Evidence-Based Laboratory Medicine: How Well Do Laboratories Follow Recommendations and Guidelines? The Cardiac Marker Guideline Uptake in Europe (CARMAGUE) Study

To the Editor:

The original Cardiac Marker Guideline Uptake in Europe (CARMAGUE) study (1) surveyed laboratory practice against the then current clinical practice recommendations (2). The survey was repeated after the publication of the universal definition to see if newer recommendations were being followed (3, 4). An updated version of the questionnaire was implemented as a Web-based form linked to a database and was tested and validated. Data extraction to a spreadsheet allowed direct tabulation of the numbers of responses and combinations of responses for each question. A link to this form was sent via local representatives to a representative sample of laboratories in each country surveyed. The survey is available on the Web site http://www.carmague.fi/2/. Responses were obtained from 303 laboratories in 28 countries. The responders were from a full range of laboratories: 34% university hospital laboratories, 36% district hospitals, 25% central hospitals, and 5% primary care facilities. Ninety-five percent of the laboratories used troponin as the preferred marker for routine diagnosis of suspected acute coronary syndromes. Fifty percent of the laboratories use troponin T, and 45% used troponin I. Thirty-one percent of the laboratories used troponin as the sole marker, but 69% combined troponin measurement with another marker and offered other marker tests in suspected cases of acute coronary syndrome (Table 1). The majority of laboratories used either the 10% CV (41.1%) or the 99th percentile (37.9%) as the decision limit, comparable to the percentages in the previous survey. The upper reference limit came from the manufacturers’ data sheets (61.6%) or from the published literature (29.6%). The decision limit for myocardial infarction (MI) came from the manufacturer’s data sheet in 51.9% of the laboratories surveyed. Only 25% of the laboratories measured their turnaround time as the time from sample receipt to when validated results become available. Forty-five percent of the laboratories measured turnaround time as the time from sample receipt to when validated results become available. Only 32% of the laboratories used heparinized plasma. Point-of-care testing was performed without quality control and laboratory supervision in 32 of 77 laboratories. Point-of-care testing was not calibrated to the routine laboratory method in 67% of these laboratories. Only 43% of laboratories had a defined protocol or recommendations for troponin measurement, less than the 46% seen in 2006. Internal quality assurance for troponin measurement was not used in 3.3% of the laboratories. External quality assurance for troponin measurement was not undertaken by 21 (6.8%) of 307 laboratories, less than that (8.9%) seen in 2006, but not significantly different.

The second CARMAGUE survey produced results across a wider range of European countries. Although it is not a comprehensive study, the second survey provides an indication of current practice. The most concerning aspect was how little laboratory practice has changed despite clear guidelines and an increasing evidence base. Laboratories continue to offer myoglobin, creatine kinase, and the creatine MB isoenzyme for the diagnosis of MI, despite the documented inferiority of these tests to cardiac troponin measurement and despite the guideline recommendations. In addition, laboratories continue to offer creatine kinase MB activity, a test known to be methodologically inadequate, as well as aspartate transaminase and lactate dehydrogenase. Laboratories are using manufacturers’ data for the reference interval for decision limits. The wide range of choice of decision limits may in part represent laboratory conservatism, physician resistance, or a feeling that assay performance is inadequate for using a 99th percentile value. There is a need for independent validation of both assay performance and 99th percentile values to provide decision limits for MI independent of manufacturers’ claims, to appraise analytical performance, and to reference populations.

Table 1. Percentages of laboratories offering biomarkers in addition to troponin in suspected cases of acute coronary syndrome.

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Percentage of laboratories</th>
</tr>
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<tbody>
<tr>
<td>Myoglobin</td>
<td>11.0%</td>
</tr>
<tr>
<td>Creatine kinase</td>
<td>59.0%</td>
</tr>
<tr>
<td>Creatine kinase isoenzyme activity</td>
<td>8.3%</td>
</tr>
<tr>
<td>Aspartate transaminase</td>
<td>34.0%</td>
</tr>
<tr>
<td>Lactate dehydrogenase</td>
<td>30.0%</td>
</tr>
<tr>
<td>Lactate dehydrogenase isoenzyme 1</td>
<td>1.0%</td>
</tr>
<tr>
<td>Hydroxybutyrate dehydrogenase</td>
<td>2.4%</td>
</tr>
<tr>
<td>Lactate dehydrogenase isoenzymes</td>
<td>0.5%</td>
</tr>
</tbody>
</table>
critically. These studies should be performed in real-world environments to reflect the fact that the equipment in use measures a range of different analytes on a 24-h basis.

Quality-assurance programs are still not used by 100% of the laboratory community. Worryingly, there appears to be a large disconnect between the laboratory service and the clinicians who use the laboratory. This issue is manifested as a lack of proper measurement of turnaround time (by the laboratory) and as point-of-care testing occurring without laboratory involvement (by the clinician). These 2 factors may not be unrelated. Of most concern is the lack of agreed protocols between the laboratory and the clinician, although all previous (5) and current (3, 4) recommendations suggest a sample-timing schedule. Laboratory scientists need to be actively collaborating with clinicians to define protocols (and vice versa). The role of biomarkers in diagnosis will become substantially more confusing with the advent of high-sensitivity troponin methods and novel analytes.

There is no longer a debate about which test should be used for the diagnosis of MI. The question is why do laboratories persist in non-evidence-based behavior? And why are they not talking with their clinicians?

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