Letter to the Editor

Falsely elevated troponin I attributed to collection tubes using the Vitros ECiQ system

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Cardio-specific troponins (i.e., cTnI and cTnT) have become the mainstay for diagnosing and monitoring myocardial damage (1, 2). However, false-positive results for cTnI have been reported, primarily caused by interferents, such as heterophilic antibodies, rheumatoid factor, macrocomplexes, hemolysis and fibrin (3–5). Recently, falsely elevated cTnI attributed to inadequate centrifugation have been reported (6). We have observed another potential source of false positive results attributed to collection tubes.

Our study was performed in the Laboratory Medicine Center, Affiliated Hospital of Nantong University, and the ethical approval was obtained from the Research Ethical Committee, College of Medicine, Nantong University. Our objective was to assess whether serum/plasma samples were adequate for the assay of cTnI using the Vitros ECiQ Immunodiagnostic system (Ortho Clinical Diagnostics, Inc., USA). Blood samples were obtained from 86 apparently healthy volunteers and collected in separator gel clot activator tubes (cat no. 230811, lots L090315, KeHua), the blood collection tubes were inverted eight times to ensure thorough mixing. All samples were centrifuged at 2000 g for 10 min and analyzed using the Vitros ECiQ system with the manufacturer’s reagents. The cTnI concentration ranges were 0.000–2.257 µg/L (separator gel clot activator tube), 0.000–0.031 µg/L (lithium heparin tube) and 0.000–0.030 µg/L (lithium heparin with gel separator tube), respectively. The reference range for cTnI in our laboratory is 0.000–0.042 µg/L (serum/plasma). In healthy volunteers, results of 0.042 µg/L may be regarded as abnormal. As shown in Table 1, we observed six samples displaying abnormally increased which were collected in separator gel clot activator tubes. Following recentrifugation (2000 g for 10 min) to exclude small cloths, bubbles or fibrin, we retested these six samples and obtained the same abnormal results. The six serum/plasma samples that yielded abnormal cTnI levels were retested using the ACCESS immunoassay analyzer (Beckman, Brea, CA, USA), and nearly identical results were obtained on specimens collected in separator gel clot activator tubes and in the other two types of primary tubes (lithium heparin tube and lithium heparin with gel separator tube).

Although cTnI is recognized as a reliable marker of myocardial damage, both the pronounced heterogeneity and the minimal amount released into the circulation represent significant challenges for measurement (3). Apple and Murakami demonstrated that there were no significant differences between cut-off thresholds for serum and plasma (7). However, we found that the discordant results were confined to individual samples. We proved that repeat centrifugation of collection tubes containing thrombin as a clot activator cannot eliminate false-positive cTnI results. A possible explanation for these obvious discrepancies might be the use of different blood collection tubes. Bowen et al. showed that collection tubes might have small analytical effects on certain assays (8). The mechanism of interference of tube components with the Vitros ECiQ system cTnI assay is not clear. Further studies are needed to clarify the exact mechanism by which serum causes such interactions and why they are confined to individual samples. Because most commercial assays differ in methodology, epitopes, form (complexed or not), and tropinin subunit (5), manufacturers should be aware of this potential problem and focus on eliminating the potential interferences.

Our results indicate that the separator gel clot activator tubes can cause variable increased cTnI results on the Vitros ECiQ system, from mild to very severe. In order to prevent misleading results and potential misdiagnosis due to the sample matrix or additional analytical interferences (9, 10), lithium heparin and lithium heparin with gel separator are recommended.
Table 1  cTnI results for serum samples compared with matched plasma samples.

<table>
<thead>
<tr>
<th>Sample no.</th>
<th>Serum cTnI, μg/L</th>
<th>Plasma cTnI, μg/L</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Separator gel clot activator Vitros/ACCESS</td>
<td>Lithium heparin Vitros/ACCESS</td>
</tr>
<tr>
<td>7</td>
<td>0.371/0.005</td>
<td>0.007/0.004</td>
</tr>
<tr>
<td>25</td>
<td>1.207/0.006</td>
<td>0.003/0.005</td>
</tr>
<tr>
<td>33</td>
<td>0.066/0.000</td>
<td>0.001/0.002</td>
</tr>
<tr>
<td>59</td>
<td>0.733/0.030</td>
<td>0.031/0.026</td>
</tr>
<tr>
<td>72</td>
<td>2.257/0.001</td>
<td>0.001/0.000</td>
</tr>
<tr>
<td>80</td>
<td>0.245/0.015</td>
<td>0.010/0.013</td>
</tr>
</tbody>
</table>

Vitros, Vitros ECiQ system; ACCESS, ACCESS immunoassay analyzer.

as specimen collection tubes when measuring cTnI with the Vitros ECiQ system.

Conflict of interest statement

In our study, we did not accept any funding or support from any organization and none of our team has been employed by an organization. We do not have any other conflicting interests.

References