Diagnostic Marker Cooperative Study for the Diagnosis of Myocardial Infarction

To the Editor:

Zimmerman et al report a multicenter study of the predictive power of biochemical markers for a diagnosis of myocardial infarction (MI) in 955 patients presenting with chest pain. MI diagnosis was based on creatine kinase (CK)-MB mass (7 ng/mL) and CK-MB index (2.5%) within 24 hours after emergency department arrival. Markers included CK-MB subforms, myoglobin, troponin T, troponin I, total CK-MB activity, and total CK-MB mass. Sensitivity and specificity are illustrated for hours 2, 4, 6, 10, 14, 18, and 22 after symptom onset. The authors report that CK-MB subforms, followed by myoglobin, were the most sensitive and specific for early diagnosis (ie, within 6 hours); they conclude that in the selection of a single assay, CK-MB subforms provide the earliest diagnosis.

A review of the data (Table 2) confirms that the sensitivity for CK-MB subforms or myoglobin is significantly higher than other markers at 2, 4, and 6 hours. However, contrary to the authors’ statement, the specificity for CK-MB subforms and myoglobin is significantly less ($P<0.01$) than for troponin I, troponin T, CK-MB activity, and CK-MB mass at these hours. The reporting of sensitivity and specificity alone does not yield estimates of the positive (rule-in) and negative (rule-out) predictive power of the markers. Calculations of positive predictive value ($+PV$) and negative predictive value ($-PV$) provide such estimates as follows:

$$+PV = \frac{\text{Se} \times 12.5}{\text{Se} \times 12.5 + (100 - \text{Sp}) \times 87.5 \times 100}$$

$$-PV = \frac{\text{Sp} \times 87.5}{\text{Sp} \times 87.5 + (100 - \text{Se}) \times 12.5 \times 100}$$

where 12.5 is the population frequency of MI in percent and 87.5 is its complement. Se indicates sensitivity and Sp, specificity.

The predictive values yield the following observations: (1) $+PV$ at hours 2, 4, and 6 for troponins I and T, CK-MB activity, and CK-MB mass is greater ($P<0.01$) than that for CK-MB subforms and myoglobin; (2) $-PV$ at 2 and 4 hours for the CK subforms is not significantly different from the other markers; and (3) $-PV$ of the CK-MB subforms at 6 hours is significantly higher than that of all other markers ($P<0.01$).

By predictive value analysis, CK-MB subforms have no greater early rule-in power for MI than troponins T and I, CK-MB activity, and CK-MB mass; CK-MB subforms have the highest rule-out power only at the sixth hour after chest pain onset.

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