Assessment of Serum Myoglobin as a Marker for Acute Myocardial Infarction

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The reliability of serum myoglobin as a marker for acute myocardial infarction was evaluated in 157 consecutive coronary-care admissions. Admission myoglobin was elevated in 47 of 52 patients with acute infarction. Excluding those patients who presented later than 24 hr after symptom onset, only one patient with acute infarct had a normal admission myoglobin. In 22 of 105 patients with no infarct, myoglobin was elevated in association with angina, congestive heart failure, arrhythmias, and renal insufficiency. The detection of acute infarction by serum myoglobin measurement equals that of serial serum creatine phosphokinase isoenzymes (CPK-MB) by electrophoresis, but an elevated myoglobin is not specific for what is now considered clinically significant myocardial infarction.

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The recent development of radioimmunoassays for serum myoglobin has greatly improved the sensitivity with which this measurement can be made (*1-3*). Although not specific for cardiac myoglobin, the measurement of serum myoglobin has been suggested as a rapid screening test for myocardial infarction (*4-6*). Frequently, several days are required before the appearance of characteristic cardiac enzymes in the blood or before electrocardiographic changes can confirm or exclude the diagnosis of acute myocardial infarction. This study examined the clinical reliability of serum myoglobin as a marker for acute myocardial infarction in a large group of patients admitted to a cardiac-care unit.

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METHODS

Patients studied. One hundred and fifty-seven consecutive admissions to the coronary-care unit of our hospital provided the patient population for this report. Each patient's serum myoglobin was measured upon admission. Myoglobin was also measured at 72 hr in the initial 63 admissions and at 12 and 24 hr in the subsequent 94 admissions. Routinely, serial electrocardiograms were obtained daily for 3 days and serum creatine phosphokinase isoenzymes (CPK-MB) were measured upon admission and at 12, 24, and 48 hr. The clinical and laboratory findings were reviewed in all patients.

Myoglobin measurements. The serum collected was separated from the red cells and refrigerated. Specimens collected during the day were separated immediately. Those collected after hours were stored at 4°C for up to 15 hr before separation from cells. Specimens stored overnight were frozen and thawed once before assaying. Four samples found

TABLE 1. RECOVERY OF MYOGLOBIN ADDED TO FOUR SERUM SPECIMENS

Initial myoglobin concentration (ng/ml)	Myoglobin added (ng/ml)	Total myoglobin measured (ng/ml)	% recovery
15	62	73	94
	125	142	102
15	62	74	95
	125	150	108
29	62	98	111
	125	191	129
28	62	93	105
	125	178	120

to have elevated concentrations of myoglobin were assayed immediately after collection, after 48 hours at 4°C, and after freezing 48 hr in storage at −20°C and then thawing. No differences were found in myoglobin concentration for these handling and storage conditions.

Myoglobin was measured by a commercially available radioimmunoassay kit,* following the manufacturer's current protocol without modification. This method uses rabbit antimyoglobin antibody, a total incubation time of 75 min, and separation of the "antibody-bound" from the "free" fraction by a second sheep antirabbit antibody. Assay sensitivity (B/B_0 = 90%) was found to be 30 ng/ml. During the course of this study the between-assay coefficients of variation, for three control pools containing 31, 92, and 215 ng myoglobin/ml, were 5.0%, 5.4%, and 4.6% (n = 39 assays), respectively. Acceptable recovery of myoglobin (62 and 125 ng/ml) added to patients' serum samples was demonstrated (Table 1). Dilutional parallelism was demonstrated between high-concentration patient samples and the standard curve (Fig. 1). No displacement occurred because of hemoglobin in grossly hemolyzed samples. Nonspecific binding in both the standards (buffer) and patients' samples was 8-9% of total activity. The standard dose-response curve expressed as logit% [(bound activity)/(total activity)] plotted against log dose in ng myoglobin/ml, was found to be linear, and a computer program using a linear least squares fit for this regression was used for estimations of unknown dose concentrations (7). Concentrations measured in 39 ambulatory noncardiac patients were 24 (± 4.6 s.d.) ng/ml. Except in one case, concentrations greater than 50 ng/ml were measured in all patients who had had myocardial infarctions if the samples were obtained at appropriate time intervals.

CPK. CPK-MB isoenzymes were estimated by electrophoresis† and during the course of this study were quantitated visually as either absent, trace (less than 5% of total CPK), or positive (greater than 5% total CPK).

Myocardial infarction. Presence or absence of clinically significant myocardial infarction was determined by the clinician on the basis of the patient's clinical presentation and course, serial electrocardiographic findings, and serum enzyme elevations (principally, the presence or absence of CPK-MB). Myoglobin results were then correlated with these clinical and laboratory data.

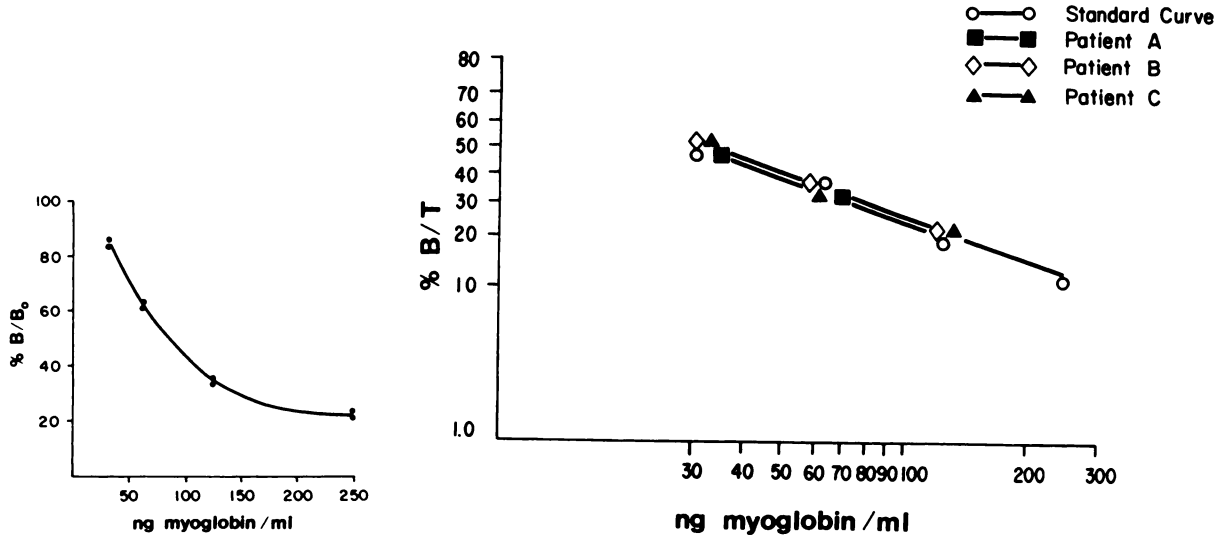

FIG. 1. (Left) Representative myoglobin standard curve. (Right) Logit/log plot of displacement observed in dilutions of three patients' samples with high initial concentrations of myoglobin.

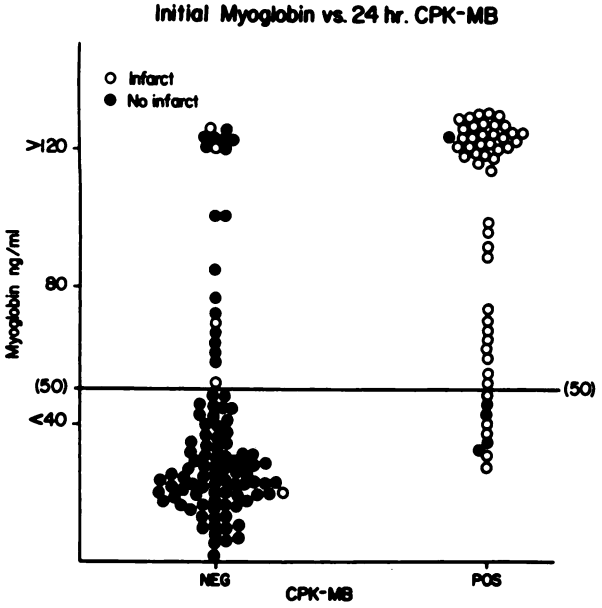

FIG. 2. Serum myoglobin and CPK-MB in 157 patients admitted for exclusion of acute myocardial infarction. (○) Patients with infarct. (●) Patients with no infarct.

RESULTS

Fifty-two patients were classified as having had an acute myocardial infarction, leaving 105 patients who had not. Figure 2 illustrates the relationship between myoglobin measured upon admission and CPK-MB in both infarcted and noninfarcted patients.

Myocardial infarct group. Table 2 summarizes the myoglobin and CPK-MB findings in the 52 patients with infarction. One patient died before a specimen for CPK-MB determination could be obtained. In 14 of 46 patients, CPK-MB was detected later than elevation of myoglobin by 4–48 hr. In one patient CPK-MB was detected in the blood 8 hr before myoglobin elevation. There was only one unexplained falsely negative myoglobin result and three unexplained falsely negative CPK-MB results.

Noninfarcted group. Table 3 summarizes the myoglobin and CPK-MB findings in the 105 patients classified as not having had an infarct. CPK-MB isoenzymes were not measured in one patient.

DISCUSSION

The value of CPK-MB isoenzyme measurements in patients with suspected myocardial infarction is well established (*8,9*). This marker generally appears in the blood 4–6 hr after acute infarction and in an appropriate clinical setting is virtually specific for myocardial infarction. Absence of CPK-MB generally excludes clinically significant myocardial infarction (*9*). Myoglobinemia has also been shown to accompany acute infarction, often preceding detectable CPK-MB (*1,4-6,10*). We have examined the sensitivity and specificity of this marker to exclude the diagnosis of myocardial infarction in a large series of patients consecutively admitted to the coronary-care unit.

Knowledge of the time elapsing between presumed myocardial injury and the time when a myoglobin specimen is obtained is necessary if results are to be correctly interpreted. Myoglobin appears in the blood within a few hours of infarction and is frequently evanescent, being missed if specimens are obtained too late—generally 6–24 hr after onset of symptoms. In this study, late specimens were a function of the time when the patient arrived at the emergency room and represent a limitation on the application of this technique.

Serum myoglobin, if measured within 6 hr of acute injury, was abnormally elevated in all but one of our patients with acute infarction. In about one third of these patients, CPK-MB was absent in the same specimen, appearing in the blood a variable time later. Similar findings have been recorded by other investigators (*4*). The sensitivity of a single-admission myoglobin determination appears to be similar to that of serial CPK-MB determinations;

TABLE 2. ACCURACY OF DIAGNOSTIC METHODS IN 52 PATIENTS WITH MYOCARDIAL INFARCTION

Method	Results: Positive no. patients	Results: False-negative no. patients	Total no. patients
Myoglobin	47	5 (9%)	52
Late sampling (>24 hr after infarction)		4	
Unexplained		1	
CPK-MB	46	5 (9%)	51
Died		1	
Late sampling (> 72 hr after infarction)		1	
Unexplained		3	

TABLE 3. ACCURACY OF DIAGNOSTIC METHODS IN 105 PATIENTS WITHOUT MYOCARDIAL INFARCTION

Method	Results		Total no. patients
	Negative no. patients	False-positive no. patients	
Myoglobin	83	22 (20%)	105
Acute congestive heart failure, angina		6	
Cardioversion		3	
Tachyarrhythmias		3	
Pacemaker failure		1	
Cardiac contusion		1	
Renal failure		6	
Fever, chills (pneumococcal pneumonia)		1	
No coronary-artery disease (catheterization)		1	
CPK-MB	99	5 (4%)	104
Angina		3	
Chronic renal failure		2	

CPK-MB was not detected in three patients with infarction when specimens were obtained at appropriate time intervals.

An elevated serum myoglobin, however, was not as specific as CPK-MB for myocardial injury, since the former appeared in the blood after a number of both cardiac and noncardiac events. It is possible that elevations of myoglobin associated with prolonged angina, congestive heart failure, and arrhythmias are indicative of myocardial damage that is now considered clinically insignificant, and thus is reflective of assay sensitivity. Reichlin et al. (*3*) also identified a similar group of patients with elevated myoglobin but without clinical infarction, although this was not reported by Stone et al. (*1*). The relative sensitivity of serum myoglobin and serum CPK-MB measurements may be clarified when radioimmunoassays for CPK-MB become more widely available (*11,12*).

As expected, myoglobin elevations occurred in the presence of significant skeletal-muscle trauma (*13*), as was seen after cardioversion or shaking chills related to sepsis. Our patients received no intramuscular injections after admission to the coronary-care unit, and minor trauma did not appear to be a factor in this study.

Decreased renal clearance was accompanied by elevations of serum myoglobin, as has been reported by others (*14*). In our study, myoglobin concentrations greater than 50 ng/ml were encountered when the serum creatinine exceeded 1.8–2.0 mg/dl.

It is necessary to examine carefully what constitutes a normal serum myoglobin for the patient population studied. In our study with this particular assay, the upper limit of normal was found to be 40 ng/ml, which is lower than normal values reported by others (*2,4*). Although the manufacturer suggests a normal range of 6–85 ng/ml, Kubasik et al. (*15*) recently reported that their normal range for ambulatory patients using this same assay is essentially the same as ours. Run-to-run assay precision was excellent: approximately ±4 ng/ml (2 s.d.) at 40 ng/ml. We found no difference in measurable immunoreactive myoglobin concentration among specimens run immediately, after storage for 48 hr at 4°C, and after one freeze-thaw cycle. Although patients may arrive for treatment at any hour—so that specimens are taken at all hours—it does not appear necessary to process samples immediately.

In conclusion, the measurement of serum myoglobin upon admission appears to identify almost all patients with acute myocardial infarction. Its sensitivity is at least equal to that of the serial measurement of CPK-MB by electrophoresis. Myoglobin elevations, however, are not specific for what is now considered clinically significant myocardial damage, and were observed in other cardiac and noncardiac situations. If further studies confirm the low false-negative rate, the measurement of serum myoglobin may be a rapid, reliable means of excluding significant myocardial injury.

FOOTNOTES

* Nuclear Medical Systems, Inc., Newport Beach, CA.
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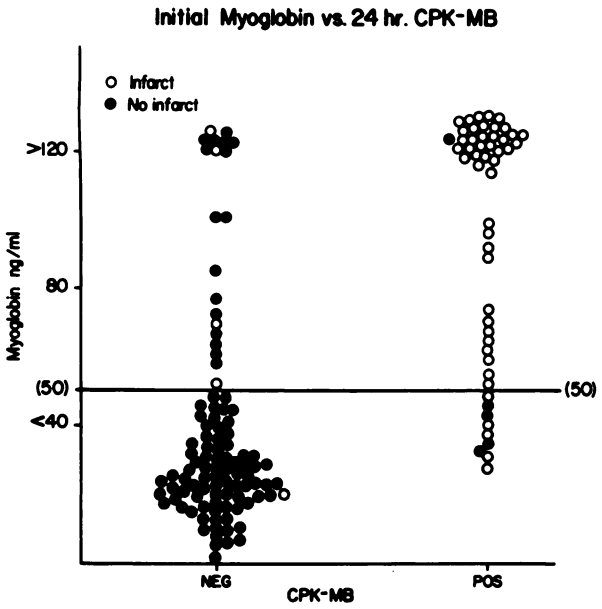

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