of a functional residual lumen obstruction after IVUS-guided balloon angioplasty. This may explain a similar clinical outcome reported after those coronary interventions. (J Am Coll Cardiol 1999;34:1899–906)

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The high incidence of restenosis remains a major drawback of balloon coronary angioplasty. Several studies described a better long-term clinical or angiographic outcome following an optimal postprocedural result (1–3). Several alternative treatment modalities have been evaluated in order to optimize the initial angiographic success, i.e., directional atherectomy (4,5), coronary stent implantation (6–8) and intravascular ultrasound (IVUS) guided stent implantation (9). These studies involving atherectomy and coronary stent implantation confirmed earlier reports that an optimal, i.e. larger, procedural result is relevant for both angiographic and clinical long-term outcome (4–8). Several IVUS studies documented the presence of coronary atherosclerosis with compensatory lumen enlargement in the adjacent angiographically normal reference artery segments (10–12). This novel insight into the dynamic atherosclerotic process resulted in the evaluation of IVUS-guided balloon angioplasty with balloons otherwise considered to be oversized. Recent studies have indicated that the use of upsized balloons guided by IVUS is safe and results in a similar long-term angiographic and clinical outcome as reported after stent implantation (13,14).
The usefulness of coronary angiography in assessing residual lumen obstruction after coronary angioplasty is limited (15). A recently published multicenter study, Dopper End points Balloon Angioplasty Trial Europe (DEBATE), indicated the additional value of a physiological parameter, i.e. distal intracoronary blood flow velocity reserve (CFVR), in the evaluation of the postprocedural angiographic result (16). In spite of its clinical relevance, only a limited number of studies have been performed concerning the relationship between the arterial dimensions and physiological responses following adjunctive stent implantation (17,18). In conjunction, these studies underlined the importance of optimizing the angiographic result and physiological status following standard balloon angioplasty. However, postprocedural measurements of CFVR are sensitive to temporary baseline blood flow velocity fluctuations (19–21), indicating that hyperemic blood flow velocity is potentially a better physiological variable for the evaluation of residual lumen obstruction following coronary interventions.

Consequently, the purpose of this study was to determine the physiological gain after standard balloon angioplasty and adjunctive IVUS-guided balloon angioplasty and stent implantation by serial measurements of distal hyperemic blood flow velocity.

**METHODS**

**Patients.** Patients with de novo or restenotic single vessel disease of native coronary arteries and normal left ventricular function referred to our institution for elective stent implantation (n = 20) were studied prospectively. Inclusion criteria were:

1) angina pectoris refractory to medical therapy,
2) proximal coronary lesion suitable for stent implantation.

Exclusion criteria were:

1) multilesion one-vessel disease,
2) functional or total coronary occlusion,
3) previous cardiac surgery,
4) electrocardiographic evidence of left ventricular hypertrophy or conduction abnormalities,
5) previous Q-wave myocardial infarction, and
6) non-Q-wave myocardial infarction less than one week before PTCA.

The protocol was approved by the Institutional Ethics Committee and all patients gave written informed consent.

**Cardiac catheterization.** Therapy with all antianginal medication was continued until cardiac catheterization. All patients received aspirin (100 mg) administered orally the night before percutaneous transluminal coronary angioplasty (PTCA). Lorazepam (1 mg) was orally administered before the procedure. Cardiac catheterization was performed in all patients by the percutaneous femoral approach. All patients received unfractionated heparin (7,500 IU) intravenously as a bolus at the beginning of the procedure. Additional heparin was administered if the procedure lasted more than 90 min. Nitroglycerin (0.1 mg intracoronary) was administered before quantitative coronary angiography (QCA) and every 30 min throughout the procedure. Consecutive balloon inflations of 1–2 min duration were performed until an angiographically satisfactory result as determined by the consensus of two experienced operators was obtained after an additional waiting time of 10 min. Single coronary stents (Palmaz-Schatz, Johnson & Johnson, Warren, New Jersey) were deployed using high balloon inflation pressures (14 ± 3 atm).

**Quantitative coronary angiography.** Off-line analysis of the angiographic severity of the coronary narrowing was performed using an automated contour detection algorithm (QCA-CMS Version 3.32, MEDIS, Leiden, the Netherlands) (22). The outer diameter of the centered, fluid-filled guiding catheter was used as a calibration device to obtain absolute arterial dimensions. Two orthogonal projections of the coronary artery lesion during the end-diastolic phase were used to assess biplane analysis of the minimal lumen diameter (MLD), minimal lumen area (MLA), percent diameter stenosis (%DS) and percent area stenosis (%AS) of the coronary narrowing. On-line QCA analysis was performed to determine the balloon size for standard balloon angioplasty. Quantitative coronary angiography was performed in the same projections before and after standard balloon angioplasty, IVUS-guided balloon angioplasty and stent implantation. Quantitative coronary angiography after high-pressure stent implantation was performed according to the method described by Reimers et al., excluding the stented segment from the calculation of the reference diameter (23). The nominal balloon:artery ratio was defined as the ratio between the nominal balloon size according to the inflation pressure used and the QCA-measured interpolated reference diameter at the site of the MLD. The QCA balloon:artery ratio was defined as the ratio between the QCA-measured size of the balloon and the QCA-measured reference diameter. angiographic grading of cor-

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**Abbreviations and Acronyms**

- ANOVA = analysis of variance
- %AS = percent area stenosis
- CFVR = distal coronary flow velocity reserve
- CLOUT = Clinical Outcomes with Ultrasound Trial
- DEBATE = Doppler End points Balloon Angioplasty Trial Europe
- %DS = percent diameter stenosis
- IVUS = intravascular ultrasound
- MLA = minimal lumen area
- MLD = minimal lumen diameter
- PTCA = percutaneous transluminal coronary angioplasty
- QCA = quantitative coronary angiography
- rCFVR = relative coronary flow velocity reserve
- %AS = percent area stenosis
- ANOVA = analysis of variance
- IVUS = intravascular ultrasound
- MLA = minimal lumen area
- MLD = minimal lumen diameter
- PTCA = percutaneous transluminal coronary angioplasty
- QCA = quantitative coronary angiography
- rCFVR = relative coronary flow velocity reserve
Intravascular dissections was performed according to the criteria of the National Heart, Lung, and Blood Institute Percutaneous Transluminal Coronary Angioplasty Registry (24). Intravascular ultrasound analysis. Intravascular imaging was performed using a 2.9F monorail system with a 30 MHz mechanically rotating ultrasound transducer (CardioVascular Imaging Systems, Inc., Sunnyvale, California). After standard balloon angioplasty, the imaging catheter was positioned distal to the dilated segment and ultrasound gain was adjusted to allow maximal gray scale differentiation. Images were recorded continuously on a VHS-tape during manual pull-back of the transducer. After an intravascular ultrasound study was completed, the videotape was reviewed to determine the optimal reference sites. Measurements were taken from both the proximal and distal reference segment. A proximal or distal segment alone was used as a reference segment in the case of a lesion adjacent to a bifurcation. The maximal diameters of the reference lumen and vessel (the external elastic membrane) were measured. The size of the upsized balloon was determined by using the following equation employing measurements from either the proximal or distal reference site: balloon size = (maximal lumen diameter + maximal vessel diameter)/2.

Intravascular ultrasound was performed after stent implantation to evaluate optimal stent deployment, i.e. circular deployment of the stent and avoidance of echo-free spaces between the stent and the inner vascular wall. Off-line IVUS analysis was performed to determine the MLD, MLA (Fig. 1), the area of the external elastic membrane (vessel area) and the percentage plaque area (vessel area minus MLA) after each intervention. The intraobserver and interobserver variability of the aforementioned IVUS variables at our center were reported previously (25).

Coronary blood flow analysis. All coronary blood flow velocity measurements with the Doppler angioplasty guide wire (FloWire, EndoSonics, Rancho Cordova, California) were performed as previously described (26,27). The tip of the Doppler guide wire was placed distal to the stenosis and manipulated until an optimal and stable blood flow velocity...
signal was obtained. After on-line assessment of the baseline average peak velocity, hyperemia was induced by the administration of an intracoronary bolus of adenosine (12 μg in the right coronary artery; 18 μg in the left coronary artery). Pressure recording through the guiding catheter was carefully monitored to exclude signs of obstruction of flow during hyperemia. Distal coronary flow velocity reserve was defined as the ratio of the maximal hyperemic/baseline average peak velocity. These blood flow velocity measurements were performed at the same location after each intervention (Fig. 1). The reference CFVR was determined in an adjacent, angiographically normal coronary artery after completion of the procedure. The relative CFVR (rCFVR) was defined as the ratio of the distal/reference CFVR.

**Statistical analysis.** Continuous variables are presented as mean ± SD. Chi-square analysis was used for comparison of the different types of coronary dissections after standard balloon angioplasty and IVUS-guided balloon angioplasty. Analysis of variance (ANOVA) for ordered groups (considering a significant linear trend) was used to compare continuous data between the subsequent interventions, i.e., before balloon angioplasty, after balloon angioplasty, after IVUS-guided balloon angioplasty and after stent implantation. A two-tailed paired t test (or Wilcoxon test for nonparametric data) was used to identify differences between blood flow velocity variables or geometric dimensions of the dilated coronary artery after the subsequent types of intervention, in specific after IVUS-guided balloon angioplasty and stent implantation. Statistical analysis was performed with SSPS (SPSS Inc., Chicago, Illinois) software for Macintosh, version 6.1.1. A p value <0.05 was considered statistically significant.

**RESULTS**

**Patients.** Baseline characteristics of the patients studied (mean age 54 ± 11 years, range 36–73 yr) are depicted in Table 1. Ten patients were treated for a de novo lesion and 10 patients for a restenotic lesion. All patients underwent elective stent implantation for a proximal lesion using a 15 mm (n = 5) or an 18 mm (n = 5) Palmaz-Schatz stent. All procedures were successfully completed without ischemic complications.

**Quantitative coronary angiographic and intravascular ultrasound data.** The mean angiographic reference diameter before balloon angioplasty was 3.37 ± 0.62 mm. Standard balloon angioplasty (nominal balloon:artery ratio = 1.07 ± 0.15) improved the MLD from 1.05 ± 0.39 mm to 2.18 ± 0.38 mm and the %DS from 68 ± 13% to 34 ± 13% (both p < 0.0001, Table 2).

Intravascular ultrasound analysis after standard balloon angioplasty of the reference segment showed an MLD of 4.3 ± 0.5 mm and a maximal vessel diameter of 4.9 ± 0.4 mm (mean diameter: 4.58 ± 0.36 mm, MLA: 12.7 ± 1.9 mm², percent plaque: 13 ± 12%). The balloons were upsized by 0.98 ± 0.26 mm (range 0.53–1.50 mm, p < 0.0001) to a nominal diameter of 4.41 ± 0.28 mm. This resulted in an increased nominal and QCA-measured balloon:artery ratio (Table 2). Quantitative coronary angiography and IVUS showed an increase in luminal dimensions after IVUS-guided balloon angioplasty (Tables 2 and 3). Adjunctive stent deployment was successful in all patients according to the IVUS criteria. Stent implantation resulted in a further increase in luminal dimensions (Tables 2 and 3). All continuous data showed a significant trend across the subsequent types of intervention.

**Blood flow velocity data.** Heart rate and mean aortic pressure did not differ between the serial blood flow velocity measurements (Table 4). The CFVR increased after standard balloon angioplasty from 1.5 ± 0.6 to 2.6 ± 0.7 towards the CFVR measured in the normal adjacent coronary artery (3.2 ± 0.7, rCFVR: 0.83 ± 0.22), despite an increase from 12 ± 5 cm/s to 22 ± 10 cm/s (p < 0.0001, Table 4) in baseline blood flow velocity. Adjunctive IVUS-guided balloon angioplasty resulted in a further increase in hyperemic blood flow velocity (Table 4), while a nonsignificant increase of baseline blood flow velocity precluded a further increase in CFVR and rCFVR (Table 4, Fig. 1). All blood flow velocity variables did not reveal changes after

**Table 1. Baseline Characteristics of the Study Patients**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n = 20 Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>54 ± 11 (range 36–73)</td>
</tr>
<tr>
<td>Male</td>
<td>17 (85%)</td>
</tr>
<tr>
<td>Functional class CCS:</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>3 (15%)</td>
</tr>
<tr>
<td>III</td>
<td>13 (65%)</td>
</tr>
<tr>
<td>IV</td>
<td>4 (20%)</td>
</tr>
<tr>
<td>Systemic hypertension</td>
<td>7 (35%)</td>
</tr>
<tr>
<td>Cigarette smoking</td>
<td>11 (55%)</td>
</tr>
<tr>
<td>Total cholesterol &gt;6.5 mmol/l</td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1 (5%)</td>
</tr>
<tr>
<td>Family history</td>
<td>5 (25%)</td>
</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>6 (30%)</td>
</tr>
<tr>
<td>Medication:</td>
<td></td>
</tr>
<tr>
<td>beta-blocker</td>
<td>19 (95%)</td>
</tr>
<tr>
<td>nitrate</td>
<td>10 (50%)</td>
</tr>
<tr>
<td>calcium-antagonist</td>
<td>13 (65%)</td>
</tr>
<tr>
<td>ace-inhibitor</td>
<td>2 (10%)</td>
</tr>
<tr>
<td>Coronary artery dilated:</td>
<td></td>
</tr>
<tr>
<td>LAD</td>
<td>11 (55%)</td>
</tr>
<tr>
<td>RCA</td>
<td>5 (23%)</td>
</tr>
<tr>
<td>LCx</td>
<td>4 (20%)</td>
</tr>
<tr>
<td>Lesion type (ACC/AHA):</td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>1 (5%)</td>
</tr>
<tr>
<td>B1</td>
<td>10 (50%)</td>
</tr>
<tr>
<td>B2</td>
<td>7 (35%)</td>
</tr>
<tr>
<td>C</td>
<td>2 (10%)</td>
</tr>
</tbody>
</table>

ACC/AHA = American College of Cardiology/American Heart Association; CCS = Canadian Cardiovascular Society; LAD = left anterior descending coronary artery; RCA = right coronary artery; LCx = left circumflex coronary artery.
stent implantation (Table 4). Furthermore, the hyperemic coronary blood flow velocity responses of patients using calcium antagonists did not differ from those not using calcium antagonists before PTCA (19 ± 9 cm/s vs. 15 ± 9 cm/s; p = 0.40), after standard balloon angioplasty (53 ± 19 cm/s vs. 44 ± 22 cm/s; p = 0.37), after IVUS-guided balloon angioplasty (62 ± 25 cm/s vs. 54 ± 20 cm/s; p = 0.48) and after stent implantation (65 ± 28 cm/s vs. 55 ± 19 cm/s; p = 0.41). All continuous data (with exception of heart rate and mean aortic pressure) showed a significant trend across the subsequent types of intervention.

Coronary dissections. Angiography of the treated coronary artery immediately after stent implantation revealed type A coronary dissections in 3/20 patients and type B dissections in 7/20 patients. A nonsignificant increase in type A dissections was noted after IVUS-guided balloon angioplasty (type A in six patients, type B in eight patients, χ² = 2.07; p = 0.36). The number of coronary dissections decreased by stent implantation; three type B dissections and one type C dissection were noticed in an adjacent segment after stent implantation (χ² = 13.8; p < 0.01).

The hyperemic blood flow velocity measurements of patients without coronary dissections did not differ from those patients with coronary dissections after standard balloon angioplasty (51.2 ± 25.3 cm/s vs. 48.3 ± 14.3 cm/s; p = 0.76) or after IVUS-guided balloon angioplasty (58.7 ± 22.2 cm/s vs. 59.2 ± 24.0 cm/s, p = 0.96).

**DISCUSSION**

This study demonstrates for the first time that adjunctive IVUS-guided balloon angioplasty induces an additional increase in hyperemic blood flow velocity related to a reduction of residual lumen obstruction. Subsequent stent implantation resulted in a further increase of coronary luminal dimensions while the hyperemic blood flow velocity parameters remained unchanged, indicating the absence of a functional residual lumen obstruction after IVUS-guided balloon angioplasty. Furthermore, this study confirms an earlier report showing that IVUS facilitates the safe use of balloons traditionally considered oversized with respect to the occurrence of coronary dissections (13).

**Coronary lumen enlargement after IVUS-guided balloon angioplasty and stent implantation.** Successful conventional balloon angioplasty results in a 30%–50% residual lumen obstruction immediately after the procedure. Several studies reported better long-term angiographical and clinical outcomes as a result of lower residual lumen obstructions after PTCA (<30 %DS) (1–3). However, the use of oversized balloons was complicated by the frequent occurrence of dissections and ischemic complications after PTCA (28,29). Roubin et al. (28) demonstrated that the size of the balloon was an independent predictor for emergency bypass graft surgery as larger balloons (nominal balloon:artery ratio = 1.13 ± 0.14) increased the rate of severe dissections. Consequently, several alternative angioplasty techniques

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**Table 2. Quantitative Coronary Angiography Variables in 20 Patients Before and After Standard Balloon Angioplasty, After IVUS-Guided Balloon Angioplasty and After Stent Implantation**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Before BA</th>
<th>After Standard BA</th>
<th>After IVUS-Guided BA</th>
<th>After Stent-Implantation</th>
</tr>
</thead>
<tbody>
<tr>
<td>MLD (mm)</td>
<td>1.05 ± 0.39</td>
<td>2.18 ± 0.38*</td>
<td>2.73 ± 0.52*</td>
<td>3.84 ± 0.51*</td>
</tr>
<tr>
<td>MLA (mm²)</td>
<td>0.95 ± 0.61</td>
<td>3.91 ± 1.35*</td>
<td>6.43 ± 2.67*</td>
<td>11.82 ± 2.91*</td>
</tr>
<tr>
<td>%DS</td>
<td>68 ± 13</td>
<td>34 ± 13*</td>
<td>19 ± 22*</td>
<td>9 ± 21*</td>
</tr>
<tr>
<td>%AS</td>
<td>88 ± 7</td>
<td>55 ± 15*</td>
<td>30 ± 46*</td>
<td>-22 ± 48*</td>
</tr>
<tr>
<td>Nominal B:A ratio</td>
<td>-</td>
<td>1.07 ± 0.14</td>
<td>1.35 ± 0.21*</td>
<td>1.40 ± 0.21</td>
</tr>
<tr>
<td>QCA B:A ratio</td>
<td>-</td>
<td>0.97 ± 0.14</td>
<td>1.22 ± 0.22*</td>
<td>1.29 ± 0.24</td>
</tr>
<tr>
<td>Gain (mm)</td>
<td>-</td>
<td>1.13 ± 0.43</td>
<td>1.69 ± 0.60*</td>
<td>2.79 ± 0.61*</td>
</tr>
<tr>
<td>Acute recoil (mm)</td>
<td>-</td>
<td>0.98 ± 0.47</td>
<td>1.24 ± 0.59</td>
<td>0.52 ± 0.65*</td>
</tr>
</tbody>
</table>

*p < 0.05 compared with the paired values of the previous measurement.

<table>
<thead>
<tr>
<th>Variable</th>
<th>After BA</th>
<th>After IVUS-guided BA</th>
<th>After Stent-Implantation</th>
</tr>
</thead>
<tbody>
<tr>
<td>MLA/reference LA</td>
<td>0.61 ± 0.15</td>
<td>0.86 ± 0.28*</td>
<td>1.09 ± 0.19*</td>
</tr>
<tr>
<td>% plaque area</td>
<td>63 ± 12</td>
<td>53 ± 13*</td>
<td>42 ± 12*</td>
</tr>
</tbody>
</table>

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**Table 3. Intravascular Ultrasound Variables After Standard Balloon Angioplasty, After IVUS-Guided Balloon Angioplasty and After Stent Implantation**

<table>
<thead>
<tr>
<th>Variable</th>
<th>After standard BA</th>
<th>After IVUS-guided BA</th>
<th>After Stent-Implantation</th>
</tr>
</thead>
<tbody>
<tr>
<td>MLD (mm)</td>
<td>2.93 ± 0.48</td>
<td>3.11 ± 0.54*</td>
<td>3.93 ± 0.29*</td>
</tr>
<tr>
<td>MLA (mm²)</td>
<td>7.53 ± 1.55</td>
<td>10.24 ± 2.22*</td>
<td>13.39 ± 1.80*</td>
</tr>
<tr>
<td>EEM area (mm²)</td>
<td>21.75 ± 6.04</td>
<td>22.93 ± 4.40</td>
<td>23.72 ± 4.98</td>
</tr>
<tr>
<td>MLA/reference LA</td>
<td>0.61 ± 0.15</td>
<td>0.86 ± 0.28*</td>
<td>1.09 ± 0.19*</td>
</tr>
<tr>
<td>% plaque area</td>
<td>63 ± 12</td>
<td>53 ± 13*</td>
<td>42 ± 12*</td>
</tr>
</tbody>
</table>

*p < 0.05 compared with the paired values of the previous measurement.

EEM = external elastic membrane; reference LA = lumen area of the reference segment. Other abbreviations as in Table 2.
Coronary Flow After IVUS-Guided PTCA

Hemodynamic and Distal Blood Flow Velocity Variables Measured Before and After Standard Balloon Angioplasty, After IVUS-Guided Balloon Angioplasty and After Stent Implantation in All Patients

<table>
<thead>
<tr>
<th></th>
<th>Before BA</th>
<th>After Standard BA</th>
<th>After IVUS-Guided BA</th>
<th>After Stent-Implantation</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (beats/min)</td>
<td>62.4 ± 10.1</td>
<td>61.4 ± 9.9</td>
<td>61.9 ± 8.9</td>
<td>63.1 ± 10.3</td>
</tr>
<tr>
<td>MAP (mm Hg)</td>
<td>85.3 ± 7.2</td>
<td>85.1 ± 8.7</td>
<td>86.0 ± 9.9</td>
<td>86.0 ± 12.0</td>
</tr>
<tr>
<td>Base-APV (cm/s)</td>
<td>11.8 ± 5.5</td>
<td>21.6 ± 9.7*</td>
<td>24.8 ± 13.7</td>
<td>25.6 ± 15.9</td>
</tr>
<tr>
<td>Hyp-APV (cm/s)</td>
<td>17.4 ± 9.2</td>
<td>49.8 ± 20.1*</td>
<td>59.1 ± 22.9*</td>
<td>61.2 ± 24.7</td>
</tr>
<tr>
<td>CFVR</td>
<td>1.51 ± 0.60</td>
<td>2.63 ± 0.69*</td>
<td>2.69 ± 0.80</td>
<td>2.81 ± 1.10</td>
</tr>
<tr>
<td>rCFVR</td>
<td>0.48 ± 0.18</td>
<td>0.83 ± 0.22*</td>
<td>0.87 ± 0.23</td>
<td>0.88 ± 0.26</td>
</tr>
</tbody>
</table>

*p < 0.05 compared with the paired values of the previous measurement.
Base-APV = baseline average peak velocity; CFVR = coronary blood flow velocity reserve; HR = heart rate; Hyp-APV = hyperemic average peak velocity; MAP = mean aortic pressure; rCFVR = relative coronary blood flow velocity reserve. Other abbreviations as in Table 2.

(i.e. directional atherectomy, coronary stent implantation) were employed in order to obtain a larger sized lumen directly after PTCA without the occurrence of severe coronary complications (4–8). Two recently published studies by Stone et al. [Clinical Outcomes with Ultrasound Trial (CLOUT) pilot study] (13) and Haase et al. (14) demonstrated the safe use of upsized balloons when guided by IVUS. Furthermore, Haase et al. demonstrated “sten-like” long-term angiographical and clinical outcomes after IVUS-guided balloon angioplasty (14). This principle was based on the presence of compensatory vessel enlargement at the site of the lesion to preserve a larger lumen, the so-called “Glagov phenomenon” (11,12). The extension of atherosclerosis and compensatory vessel enlargement to the reference segment may result in an angiographical underestimation of the true size of the reference segment (10). In the forementioned IVUS-guided balloon angioplasty studies, different strategies were used to determine the optimal balloon size, resulting in different balloon:artery ratios of 1.30 ± 0.17 (13) and 1.38 ± 0.25 (14). The CLOUT pilot study reported a reduction of residual lumen obstruction from 28 ± 15 to 18 ± 14 %DS without an increase in the incidence of coronary dissections as determined by angiography. In this study, balloons were upsized using the average of the maximal vessel diameter and the maximal lumen diameter of the adjacent reference segments assessed by IVUS analysis. This resulted in a slightly larger balloon: artery ratio of 1.35 ± 0.21 as compared with the CLOUT pilot trial. Nevertheless, the lumen enlargement after IVUS-guided balloon angioplasty (19 ± 22 %DS) was similar to the results of the CLOUT trial. These angiographic results after IVUS-guided balloon angioplasty are in accordance with angiographic studies after adjunctive stent implantation using conventional balloon pressures of ~10 atm (6–8). However, the use of higher balloon pressures (15 atm) for in stent balloon inflations produced less residual lumen obstruction (1 ± 9 %DS) (9). Colombo et al. described an even more pronounced lumen enlargement (to −9 ± 15 %DS) after stent implantation using oversized balloons with high-pressure inflation. These results were similar to the angiographic results of this study immediately after IVUS-guided stent implantation.

This study did not demonstrate an increase in coronary dissections after IVUS-guided balloon angioplasty, taken into account the limited number of patients studied. These findings are in accordance with the studies of Haase et al. and Stone et al., indicating the safe use of IVUS-guided balloon angioplasty.

Hemodynamic response after IVUS-guided balloon angioplasty and coronary stent implantation. Several studies, including this study, showed a normalization of the CFVR (>2.5) after standard balloon angioplasty (16,30). However, there are a limited number of studies evaluating balloon angioplasty and adjunctive coronary interventions in relation to coronary hemodynamics (17,18). A reduced or nearly normal coronary flow reserve after balloon angioplasty may improve towards the value of the reference coronary flow reserve of the normal adjacent coronary artery after coronary stent implantation (17,18). The results of a recently published multicenter study (DEBATE) have demonstrated the prognostic value of an optimal angiographic result (DS < 35%) in conjunction with a normalization of CFVR (>2.5) after balloon angioplasty (16). The aforementioned angiographic studies supporting the concept “the bigger, the better,” as well as the DEBATE-study, underline the clinical relevance of optimizing the procedural result. This study indicates that IVUS-guided balloon angioplasty following balloon angioplasty results in an optimal procedural, angiographical and hemodynamic outcome. The alterations in coronary hemodynamics in relation to residual lumen obstruction were evaluated by the hyperemic blood flow velocity values. In a recent study we demonstrated two different baseline flow velocity responses following balloon angioplasty or stent implantation. A normalized CFVR was associated with a normal baseline flow velocity following intervention, while an impaired CFVR (<2.5) was associated with an increase in baseline blood flow velocity, which may be caused by a temporary loss of the microvascular autoregulation (21). In this study, the hyperemic blood flow velocity increased after standard balloon angioplasty and subsequent IVUS-guided balloon angioplasty. The study of Haase et al. demonstrated a clinical outcome following IVUS-guided balloon angio-
plasty similar to the reported results after stent implantation (14). This study demonstrates that adjunctive stent implantation does not yield a further gain in the hyperemic blood flow velocity, indicating the absence of a functional residual lumen obstruction after IVUS-guided balloon angioplasty, which may explain a similar long-term clinical outcome following IVUS-guided balloon angioplasty as compared with stent implantation. Furthermore, the present results are in accordance with experimental data in the classic study of Gould et al. (31), describing a curvilinear relationship between the severity of short-term artificial coronary lesions and hyperemic blood flow in healthy sedated dogs, i.e., a plateau phase of hyperemic flow in coronary residual lumen obstructions <30%.

**Study limitations.** These results were obtained from a small uniform selected group of patients with one-vessel disease and large reference diameters (i.e. 3.37 ± 0.62 mm), which limits the extrapolation of the present findings to other patient categories. The relative large reference diameter as well as the initial results after balloon angioplasty may be responsible for the differences between other studies showing an increase in coronary flow reserve after adjunctive stent implantation (17,18).

A limitation of this study is the lack of intracoronary pressure measurements. The pressure gradient or corresponding fractional flow reserve across the treated lesion may be used as another physiological variable for the residual lumen obstruction after different treatment modalities. A recent study suggests that the assessment of the pressure gradient by means of a guide wire may serve as an alternative for IVUS to optimize stent implantation (32). The complexity of the present protocol precluded additional pressure measurements in our study. Furthermore, blood flow velocity alterations may not be interpreted as changes due to fluctuations in the diameter of the epicardial coronary segment as a result of alpha-mediated vasoconstriction induced by mechanical stretch and hypoperfusion during balloon inflation (33,34). Nitroglycerin (intracoronary) was administered throughout the procedure in order to minimize this confounding factor.

The site of the repeated blood flow velocity measurements was determined by angiography, although this method for making repeated measurements may have been a contributing factor in the variations noted.

Hyperemic blood flow velocity is subject to an interpatient variability related to a variety of physiologic (35–37) and pathophysiologic conditions of epicardial conduits or the distal microvascular bed (38–41). These confounding factors were limited by the inclusion criteria and, again, by serial observations in individual patients. However, the various interventional techniques used may induce different degrees of medial injury resulting in different grades of platelet activation, microembolization of platelet aggregates, and the release of platelet-mediated vasoconstrictor products may influence hyperemic flow (42). Nevertheless, each patient received aspirin before the procedure, limiting platelet aggregation. Furthermore, there was no variability in hyperemic blood flow velocity between those patients with and those without coronary dissections, which suggests that the effect of this potential factor was limited. Moreover, even if stent implantation may not add any acute advantage in terms of distal perfusion following optimal IVUS-guided PTCA, this aspect does not take into consideration subacute recoil, next day lumen loss and chronic remodeling. This study was not designed to measure subacute recoil after the different types of interventions and therefore did not allow the exclusion of the possibility of an additional protective role of stenting despite IVUS-guided balloon angioplasty.

**Clinical implications.** Intravascular ultrasound guided balloon angioplasty safely provided a direct lumen enlargement and increase in hyperemic blood flow velocity as compared with standard balloon angioplasty. Despite additional lumen enlargement, adjunctive IVUS-guided stent implantation did not create a further improvement in the hemodynamic results. This suggests the presence of a plateau-phase of the optimal hemodynamic response in relation to the residual lumen obstruction, which can be achieved using IVUS-guided balloon angioplasty. Preliminary results of the SIPS (Strategy of ICUS guided PTCA and Stenting) trial demonstrated a lower rate of target lesion revascularization at 6 months follow-up in patients treated with IVUS-guided balloon angioplasty as compared with patients treated with standard balloon angioplasty (43). In an observational study Haase et al. also revealed clinical outcomes after IVUS-guided balloon angioplasty similar to stent implantation (14). Moreover, results of an ongoing clinical trial revealed similar promising long-term outcomes regarding the target lesion revascularization rate (7.8% vs. 12.9%; p = 0.08) and event-free survival (90% vs. 82%; p = 0.05) after IVUS-guided balloon angioplasty as compared with provisional stent implantation (44).

In conjunction, the data from these clinical trials suggest that IVUS-guided balloon angioplasty may serve as an alternative for stent implantation resulting in a similar clinical outcome.

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**Reprint requests and correspondence:** Dr. Jan J. Piek, Dept. of Cardiology, B2-108, Academic Medical Center, Meibergdreef 9, 1105 AZ, Amsterdam, the Netherlands P.O. Box: 22700, 1100 DD, Amsterdam, the Netherlands. E-mail: j.j.piek@amc.uva.nl.

**REFERENCES**

van Liebergen et al.  
Coronary Flow After IVUS-Guided PTCA  
JACC Vol. 34, No. 7, 1999  
December 1999;1899–906


43. Hodgson JM, Roskamm H, Frey AW. Target lesion revascularization performed after ultrasound-guided intervention: findings after 6-months follow-up from the strategy of ICUS guided PTCA and stenting (SIPS) trial [abstract]. Circulation 1997;96:1–582.