Visualization of Discrete Microinfarction After Percutaneous Coronary Intervention Associated With Mild Creatine-MB Elevation

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Background—Mild elevations in creatine kinase-MB (CK-MB) are common after successful percutaneous coronary interventions and are associated with future adverse cardiac events. The mechanism for CK-MB release remains unclear. A new contrast-enhanced MRI technique allows direct visualization of myonecrosis.

Methods and Results—Fourteen patients without prior infarction underwent cine and contrast-enhanced MRI after successful coronary stenting; 9 patients had procedure-related CK-MB elevation, and 5 did not (negative controls). The mean age of all patients was 61 years, 36% had diabetes, 43% had multivessel coronary artery disease, and all had a normal ejection fraction. Twelve patients (86%) received an intravenous glycoprotein IIb/IIIa inhibitor; none underwent atherectomy, and all had final TIMI 3 flow. Of the 9 patients with CK-MB elevation, 5 had a minor side branch occlusion during stenting, 2 had transient ECG changes, and none developed Q-waves. The median CK-MB was 21 ng/mL (range, 12 to 93 ng/mL), which is 2.3× the upper limit of normal. Contrast-enhanced MRI demonstrated discrete regions of hyperenhancement within the target vessel perfusion territory in all 9 patients. Only one developed a new wall motion abnormality. The median estimated mass of myonecrosis was 2.0 g (range, 0.7 to 12.2 g), or 1.5% of left ventricular mass (range, 0.4% to 6.0%). Hyperenhancement persisted in 5 of the 6 who underwent a repeat MRI at 3 to 12 months. No control patient had hyperenhancement.

Conclusions—Contrast-enhanced MRI provides an anatomical correlate to biochemical evidence of procedure-related myocardial injury, despite the lack of ECG changes or wall motion abnormalities. Mild elevation of CK-MB after percutaneous coronary intervention is the result of discrete microinfarction. (Circulation. 2001;103:2780-2783.)

Key Words: creatine kinase ■ magnetic resonance imaging ■ angioplasty

Creatine kinase-MB (CK-MB) elevation occurs in 5% to 30% of patients after percutaneous coronary intervention (PCI)1-5 and is associated with increased mortality.3,4,6,7 Importantly, even patients with minimal CK-MB elevation (<3× upper limit of normal) and otherwise successful PCI seem to be at an increased risk for adverse outcomes.4,6,7 The mechanism responsible for procedure-related CK-MB elevation is unclear. Because the majority of patients have no other clinical evidence of myocardial infarction, there is debate regarding whether myonecrosis has actually occurred.2,5,6,8

The ability to identify and quantify myocardial necrosis in vivo has recently been demonstrated using a contrast-enhanced MRI technique, in which infarcted tissue is distinguished as a hyperenhanced region.9,10 Because this technique is capable of visualizing small regions of myonecrosis that are not otherwise evident with noninvasive myocardial imaging, we hypothesized that contrast-enhanced MRI would provide a direct anatomical correlate to biochemical evidence of myocardial injury in patients undergoing successful PCI and, therefore, provide insight into the mechanism of procedure-related CK-MB elevation.

Methods

Study Population

All 14 patients without evidence of prior myocardial infarction by history and noninvasive testing who underwent a successful elective PCI at Northwestern Memorial Hospital between August 1999 and August 2000 and who had a cardiac MRI within 4 weeks of PCI (median, 2 days) were investigated. Blood samples for CK and CK-MB were obtained at 4 and at 12 to 24 hours after PCI or until a peak level was established. CK-MB was quantified if the total CK was >100 IU/L. Study patients included 9 with procedure-related CK-MB elevation (>9 ng/mL) and 5 negative controls (no elevation). Four patients (2 in the index group and 2 controls) had rest or prolonged angina and were enrolled only after myocardial infarction was ruled out by serial CK-MB and troponin I determinations to limit the possibility that myocardial necrosis was present before PCI. All patients gave informed consent to the study protocol, which was approved by the Northwestern Institutional Review Board. The safety of performing MRI soon after coronary stent placement has been previously confirmed.11
MRI Protocol
Cine images were acquired on a 1.5T scanner (Siemens Sonata) with full ventricular coverage. Contrast-enhanced images were acquired 5 to 10 minutes after intravenous gadoteridol administration (0.1 mmol/kg) using a breath-hold segmented gradient-echo pulse sequence, as previously described. This sequence produces strongly T1-weighted images due to the use of an inversion pulse before image acquisition. In 2 of the 9 patients with CK-MB elevation, MRI was performed before and after PCI. Six of the patients with CK-MB elevation had a follow-up MRI at 3 to 12 months.

Image Analysis
Regional wall motion from the cine MRI, regional contrast-enhancement from the contrast-enhanced MRI, and the perfusion territory of the target vessel from the coronary angiogram were scored by the consensus of 2 observers using a 14-segment model. Each modality was interpreted with the observer blinded to patient identity and to the results of the other modalities.

Results
Patient Characteristics and Procedural Variables
The 14 patients ranged in age from 40 to 77 years (mean, 61 years); 5 (36%) had diabetes mellitus, and 6 (43%) had multivessel coronary disease (Table). All had normal left ventricular systolic function on contrast ventriculography or echocardiography, and all underwent angiographically successful coronary stent placement. Twelve (86%) received periprocedural intravenous glycoprotein IIb/IIIa receptor blockade. None underwent atherectomy. No patient had angiographic evidence of distal embolization, thrombus, transient abrupt closure, or transient slow flow. All had normal TIMI 3 flow at procedure completion. No patient developed Q-waves. There were no procedure-related major (>1.5 mm diameter) side-branch occlusions.

Of the 9 patients in the CK-MB elevation group, 5 had intraprocedural occlusion of a minor side branch (≤1.5 mm diameter), one developed medial dissection (which resolved with stenting), and 2 had transient ST-segment changes during the procedure that resolved spontaneously. These findings were absent in the control patients. Procedural vessel location did not differ between groups. In those with CK-MB elevation, the median peak CK and CK-MB were 245 IU/L (range, 146 to 709 IU/L) and 21 ng/mL (range, 12 to 93 ng/mL), respectively. Six of the 9 peak CK-MB levels were >3 the upper limit of normal (median, 2.3-fold elevation).

MRI Findings
All patients with procedure-related CK-MB elevation had myocardial hyperenhancement within the target vessel perfusion territory. Hyperenhancement was not observed in the control patients. Hyperenhancement was present immediately adjacent to the implanted stent in 3 patients, all of whom developed minor side-branch occlusion. Figure 1 shows examples of this pattern of hyperenhancement in 2 of these patients. In the remaining 6 patients, the hyperenhancement was located more distally in the myocardium subtended by the stented artery. Figure 2 shows examples of this hyperenhancement pattern. Assuming a myocardial specific gravity of 1.05 g/cm³, the median mass of infarcted tissue based on the volume of hyperenhanced myocardium was 2.0 g (range, 0.7 to 12.2 g), or 1.5% of the mass of the left ventricle (range, 0.4% to 6.0%). The mass of infarcted tissue was related to the peak CK-MB level (r=0.61, P=0.02). Only one patient with CK-MB elevation developed a new regional wall motion abnormality by cine MRI. Hyperenhancement persisted in 5 of 6 patients who underwent repeat MRI at 3 to 12 months (Figures 1 and 2).
Discussion

The mechanism of cardiac enzyme release after otherwise successful PCI has been disputed. Although myocellular necrosis has been implicated, severe ischemia without infarction has also been invoked. In the current study, all patients with CK-MB elevation had discrete hyperenhancement in the target vessel perfusion territory. None of the CK-MB negative controls had hyperenhancement. Because hyperenhancement is known to occur after irreversible myocellular injury but not after severe but reversible injury, such as myocardial stunning, the data provide evidence that PCI-related CK-MB elevation is due to new myonecrosis.

Our results are consistent with a recent consensus document on the redefinition of myocardial infarction, which states that despite the lack of complementary clinical evidence, a typical rise and fall of cardiac enzymes recovered from blood samples after PCI should be considered an acute myocardial infarction. One potential limitation of the present study is the lack of uniform MRI testing before PCI to rule out preexisting infarction. However, careful patient selection to limit this possibility, the lack of hyperenhancement in the control group, and the significant correlation between procedural CK-MB peak level and hyperenhancement mass (r=0.61, P=0.02) strongly suggest that the infarction occurred at the time of PCI.

Peak CK-MB level >3x the upper limit of normal has been recommended as the threshold for determining an infarction in the setting of PCI. In the current study, the majority of patients with hyperenhancement had CK-MB levels less than this threshold (6 of 9 patients). Perhaps because of the small amount of necrosis (median, 2 g), only 2 patients had transient ECG changes, none developed Q-waves, and only one developed a new wall motion abnormality. As a point of comparison, we note that, in general, >10 g of myocardial tissue must be injured before detection by radionuclide perfusion imaging.

Myonecrosis in the setting of successful PCI may result from transient vessel closure, side-branch compromise, coronary dissection, and distal embolization. Interestingly, we observed 2 different patterns of myonecrosis in the current study. In 3 patients, the necrotic tissue was immediately adjacent to the implanted stent, whereas in the remaining 6 patients, the necrotic tissue was located more distally in the myocardium subtended by the stented artery. All 3 patients with myonecrosis immediately adjacent to the stent had incidental minor side-branch occlusion. No patient had angiographic evidence of transient abrupt closure, thrombus, distal embolization, or major (>1.5 mm) side-branch occlusion. The cohort studied is representative of contemporary coronary interventions with a predominance of stent use (100%) and adjunctive glycoprotein IIb/IIIa receptor blockade (86%). In this cohort, the data support 2 pathways by which myonecrosis occurs after successful PCI: (1) incidental minor side-branch occlusion and (2) microvascular obstruction from distal embolization of plaque contents (platelets, thrombus, and/or atheroma).

The process by which procedural CK-MB elevation confers increased risk for future adverse outcomes was not addressed, nor can we conclude whether the level of increased risk is the same for the 2 patterns of myonecrosis observed. This issue will require further investigation.

In summary, this study is the first to provide an anatomic correlate to biochemical evidence of myocardial injury during PCI. The findings indicate that CK-MB elevation after PCI is the result of discrete microinfarction.
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