Prediction of Clinical Outcome After Mechanical Revascularization in Acute Myocardial Infarction by Markers of Myocardial Reperfusion

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OBJECTIVES
We sought to evaluate and compare recently suggested parameters of reperfusion after angioplasty in acute myocardial infarction (AMI) for risk stratification during long-term follow-up.

BACKGROUND
Abnormal myocardial perfusion has a detrimental impact on survival. Several parameters of reperfusion have been evaluated in controlled study populations for risk stratification.

METHODS
In 253 consecutive patients undergoing intervention in AMI on a native coronary vessel, angiographic myocardial blush grade (MBG), corrected TIMI (thrombolysis in myocardial infarction) frame count (CTFC) and persistent ST-segment elevation (STE) were determined to evaluate reperfusion. This was a high-risk population, including referral for treatment failure at a primary center in 29.2%, failed thrombolysis in 22.1% and cardiogenic shock in 13.4% of cases.

RESULTS
In addition to age, patient referral, LBBB and heart rate on admission, MBG 0 to 1 (odds ratio [OR] = 3.23, p < 0.001), CTFC (OR = 1.01, p = 0.015) and persistent STE >2 leads (OR = 3.46, p = 0.010) were univariate predictors of mortality during a 22.1±15.6 months follow-up. Myocardial blush grade 0 to 1 (OR = 2.17, p = 0.033) and persistent STE (OR = 3.61, p = 0.017) persisted as independent predictors of mortality, whereas CTFC failed. Differences in mortality between reperfusion groups at 30 days remained throughout the complete follow-up. In sequential Cox models, the predictive power of clinical data alone for mortality (model chi-squared 55.8) was strengthened by adding MBG (model chi-squared 64.2) and ECG postintervention (model chi-squared 69.2).

CONCLUSIONS
Myocardial blush grade 0 to 1 and persistent STE are independent predictors for long-term mortality after angioplasty in AMI. Corrected TIMI frame count is a less powerful predictor. Combining both parameters to consider quality of reperfusion in the myocardium at risk and extent of the infarct zone increases the predictive power. (J Am Coll Cardiol 2003;41:532–8) © 2003 by the American College of Cardiology Foundation

Early restoration of patency and adequate antegrade reflow in the infarct-related artery has been the primary objective of treatment strategies in patients with acute myocardial infarction (AMI) (1,2). In recent years, there has been increasing recognition that the objective should be extended to the achievement of adequate reperfusion on the myocardial tissue level (3–5). A lack of myocardial reperfusion in spite of restored (Thrombolysis In Myocardial Infarction [TIMI]-3) flow, the “no-reflow” phenomenon, initially has been described by myocardial contrast echocardiography and confirmed by other imaging techniques such as positron emission tomography (3,6). Impaired myocardial reperfusion after AMI is associated with an increased rate of left ventricular (LV) dysfunction, complications and impaired survival (4–8).

Several parameters by which myocardial microcirculation can be easily and reproducibly assessed have been suggested. Among them are the angiographic myocardial blush grade (MBG), the corrected TIMI frame count (CTFC) and the early persistence of ST-segment elevation (STE) (9–13). The myocardial blush relates to the contrast opacification of the myocardial bed subtended by the infarct artery. The CTFC is a quantitative index of the coronary flow in the infarct-related artery, and persistent STE appears to reflect inadequate restoration of perfusion on the myocardial tissue level. The comparative value of different markers of reperfusion easily to be obtained during the acute stage of AMI in a nonselected high-risk population for prediction of follow up clinical events has not been evaluated. The present study was undertaken: 1) to compare CTFC, low MBG and persistent STE regarding their predictive value for mortality during long-term follow up in a cohort of high-risk AMI patients undergoing mechanical reperfusion therapy at a referral center, and 2) to determine if the prognostic value for mortality can be improved by a combination of parameters of microvascular reperfusion.
Abbreviations and Acronyms

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tr>
<td>AMI</td>
<td>acute myocardial infarction</td>
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<td>CTFC</td>
<td>corrected TIMI frame count</td>
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<td>LBBB</td>
<td>left bundle branch block</td>
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<td>LV</td>
<td>left ventricular, left ventricle</td>
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<tr>
<td>MBG</td>
<td>myocardial blush grade</td>
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<tr>
<td>PTCA</td>
<td>percutaneous transluminal coronary angioplasty</td>
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<td>STE</td>
<td>ST-segment elevation</td>
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<td>TIMI</td>
<td>Thrombolysis In Myocardial Infarction</td>
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METHODS

Study population. Two hundred fifty-three consecutive patients with first AMI undergoing mechanical revascularization within 12 h of symptom onset at the University Clinic Aachen from January 1996 through November 1999 were included in the study. Inclusion criteria were 1) typical anginal pain lasting >30 min, 2) ST-segment elevation of >0.2 mV in at least two contiguous ECG leads. All patients were considered regardless of hemodynamic status, infarct vessel and possible thrombolytic therapy before the intervention. Patients presenting >12 h after onset of symptoms were considered for PTCA only if they had signs of recurrent myocardial infarction. Twelve-lead electrocardiogram was repeated 1 h after PTCA. On the last coronary angiogram after revascularization, MBG and CTFC were determined.

Coronary angiography and angioplasty. Coronary angiography was done with a frame rate of 12.5/s. Coronary angiograms were analyzed off-line (QuantCor, CAAS II, Siemens, Erlangen, Germany). Acetylsalicylic acid (100 mg daily) and ticlopidine (250 mg twice daily) were given during follow up.

Myocardial blush grade (MBG) was graded by a blinded experienced interventionalist on the final angiogram based on the visual assessment of contrast opacification of the myocardial territory subtended by the infarct vessel, as described previously (9). Myocardial blush grade was defined as follows: 0 = no myocardial blush or contrast density; 1 = minimal myocardial blush or contrast density; 2 = moderate myocardial blush or contrast density but less than that obtained during angiography of a contralateral or ipsilateral noninfarct-related coronary artery; and 3 = normal myocardial blush or contrast density, comparable to that obtained during angiography of a contralateral or ipsilateral noninfarct-related coronary artery. Myocardial blush grade 0 and 1 were combined in the results. From multiple orthogonal projections, the single view was chosen that best isolated the myocardial infarct zone in question.

The CTFC was determined on the final angiogram to objectively assess coronary blood flow as a continuous variable, as described recently (11). In brief, the number of frames required for dye to reach standardized distal landmarks was counted and divided by 1.7 for the left anterior descending artery to obtain the corrected frame count. Subsequently, the number of frames was multiplied by 30 and divided by 12.5 to report a cine frame count in accordance with standard methods (11). A CTFC ≥40 was used to identify patients with depressed reperfusion, as opposed to patients with a CTFC <40, as described previously (11). Intra- and interobserver variability in the assessment of MBG and CTFC were determined from a random sample of 30 films scored by Ph.H. and R.H. Assessment of intraobserver variability demonstrated a kappa of 0.92 for the MBG and a mean deviation of 0.6 ± 0.4 frames for the CTFC. Assessment of interobserver variability demonstrated a kappa of 0.87 for the MBG and a mean deviation of 0.9 ± 0.5 frames for the CTFC.

Electrocardiogram analysis. Electrocardiograms were done on admission to hospital (first ECG) and in the coronary care unit 1 h after primary angioplasty. The STE was evaluated 0.06 s after the end of the QRS-complex in the 12-lead ECG. Electrocardiogram leads demonstrating a STE of more than 0.1 mV after angioplasty were considered to show persistent STE. The number of ECG leads with persistent STE was used as a parameter to assess the size of the myocardial area with failed reperfusion. Persistent STE in >2 leads on a 12-lead ECG was considered an indicator for more extensive impairment of reperfusion. In addition, ECGs done after intervention were classified based on resolution of STE compared with the baseline ECG. The categories for classification were normalized, improved or unchanged, as previously described (14).

Clinical follow-up. Follow-up information on patient survival was obtained in all 253 patients. Data were obtained by telephone contact with the patient, with one of his or her immediate relatives and complemented by information obtained by the patient’s general physician or patient charts from recurrent hospital admissions. In case neither patient nor relatives could be contacted and patient’s general physician did not know about the patient’s outcome, the local population registries were contacted to obtain information about the patient’s possible death or current location.

Statistical analysis. Analysis was performed using SAS V8.2 software (SAS Institute Inc., Cary, North Carolina). Continuous variables are presented as mean ± SD and were compared using Student t test, Wilcoxon test, or ANOVA, as appropriate. Dichotomous variables were compared using chi-squared statistics or Fisher’s exact test. Patient survival was analyzed and Kaplan-Meier curves were constructed. Differences between survival curves were evaluated using the log-rank test. Receiver operating characteristics curves were calculated, which considered MBG alone or MBG divided by number of ECG leads with persistent STE for prediction of mortality. Cox proportional hazard regression was used to determine the independent predictors of mortality. Univariate predictors with p < 0.1 were included in the multivariate analysis. Values of p ≤ 0.05 were considered to indicate statistical significance.
Table 1. Baseline Clinical and Angiographic Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Dead (n = 62)</th>
<th>Alive (n = 191)</th>
<th>p</th>
</tr>
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<tbody>
<tr>
<td>Age (yrs)</td>
<td>63.6 ± 10.8</td>
<td>58.3 ± 11.7</td>
<td>0.002</td>
</tr>
<tr>
<td>Chest pain to hospital (h)</td>
<td>4.8 ± 5.7</td>
<td>3.8 ± 4.5</td>
<td>0.336</td>
</tr>
<tr>
<td>Door to needle time (h)</td>
<td>2.0 ± 2.2</td>
<td>1.9 ± 2.0</td>
<td>0.892</td>
</tr>
<tr>
<td>Female</td>
<td>17 (27%)</td>
<td>31 (16%)</td>
<td>0.082</td>
</tr>
<tr>
<td>Cardiogenic shock</td>
<td>11 (18%)</td>
<td>23 (12%)</td>
<td>0.171</td>
</tr>
<tr>
<td>Heart rate before PTCA (beats/min)</td>
<td>90.7 ± 26.5</td>
<td>73.3 ± 16.4</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Patient referral</td>
<td>24 (39%)</td>
<td>50 (26%)</td>
<td>0.063</td>
</tr>
<tr>
<td>No. of diseased vessels</td>
<td>2.1 ± 0.8</td>
<td>1.7 ± 0.7</td>
<td>0.002</td>
</tr>
<tr>
<td>Peak creatine kinase (U/l)</td>
<td>1,492 ± 1,713</td>
<td>914 ± 1,166</td>
<td>0.004</td>
</tr>
<tr>
<td>Abciximab</td>
<td>30 (48%)</td>
<td>92 (48%)</td>
<td>1.000</td>
</tr>
<tr>
<td>IABP</td>
<td>25 (41%)</td>
<td>11 (6%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Stent</td>
<td>42 (68%)</td>
<td>151 (79%)</td>
<td>0.058</td>
</tr>
<tr>
<td>Target vessel: left anterior descending</td>
<td>24 (39%)</td>
<td>80 (42%)</td>
<td>0.626</td>
</tr>
<tr>
<td>Baseline TIMI flow 3</td>
<td>7 (11%)</td>
<td>67 (35%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>22 (36%)</td>
<td>67 (35%)</td>
<td>1.000</td>
</tr>
<tr>
<td>Left bundle branch block</td>
<td>14 (23%)</td>
<td>11 (6%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Markers of reperfusion</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postprocedure TIMI flow 3</td>
<td>50 (80%)</td>
<td>173 (91%)</td>
<td>0.064</td>
</tr>
<tr>
<td>MBG 0/1</td>
<td>39 (63%)</td>
<td>61 (32%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>MBG 2</td>
<td>14 (23%)</td>
<td>60 (31%)</td>
<td>0.206</td>
</tr>
<tr>
<td>MBG 3</td>
<td>9 (14%)</td>
<td>70 (37%)</td>
<td>0.004</td>
</tr>
<tr>
<td>CTFC (frames)</td>
<td>42.6 ± 32.2</td>
<td>32.8 ± 23.9</td>
<td>0.012</td>
</tr>
<tr>
<td>ECG leads with ST-segment elevation post PTCA</td>
<td>4.42 ± 1.87</td>
<td>3.20 ± 2.22</td>
<td>0.001</td>
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</table>

CTFC = corrected TIMI frame count; IABP = intraaortic balloon pump; MBG = myocardial blush grade; PTCA = percutaneous transluminal coronary angioplasty; TIMI = Thrombolysis In Myocardial Infarction

RESULTS

Patient population. Baseline characteristics of the 253 patients included in the analysis are given in Table 1. The study cohort consisted of a high-risk group of patients. Seventy-four patients (29.2%) were referrals from other centers because of cardiogenic shock, failed thrombolysis or persistent chest pain after conventional treatment. Thirty-four patients (13.4%) presented in cardiogenic shock, and 56 patients (22.1%) underwent rescue angioplasty for failed thrombolysis. In 36 patients (14.2%), placement of an intra-aortic balloon pump for sustained hypotension was required.

Interventional procedure and late clinical outcome. In 193 patients (76.3%), stent placement was used to optimize the interventional result, and in 122 patients, (48.2%) glycoprotein IIb/IIIa receptor antagonists were administered.

Thirty-six patients (14.2%) had died at 30-day follow up, 49 patients (19.4%) at 180-day follow-up and 62 patients (24.5%) during the total follow-up period (22.1 ± 15.6 months).

Myocardial perfusion status and effect on outcomes. Data on MBG and CTFC at the end of the interventional procedure as well as interpretable ECGs on admission could be obtained in all patients. After the interventional procedure no ECG was available in eight patients because of death of the patient, and 25 patients were excluded from the evaluation of STE because of left bundle branch block (LBBB). Seventy-nine patients had MBG 3, 74 patients MBG 2 and 100 patients MBG 1. Seventy-one patients had a CTFC ≥40 and 182 patients a CTFC <40. One hundred forty-nine patients had persistent STE in ≥2 ECG leads; 71 patients had less extensive persistent STE changes.

Patients who died during long-term follow-up were of higher age, had more diseased coronary arteries, a higher heart rate before intervention, more frequent LBBB, a higher peak creatine kinase level, required more frequently placement of an intra-aortic balloon pump, had less frequent TIMI flow 3 at baseline, a higher CTFC, a higher number of ECG leads with persistent STE, more frequent BG = 0 and less frequent BG = 3 (Table 1). Considering the level of ST-segment resolution, mortality for patients with persistence of STE after angioplasty >0.7 of first ECG was 37% compared with 22% with improved ECG (persistence of STE 0.3 to 0.7) and 18% for patients with normalized ECG (persistence of STE <0.3) (p = 0.037).

Perfusion parameters to predict survival during follow-up. Coronary CTFC, ECG following intervention and the MBG category allowed prediction of patient mortality at 30 days and during long-term follow-up. Cumulative survival curves for the three parameters are displayed in Figure 1. Log-rank statistics demonstrated highly significant differences between the groups for each parameter. Differences in mortality observed at 30-day follow-up between the blush grade groups persisted at 1-year follow-up and during the complete follow-up period (Table 2). Further subanalysis considering patients with persistence of STE in ≥2 ECG leads demonstrated mortality during follow-up of 4% for patients with no ECG lead demonstrating persistent STE (N = 28), 5% for patients with one ECG lead with
persistent STE (n = 21) and 14% for patients with two ECG leads with persistent STE (n = 22).

Univariate predictors of cumulative mortality by Cox proportional hazard regression analysis were age >70 years, patient referral, heart rate on admission >100 beats/min, LBBB on admission, CTFC, persistent STE in >2 ECG leads after PTCA and MBG 0 to 1 (Table 3). In a multivariate analysis, MBG 0 to 1 and persistent STE in >2 ECG leads remained independent determinants of mortality, in addition to advanced age, patient referral, heart rate on admission and LBBB (Table 4); CTFC did not have the power to persist as an independent predictor. Considering in a multivariate analysis only those 223 patients with TIMI flow 3 postprocedure, the same variables, including persistent STE in >2 ECG leads and MBG 0 to 1, remained independent determinants of mortality. Considering level of ST-segment resolution instead of number of ECG leads with persistent STE was also a univariate predictor of mortality (OR = 2.95, 95% CI 1.65 to 6.45, p = 0.015 for incomplete resolution compared with normalized ECG).

Sequential Cox hazard models for the prediction of cumulative mortality were devised to assess the incremental contribution of MBG and number of ECG leads with persistent STE to the clinical evaluation of the patient. Age>70 years, patient being a referral, heart rate prior to intervention and LBBB entered the clinical model (chi-squared 55.8, p < 0.0001). The addition of MBG being 0 to 1 increased the power of the model (chi-squared 64.2, p < 0.0001) and subsequent addition of the number of ECG leads with persistent STE further increased the power of the model (chi-squared 69.2, p < 0.0001).

The combination of MBG and 1 (number of ECG leads demonstrating persistent STE after PTCA) had a higher accuracy to predict mortality than MBG alone (area under the ROC curve 0.71, 95% CI 0.65 to 0.77 for MBG/

Table 2. Relation of Myocardial Perfusion Grade to Mortality

<table>
<thead>
<tr>
<th>MBG 0/1 (n = 100)</th>
<th>MBG 2 (n = 74)</th>
<th>MBG 3 (n = 79)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death at 30 days</td>
<td>26.0%</td>
<td>9.9%</td>
<td>3.9%</td>
</tr>
<tr>
<td>Death at 1 year</td>
<td>35.1%</td>
<td>13.4%</td>
<td>9.4%</td>
</tr>
<tr>
<td>Death during F/U</td>
<td>39.0%</td>
<td>18.3%</td>
<td>12.4%</td>
</tr>
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</table>

F/U = follow-up; MBG = myocardial blush grade.

Figure 1. Cumulative survival in 253 patients after mechanical revascularization for acute myocardial infarction stratified by myocardial blush grades (MBG, left), corrected TIMI frame counts (CTFC, middle) and persistent ST-segment elevation in >2 or >2 electrocardiographic (ECG) leads after PTCA (percutaneous transluminal coronary angioplasty) (ECG post PTCA, n = 220, right). P values represent log-rank for trend. MI = myocardial infarction.

Table 3. Univariate Cox Model Predictors of Cumulative Mortality

<table>
<thead>
<tr>
<th>OR</th>
<th>95% CI</th>
<th>p</th>
</tr>
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<tbody>
<tr>
<td>Age &gt;70 yrs</td>
<td>2.23</td>
<td>1.20–4.14</td>
</tr>
<tr>
<td>Patient referral</td>
<td>1.77</td>
<td>1.01–3.12</td>
</tr>
<tr>
<td>Heart rate pre PTCA</td>
<td>4.06</td>
<td>2.11–7.78</td>
</tr>
<tr>
<td>&gt;100 beats/min</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LBBB</td>
<td>3.12</td>
<td>1.51–6.49</td>
</tr>
<tr>
<td>MBG 0–1 vs. MBG 2–3</td>
<td>3.23</td>
<td>1.82–5.88</td>
</tr>
<tr>
<td>ST-segment elevation in &gt;2 leads post PTCA</td>
<td>3.46</td>
<td>1.35–8.86</td>
</tr>
<tr>
<td>CTFC (frame)</td>
<td>1.01</td>
<td>1.00–1.02</td>
</tr>
</tbody>
</table>

CI = confidence interval; CTFC = corrected TIMI frame count; LBBB = left bundle branch block; MBG = myocardial blush grade; OR = odds ratio; PTCA = percutaneous transluminal coronary angioplasty.
Markers of Myocardial Reperfusion

Table 4. Multivariate Cox Model Predictors of Cumulative Mortality

<table>
<thead>
<tr>
<th>Predictor</th>
<th>OR</th>
<th>95% CI</th>
<th>p</th>
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<tbody>
<tr>
<td>Age &gt;7 yrs</td>
<td>3.87</td>
<td>2.64–5.66</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Heart rate pre PTCA</td>
<td>4.68</td>
<td>3.15–6.95</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>&gt;100 beats/min</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LBBB</td>
<td>3.36</td>
<td>1.79–6.32</td>
<td>0.013</td>
</tr>
<tr>
<td>ST-segment elevation in</td>
<td>3.61</td>
<td>2.10–6.18</td>
<td>0.017</td>
</tr>
<tr>
<td>&gt;2 leads post PTCA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MBG 0–1 vs MBG 2–3</td>
<td>2.17</td>
<td>1.52–3.23</td>
<td>0.033</td>
</tr>
</tbody>
</table>

Abbreviations as in Table 3.

number of ECG leads with persistent STE vs. 0.63, 95% CI 0.57 to 0.70 for MBG alone, p = 0.029) (Fig. 2). Patients with a MBG of 3 and persistent ST-segment elevation in ≤2 ECG leads had a mortality of 0% at long-term follow-up. Patients with a MBG of 0, 1 or 2 and persistent STE in ≤2 ECG leads had a mortality of 13% at long-term follow-up, whereas patients with a MBG of 0, 1 or 2 and persistent STE in >2 ECG leads had a mortality of 47% during long-term follow-up (Fig. 3).

DISCUSSION

This study evaluated and compared simple-to-determine invasive and noninvasive markers of reperfusion after AMI regarding their predictive value for mortality. The principle findings were: 1) myocardial blush score and persistent STE after coronary intervention are independent predictors of long-term mortality, 2) a combination of MBG to define the quality of nonreperfusion and the number of ECG leads with persistent STE to define the extent of nonreperfusion allows even improved prediction of mortality during follow-up, 3) CTFC for assessment of coronary blood flow in the infarct-related artery is less predictive.

Reperfusion after myocardial infarction. Recent studies have demonstrated that myocardial perfusion and metabolism is often abnormal, despite restoration of TIMI-3 flow in the infarct-related artery (3–6,8). This “no-reflow” phenomenon is thought to be the result of microvascular obstruction. It constitutes a marker of more extensive myocardial tissue damage and is associated with poorer functional recovery, an increased frequency of congestive heart failure and adverse outcome (4,5). Thus, inadequate myocardial reperfusion compromises the potentially beneficial effect of early recanalization of the infarct-related artery. Several clinically applicable markers of myocardial reperfusion have been proposed. Myocardial blush, the CTFC and persistent STE are among them. They have in common that they can be easily determined in clinical practice during the acute stage of AMI. Myocardial blush, the angiographic evidence of myocardial perfusion in the myocardial bed subtended by the infarct artery has been described by van’t Hof et al. (9). The myocardial blush scale has been found to relate to the enzymatic infarct size in patients after primary PTCA for AMI (9,15) and to have a better predictive value for long-term mortality than Killip class, TIMI grade flow, LV ejection fraction and other clinical variables. Similarly, the TIMI frame count at 90 min angiography after thrombolytic therapy has been suggested to reflect myocardial reperfusion and to be an independent predictor of inhospital and 1-month clinical outcome (11,16). Early persistence of STE despite a patent infarct artery has also been shown to be a predictor of higher in-hospital and long-term mortality (12,13,17). Different parameters to assess persistent STE after revascularization procedures in AMI have been described. Some of them consider a ratio of preintervention STE to postintervention STE. This has been shown to be a useful index to assess improvement of reperfusion after PTCA in the area at risk. However, it yields no information on the extent of the myocardial area remaining at risk. The number of ECG leads with persistent STE as evaluated in this study may allow better assessment of the area remaining at risk after PTCA in AMI. Recently, TIMI myocardial perfusion grade and persistence of STE after intervention have been shown to be associated with infarct size as assessed by single photon emission computed tomography (18). Thus, the mortality differences between the different perfusion groups are likely to relate to differences in infarct size.

Prediction of patient outcome. Optimal prediction of LV function and patient outcome after AMI requires accurate evaluation of microvascular dysfunction. The optimal parameter to assess impairment of microvascular function after AMI should allow an assessment of the extent and quality of nonreperfusion. Myocardial blush and the number of ECG leads with persistent STE proved to be independent predictors of mortality during long-term follow-up. Myocardial blush grade reflects the quality of reperfusion for a given perfusion bed. It reflects the microvascular function of a perfusion bed irrespective of the size of the myocardial
Thus, MBG is limited by the lack of information on the size of the endangered perfusion bed. The same difficulty applies to the CTFC. In addition, the CTFC determined in the epicardial artery is only an indirect parameter of the microvascular function of the subtended perfusion bed. In contrast, the 12-lead ECG yields information about the extent of the area at risk.

In this study, a combination of MBG and number of ECG leads with persistent STE after interventional revascularization was of incremental value for the prediction of patient outcome. This approach combined an assessment of the quality of reperfusion by the MBG with an assessment of the extent of the reperfusion defect using the number of ECG leads showing persistent STE, thereby increasing the predictive power of the model.

Several therapeutic strategies have been described to improve reperfusion in patients with AMI, including mechanical protection devices and pharmacological treatment to specifically improve microvascular function on the myocardial tissue level (19,20). The proposed markers of reperfusion may be used as surrogate study end points in clinical trials (4–11,17) to test the effect of these emerging new therapeutic strategies. Compared with the standard clinical end point, mortality, the use of these surrogate end points in trials analyzing the effect of strategies designed to improve reperfusion after AMI may allow a reduction of required patient numbers (4). The choice of the surrogate marker to be used in future trials has to recognize its predictive accuracy.

**Study limitations.** The mortality rate during follow-up was higher in this study as compared with that in other recently published studies (21,22). However, in several of these studies only patients conforming to special inclusion criteria were part of the analysis, whereas patients with very high risks were excluded. In contrast, all consecutive patients with AMI undergoing angioplasty at this referral center were included in this study, resulting in a study population with multiple high-risk characteristics. For patients with normal or intermediate myocardial blush, survival rates similar to previously reported data were found in this study (15). Thus, the overall high mortality is likely to reflect in particular the inclusion of a high rate of patients with very poor baseline characteristics. The overall mortality rate as well as the mortality rates for all patient groups reported in this study may, in fact, better represent those to be expected in an unselected patient population at a referral center. Corrected TIMI frame count was no independent predictor of mortality in this study. It might have become an independent predictor of mortality in addition to myocardial blush with higher patient numbers, as in a recent study on 800 patients (23).

This study evaluated patient survival in a retrospective fashion. Patients were not routinely followed up at predefined time intervals. Rather, patients were contacted only
at one time point. However, due to intensive efforts, a complete follow-up could be obtained regarding patient mortality. Coronary angiograms were recorded at a speed of 12.5 fps. This might have resulted in minor differences of the determined CTFC compared with those that would have been determined with a speed of 30 fps. Finally, the number of patients included in the analysis was limited because of confinement of patients’ inclusion to one large referral center. Larger studies to confirm the results are required. The limited patient number may have restricted the ability to demonstrate differences in mortality, myocardial blush and ST resolution between anterior versus inferior MI and for survival as a function of time to reperfusion although these associations have been demonstrated in larger studies.

Conclusions. Myocardial blush and persistent STE after intervention in AMI are independent predictors of mortality. A combination of both parameters to consider quality of reperfusion in the endangered perfusion bed and extent of the injured myocardium is likely to further increase the predictive accuracy. Further studies are required to examine whether they allow superior assessment of mechanical and pharmacological strategies aiming at the improvement of myocardial perfusion and clinical outcome of patients with AMI.

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