Is the Myocardial Blush Grade Scored by the Operator During Primary Percutaneous Coronary Intervention of Prognostic Value in Patients With ST-Elevation Myocardial Infarction in Routine Clinical Practice?

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Background—Multiple trials have documented that myocardial blush grade (MBG) after primary percutaneous coronary intervention (PCI) for ST-elevation myocardial infarction (STEMI) has prognostic value for long-term clinical outcome. However, to the best of our knowledge, no study has determined the clinical use of MBG in routine clinical practice. We determined the prognostic value of MBG scored by the operator during primary PCI in consecutive patients with STEMI.

Methods and Results—The prognostic value of MBG scored by the operator in relation to 1-year all cause mortality was evaluated in all patients with STEMI who underwent primary PCI between January 2004 and July 2008 in our hospital. The incidence of MBG 0, 1, 2, and 3 was 12%, 14%, 36%, and 38%, respectively, in 2118 consecutive patients with STEMI. Follow-up of all 2118 patients showed a 1-year all cause mortality rate of 8% (168 of 2118): 24%, 10%, 6%, and 4%, respectively, among patients with MBG 0, 1, 2, and 3 (P<0.001). In the 1763 patients with Thrombolysis in Myocardial Infarction (TIMI) flow grade 3 after PCI, these mortality rates were 17%, 10%, 6%, and 4%, respectively (P<0.001). MBG scored by the operator was a strong independent predictor of 1-year all cause mortality corrected for other well-known predictive variables, including TIMI flow grade.

Conclusions—MBG scored by the operator during primary PCI has prognostic value for 1-year all cause mortality in patients with STEMI in routine clinical practice. Therefore, the MBG should be documented, in addition to the TIMI flow grade, during primary PCI in patients with STEMI in standard PCI reports in routine clinical practice. (Circ Cardiovasc Interv. 2010;3:00-00.)

Key Words: acute myocardial infarction • percutaneous coronary intervention • myocardial blush grade • routine clinical practice

Depending on the duration of coronary occlusion, myocardial infarction leads to necrosis of myocytes and eventually to destruction of the microvascular bed.1 The primary goal of primary percutaneous coronary intervention (PCI) for ST-elevation myocardial infarction (STEMI) is restoration of epicardial blood flow to provide perfusion into the infarcted part of the myocardium. The rate of restoration of epicardial blood flow after PCI can be assessed by the angiographic Thrombolysis in Myocardial Infarction (TIMI) flow grade.2,3 TIMI flow grade is associated with clinical outcome.4,5 In ≈90% of the patients with STEMI, restored epicardial blood flow, defined as TIMI flow grade 3, is achieved after primary PCI.6–8 However, despite restored epicardial blood flow, a substantial percentage of patients have signs of impaired myocardial reperfusion and therefore have an impaired prognosis.9,10

Clinical Perspective on p 000

Myocardial blush grade (MBG) is a simple visual angiographic assessment of myocardial perfusion in the infarct area, as first described by van’t Hof et al1; MBG seems to be of additional value, especially in patients with restored epicardial blood flow because MBG reflects the extent of damage of the microvascular bed. In several studies, the MBG is associated with ST-segment elevation resolution, enzymatic infarct size, left ventricular function, and long-term mortality.6,7,11,12 Therefore, MBG is often used as an end point in clinical trials. In routine clinical practice, MBG is not often used as a prognostic tool, possibly because of concerns

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that the subjectivity of the operator will limit its prognostic value. Until now, no studies have validated the prognostic value of MBG scored by the operator during primary PCI in routine clinical practice, but they have relied on independent core laboratory or experienced observers blinded to all clinical data. In this study, we evaluated the relation between MBG scored by the operator during primary PCI and 1-year all-cause mortality in patients with STEMI and its additional prognostic value when TIMI flow grade 3 is achieved after primary PCI.

Methods

Patient Population
In this “real-world” analysis, all consecutive patients with STEMI were included who were treated with primary PCI from January 2004 to July 2008 in our hospital. During this period, 1599 patients with STEMI were included in 1 of our randomized controlled trials. Our trials include TAPAS (Thrombus Aspiration during Percutaneous coronary intervention in Acute myocardial infarction Study; n=1071),13,14 Diver versus Export (n=80),15 and ADAPT (Adenosine Administration during and after Primary percutaneous coronary intervention in acute myocardial infarction; n=448).16 These trials included patients with suspected STEMI in the period between January 2005 and July 2008. Trial exclusion criteria were rescue PCI after thrombolysis, cardiogenic shock, known disease with a life expectancy of <6 months, and lack of informed consent. For this study, no exclusion criteria were used, and all patients with STEMI included in our trials (trial patients) and all patients with STEMI not included in our trials (nontrial patients) were analyzed.

Treatment
From January 2004 to January 2005, patients with STEMI were treated with conventional PCI (balloon angioplasty followed by stent implantation). From January 2005 to December 2006, conventional PCI and thrombus aspiration followed by stent implantation were randomly performed in context of the TAPAS trial.13,14 Thrombus aspiration became the preferred treatment since December 2006. Most patients received bare-metal stents. Acute pharmacotherapy was according to current international guidelines, including aspirin, clopidogrel, and the glycoprotein IIb/IIa inhibitor abciximab.17 Maintenance pharmacotherapy consisted of aspirin, clopidogrel for at least 1 month, b-blockers, lipid-lowering agents, and angiotensin-converting enzyme inhibitors or angiotensin-II receptor blockers.

Angiographic Analysis
The operators scored the TIMI flow grades (operator TIMI flow grade) and MBG (operator MBG) during the PCI procedure and registered the outcome in the catheterization laboratory database. In all patients, TIMI flow grade was scored before PCI, and TIMI flow grade and MBG were scored after PCI. The operators scored the TIMI flow grade and MBG (operator MBG) on recorded angiograms, as previously described.13-16

End Points and Definitions
TIMI flow grade was classified as 0: no antegrade flow, 1: minimal antegrade flow into the obstructed segment, 2: slow antegrade flow into the distal bed, and 3: normal antegrade flow into the distal bed.2 The MBG was determined by the contrast density in an angiographic projection that isolated the distal myocardial region of the infarct-related artery. Detailed description of the angiographic requirements to assess the MBG has been published previously by van ‘t Hof et al.17 MBG of the myocardial infarct region was classified as 0: no

![Figure 1. Flow diagram of inclusion](image)

Figure 1. Flow diagram of inclusion. Patients with STEMI were included in this study when TIMI flow grades and MBG were scored by operator during primary PCI and in trial patients also scored by independent core laboratory. Our clinical trials include TAPAS,13,14 Diver versus Export,15 and ADAPT.16 1071),13,14 Diver versus Export (n=80),15 and ADAPT.16

myocardial blush, 1: minimal myocardial blush, 2: moderate myocardial blush, or 3: normal myocardial blush, all compared with the MBG of myocardial regions of noninfarct-related arteries. Persisting myocardial blush was also graded as 0 because this is considered to be extravasation of angiographic contrast medium associated with hemorrhage.18 Enzymatic infarct size was determined as peak creatinine kinase. All cause 1-year mortality was collected using municipal civil registries. Because only patients who are lost to follow-up by municipal civil registries could not be tracked, this system provides completeness of follow-up with regard to vital status in >99% of patients admitted to our department.

Statistical Analysis
Normally distributed continuous variables are presented as mean±SD and were compared using a 2-tailed Student t test. Skewed distributed continuous variables are presented as median with interquartile range and were compared using a Mann-Whitney U test. Categorical variables are presented as number and percentage and were compared using the χ2 test or Fisher exact test. To determine the agreement between operators and core laboratory scoring, unweighted kappa was used with TIMI flow grades and MBG grouped as 0 or 1 versus 2 or 3. The additional predictive value for 1-year all cause mortality by operator MBG compared with the often used prognostic scores during the procedure, TIMI flow grade before and after PCI, was evaluated by receiver operating characteristic curves. Logistic regression analysis for mortality was performed using well-known prognostic variables: age, anterior infarction, peak creatinine kinase, TIMI flow grade before and after PCI, and MBG. A large enzymatic infarct size was defined as creatinine kinase peak at least 15 times the upper limit of the normal values. Independent predictors of 1-year all cause mortality were identified using the backward stepwise regression. Statistical significance was defined as a 2-sided P value of <.05. Statistical analysis was performed using SPSS software version 16.0 (SPSS Inc, Chicago, Ill).

Results

Study Population
A total of 2375 patients with STEMI underwent primary PCI in our hospital in the 4.6-year period (Figure 1). In 89% (2118 of 2375) of the patients, immediate TIMI flow grades and MBG were scored by the operator. In trial patients, TIMI flow grades and MBG were scored in 86% (1375 of 1599) by operator as well as by core laboratory. In nontrial patients, TIMI flow grades and MBG were scored in 96% (743 of 776) by operator. Compared with trial patients, nontrial patients had worse angiographic characteristics and a higher 1-year all cause mortality rate (Table 1). In all consecutive patients with STEMI, operator TIMI flow grade 3 and operator MBG 3
after PCI were achieved in 83% and 38%, and operator TIMI flow grade 0 and operator MBG 0 after PCI were scored in 2% and 12% of the patients. In trial patients, operator TIMI flow grade 3 and operator MBG 3 after PCI were achieved in 85% and 40%, and operator TIMI flow grade 0 and operator MBG 0 after PCI were scored in 1% and 5% of the patients. In nontrial patients, operator TIMI flow grade 3 and operator MBG 3 after PCI were achieved in 80% and 35%, and operator TIMI flow grade 0 and operator MBG 0 after PCI were scored in 4% and 24% of the patients. One-year all

| Table 1. Characteristics of All Consecutive STEMI Patients, Divided in Trial and Nontrial Patients |
|-------------------------------------------------|--------------------------------------------------------------------------------------------------|
| All Patients (n=2118) | Trial Patients (n=1375) | Nontrial Patients (n=743) | P |
| General characteristics |
| Age, y (mean±SD) | 63.1±12.9 | 62.8±12.6 | 63.7±13.4 | 0.134 |
| Male sex | 1502 (71) | 996 (72) | 506 (68) | 0.036 |
| Previous PCI | 146 (7) | 84 (6) | 62 (9) | 0.035 |
| Previous CABG | 41 (2) | 23 (2) | 18 (3) | 0.198 |
| Angiographic characteristics |
| Infarct-related artery |
| LAD | 888 (42) | 568 (41) | 320 (43) | 0.434 |
| CX | 346 (16) | 233 (17) | 113 (15) | 0.302 |
| RCA | 850 (40) | 569 (41) | 281 (38) | 0.110 |
| Graft | 11 (0.5) | 1 (0.1) | 10 (1.3) | <0.001 |
| Left main | 23 (1.1) | 4 (0.3) | 19 (2.6) | <0.001 |
| Operator TIMI flow grade | |
| 0 | 1257 (59) | 784 (57) | 473 (64) | 0.003 |
| 1 | 175 (8) | 110 (8) | 65 (9) | |
| 2 | 324 (15) | 235 (17) | 89 (12) | |
| 3 | 362 (17) | 246 (18) | 116 (16) | |
| Ischemic time, minutes (median [IQR]) | 185 (135 to 285) | 180 (130 to 285) | 190 (135 to 280) | 0.445 |
| Ischemic time >6 h | 299 (16) | 92 (16) | 207 (16) | 0.830 |
| Procedural characteristics |
| Administration of glycoprotein IIb/IIIa inhibitor | 1780 (84) | 1267 (92) | 513 (69) | 0.001 |
| IABP | 180 (9) | 67 (5) | 113 (16) | <0.001 |
| Clinical chemistry |
| Creatinine kinase peak U/L (median [IQR]) | 737 (292 to 1687) | 716 (282 to 1687) | 781 (333 to 1687) | 0.433 |
| CK-myocardial band peak U/L (median [IQR]) | 76 (31 to 156) | 78 (32 to 170) | 72 (30 to 132) | 0.007 |
| Follow-up |
| 1-year mortality | 168 (8) | 53 (4) | 115 (16) | <0.001 |

Data are presented as n (%) unless otherwise indicated. P value represents the difference between trial patients and nontrial patients. Ischemic time was recorded in 1866 consecutive STEMI patients, 1282 trial patients, and 584 nontrial patients. CABG indicates coronary artery bypass grafting; LAD, left anterior descending artery; CX, left circumflex artery; RCA, right coronary artery; IABP, intra-aortic balloon pump; TIMI, Thrombolysis in Myocardial Infarction; IQR, interquartile range; MBG, myocardial blush grade.
cause mortality was 8% (168 of 2118) in all consecutive
patients with STEMI, 4% (53 of 1375) in the trial patients,
and 16% (115 of 743) in the nontrial patients.

Agreement Between Operator and Core Laboratory
Scoring of MBG and TIMI Flow Grade
The incidence of the overall scored grades of myocardial
blush between operators and core laboratory in trial patients
is compatible (Figure 2). The highest agreement between
operators and core laboratory was in TIMI flow grade before
PCI (kappa 0.81) compared with TIMI flow grade after PCI
(kappa 0.62) and MBG (kappa 0.47), when grouped in 0 or 1
versus 2 or 3. The kappa was lower for TIMI flow grade after
PCI because of the high incidence of grade 2 and 3 (Figure 3).

Prognostic Value of MBG Scored by the Operator
There were strong relations among operator TIMI flow grade
before PCI ($P < 0.006$), operator TIMI flow grade after PCI
($P < 0.001$), operator MBG ($P < 0.001$), and 1-year all cause
mortality in all consecutive patients with STEMI (Figure 4).
Per grade of myocardial blush, the prognosis decreased with
a markedly poor prognosis for operator MBG 0 (Figure 5).
Compared with operator MBG, the relation between core
laboratory MBG and mortality was similar (core laboratory
MBG 0, 1, 2, 3: 15.3%, 4.6%, 2.8%, 2.9%, respectively; $P < 0.001$).
In nontrial patients alone, a similar and significant
relation between operator MBG and mortality was found.

In the 83% of patients with operator TIMI flow grade 3
after PCI, operator MBG was 0 in 7%, 1 in 11%, 2 in 37%,
and 3 in 45% of the patients. In these patients with restored
epicardial flow after PCI, operator MBG remained a strong
predictor for mortality (Figure 6). The receiver operating characteristic analysis showed that
operator MBG had additional predictive value for 1-year all
cause mortality compared with TIMI flow grade before and
after PCI (Figure 7). Multivariable analysis showed that
operator MBG is a strong and independent predictor of 1-year
mortality corrected for age, anterior infarction,
enzymatic infarct size, and TIMI flow grade before and after
PCI (Table 2).

Discussion
In this real-world study, we show that MBG scored by the
operator during the PCI procedure, as a determinant of
myocardial reperfusion, is a strong predictor of long-term
mortality in patients with STEMI treated with primary PCI.
After correction for other predictive variables (age, anterior
infarction, enzymatic infarct size, and TIMI flow grade
before and after PCI), MBG remains an independent prog-
nostic variable (odds ratio of MBG 0 or 1 versus 2 or 3: 2.75;
95% CI: 1.95 to 3.86; $P < 0.001$). Moreover, in patients with
restored epicardial blood flow after primary PCI, operator
MBG has additional prognostic value.

Restoration of the epicardial blood flow to provide myo-
cardial reperfusion has been the target for treatment of
patients with myocardial infarction for many years.2,3 With
primary PCI, a restored epicardial blood flow is achieved in
$\approx 90\%$ of the patients in several trials.7, 8,19,20 The prognostic
value of epicardial blood flow, classified as TIMI flow grade,
is well known.4,5 Our study also shows that operator TIMI
flow grade before and after PCI are predictors of long-term
mortality in routine clinical practice. However, TIMI flow
grade does not describe the reperfusion of the infarcted
myocardium. Van’t Hof et al described MBG as a visual
assessment of angiographic contrast density in the myocardial
region of the infarct-related artery as a reflection of myocar-
dial reperfusion. Several trials have shown the prognostic
value of retrospective scored MBG by experienced obser-
vers or independent core laboratory blinded to all clinical
data.5,7,11,12,19 To the best of our knowledge, this study is the
first that uses MBG obtained during the PCI procedure in
routine clinical practice. We show that operator MBG is a
predictor of long-term mortality in patients with STEMI
treated with primary PCI. Furthermore, this study had the
capacity to identify progressively decreasing prognosis per
grade of myocardial blush, with a markedly poor prognosis in MBG 0.

That the restored epicardial blood flow is not identical to restored myocardial perfusion can be explained as follows. Myocardial perfusion is related to the extent of myocardial necrosis caused by microvascular dysfunction. This depends partly on the duration of coronary artery occlusion, the size of the myocardium supplied by the infarct-related artery, and the quality of collateral circulation. However, besides disturbed reperfusion by epicardial or collateral vessels, the impaired microvascular perfusion can also be caused by edema, inflammation, neurohormonal reflexes, vasoconstriction, and spontaneous or PCI-induced distal atherothrombotic embolization.10,21,22 In 11% to 50% of the patients with STEMI no or reduced myocardial perfusion ("no reflow") is observed after PCI, despite restored epicardial blood flow.7,10,12,19,23 This impaired myocardial perfusion is associated with decreased clinical outcomes, and therefore, restored epicardial blood flow is no guarantee for restored myocardial viability and clinical outcome.10,12,21 In our study, 18% had impaired myocardial blush despite TIMI flow grade 3 after PCI. In these patients with MBG 0 or 1, a mortality rate of 17% and 10% was observed compared with a mortality rate of 6% and 4% when MBG 2 or 3 was achieved (P<0.001). In the receiver operating characteristic analysis, the predictability of 1-year mortality increased using MBG beyond the TIMI flow grade before and after PCI. Furthermore, in multivariable analysis, MBG remained an independent predictor after adjustment for other known prognostic variables, including TIMI flow grade after PCI. Therefore, MBG identifies an additional patient population at risk on top of TIMI flow grade. This implicates that documentation of MBG has prognostic value in routine clinical practice, in particular when TIMI flow grade 3 is achieved after PCI.

As is the case for TIMI flow grade, MBG is a subjective angiographic parameter. In the trial patients, the incidence of the different grades of myocardial blush was comparable...
Conclusions and Implications
Angiographic MBG scored by the operator during primary PCI in patients with STEMI is an independent predictor for
1-year all-cause mortality in routine clinical practice. Even when TIMI flow grade 3 is achieved after PCI, operator MBG has an additional predictive value. Furthermore, probably, this is the first study that could categorize MBG in 4 groups with decreasing prognostic per grade, with a markedly poor prognosis in MBG 0. Compared with other functional outcome parameters, such as in MRI and echocardiography, the operator-scored MBG has the important practical advantage that it is assessed directly after the primary PCI procedure. This all implicates that MBG scored by the operator during temporary coronary occlusion in the dog. Clinical findings through hospital discharge. Circulation. 1987;76:142–154.


Myocardial blush grade (MBG) is a simple visual angiographic assessment of myocardial perfusion of the infarct area. Multiple clinical trials have determined the prognostic value of post hoc core laboratory-scored MBG in patients with ST-elevation myocardial infarction. However, no study has determined the clinical use of MBG scored by the interventional cardiologist in routine clinical practice, possibly because of concerns that the subjectivity of the operator will limit its prognostic value. In this study, we found that operator-scored MBG during primary percutaneous coronary intervention was an independent predictor of 1-year all cause mortality in 2118 consecutive patients with ST-elevation myocardial infarction. Furthermore, our cohort was large enough to categorize MBG in 4 groups with decreasing prognosis per grade, with a markedly poor prognosis in MBG 0. Compared with other functional outcome parameters, such as in MRI and echocardiography, the operator-scored MBG has the important practical advantage that it is assessed directly after the primary percutaneous coronary intervention procedure. This indicates that operator-scored MBG is a valuable tool in early risk stratification in routine clinical practice with the opportunity to intensify the treatment for high-risk patients.

CLINICAL PERSPECTIVE

Myocardial blush grade (MBG) is a simple visual angiographic assessment of myocardial perfusion of the infarct area. Multiple clinical trials have determined the prognostic value of post hoc core laboratory-scored MBG in patients with ST-elevation myocardial infarction. However, no study has determined the clinical use of MBG scored by the interventional cardiologist in routine clinical practice, possibly because of concerns that the subjectivity of the operator will limit its prognostic value. In this study, we found that operator-scored MBG during primary percutaneous coronary intervention was an independent predictor of 1-year all cause mortality in 2118 consecutive patients with ST-elevation myocardial infarction. Furthermore, our cohort was large enough to categorize MBG in 4 groups with decreasing prognosis per grade, with a markedly poor prognosis in MBG 0. Compared with other functional outcome parameters, such as in MRI and echocardiography, the operator-scored MBG has the important practical advantage that it is assessed directly after the primary percutaneous coronary intervention procedure. This indicates that operator-scored MBG is a valuable tool in early risk stratification in routine clinical practice with the opportunity to intensify the treatment for high-risk patients.
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