DIAGNOSTIC NUCLEAR MEDICINE

Behavior of Serum Myoglobin During Cardiac Catheterization: Concise Communication

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We have studied 28 patients undergoing coronary angiography by the Judkins technique to determine whether serum myoglobin (MG) might be useful as an indicator of myocardial injury during routine cardiac catheterization and coronary angiography. MG was measured immediately before and after the procedure, and 4 hr later. The study population failed to show a rise of MG outside the normal range in spite of angina, hypotension, or severe coronary disease. Four patients premedicated with intramuscular pentobarbital (positive control) showed a consistent rise, with a range 1.5–3 times normal ($p < 0.001$). We conclude that injury to myocardial or peripheral tissues occurring during coronary angiography does not raise myoglobin in venous blood above normal levels in the absence of myocardial infarction or preoperative intramuscular injection. Myoglobin, therefore, provides a useful test for the exclusion of myocardial infarction following coronary angiography.

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Serum myoglobin as determined by radioimmunoassay shows great promise as a clinically useful indicator of acute myocardial infarction (*1–5*). It is the earliest and most sensitive chemical sign of acute infarction, and frequently peaks earlier than creatinine phosphokinase (*3–5*). It is nonspecific, however, and may be elevated in skeletal muscle trauma, rhabdomyolysis, and renal failure (*6*). Myoglobin levels do not rise with angina alone in the absence of acute myocardial infarction (*2,3*).

A rapid, reliable test for assessing the presence of myocardial damage during cardiac catheterization and coronary angiography would be desirable. Catheterization could theoretically cause release of both cardiac and peripheral myoglobin. Earlier work (*1*) has suggested that myoglobin levels do not rise following routine uncomplicated coronary angiography. This series, however, was limited in size. Furthermore, no study has questioned whether a peripheral-venous sample might be as reliable as a sample from the coronary sinus. Because of the great potential of myoglobin as a sensitive indicator of acute myocardial infarction, we studied its behavior during cardiac catheterization and coronary angiography.

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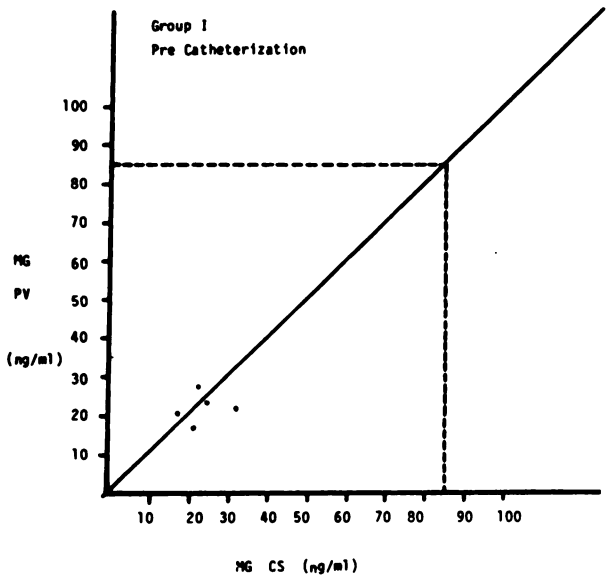
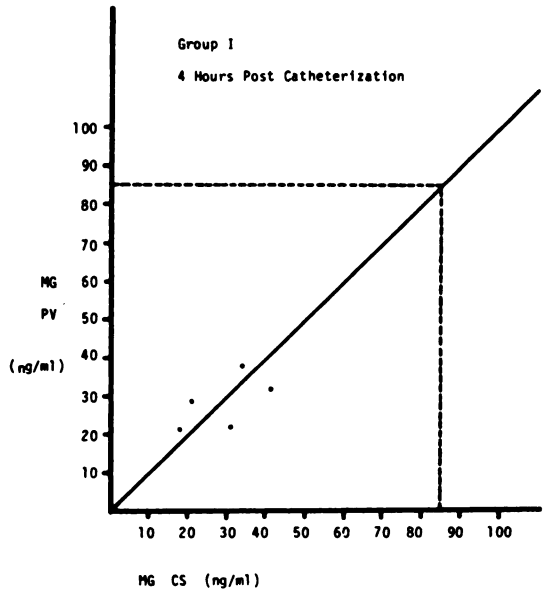
METHODS

The study involved 28 consecutive adult patients who underwent routine cardiac catheterization and coronary angiography by the Judkins technique between October 1978 and July 1979. The patients were selected on the basis of: (a) Need for coronary angiography to define the presence or extent of coronary artery disease in the absence of valvular, myocardial, or pericardial disease; (b) absence of prior muscle injury, recent acute myocardial





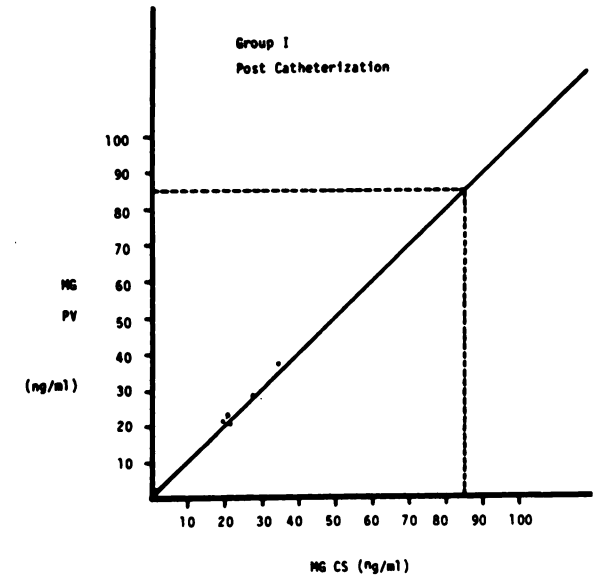


FIG. 1. GROUP 1: (Five patients without i.m. premedication) Coronary-sinus and peripheral-venous myoglobin compared. A. Precatheterization; B. Just after catheterization; C. 4 hr after catheterization. Abbreviations: MG = myoglobin, PV = peripheral venous, CS = coronary sinus. Dashed line delineates upper limit of normal.

infarction, and renal failure; and (c) lack of need for exercise, pacing, or ergonovine stimulation during catheterization.

The patients were divided into three groups. Group 1 included five who received no intramuscular injections and in whom the coronary sinus could be selectively cannulated with a Zucker pacing catheter. Patients were selected for Group 1 only by success in cannulation of the coronary sinus at the beginning of the procedure; if this could not be done after a reasonable attempt, they were excluded from the study. In this group, paired peripheral-venous and coronary-sinus samples were analyzed to evaluate the contributions of peripheral or myocardial tissues to any detected rise of myoglobin. If cardiac myoglobin were liberated, then coronary-sinus levels might be higher than peripheral-venous levels, whereas if only peripheral tissue were injured, both would likely be equal. There were 19 patients in Group 2. They were similar to those in Group 1 in that they received no intramuscular injections, but differed in that only their peripheral-venous myoglobins were determined; no attempt was made to catheterize the coronary sinus in these patients. Group 3 consisted of four patients who received intramuscular premedication with pentobarbital, 100 mg, but were otherwise treated as in Group 2. Group 3 served as the positive control for the study.

All patients received pre- and postcatheterization electrocardiograms. Serial CPK, SCOT, and LDH determinations were done when clinical suspicion of myocardial infarction was high. Blood for myoglobin determination was drawn before catheterization, immediately after catheterization, and 4 hr after catheterization. Myoglobin was determined with a commercial radioimmunoassay kit, whose accuracy and reliability had been established previously (*3*). Normal serum myoglobin by this method is <85 ng/ml.

Statistical comparisons used the Wilcoxon signed rank test for paired coronary-sinus and peripheral-venous samples in Group 1, and for paired pre- and postcatheterization observations in Groups 1 and 2. We used the Wilcoxon rank sum test for comparisons between Groups 2 and 3. Confidence limits of the means were determined using the method of standard confidence intervals for single samples based upon the *t* distribution.

RESULTS

Group 1: None of the patients showed a rise in either coronary-sinus or peripheral-venous myoglobin during coronary angiography (Figs. 1a, 1b, 1c). There were

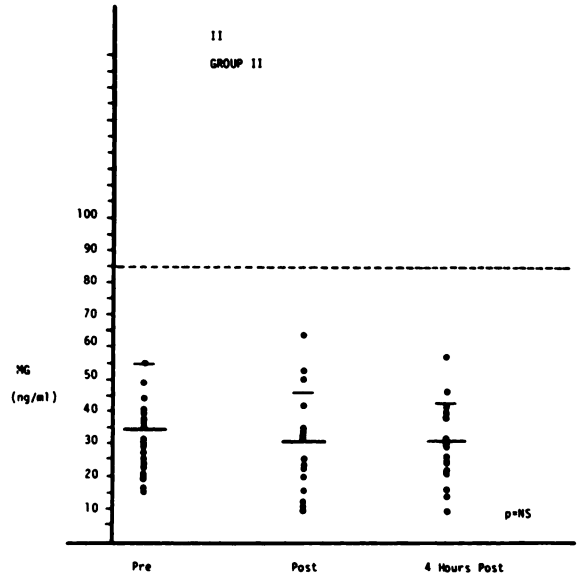


FIG. 2. GROUP 2: (Nineteen patients without i.m. premedication) Peripheral-venous myoglobin pre-, postcatheterization, and 4 hr later.

minimal differences (p = NS) between paired coronary-sinus and peripheral-venous samples, for populations means (Figs. 1a, 1b, 1c.). Mean values (and range) expressed in ng/ml were as follows: coronary-sinus precatheterization 23.3 (16.3-32.6); postcatheterization 25.1 (19.9-34.5); and 4 hr after catheterization 29.5 (18.2-42.3) (p = NS for samples paired pre- and post-, pre- and 4 hr post-). Peripheral-venous myoglobin levels were: precatheterization 21.7 (17.9-27.7); postcatheterization 26.5 (21.6-37.9); and 4 hr postcatheterization 28.5 (20.9-38.5) (p = NS for samples paired pre- and post-, pre- and 4 hr post-). Although two patients sustained vasovagal reactions with transient hypotension and four had transient chest pain requiring nitroglycerin, none was thought to have sustained myocardial infarction by clinical assessment, electrocardiogram, or serial enzyme determinations.

Group 2. With the equivalence between central- and peripheral-venous myoglobin established, we continued the study to validate the initial findings further (Fig. 2). Mean ± s.d. (with range) values for pre-, post-, and 4-hr serum myoglobin were 29.7 ± 9.7 (16.2-48.4), 31.4 ± 14.8 (9.9-63.9), and 30.9 ± 11.8 (9.5-57.0) ng/ml (p = NS). No patient in Group 2 showed a significant rise in peripheral-venous myoglobin during or after catheterization. Twelve of 20 had coronary artery disease, with 11 exhibiting severe three-vessel involvement. During the procedure two patients had severe angina, lasting less than 5 min and responding to sublingual nitroglycerin. There was no clinical, ECG, or enzyme indication that either had sustained myocardial injury. One patient without pain was referred for emergency coronary-artery bypass surgery for severe disease of the left main coronary.

Group 3. Four patients who received i.m. premedication served as the positive control. The medication was given within one hour of the precatheterization myoglobin determination. Two were abnormal on precatheterization (Fig. 3). Mean (range) values on pre-, post-, and 4-hr-postcatheterization samples were 111.1 (25.3-185.6), 165.5 (118.2-251.2), and 184.7 (109.0-228.7) ng/ml. All had three-vessel disease, but

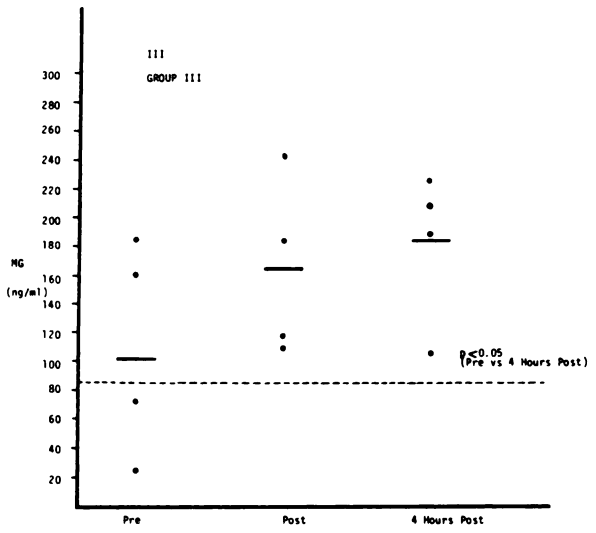


FIG. 3. GROUP 3: (Four patients with i.m. premedication) Peripheral-venous myoglobin pre- and postcatheterization, and 4 hr later.

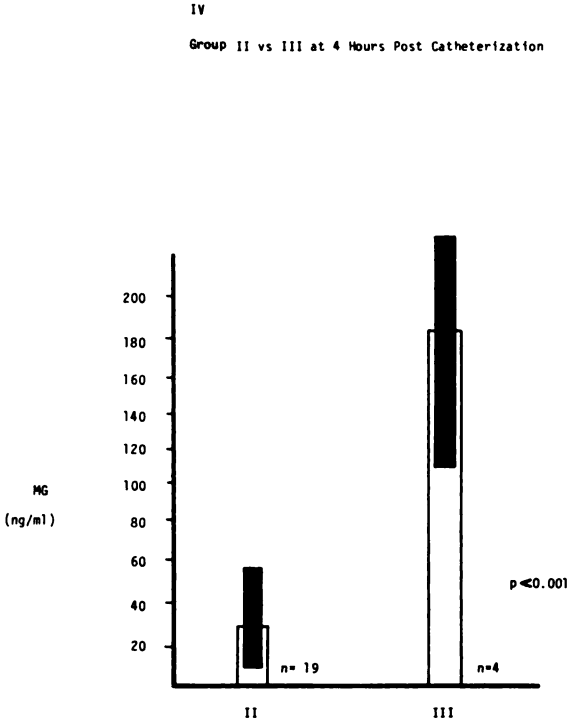


FIG. 4. Peripheral-venous myoglobin in Group 2 compared with that in Group 3 (positive controls) at 4 hr after catheterization. Mean (light bar) and range (heavy bar).

none was thought clinically to have sustained myocardial infarction. Comparison of Group 2 with Group 3 at 4 hr after catheterization (Fig. 4) demonstrates a significant difference ($p < 0.001$), serving to validate the marked sensitivity of the test, and to suggest the reliability of a normal value after the test.

Upper limits of the 99% confidence bands for the means of the peripheral-venous samples (Groups 1 and 2 combined) are 54.2 ng/ml before catheterization, 68.5 ng/ml after catheterization, and 61.2 ng/ml 4 hr later. All are well within the range of normal (<85 ng/ml). These statistical data define the limits of the variability of our test in our sample and imply a wide margin of reliability for a negative test in our protocol.

DISCUSSION

Myoglobin is liberated during any muscle necrosis. In 1956 myoglobin was discovered to be present in serum and urine following myocardial infarction (*3*). Development of a radioimmunoassay for myoglobin, with subsequent modification for shortening assay time, was completed in 1977 (*2*). Studies since then have shown that myoglobin is a highly sensitive indicator of myocardial infarction when other conditions such as rhabdomyolysis, severe skeletal muscle trauma, and renal failure can be eliminated (*3,4*). Although the exact place of myoglobin in our diagnostic armamentarium remains in question (*7,8*), there is general agreement upon its reliability as an indicator of muscle necrosis. A very significant clinical value of myoglobin lies in its early appearance following myocardial injury (*5*). In recent studies of myoglobin, all patients with clinical infarction reached a myoglobin peak by 6 hr after infarction, and most did so by 4 hr (*3,4*), thus allowing very early detection and therapeutic intervention. Equally important is the observation that if myoglobin is normal within the first 6 hr following chest pain, myocardial infarction can be virtually excluded (*3,4*).

Angina is often precipitated during the course of coronary angiography. It would be desirable to have a means for early differentiation of angina from true myocardial injury. Currently, CPK analysis can take 12–24 hr to be diagnostic, either positive or negative. Our study was designed to show whether or not determination of myoglobin in peripheral-venous samples could, in fact, be relied upon to indicate myocardial injury as a complication of routine coronary angiography. If myoglobin were found routinely to be abnormally elevated after coronary angiography, its usefulness would be doubtful. However, if myoglobin should remain within normal limits after coronary angiography in spite of occurrence of angina during the procedure, then abnormal elevation would suggest myocardial injury.

We began by studying the reliability of peripheral-venous sampling compared with central sampling. All patients whose coronary sinus was easily engaged were included in the study until this issue was resolved. Thus, by sampling simultaneously from the coronary sinus and a peripheral vein, paired samples were obtained for myoglobin comparisons. This made up Group 1, and represented our early experience with myoglobin. None of these patients was found to have myoglobin elevation even if angina occurred, and there were no chemical indications of myocardial injury. Although there were no myocardial infarctions in Group 1, it was not the sensitivity of myoglobin for determining the presence of a myocardial infarction that was in question, since this feature has been well established previously (*3,4,9*). Since samples from the coronary sinus and peripheral vein yielded similar myoglobin levels, peripheral-vein sampling alone was thought to be reliable in the setting of catheterization.

To gain further experience with myoglobin determination in association with coronary angiography, we studied an additional 19 consecutive patients using peripheral-vein sampling before, immediately after, and 4 hr after catheterization. These made up Group 2. None of these patients was found to have myoglobin elevation after catheterization in spite of angina or, in two cases, hypotension of approximately 70 mm Hg for 5 min as a result of vasovagal reaction.

Finding no patient in Groups 1 or 2 with elevated serum myoglobin, we studied four patients who were given 100 mg of intramuscular pentobarbital as premedication. All of these patients were found to have an abnormal rise in myoglobin after catheterization.

It appears that, excluding intramuscular premedication and known conditions contributing to an elevated myoglobin, one can expect peripheral-vein sampling for myoglobin determination to be a reliable indicator of myocardial injury resulting from routine coronary angiography. This finding corroborates the data of Stone, who showed that catheterization did not elevate myoglobin in nine patients (*2*). The 99% confidence bands for the means of our sample population (Groups 1 and 2), as detailed previously, disclose a wide margin of reliability for our findings. No patient would be expected to show a random rise outside the range of normal. Therefore, the absence of myoglobin rise in our sample population implies that myoglobin should not routinely be expected to rise in any population subjected to the same protocol.

In summary, the tissue trauma that is sustained during cardiac catheterization is insufficient to cause central- or peripheral-venous myoglobin to rise above the normal range, provided there has been no intramuscular injection or clinical myocardial infarction. The presence of chest pain or hypotension during cardiac catheterization, and the demonstration of severe coronary artery disease, do not alter this finding. The behavior of serum myoglobin demonstrates, therefore, that it is a useful indi-

cator for the early diagnosis or exclusion of myocardial injury following cardiac catheterization and coronary angiography.

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