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Diagnostic Accuracy of Kodak Creatine Kinase MB, Stratus Creatine Kinase MB, and Lactate

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We used receiver-operating-characteristic (ROC) curves 1, 2) and logistic discriminant analysis 3) to compare the accuracy of two creatine kinase (CK; EC 2.7.3.2) isoenzyme MB methods and lactate dehydrogenase (LD; EC 1.1.1.27) isoenzyme 1 in diagnosing acute myocardial infarction AMI). Furthermore, functions for the likelihood ratio were found 3). Given the likelihood ratio function, L(x), and the prevalence, p, the probability of disease at enzyme activity concentration x, P(D|x), can be calculated 3) as P(D|x) = L(x)/(pL(x) + 1 − p). To our knowledge, functions for the likelihood ratio for CK-MB in diagnosing AMI have not been published previously.

Stratus CK-MB (4), Kodak CK-MB (5), and LD-1 were studied in 117 patients consecutively referred with some symptoms of AMI. Activity of LD-1 was calculated from results of agarose gel electrophoresis (Paragon, Beckman) and total LD activity (6). Specimens for serum enzyme measurements were obtained at admission (day 1), and on days 2, 3, and 5 at 0800 hours. AMI was diagnosed in 41 patients, without knowledge of isoenzyme test results, according to the following criteria: development of abnormal, persistent Q or QS waves in the electrocardiogram, and (or) typical changes in serum enzymes [aspartate aminotransferase (ASAT; EC 2.6.1.1), CK, and LD].

No isoenzyme provided useful information at admission. The diagnostic accuracy of the two CK-MB methods was best on day 2, but LD-1 proved to be the best parameter on that day. The area under the ROC curves for all three variables on day 2 were 0.95. However, LD-1 had the highest chi-square test value of logistic discriminant analysis [101.21 (one degree of freedom) vs 81.13 and 82.26, respectively, for Kodak CK-MB and Stratus CK-MB]. The area under the ROC curve for the ratio Kodak CK-MB/total CK disclosed a virtually worthless test on all days (highest value 0.55).

Using peak enzyme values rather than values on specific days, we found that the two CK-MB methods showed better diagnostic accuracy than the LD-1 test. The mean (SD) area under the ROC curves for Kodak CK-MB, Stratus CK-MB, and LD-1 were 0.98 (0.02), 0.98 (0.02), and 0.96 (0.03), respectively. The chi-square test values of logistic discriminant analysis were 96.10, 92.91, and 97.98, respectively, with one degree of freedom. Adding Kodak CK-MB or Stratus CK-MB to LD-1 significantly increased the diagnostic accuracy (chi-square values of 10.56 and 3.31, respectively, with one degree of freedom). The likelihood ratio functions for peak values were L(x) = exp(−3.6890 + 0.1420x), L(x) = exp(−3.0066 + 0.2115x), and L(x) = exp(−4.4879 + 0.0204x), for Kodak CK-MB, Stratus CK-MB, and LD-1, respectively. The probability of AMI, given peak isoenzyme values at certain values of prevalence, is shown in Figure 1.

In conclusion, we found the same diagnostic accuracy for Kodak CK-MB as for Stratus CK-MB. Despite infrequent sampling, CK-MB showed as good diagnostic accuracy as...
LD-1. The combination of CK-MB and LD-1 was better than either one alone. When interpreting results from individual patients, calculating probability of AMI from likelihood ratio functions gives much more information than just classifying the results as "positive" or "negative" (3).

References


Recipients of blood transfusions run the risk of potential infection, and several procedures for the identification of high-risk donors are used, including the detection of antibody to human immunodeficiency virus (HIV), hepatitis B core antigen, and the measurement of plasma or serum alanine aminotransferase (ALT; EC 2.6.1.2) as a marker for non-A, non-B (NANB) hepatitis (1). To minimize the risk of infection from HIV when handling plasma or serum, one of the suggested procedures is heat treatment at 56 °C (2, 3).

Published data on the effects of heat treatment on ALT and aspartate aminotransferase (AST; EC 2.6.1.1) are limited. For AST, some reports showed no statistically significant differences after treatment for 0.5 or 1 h at 56 °C, although slight reductions of the mean enzyme activities were noted (4–6). For ALT, there is one report of a 63% reduction of enzyme activity in serum after heat treatment for 0.5 h (4).

We measured AST and ALT in plasma after heat treatment at 56 °C for 0.5 and 1 h (3). Heparinized plasma samples (n=20) free from hemolysis, lipemia, and icterus were obtained from healthy volunteers, and were heated in 1.5-ML polypropylene screw-capped centrifuge tubes in a dry-heating block. To measure absorbance, we used a Roche Cobas-Bio centrifugal analyzer at 37 °C. For plasma AST and ALT measurements we used reagents formulated according to the recommendations of the Deutsche Gesellschaft für Klinische Chemie (DGKC) (9) (Boehringer Mannheim, product nos. 158178 and 16101).

In addition, we measured plasma ALT with a reagent formulated according to the International Federation of Clinical Chemistry (IFCC) recommendations (10), differences of ALT activity having been observed between use of the two reagent formulations (11). We used the IFCC reagent (Boehringer Mannheim, product no. 487325) either (a) excluding pyridoxal phosphate or (b) with addition of pyridoxal phosphate, 0.10 mmol/L, and no preincubation step.

For all methods, within-batch precision studies gave CV <1% for assays of a bovine control serum (n=25). Using the DGKC reagent, we obtained a mean value for plasma AST of 17.3 (SD 6.8) U/L (range, 12–29 U/L). After heat treatment at 56 °C for 0.5 and 1 h, the mean value changed to 19.0 (SD 5.6) and 18.6 (SD 5.3) U/L, respectively (not statistically significant: P >0.05).

However, ALT activity in plasma was markedly reduced (P<0.01) after heat treatment at 56 °C for 0.5 and 1 h, as assayed with either reagent (Table 1). Without preincubation, adding pyridoxal phosphate to the IFCC reagent did not restore the apparent plasma ALT activity to preheating values. Further studies will be required to demonstrate whether preincubation with pyridoxal phosphate reactivates plasma ALT after heat treatment, because the preincubation procedure is known to affect ALT measurements (12).

In conclusion, the effects of heat treatment were much greater than other preanalytical variables described for plasma ALT measurements (13), and alternative procedures should be used for handling "high risk" samples.

Table 1. Effect of Heat Treatment at 56 °C on Plasma ALT (U/L)

<table>
<thead>
<tr>
<th></th>
<th>No treatment</th>
<th>0.5 h</th>
<th>1 h</th>
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<tbody>
<tr>
<td><strong>DGKC reagent</strong></td>
<td></td>
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</tr>
<tr>
<td>Mean (SD)</td>
<td>13.4 (4.9)</td>
<td>5.0 (2.8)</td>
<td>5.0 (2.9)</td>
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<tr>
<td>Range</td>
<td>5–24</td>
<td>1–11</td>
<td>1–13</td>
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<tr>
<td><strong>IFCC reagent without pyridoxal phosphate</strong></td>
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<td></td>
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<tr>
<td>Mean (SD)</td>
<td>16.5 (6.4)</td>
<td>7.3 (3.1)</td>
<td>5.8 (3.0)</td>
</tr>
<tr>
<td>Range</td>
<td>8–32</td>
<td>4–16</td>
<td>3–16</td>
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<tr>
<td><strong>IFCC reagent with pyridoxal phosphate</strong></td>
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<td></td>
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<tr>
<td>Mean (SD)</td>
<td>17.8 (6.8)</td>
<td>6.3 (2.8)</td>
<td>4.7 (2.1)</td>
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<tr>
<td>Range</td>
<td>8–31</td>
<td>3–12</td>
<td>2–10</td>
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References