Early and Rapid Diagnosis of Perioperative Myocardial Infarction in Aortocoronary Bypass Surgery by Immunoturbidimetric Myoglobin Measurements*

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Study objectives: To evaluate measurements of myoglobin in the diagnosis of perioperative myocardial tissue damage in aortocoronary bypass surgery. A new immunoturbidimetric myoglobin assay, which yields quantitative concentrations of myoglobin within approximately 1 min, was used.

Design: Prospective clinical study.

Patients: Thirty-two patients scheduled for elective aortocoronary bypass surgery.

Measurements and results: Myoglobin concentrations in patients without perioperative myocardial infarction (n=37) increased with aortic unclamping, peaked after 1 h, and decreased to almost baseline values within 4 h. By contrast, myoglobin concentrations in patients with perioperative myocardial infarction (n=5) further increased after 1 h of aortic unclamping and were significantly higher (p<0.05) than in patients without myocardial infarction as soon as 3 h after aortic unclamping. In all patients with myocardial infarction, myoglobin concentrations exceeded 400 μg/L over a minimum period of 4 h. Ten of 27 patients without perioperative myocardial infarction had episodes of minor perioperative myocardial ischemia (defined as ST-T segment changes in the ECG without a concomitant increase in the activity of creatine kinase isoenzyme MB). Myoglobin concentrations (but not creatine kinase isoenzyme MB activity) were significantly higher in these 10 patients when compared to the 17 completely uneventful cases.

Conclusions: Plasma concentrations of myoglobin are a sensitive marker of perioperative myocardial tissue damage in aortocoronary bypass surgery. Myoglobin measurements with the immunoturbidimetric assay have an important contribution to make to the early and rapid diagnosis of perioperative myocardial infarction.

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Myoglobin measurements are useful in the early diagnosis of myocardial infarction in nonsurgical patients. Although data are limited, plasma concentrations of myoglobin seem to be of diagnostic and prognostic value in patients undergoing cardiac surgery as well; however, until recently, serum myoglobin only could be measured by time-consuming radioimmunoassays or by a rapid semiquantitative latex agglutination test. Consequently, myoglobin measurements remained of minor importance in clinical practice. A new quantitative and rapid immunoturbidimetric myoglobin assay (assay time, approximately 1 min) is now commercially available for use in emergency laboratories. The aim of this study, therefore, was to evaluate this new myoglobin assay in the early and rapid diagnosis of perioperative myocardial tissue damage in aortocoronary bypass surgery.

Materials and Methods

Patients

After institutional approval and informed consent, 32 patients scheduled for elective aortocoronary bypass surgery were studied (27 men and 5 women; median age, 61.5 years; range, 45 to 73 years). Perioperative myocardial infarction was diagnosed in the case of ECG changes indicating perioperative ischemia and creatine kinase isoenzyme MB (CK-MB) activity exceeding 20 U/L 20 h after aortic unclamping. Values for CK-MB activity greater than 20 U/L 20 h after aortic unclamping were assumed to indicate myocardial tissue damage exceeding the inevitable amount in aortocoronary bypass surgery. Five of the 32 patients (group 1) sustained perioperative myocardial infarction. Group 1 comprised 2 patients with new Q waves and CK-MB activity greater than 100 U/L 20 h after aortic unclamping and 3 patients with new ST elevation or negative T waves and CK-MB activity greater than 20 U/L 20 h after aortic unclamping. The remaining 27 patients without perioperative myocardial infarction (group 2) comprised 10 patients with clinical or ECG signs of perioperative myocardial ischemia (group 2A) and 17 patients with a completely uneventful perioperative course (group 2B).

Surgical Techniques

Standard cardiopulmonary bypass technique with moderate systemic hypothermia was used in all patients. Myocardial protection was achieved by infusion of cold hyperkalemic cardioplegic solution (modified St. Thomas solution) and additional topical cooling. Median aortic crossclamping time was 57.5 min (range, 36 to 106 min), and a median of 4 grafts (range, 1 to 5 grafts) per patient was implanted (19 of them arteria mammaria interna grafts).

Measurements

In all patients, ECG recordings were obtained before surgery, immediately after surgery, on the first postoperative day, and before

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discharge from the hospital. During surgery, patients were monitored by a five-electrode ECG system (including one precordial unipolar lead in the V₅ position) and computerized on-line ST-T segment analysis. Patients had transesophageal echocardiographic monitoring for regional wall motion abnormalities during surgery. Additional ECG or echocardiographic investigations were performed in some patients according to clinical necessities.

Serial samples of venous blood were obtained before induction of anesthesia, before surgery, before cardiopulmonary bypass, after aortic unclamping, and at 1, 2, 3, 4, 8, 12, 16, and 20 h later. The CK-MB activity was measured by immunoinhibition using a commercial test kit (Merck). Myoglobin concentrations were measured by a rapid, quantitative immunoturbidimetric assay⁴⁷ (Turbiquant Myoglobin; Behringwerke AG, Marburg, Germany). The upper limit of the reference interval of this assay is 75 µg/L.

Statistics

Median and interquartile range were calculated to describe continuous variables. Wilcoxon's signed rank test and the Mann-Whitney U test were used for group comparison. A p value less than 0.05 was considered to indicate statistical significance.

RESULTS

Myoglobin Release in Perioperative Myocardial Infarction

Release of myoglobin after aortic unclamping was significantly different in patients with (group 1) and without (group 2) perioperative myocardial infarction (Fig 1, left). In patients without perioperative myocardial infarction, myoglobin concentrations peaked 1 h after aortic unclamping (median, 320 µg/L) and decreased rapidly thereafter (median myoglobin concentration 4 h after aortic unclamping, 136 µg/L; p = 0.001; Fig 1, left). In contrast, myoglobin concentrations in patients with perioperative myocardial infarction further increased after 1 h of aortic unclamping and were significantly higher as early as 3 h after aortic unclamping (median myoglobin concentration, 390 µg/L at 1 h, 388 µg/L at 4 h, and 665 µg/L at 12 h after aortic unclamping; Fig 1, left). The CK-MB activity increased 2 h after aortic unclamping in patients with (group 1) and without (group 2) perioperative myocardial infarction. Values for CK-MB activity were significantly higher (p<0.007) in patients with perioperative myocardial infarction within 8 h after aortic unclamping onward (Fig 1, right).

Myoglobin Concentrations in Patients Without Perioperative Myocardial Infarction

Twenty-seven patients did not fulfill criteria of perioperative myocardial infarction (CK-MB>20 µg/L h after aortic unclamping together with ECG signs of ischemia). Ten (group 2A) of these 27 patients had clinical or ECG signs of perioperative myocardial ischemia; 3 patients showed ST segment elevation during surgery, accompanied by wall motion abnormalities in transesophageal echocardiography (2 of them had surgical revision of their grafts; in 1, extracorporeal circulation was reestablished and medical treatment initiated), and 7 patients had transient ST segment elevation or negative T waves in at least 2 leads immediately after surgery. The release of myoglobin in these 10 patients (group 2A) was characterized by a second pronounced increase 2 to 12 h after aortic unclamping. In these 10 patients (group 2A), myoglobin concentrations were significantly higher than in the 17 patients without clinical or ECG signs of ischemia (group 2B) from 8 to 16 h after aortic unclamping onward (Fig 2). Values for CK-MB activity,
A single measurement of myoglobin at a given time after aortic unclamping is often of limited diagnostic value, due to a considerable variation in myocardial tissue damage in uneventful cases. Therefore, diagnosis of perioperative myocardial infarction must be based on changes in myoglobin concentration over a 4-h period. Then, repeated measurements of myoglobin have an important contribution to make in the early and rapid diagnosis of suspected perioperative myocardial infarction. Four of 27 patients without perioperative myocardial infarction had myoglobin concentrations exceeding 400 μg/L for a period of 4 h. Myoglobin is released in significant amounts from ischemic myocardium, although ischemia does not lead to an increase in CK-MB activity in the plasma.\textsuperscript{11,12} In fact, three of these four patients showed ECG or clinical evidence of myocardial ischemia. Thus, in some cases, prolonged elevated concentrations of myoglobin obviously result from minor myocardial tissue damage not detected by measurements of CK-MB activity. In these cases, extended myocardial necrosis must be excluded by CK-MB measurements subsequently.

Using continuous perioperative Holter monitoring, ST-T segment changes indicating ischemia are found in more than 50 percent of all patients undergoing aortocoronary bypass surgery.\textsuperscript{13} In our patients, routine monitoring identified episodes of minor perioperative myocardial ischemia in 10 of 27 patients without perioperative myocardial infarction. These episodes of ischemia are accompanied by a significant release of myoglobin into the plasma, but not a release of CK-MB, as measured as activity. Thus, our results indicate that myoglobin measurements might be superior to measurements of CK-MB activity in the laboratory diagnosis of minor perioperative myocardial tissue damage. In the absence of an alternative accepted criterion or standard in the diagnosis of perioperative myocardial tissue damage, we cannot evaluate the sensitivity and specificity of myoglobin and CK-MB activity independently.

Although myoglobin lacks cardiосpecificity, myoglobin measurements in coronary sinus blood samples identified the myocardium as the major source of myoglobin release in patients undergoing cardiac surgery.\textsuperscript{3} Sternotomy without cardiac surgery does not cause a distinct increase in plasma levels of myoglobin.\textsuperscript{3} Myoglobin is rapidly cleared from the blood by the kidneys.\textsuperscript{4,9} Renal function did not differ between patients with and without perioperative myocardial infarction, and impaired renal function cannot account for the differences in myoglobin concentrations observed. Nevertheless, it is recommended that the diagnosis of perioperative myocardial infarction be confirmed by more cardiac-specific marker proteins subsequently. Creatine kinase isoenzyme MB is re-

**Figure 2.** Myoglobin level in 27 patients without perioperative myocardial infarction, including patients with episodes of perioperative myocardial ischemia (n = 10) and completely uneventful cases (n = 17). by contrast, did not differ significantly between these two groups.

**Diagnostic Performance of Serial Myoglobin Measurements**

A single myoglobin concentration at a given time after aortic unclamping was of limited diagnostic value in our patients. By contrast, changes in myoglobin concentrations over a 4-h period identified suspected perioperative myocardial infarction. All patients with perioperative myocardial infarction showed myoglobin concentrations exceeding 400 μg/L for a minimum period of 4 h. Only 4 of 27 patients without perioperative myocardial infarction also showed myoglobin concentrations exceeding 400 μg/L for a period of 4 h. Three of them had clinical or ECG signs of perioperative myocardial ischemia (group 2A).

**DISCUSSION**

Some myocardial tissue damage is inevitable in aortocoronary bypass surgery and leads to an increase in plasma concentrations of myocardial marker proteins in uneventful cases as well.\textsuperscript{9} Therefore, only a persisting increase in marker proteins, which is caused by an ongoing release from ischemic myocardium, indicates perioperative myocardial infarction.\textsuperscript{5,8} The biological half-life of myoglobin\textsuperscript{6,9} in the systemic circulation is shorter compared to CK-MB\textsuperscript{10} (20 min vs 13 h). Consequently, myoglobin is cleared from plasma more rapidly in uneventful cases, and myoglobin measurements discriminate between patients with and without perioperative myocardial infarction several hours earlier than measurements of CK-MB activity do. Myoglobin concentrations in patients without perioperative myocardial infarction decrease to almost baseline values within 4 h after aortic unclamping.
leased from injured myocardium over several hours and, due to its plasma half-life of approximately 13 h, remains increased in the circulation for several days. Therefore, CK-MB measurements cannot distinguish preoperative, intraoperative, and postoperative events, but integrates them over time. Because of its short plasma half-life, myoglobin can be useful in identifying the exact onset of perioperative myocardial infarction. Three of five patients with perioperative myocardial infarction had a continuous rise in their myoglobin concentrations after aortic unclamping, indicating intraoperative myocardial infarction. Two of them showed an initial decrease (characteristic of uncomplicated cases), followed by a pronounced second increase. Myoglobin concentrations in these two patients indicate the onset of myocardial necrosis in the early postoperative period.

In summary, myoglobin concentrations are a sensitive marker of perioperative myocardial tissue damage. Myoglobin measurements with the immunoturbidimetric assay have an important contribution to make in the early and rapid diagnosis of perioperative myocardial infarction in aortocoronary bypass surgery.

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