unspecified stabilizers, plasticizers, and other components, matrix effects could still be a possibility if other specimen preparation protocols are used.

References

Fig. 1. Patient sirolimus whole-blood specimens analyzed without (A and C) and with (B and D) SPE cleanup: comparison of results obtained by calibration with the Chromsystems materials vs in-house calibrators.
1 Pt Cal and 4 Pt Cal, one- and four-point calibration, respectively; Cal, calibrators.

Cardiac Troponin and Creatine Kinase MB Monitoring during In-Hospital Myocardial Reinfarction, Fred S. Apple* and MaryAnn M. Murakami (Department of Laboratory Medicine and Pathology, Hennepin County Medical Center and University of Minnesota School of Medicine, Minneapolis, MN; * address correspondence to this author at: Hennepin County Medical Center, Clinical Laboratories P4, 701 Park Ave., Minneapolis, MN 55415; fax 612-904-4229, e-mail fred.apple@co.hennepin.mn.us)

Cardiac troponin monitoring for detection of myocardial injury has been designated the new standard for differ-
entiating the diagnosis of unstable angina and non-ST-elevation myocardial infarction (NSTEMI) in acute coronary syndrome patients (1–4). Increased cardiac troponin I (cTnI) or T (cTnT) in the clinical setting of ischemia is defined as an acute MI and has been endorsed by the European Society of Cardiology, American College of Cardiology, the American Heart Association, the IFCC, and the Epidemiology World Council (1–6). One of the challenges that confronts cardiac troponin monitoring encompasses the clinical setting of myocardial reinfarction within a short time period after an initial MI. Because cardiac troponins can remain increased in the circulation for up to 5 (cTnI) or 10 days (cTnT) after an acute MI, in theory, the role for monitoring cardiac troponins during reinfarction has been questioned. The European Society of Cardiology/American College of Cardiology consensus document notes that in the clinical setting of a reinfarction, creatine kinase MB (CKMB) may be more useful for monitoring for MI because CKMB remains increased for only 2–4 days after an acute MI (1–4). There are only two case reports in the literature, both from a previous report from our laboratory, that redressed the role of cardiac troponin monitoring in reinfarction (7).

The purpose of this study was to compare the patterns of increases and decreases in cTnI and CKMB mass in a series of nine MI patients who experienced an in-hospital myocardial reinfarction (MI extension) within 4 days of the initial MI event. Over a period of 16 months (September 1999 through February 2001), nine MI patients were identified who experienced a myocardial reinfarction during hospitalization for an MI. With appropriate Investigational Review Board approval, we obtained plasma (heparin) during and after both the initial MI and during the reinfarction episode. All plasma samples were analyzed fresh, within 2 h of draw time, by both the Dade Dimension RxL cTnI and CKMB mass immunoassays (7, 8). Upper reference limits at the time these data were collected were 0.8 µg/L for cTnI and 5.0 µg/L for CKMB, with total imprecision (CVs) at these concentrations of 11.5% and 5.5%, respectively (7, 8). MI patients initially presented within 12 h of experiencing symptoms of ischemia (e.g., chest pain, chest discomfort) with or without electrocardiographic (ECG) evidence of myocardial ischemia (ST-segment depression, ST-segment elevation, T-wave inversion, or Q-waves). Patients were considered to have either an ST-elevation MI (ST elevation or Q-wave with an increased cTnI) or a NSTEMI (no ST elevation or Q-wave but with an increased cTnI) on the basis of both serial ECG and cTnI determinations over 12–24 h after presentation for both the initial or reinfarction events. For patients with an initial STEMI, reinfarction was defined based on new onset of ischemic symptoms and a pattern of increasing cTnI during serial monitoring.

The following case presentation is representative of our series of nine patients studied. Patient 9 was hospitalized January 4–10, 2000, for a NSTEMI (non-Q-wave MI per chart documentation) and negative adenosine stress test. The peak cTnI at 24 h after onset of chest pain was 1.3 µg/L (peak CKMB = 11.5 µg/L) and returned to normal 3 days after the event (cTnI = 0.6 µg/L; CKMB = 5.0 µg/L). At 72 h after presentation, the patient experienced new-onset chest pain, described as a burning pain in the left shoulder, arm, and epigastrium. Although nitroglycerin provided some relief, the ECG demonstrated only nonspecific T-wave abnormalities, no different from the initial presentation, which had resolved to a normal rhythm during the initial 2 days of hospitalization. New onset of symptoms in combination with recurring T-wave abnormalities and increasing cTnI values were used for the diagnosis of reinfarction. The initial cTnI on the suspected reinfarction (day 4) was increased at 1.4 µg/L (with a corresponding CKMB of 11.0 µg/L). Cardiac catheterization, performed on day 4 after the reinfarction and 2 h after the 1.4 µg/L cTnI finding, revealed 85% distal left anterior descending stenosis, 95% mid-right coronary artery narrowing, and a 80% occluded circumflex proximally; stents were successfully placed within both the distal and proximal right coronary artery.

The mean age of the nine patients studied was 66.2 years (median, 63 years; range, 50–84 years). Six of nine were males; four were African American and five were Caucasian. All reinfarctions occurred in the hospital and within 24–96 h of the initial index presentation. The mean time from onset of chest pain to initial presentation was 5.2 h (median, 4.0 h; range, 1–12 h). Shown in Fig. 1 are the serial cTnI and CKMB concentrations vs time profiles for each patient during both their initial MI presentation and the reinfarction events. Four patients presented initially with a STEMI (patients 1, 4, 5, and 7). Three of nine patients presented with both increased cTnI and CKMB (patients 1, 2, and 8). However, at reinfarction, six of nine patients had increased baseline cTnI (patients 1, 2, 3, 4, 7, and 8) compared with only three of nine patients with a borderline increased CKMB (patients 1, 3, and 7). Overall, the profiles of each biomarker paralleled each other. In the patients in whom the last cTnI concentration from the initial biomarker orders were increased (patients 1, 4, 5, 7, 8, and 9), all reinfarctions showed substantial secondary increases above the previous cTnI value.

Although preliminary, our findings in nine myocardial reinfarction patients demonstrated that CKMB analysis is not clinically relevant, or cost-effective, in the differential diagnosis of myocardial reinfarction in acute coronary syndrome patients when cardiac troponin monitoring is available. Previously, we demonstrated similar findings in two case studies (7). Furthermore, Bodor et al. (9) also have described similar findings in six patients who had a second MI 52–288 h after the occurrence of the first MI. We encourage others to test our hypothesis to be able to dispel the theoretical rational for use of CKMB in addition to cardiac troponin testing, expediting the cost-effective adaptation favoring only cardiac troponin monitoring in testing for MI or reinfarction.
The use of cardiac troponin assays has become equal to and greater than use of either total CK and CKMB assays in clinical practice (12). Monitoring of cardiac troponins is therefore not limited by assay availability.

The reported incidence rate of reinfarction appears to be <20% (13). Few studies have examined the secondary increases in cardiac biomarkers during an early recurrent infarction (reinfarction extension). In the largest series of patients studied, Marmor et al. (14) documented a secondary increase in CKMB activity that occurred a mean (SD) of 10 (4) days after the initial infarct, but in only 17% of patients (34 of 200). Morrison et al. (15), examining the release of CKMB to estimate infarct size in 35 MI patients, contended that the appearance of a second peak of CKMB before the return of the enzyme to baseline was not associated with an infarct extension. Eisenberg et al. (13) stratified 50 chest pain patients for MI based on a 50% change in CKMB concentrations, independent of whether CKMB was normalized between the initial and recurrent infarctions. We recognize that the current study has limitations in that more extensive clinical information was not available, but its primary goal of demonstrating comparative biomarker profiles was achieved.

We could not identify any citations in either MedLine or PubMed searches for studies addressing cTnI and CKMB monitoring in myocardial reinfarction as a diagnostic tool. Our observations infer that cardiac troponin monitoring, specifically cTnI as shown in the current study, is sufficient as an individual cardiac biomarker to rule in and rule out MI and/or reinfarction in clinical practice. Although cTnI and cTnT concentrations have been shown to be negatively biased when heparin plasma has been used vs serum as a sample for some troponin assays (16), the findings of this study, based on serial observations, were unlikely to be influenced by the specimen collection tube used. Because cTnI remains in-

Fig. 1. Time (hours) vs cardiac biomarker (cTnI and CKMB mass) profiles in nine MI patients who experienced a reinfarction during hospitalization.

- cTnI; □ CKMB. Arrows indicate the time reinfarction was suspected by clinicians, according to medical records.
creased for longer periods after an initial MI (up to 10 days), independent validation for cTnT should be carried out as a biomarker for reinfarction. Given the limited financial resources in laboratories and healthcare, clinicians should consider monitoring just cardiac troponins for the diagnosis of MI or in-hospital infarction.

References


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