Intracoronary Stenting and Risk for Major Adverse Cardiac Events During the First Month

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Background—Our rationale for this study was to analyze the risk for procedural failure of attempted stenting and the risk for major adverse cardiac events (MACE) after success and to develop a risk stratification protocol for successful procedures.

Methods and Results—Stenting was attempted in 2894 procedures during the 5-year study period (success in 98.3% of 3815 lesions). After failure, the MACE rate was 42.6%. The risk for failure was higher for lesions in the left circumflex coronary artery or in venous bypass grafts and after an acute occlusion before stenting; it increased with stenosis length or grade and decreased with vessel size and growing institutional experience in stenting. After success, death occurred in 0.8%, death or myocardial infarction in 2.0%, and any MACE in 3.6%. Independent risk factors for MACE were older age, diabetes, acute myocardial infarction, unstable angina, impaired left ventricular function, residual dissections, stent overlap, longer stented segments, and a postprocedural regimen without ticlopidine. Procedural factors were substantially stronger predictors than operator-independent variables available before procedures. Overall, the risk declined after the first 3 days. Two major factors exhibited time-dependent variations of their influence: while residual dissections were the dominant risk factor within the first 3 days with a reduction after that, no protective effect of ticlopidine could be identified before day 3. From these results, we derived a risk stratification protocol for individual procedures.

Conclusions—These results underscore the importance of optimal angiographic results and the need for antiplatelet regimens with immediate onset. Our risk stratification protocol may guide individual postprocedural care and allow us to compare risk profiles of different study populations and to devise quality control programs for stenting. (Circulation. 1998;98:104-111.)

Key Words: stents ▪ coronary disease ▪ risk factors ▪ platelet aggregation inhibitors

Coronary stenting has become an established treatment for suboptimal results after conventional angioplasty (PTCA), and it reduces restenosis rates in comparison with PTCA. The use of stents has been growing continuously beyond these indications, and today stents are a ubiquitous routine in interventional cardiology.

Although stenting is technically more difficult than standard PTCA, it can be achieved with a high primary success rate (94% to 97%). However, most studies reporting procedural success rates have included only selected patients, for example, those with less complex stenoses. These data might not be applicable to many patients in the increasing routine use of stents. A comprehensive analysis of the risk of procedural failure and the associated risk of MACE is warranted.

Technical refinements and improvements of postprocedural antithrombotic therapy have reduced the rate of MACE during early follow-up. However, the MACE rates may vary substantially, depending on clinical, angiographic, and procedural characteristics, and a comprehensive analysis of the risk for MACE is not available. A protocol for individual risk stratification may not only guide the necessary follow-up care and treatment but also allow us to devise quality control programs for interventional procedures with stent placement.

The rationale of the present study was therefore to analyze the risk for procedural failure of attempted stent placement and the risk for MACE after successful stenting and to develop a risk stratification protocol for successful procedures.

Methods

Patient Population

During the 5-year study period between May 1992 and May 1997, stent placement was attempted during 2894 consecutive procedures (2444 patients, 3815 lesions); 73 additional procedures in patients with cardiogenic shock or mechanical ventilation before PTCA were excluded from this analysis.
Stent Placement

Before stenting, no additional alternative technique (ie, rotational atherectomy, laser, or other debulking devices) was used. Implantation of various slotted-tube–type stents was performed as previously described.\(^7\) The majority were hand-cramped on the angioplasty balloon catheters (95.4%). Intravascular ultrasound studies were performed in only a minority of procedures (8.3%).

Clinical Management After Success

Three different antithrombotic regimens were used: full anticoagulation (18.7% of procedures), combined antiplatelet therapy (79.7%), and aspirin alone (1.6%). All patients were given aspirin (100 mg BID) and intravenous heparin for 12 hours (target partial thromboplastin time, 80 to 100 seconds). Patients with full anticoagulation received the coumarin derivative phenprocoumon (Marcumar; Hoffmann-La Roche), and intravenous heparin was continued until a target international normalized ratio of 3.5 to 4.5 was achieved. Patients assigned to combined antiplatelet therapy received ticlopidine (250 mg BID; Tiklyd, Sanofi-Winthrop). Ticlopidine or phenprocoumon was given for 4 weeks. Because of the pivotal role of ticlopidine,\(^3\),\(^1\),\(^1\) postprocedural regimens are categorized as either with or without ticlopidine.

A complete 30-day follow-up is available for all procedures; all patients were seen as outpatients 1 month after discharge or were contacted by telephone.

Definitions

Procedural success was defined as successful stent placement at the desired position with <30% residual stenosis. MACE were death of cardiac or procedure-related origin, MI, and repeat target lesion revascularization by PTCA or coronary artery bypass graft surgery during a 30-day follow-up. Institutional experience was the time between the day of the procedure and the beginning of the study (May 1, 1992). The following assessments were performed by the operator at the end of the procedure: LV function was categorized as normal in the absence of wall motion abnormalities, slightly impaired if 1 or 2 of 7 ventricular segments were hypokinetic, impaired if several segments were hypokinetic or 1 or 2 akinetic, and severely impaired if several segments were akinetic with only 1 or 2 normal segments. A residual dissection was noted in the presence of a small (<5-mm) dissection in the stented or adjacent segment; dissections >5 mm for which a necessary coverage with additional stents could not be achieved for procedural or technical reasons were defined as substantial residual dissections. Quantitative angiographic analysis was performed off-line on a commercially available system with edge-detection algorithms (CMS, Medis Medical Imaging Systems) by trained technicians not involved in the procedures and unaware of the operator’s qualitative assessments. Measurements of minimal luminal diameter and reference diameter (before and at the conclusion of the procedure), of stenosis length, of the minimal diameter of the largest balloon at maximum inflation pressure, and of the length of the stented segment were obtained.

Data Analysis and Statistics

Data were continuously assessed and entered into a relational database. Clinical data were recorded to define procedures, and angiographic data were assessed for individual lesions treated during a procedure. Analyses were performed with S-Plus software (Math-Soft), expanded by a function library by Harrell. Statistical significance was assumed at \(P<0.05\).

The risk of procedural failure was calculated per lesion with a logistic regression model based on factors available before procedures. Odds ratios were computed for significant correlates. For continuous variables, these refer to the ratio between the odds for the 1st and 3rd quartiles. No significant changes in regression coefficients were observed in 1000 bootstrap replications,\(^5\) even after a potential clustering effect for interventions in >1 lesion was accounted for. We did not limit the number of variables entered into the analysis. However, an unrestricted model yielded the best Akaike’s information criterion (model \(\chi^2\) minus twice the number of parameters aside from the intercept).\(^6\) The reliability of the model was assessed by cross-validation. The model was fitted to 200 bootstrap replications (training sample) and to the original data (test sample) with a good agreement (bootstrap estimate for slope shrinkage, \(-0.70\)).\(^7\)

The risk for MACE was analyzed per procedure with Cox proportional hazard models. Hazard ratios were computed for significant correlates. For interventions in >1 lesion, angiographic variables of 1 randomly assigned lesion were entered into the analysis; for lesion length and length of stented segments, we analyzed the sum of measurements of all lesions to avoid missing an additive role. For the Cox model, the proportional hazard assumption over time was initially tested for each variable. A time-dependent covariable was added to variables that did not satisfy this assumption (product of variable with log-transformed time-to-event). The Cox model was validated in 2 ways: first, the model was fitted to 200 bootstrap samples (training sample) and to the original data (test sample); the resulting correlation was very close (bootstrap estimate for slope shrinkage, 0.79). Second, the survival predicted from 200 bootstrap replications correlated well with the actual Kaplan-Meier survival in all time intervals analyzed. To define subgroups of patients with different risks for MACE, linear risk predictors for each procedure were derived from Cox model analysis. Quartile values were used to differentiate risk groups. On the basis of this model, we developed software to predict the risk for MACE. The program assigns a patient to 1 predicted risk group after actual parameters are entered. Detailed subgroup analysis was made by use of the CART.\(^8\)

The knots of the first 4 divisions are presented unless a subgroup had <50 cases and <10 events.

Results

Stent placement was attempted in 3815 lesions during 2894 procedures in 2444 patients. Procedural success was achieved in 98.3% of lesions and 97.9% of procedures. The reasons for procedural failure were inability to reach or cross the primary target lesion with the stent (n=19), inability to cross an already placed stent with another stent to reach an additional distal target lesion (as defined by a residual stenosis >30% or a substantial dissection extending distally; n=29), inability to achieve adequate flow or a distal thrombus with TIMI flow <2 (n=12), and a perforation of a venous bypass graft (n=1). In 53 procedures, a stent was lost before implantation (0.8% of total number of stents implanted); in 6 of these, no final success could be achieved (resulting in 1 MACE). In 47 procedures, the stent could be withdrawn from the coronary circulation and was lost in the aorta or the peripheral circulation without any associated clinical complication. In 6 of the 53 procedures, a stent was lost within the coronary circulation. Five of these were recovered; 1 was pressed against the vessel wall with an additional stent. All 6 cases were finished successfully without any subsequent MACE.

Failure was associated with a 42.6% MACE rate compared with 3.6% after successful procedures (OR=19.9; 95% CI, 11.0 to 35.3), with 8.2% deaths compared with 0.9%
Risk Analysis for Coronary Stenting

TABLE 1. Factors Analyzed for Risk of Procedural Failure

<table>
<thead>
<tr>
<th></th>
<th>Successful</th>
<th>Unsuccessful</th>
<th><em>P</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>2383</td>
<td>61</td>
<td></td>
</tr>
<tr>
<td>No. of procedures</td>
<td>2833</td>
<td>61</td>
<td></td>
</tr>
<tr>
<td>No. of lesions</td>
<td>3750</td>
<td>65</td>
<td></td>
</tr>
<tr>
<td>Patient age, y</td>
<td>63.0±10.8</td>
<td>64.1±10.5</td>
<td>0.73</td>
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<tr>
<td>Female sex, %</td>
<td>22.6</td>
<td>26.2</td>
<td>0.38</td>
</tr>
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<td>Cardiovascular risk factors, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>16.5</td>
<td>18.3</td>
<td>0.60</td>
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<tr>
<td>Hypercholesterolemia</td>
<td>38.6</td>
<td>37.7</td>
<td>0.41</td>
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<tr>
<td>Arterial hypertension</td>
<td>56.3</td>
<td>50.8</td>
<td>0.34</td>
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<td>Smoking</td>
<td>36.8</td>
<td>36.1</td>
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<tr>
<td>Unstable angina, %</td>
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<td>27.9</td>
<td>0.64</td>
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<tr>
<td>LV function, %</td>
<td>56.2</td>
<td>60.7</td>
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<tr>
<td>Normal</td>
<td>56.2</td>
<td>60.7</td>
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<tr>
<td>Slightly impaired</td>
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<td>11.4</td>
<td></td>
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<tr>
<td>Impaired</td>
<td>20.2</td>
<td>21.3</td>
<td></td>
</tr>
<tr>
<td>Severely impaired</td>
<td>4.2</td>
<td>6.6</td>
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<td>Target vessel, %</td>
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</tr>
<tr>
<td>LAD</td>
<td>41.9</td>
<td>32.3</td>
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<tr>
<td>LCx</td>
<td>17.3</td>
<td>27.7</td>
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<tr>
<td>Left main</td>
<td>1.7</td>
<td>1.5</td>
<td></td>
</tr>
<tr>
<td>RCA</td>
<td>34.2</td>
<td>27.7</td>
<td></td>
</tr>
<tr>
<td>Bypass grafts</td>
<td>4.8</td>
<td>10.8</td>
<td></td>
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<tr>
<td>ACC/AHA lesion characteristics, %</td>
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<td></td>
<td>0.12</td>
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<tr>
<td>A</td>
<td>7.5</td>
<td>3.1</td>
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<tr>
<td>B1</td>
<td>18.6</td>
<td>10.9</td>
<td></td>
</tr>
<tr>
<td>B2</td>
<td>39.9</td>
<td>48.4</td>
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<tr>
<td>C</td>
<td>34.1</td>
<td>37.5</td>
<td></td>
</tr>
<tr>
<td>Ostial lesions, %</td>
<td>10.6</td>
<td>7.7</td>
<td>0.35</td>
</tr>
<tr>
<td>Chronic occlusions (&gt; 1 month old), %</td>
<td>6.0</td>
<td>9.2</td>
<td>0.35</td>
</tr>
<tr>
<td>Acute occlusion before stenting, %</td>
<td>4.3</td>
<td>10.7</td>
<td>0.028</td>
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<tr>
<td>Thrombus present before intervention, %</td>
<td>27.9</td>
<td>18.5</td>
<td>0.29</td>
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<tr>
<td>% stenosis before intervention</td>
<td>74.5±16.1</td>
<td>81.6±15.1</td>
<td>0.0015</td>
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<tr>
<td>Reference diameter, mm</td>
<td>3.04±0.54</td>
<td>2.90±0.62</td>
<td>0.0012</td>
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<tr>
<td>Lesion length, mm</td>
<td>10.7±5.9</td>
<td>12.4±7.6</td>
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<td>Institutional experience in stenting technique, y</td>
<td>3.79±0.94</td>
<td>3.06±1.13</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

(OR = 10.5; CI, 3.0 to 29.3) and 14.8% death or MI compared with 2.0% (OR = 8.4; CI, 3.5 to 18.3). Unsuccessful procedures with MACE (n=26) differed from uneventful procedures with regard to vessel size (2.80±0.62 versus 3.11±0.61 mm; P = 0.05), and they showed a trend toward more unstable angina (42% versus 17%; P = 0.06).

Risk for Procedural Failure of Stent Placement

In view of the poor outcome after failure, we analyzed all variables available before procedures to identify risk factors for failure. All procedures with attempted stent placement are described in Table 1, distinguishing successful from unsuccessful procedures. All factors were entered into a multivariate logistic regression analysis; the resulting P values are listed in the Table. The 6 significant risk factors for procedural failure are illustrated in Figure 1: the risk increased with stenosis length and grade but decreased with vessel size; it was higher in the case of an acute occlusion before stenting (after the initial PTCA) and for lesions in venous bypass grafts or the LCx. The most significant factor was the institutional experience in stent placement technique: with increasing practice during the 5 years, procedural failure was less likely (Figure 2).

Risk for MACE After Successful Stent Placement

The overall incidence of MACE was 3.6% (n = 102). In 65 events, the cause was stent occlusion verified by angiography or autopsy; 20 were repeat PTCA with patent stents but nonocclusive dissections in neighboring segments or side branches; 3 were MIs due to side branch occlusions after stenting; 12 were deaths of cardiac origin without evidence of stent occlusion; and 2 were procedure-related noncardiac deaths. No other deaths occurred during the study period. The
The association of all factors with MACE is summarized in Table 2, with \( P \) values from the Cox model. Independent risk factors were older age, diabetes, acute MI, unstable angina, impaired LV function, residual dissections, stent overlap, and longer stented segments; a postprocedural regimen with ticlopidine was a significant protective factor (Figure 3).

This analysis is based on 4 categories of factors: (1) clinical data; (2) lesion characteristics, both available before procedures and operator-independent; (3) procedural factors describing the intervention and the final results; and (4) the postprocedural antithrombotic regimen (categorized as with or without ticlopidine). These 4 categories are separated by thin lines in Table 2. To assess the contribution of each category to the strength of the final Cox model, we analyzed partial models with variables from the respective categories. These results are illustrated in Figure 4 in a comparison of the \( \chi^2 \) of the partial models. The models with variables available before the procedure that are operator-independent yield a relatively low \( \chi^2 \), indicating only a minor contribution to the strength of the full model. The model with procedural variables yields a high \( \chi^2 \), which is further increased if the

### TABLE 2. Factors Analyzed for Risk of MACE After Successful Stent Placement

<table>
<thead>
<tr>
<th></th>
<th>Without MACE</th>
<th>With MACE</th>
<th>( P^* )</th>
</tr>
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<tbody>
<tr>
<td>No. of procedures</td>
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<td>Patient age, y</td>
<td>62.9±10.8</td>
<td>66.4±10.4</td>
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<td>Female sex, %</td>
<td>22.3</td>
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<td>Cardiovascular risk factors, %</td>
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<td>Diabetes mellitus</td>
<td>16.1</td>
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<td>Hypercholesterolemia</td>
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<td>56.1</td>
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<td>Smoking</td>
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<td>29.4</td>
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<td>Slightly impaired</td>
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<td>Target vessel, %</td>
<td>LAD</td>
<td>41.2</td>
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<td>LCx</td>
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<td>Bypass grafts</td>
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<td>ACC/AHA lesion characteris, %</td>
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<td>C</td>
<td>32.1</td>
<td>50.0</td>
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<td>Ostial lesions, %</td>
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<td>10.8</td>
<td>0.66</td>
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<td>Chronic occlusions (( &gt;1 ) month old), %</td>
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<td>6.9</td>
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<td>Acute occlusion before stenting, %</td>
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<td>Thrombus present before intervention, %</td>
<td>26.4</td>
<td>43.1</td>
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<td>% stenosis before intervention</td>
<td>75.2±15.7</td>
<td>78.0±17.2</td>
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<td>Reference diameter before intervention, mm</td>
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<td>3.02±0.56</td>
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<td>Cumulative lesion length, mm</td>
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<td>16.9±11.0</td>
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<td>Institutional experience in stenting technique, y</td>
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<td>3.51±1.16</td>
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<td>Intervention ( &gt;1 ) lesion, %</td>
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<td>0.68</td>
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<tr>
<td>Type of stent, %</td>
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<td>56.9</td>
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<td>ID</td>
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<td>ACS Multilink</td>
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<td>Exotic</td>
<td>1.6</td>
<td>1.0</td>
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<td>Combination of different stent types</td>
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<td>4.9</td>
<td>0.56</td>
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<tr>
<td>Balloon-to-vessel ratio</td>
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<td>1.04±0.11</td>
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<td>Maximum balloon pressure, atm</td>
<td>13.9±3.3</td>
<td>13.2±3.7</td>
<td>0.12</td>
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### TABLE 2. Continued

<table>
<thead>
<tr>
<th></th>
<th>Without MACE</th>
<th>With MACE</th>
<th>( P^* )</th>
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<tr>
<td>% stenosis after stenting</td>
<td>5.8±9.6</td>
<td>7.3±10.2</td>
<td>0.73</td>
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<tr>
<td>Cumulative length of stented segments, mm</td>
<td>22.5±15.4</td>
<td>32.1±24.2</td>
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<td>Overlapping stents, %</td>
<td>15.9</td>
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<td>Thrombus present after stenting, %</td>
<td>6.8</td>
<td>18.6</td>
<td>0.085</td>
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<td>Slow distal flow after stenting (TIMI 1–2( ^{-1/2} )), %</td>
<td>5.6</td>
<td>11.8</td>
<td>0.75</td>
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<td>Residual dissection after stenting, %</td>
<td>20.9</td>
<td>40.2</td>
<td>(&lt;0.0001)</td>
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<td>Substantial residual dissection</td>
<td>2.3</td>
<td>16.7</td>
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<td>Postprocedural regimen with ticlopidine, %</td>
<td>80.4</td>
<td>61.8</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

Abbreviations as in Table 1.

*\( P \) values as calculated by Cox proportional hazard model; data were analyzed per procedure (model \( \chi^2=177 \)).

association of all factors with MACE is summarized in Table 2, with \( P \) values from the Cox model. Independent risk factors were older age, diabetes, acute MI, unstable angina, impaired LV function, residual dissections, stent overlap, and longer stented segments; a postprocedural regimen with ticlopidine was a significant protective factor (Figure 3).

This analysis is based on 4 categories of factors: (1) clinical data; (2) lesion characteristics, both available before procedures and operator-independent; (3) procedural factors describing the intervention and the final results; and (4) the postprocedural antithrombotic regimen (categorized as with or without ticlopidine). These 4 categories are separated by thin lines in Table 2. To assess the contribution of each category to the strength of the final Cox model, we analyzed partial models with variables from the respective categories. These results are illustrated in Figure 4 in a comparison of the \( \chi^2 \) of the partial models. The models with variables available before the procedure that are operator-independent yield a relatively low \( \chi^2 \), indicating only a minor contribution to the strength of the full model. The model with procedural variables yields a high \( \chi^2 \), which is further increased if the

### Figure 3. Hazard ratios for independent risk factors for MACE after successful stenting identified by Cox analysis (for age calculated for 1st vs 3rd quartile; ie, 71.1 vs 55.8 years; for impaired LV function, impaired vs normal; for length of stented segment, 30 vs 15 mm; for residual dissection, substantial vs no residual dissection); hazard ratios are displayed on a logarithmic scale.

### Hazard Ratio and 95% CI

- age
- diabetes
- acute MI
- unstable angina
- impaired LV function
- length of stented segment
- residual dissection
- stent overlap
- ticlopidine

0.1 1 10 20

- Hazard ratios for independent risk factors for MACE after successful stenting identified by Cox analysis (for age calculated for 1st vs 3rd quartile; ie, 71.1 vs 55.8 years; for impaired LV function, impaired vs normal; for length of stented segment, 30 vs 15 mm; for residual dissection, substantial vs no residual dissection); hazard ratios are displayed on a logarithmic scale.
adjunct postprocedural regimen is included. These analyses indicate a dominant contribution of these operator-dependent factors to the risk for MACE.

Time Dependency of Risk Factors

Figure 5A shows the cumulative incidence of MACE. There is an apparent decline in the risk for MACE, with >50% of events occurring in week 1. This decreasing hazard as a function of time is illustrated in Figure 5B. All significant factors were tested for temporal variations of their influence. The 2 factors identified are illustrated in Figure 5C. Residual dissections constituted a major risk factor during the first 3 days, with a decreasing weight afterward. An opposing effect was seen for a regimen without ticlopidine: during the first 2 days, this did not constitute a significant risk; however, the hazard ratio later increased significantly, peaking after 1 week. This signifies that a protective effect of ticlopidine could not be identified before day 3.

Risk Stratification

We used a CART model to define subgroups with distinct MACE rates (Figure 6). The primary risk factor was the grade of residual dissection: in its presence, the MACE rate increased from 2.1% to 8.4%. It increases further for subgroups with length of stented segment >15 mm and substantial residual dissections to a maximum of 27.8%. Conversely, the lowest event rate of 0.5% could be found in a large group of ≈30% of all procedures (n=844) in patients with normal LV function, a postprocedural regimen with ticlopidine, and no acute MI.

To calculate individual risks of procedures based on actual parameters, linear risk predictors were derived from the Cox model with all variables. This risk stratification protocol defines 3 risk groups on the basis of the quartiles of the study population. The 2 quartiles with the lowest risk were condensed to 1 low-risk group because the quartile values were not significantly different (0.4% and 1.0%). This model therefore identified a large group with a low risk and 2 smaller groups with intermediate and high risk. Figure 7 shows the cumulative MACE rates for these groups. This graph illustrates that in the high and intermediate risk groups, events occurred throughout the observation period. In the low-risk group, however, no event occurred after day 15.
Discussion

In the present study, we provide a comprehensive analysis of the risk for procedural failure of coronary stenting as well as the risk for MACE after procedural success, and we describe a protocol for individual risk stratification. This analysis included all patients treated at our institutions during a 5-year period; only patients with cardiogenic shock or mechanical ventilation before the procedure were excluded. Therefore, the study population represents the full spectrum of symptomatic coronary artery disease, including many patients with acute coronary syndromes and technically complex lesions who had been excluded from several previous trials.

Procedural success was achieved in 97.9% of procedures. This success rate is higher than reported for several studies that had included only selected patients.\(^5\) However, most of these studies used stents premounted on delivery systems with unfavorable balloon catheter profiles and limited trackability. The majority of our procedures were performed with hand-mounted stents on low-profile, rapid-exchange catheters. In our analysis, procedural failure was more likely in venous bypass grafts or lesions in the LCx, after an acute occlusion before stenting (after the initial PTCA), and in smaller vessels with tighter or longer lesions. The main factor for success, however, was the institutional experience in stent placement technique. This time-dependent protective factor reflects our institutional learning curve together with continuing improvements in technique. In view of the high MACE rate observed after unsuccessful procedures, these data underscore the need for optimization of technical equipment as well as operational skills.

Our data indicate that MACE rates after successful stenting may vary substantially. CART analysis (Figure 6) shows that there are well-defined subgroups with particular high or low event rates ranging from 0.5% to 27.8%. Because these depend on applicable risk factors identified by the Cox model, any comparison with other studies would have to account for differences in risk profiles.

We had included a very large number of factors: clinical data and lesion characteristics available before an intervention, procedural factors referring to the intervention and the final results, and the postprocedural antithrombotic regimen. Nine characteristics were identified as significant and independent risk factors for MACE. Several of these factors had already been suggested by logistic regression analyzes focus-
Risk Analysis for Coronary Stenting

ing on thrombotic stent occlusion in smaller patient co-
horts. Five of the significant factors are operator-inde-
dependent, because they refer to a patient’s status before the
intervention (age, diabetes, acute MI, unstable angina, im-
paired LV function); 4 are operator-dependent, because they
refer to either the procedure itself with final results (length of
stented segment, residual dissection, stent overlap) or the
postprocedural regimen (ticlopidine). The 3 most significant
factors were all procedural variables (residual dissection,
postprocedural regimen, and length of stented segment).
Furthermore, in our analysis of partial models (Figure 4),
the models with procedural variables and ticlopidine were
the strongest, whereas models with data available before the
intervention contributed only a minor part to the strength of
the final model. These data suggest that factors describing the
procedure and the final result are the major determinants of
early outcome, with a smaller contribution by factors describ-
ing the patient’s status before the procedure.

Our data indicate that the risk for MACE is highest during
the first 3 days and decreases rapidly after that. However,
only after procedures with a low-risk profile, no event
occurred after week 2 (Figure 7B). Therefore, this study
provides only limited support for concepts of a shorter
ticlopidine regimen of only 2 weeks. We had identified 2
factors with significant temporal variations of their influence:
the risk associated with residual dissections peaks during the
first 3 days, with a decrease after that, and a protective effect
of ticlopidine cannot be identified before day 3. Residual
dissections represent a suboptimal final result. They have
been identified as the major risk factor for thrombotic stent
occlusions, which have been the predominant cause of
MACE in virtually all studies on stenting. The delayed
protective effect of ticlopidine reflects the well-known slow
onset of action of this drug. The contrasting effects of these
2 factors might be interrelated, suggesting that the early “gap”
of ticlopidine action should be compensated for either by
pretreatment with ticlopidine for several days or by more
potent antiplatelet drugs with immediate onset of action (ie,
glycoprotein IIb/IIIa receptor inhibitors) given during the
procedure and the first few days. Further studies on optimal
strategies for this early period after stenting are warranted.

Some factors included in our analyses for MACE have
been subject to major debate, for example, maximum balloon
pressure and balloon-to-vessel ratio. Neither variable was
identified as a significant factor. Both were initially deemed
important for the transition from full anticoagulation to
combined antiplatelet therapy. However, although high-
pressure stent dilatations are widely performed, controlled
data are not available. Retrospective analyses looking at the
influence of high pressure and subsequent events did not
identify an independent role of balloon pressure, and
preliminary results from 2 randomized trials did not indicate
a significant benefit for patients treated with high-pressure
balloon inflations. Final results of these and possibly other
randomized trials are necessary to define the role of balloon
pressure.

Limitations
The rate of procedural failure was low. This might have
affected the ability of the study to detect specific aspects or
predictive factors for failure and might have increased the
risk of a type II error.

All significant risk factors for procedural failure or MACE
that are available before procedures were only weak predic-
tors in our analysis (except for institutional experience); there-
fore, no inferences can be made that these might consti-
tute contraindications for stenting.

Postprocedural increases in creatine kinase have been
associated with adverse outcome, particularly with an in-
crease in late mortality. In our study, routine measurements
of creatine kinase were used only to confirm a diagnosis of the
adverse event of acute MI (in all our studies defined as
twice the upper limit of normal); small increases in enzyme
levels were not recorded in the database. Therefore, we
cannot evaluate the possible role of such a rise below the
index limit.

Intravascular ultrasound studies were performed in only a
minority of procedures. Therefore, this study does not allow
for a meaningful analysis of the role of intravascular ultra-
sound or intravascular ultrasound measurements. We used
predominantly hand-mounted slotted-tube stents; an unre-
stricted applicability of our results to other types (ie, with
delivery systems or coil stents) would have to be verified in
specific studies.

Bootstrapping procedures were performed to validate the
results of our models; additional prospective or randomized
trials may be necessary to further validate the findings of our
study.

Summary
The main findings of the present study can be summarized as
follows. Procedural success can be achieved in a very high
number of procedures. Failure is associated with a >10-fold
increase in MACE. The risk for procedural failure is higher
after an acute occlusion before stenting (after initial PTCA)
and for target lesions in the LCx or in venous bypass grafts;
it increases with stenosis length and grade and decreases with
vessel size and growing institutional experience in stenting.
These data underscore the need for optimization of technical
equipment as well as operational skills and training. After
success, the risk for MACE depends predominantly on
procedural characteristics: it is higher in the presence of
residual dissections or stent overlap and increases with the
length of the stented segment. Furthermore, the risk is
significantly lower with postprocedural ticlopidine therapy.
The risk for MACE depends to a lesser extent on operator-
independent patient characteristics available before a proce-
dure (age, diabetes, acute MI, unstable angina, impaired LV
function). The risk for MACE declines after the first 3 days.
Residual dissections are the most important risk factor for this
early period, with a decline later. Ticlopidine has no effect on
the risk for this early period but is a dominant protective
factor later. These results underscore the importance of an
optimal angiographic result and the need for an additional or
alternative antiplatelet regimen with immediate onset. The
risk stratification protocol based on our model calculations
may allow us to study more precisely the necessary individual
follow-up care, ie, the low-risk group may be the subject of
future studies on the necessary duration of antithrombotic
therapy, and the high-risk group may be the subject of studies on additional or more effective antithrombotic regimens. Furthermore, this protocol may permit an accurate comparison of different study populations. Finally, because this protocol identified procedural factors in particular, it may help to establish quality control programs for coronary stenting, which are undoubtedly needed in the future.

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