


We evaluated assay imprecision using lyophilized control sera with three different concentrations of cTnI (0.57, 5, and 15 μg/L) that were analyzed 10 times in one analytical run for the determination of within-run imprecision and 24 times on 24 different days for the determination of between-run imprecision. Our results confirmed the manufacturer’s claims that within- and between-run imprecisions (CVs) were 2.8–3.9% and 2.9–4.1%, respectively. The analytical sensitivity was 0.04 μg/L, defined as the concentration corresponding to a signal that was 2 SD above the signal detected for the 0 μg/L cTnI calibrator (n = 20).

To compare plasma and serum cTnI, 100 paired randomized blood samples were obtained from patients admitted to the Division of Cardiology (n = 64) or to the Emergency Room (n = 36) of our hospital for acute myocardial infarction (AMI) or suspected AMI. The paired samples were drawn in parallel into tubes without anticoagulant (cat. no. 367615; Becton Dickinson) and into tubes with lithium heparin (−65 IU of heparin/mL plasma considering an hematocrit of 50%; cat. no. 367684; Becton Dickinson). According to the consensus document of the European and American Cardiologists (3), blood was obtained from our patients on hospital admission, at 6 to 9 h and again at 12 to 24 h if the earlier samples were negative and the clinical index of suspicion was high. We used a cTnI cutoff for AMI at 0.6 μg/L as indicated by the manufacturer. The Dimension RxL assay, like all the other troponin assays (8), does not comply with the new consensus requirement (3) of a ≤10% CV at the 99th percentile (0.07 μg/L) of a reference group. Within 10–15 min after venipuncture, both tubes were centrifuged at 3000g for 10 min, and the serum and heparin-plasma samples were frozen at −20°C until cTnI determination. Before assay, the specimens were thawed, gently mixed by inverting the tubes five to eight times, and recentlyrifed at 3000g for 10 min.

The cTnI concentration ranges for serum and plasma were 0.24–48.5 μg/L and 0.28–48.2 μg/L, respectively, well above the detection limit of the assay (0.04 μg/L as indicated above). No significant difference was found between serum and plasma cTnI concentrations (101.7 ± 2.4%; t-test for paired data, P = 0.90), with an excellent correlation (r = 0.993; P < 0.001; cTnIplasma = 1.00 × cTnIs serum − 0.02). Whereas the ratio between plasma and serum cTnI concentrations was rather wide (range, 53.8–125%), no significant correlation was found between this ratio and the mean plasma-serum cTnI concentration (P = 0.63). Interestingly, only one sample showed a high underrate in plasma cTnI concentration compared with serum (~46%). This sample gave the same result when repeatedly analyzed (three times) to exclude sporadic error attributable to a small clot, bubble, or misidentification. For the other 99 samples, the plasma-serum cTnI ratio was between 0.76 and 1.25 (Fig. 1).

To clarify this problem, we also carried out heparin titration experiments by adding increasing volumes of heparin (5000 IU/mL) to serum aliquots of 10 samples (with cTnI between 0.24 and 20.2 μg/L) to final concen-
concentrations of 32, 62.5, and 238 IU/mL. These concentrations were chosen for the following reasons: (a) 32 IU/mL closely corresponded to the concentration in tubes used by Stiegler et al. (7); (b) 62.5 IU/mL corresponded approximately to the final plasma heparin concentration with our tubes; and (c) 238 IU/mL allowed us to verify the effects on cTnI assay of a high heparin concentration. Samples were gently mixed on a vortex-type mixer, and cTnI was determined after 30 min (6), taking into account the same dilution attributable to the added heparin solution. These 10 samples showed no significant difference between serum and plasma cTnI (t-test for paired data, P = 0.33). However, a difference whose statistical significance progressively increased with increasing heparin concentration was found between serum and heparin-serum cTnI concentrations (Table 1). The latter results were reflected by a trend toward an inverse correlation (r = -0.865; P = 0.12) between the heparin concentration and cTnI. Thus, heparin seemed to influence the cTnI assay, although the maximum decrease in cTnI detected at the highest heparin concentration tested (approximately fourfold the concentration in our tubes) was 16%. In contrast to the findings of Gerhardt et al. (6) for the cTnT assay, we did not find any difference between early and late sampling during the evolution of AMI with regard to the heparin interference on the Dade Dimension cTnI assay. Interestingly, the sample that revealed the largest difference between serum (20.2 µg/L) and plasma (10.9 µg/L) cTnI (a 46.2% decrease) showed only a 5% decrease in cTnI when heparin was added at the highest concentration. In this case, the difference between serum and plasma may be attributable to a matrix effect (9,10).

In conclusion, both serum and heparin plasma seem to be suitable samples for cTnI assay on the automated chemical analyzer Dimension RXL, but the variation between our paired plasma-serum samples was greater than the 4% between-series CV we found in our evaluation of assay imprecision. Wide scatter may be attributable to matrix effect and to heparin interferences. These effects may lead to a failure to detect small AMI, although this was not the case in our 100 paired samples.

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Table 1. Heparin titration experiments.

<table>
<thead>
<tr>
<th>Amount of heparin added, IU/mL</th>
<th>Mean cTnI, µg/L</th>
<th>Hep-S/S%</th>
<th>P-value, t-test for paired data (vs serum)</th>
</tr>
</thead>
<tbody>
<tr>
<td>32</td>
<td>7.13</td>
<td>95 ± 2.5</td>
<td>89–100</td>
</tr>
<tr>
<td>62.5</td>
<td>7.11</td>
<td>94.4 ± 3.7</td>
<td>91–103</td>
</tr>
<tr>
<td>238</td>
<td>6.81</td>
<td>89.5 ± 3</td>
<td>83–97</td>
</tr>
</tbody>
</table>

*The mean cTnI concentration of serum without heparin was 7.54 µg/L.

**Hep-S/S%, percentualized ratio between cTnI concentrations found in heparin serum and those found in serum alone.

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References


