Table 1. Patients with Increased cTnI.*

<table>
<thead>
<tr>
<th>No.</th>
<th>Age, years</th>
<th>Sex</th>
<th>cTnI μ/L</th>
<th>cTnT μ/L</th>
<th>LD1/LD2</th>
<th>CK, μ/L</th>
<th>CK-MB, μg/L</th>
<th>Cr, mg/dL</th>
<th>Diagnosis*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>67</td>
<td>M</td>
<td>1.2</td>
<td>0.79</td>
<td>0.92</td>
<td>156</td>
<td>3</td>
<td>132</td>
<td>DM; HTN</td>
</tr>
<tr>
<td>2</td>
<td>35</td>
<td>F</td>
<td>1.3</td>
<td>0.23</td>
<td>0.67</td>
<td>116</td>
<td>1</td>
<td>27</td>
<td>DM; HTN</td>
</tr>
<tr>
<td>3</td>
<td>62</td>
<td>M</td>
<td>1.4</td>
<td>0.15</td>
<td>0.67</td>
<td>100</td>
<td>1</td>
<td>36</td>
<td>DM; hepatitis C</td>
</tr>
<tr>
<td>4</td>
<td>37</td>
<td>M</td>
<td>1.5</td>
<td>0.18</td>
<td>0.51</td>
<td>687</td>
<td>8</td>
<td>39</td>
<td>Hepatic failure</td>
</tr>
<tr>
<td>5</td>
<td>77</td>
<td>M</td>
<td>3.6</td>
<td>4.25</td>
<td>0.81</td>
<td>60</td>
<td>3</td>
<td>62</td>
<td>Non-Q-wave MI; CHF</td>
</tr>
<tr>
<td>6</td>
<td>56</td>
<td>M</td>
<td>2.8</td>
<td>0.25</td>
<td>0.59</td>
<td>480</td>
<td>11</td>
<td>38</td>
<td>Non-Q-wave MI; hepatic injury</td>
</tr>
<tr>
<td>7</td>
<td>87</td>
<td>M</td>
<td>1.6</td>
<td>1.30</td>
<td>0.59</td>
<td>354</td>
<td>2</td>
<td>34</td>
<td>HTN; urosepsis; gout</td>
</tr>
</tbody>
</table>

* Reference values: cTnI <0.35 μg/L; cTnT <0.1 μg/L; lactate dehydrogenase isoenzyme 1 and 2 ratio (LD1/LD2) 0.6; creatine kinase (CK) 50–150 U/L (male), 40–120 U/L (female); CK-MB isoenzyme 0–4 μg/L; serum creatinine (Cr) <14 mg/dL.

^ DM, diabetes mellitus; HTN, hypertension; MI, myocardial infarction; CHF, chronic heart failure.

know, but my colleagues and I intend to find the answer.

References


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Greater Frequency of Increased Cardiac Troponin T than Increased Cardiac Troponin I in Patients with Chronic Renal Failure

To the Editor:

In a previous report we documented that cardiac troponin T (cTnT) was increased in 52 of 82 (63.4%) patients with end-stage renal disease (ESRD) without clear evidence of myocardial injury as defined by usual criteria, i.e., history of chest pain, compatible electrocardiographic abnormalities, and (or) concurrent increased concentrations of CK-MB or "flipped" lactate dehydrogenase isoenzymes LD1/LD2 ratio at the time of testing [1]. We were unable in that study to determine whether the increased cTnT in renal failure was due to assay cross-reactivity from skeletal muscle cTnT, reexpression of cTnT during muscle regeneration, or subclinical myocardial injury. With the availability of the more organ-specific cardiac troponin I (cTnI) assay [2], we have been able to measure cTnI concentrations in 79 of 82 patients, using the original specimens subsequently frozen and preserved from the previous study. We used the Stratus™ system (Dade International, Miami, FL) for cTnI, following the instructions of the manufacturer. The reference range in this study for cTnI is ≤0.35 μg/L; for cTnT, <0.1 μg/L. The discriminator value for cTnI is >1.5 μg/L; for cTnT, >0.2 μg/L. Interassay precision (CV) for cTnI in our laboratory is ≤10%.

Of the 79 patients with ESRD, 7 (8.9%) had measurable cTnI, with values ranging from 1.2 to 3.6 μg/L. All the other patients had undetectable cTnI, i.e., below the limit of detection of 0.35 μg/L. Salient characteristics of this subset are shown in Table 1. All of these patients had concordant increases in cTnT concentrations. In three of these ESRD patients, the cause of chronic renal failure was diabetic nephropathy. It is interesting that three additional patients also had concurrent hepatitis (drug-induced in two, hepatitis C in one) with marked increases of transaminase concentrations. Reported clinical trial data on 128 patients who had been ruled-in for acute myocardial infarction indicated that the discrimination value for cTnI was 1.5 μg/L (unpublished data, Dade International). If we use this cutoff value, none of the patients with diabetic nephropathy had diagnostic cTnI values consistent with an occult or silent infarction, although minor myocardial injury appears likely.

To determine whether the other four patients who had increases in both cTnT and cTnI experienced subclinical myocardial injury, we scrutinized the clinical findings and laboratory data. The two patients with the highest values for cTnI (3.6 and 2.8 μg/L) did have subsequent clinically confirmed non-Q-wave infarction, which was recognized during the latter part of their hospitalization. We attribute the earlier result detected in these two patients as representing subclinical infarction with later extension resulting in clinical recognition [3]. In
the remaining two patients with increased cTnI, the reasons for their increases could not be determined from clinical review.

Our data therefore suggest that cTnI is more discriminating than cTnT for myocardial injury. cTnI was increased in only 8.9% of our patients, but cTnT was increased in 63.4%. It is not surprising that this nonspecific increase of cTnT was detected in such a proportion of uremic patients because these patients can have myopathy with muscle regeneration [4]. However, this can be clearly settled only by an outcomes study. Our findings of fewer increased concentrations of cTnI than of cTnT in renal failure is in agreement with that of Bhayana et al. [5] in a smaller group (n = 8). In a study of cTnI in patients with ESRD, Katus et al. [6] suggested that cTnI is more sensitive than cTnT but did not present data to support this claim. A persistent increase of cTnT lasting over 6 months, reported by Hafner et al. [7], argues against significant myocardial injury because the serial rise and fall of cardiac markers such as CK-MB and cTnI has been documented in acute myocardial injury in the clinical setting [8, 9]. With the higher cutoff value of 0.2 μg/L for the cTnT assay as proposed by Katus et al. [7], 15 of 51 (29%) of their patients on chronic maintenance hemodialysis had increased cTnT concentrations. In our patient population, selecting 0.2 μg/L as a discriminating value still left a substantial proportion (38 of 82, 46.3%) of patients with chronic renal failure who had increased cTnT. Conversely, none of the patients with normal values for both cTnT and cTnI had clinical evidence of myocardial injury in the time frame associated with our sampling.

Both cTnT and cTnI are useful in ruling out myocardial injury, but cTnI has not been shown to be expressed in skeletal muscle, either in embryonic development or in repair states. Evidence continues to accumulate supporting the true cardiospecificity of the cTnI marker, and we consider it the preferred marker for myocardial injury in the setting of chronic renal disease.

References

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Precision and Accuracy of the Accu-Chek® Advantage® Blood Glucose Monitoring System at High Altitude

To the Editor:

Self-monitoring of blood glucose is an important tool for assessing glycemic control in people with diabetes mellitus. Recently, the Diabetes Control and Complications Trial (DCCT) [1], an unprecedented work by multiple institutions, showed that the progression of all major complications associated with this disease could be suppressed if patients were held in tighter glycemic control. One component of the DCCT was to accurately and precisely predict a patient's blood glucose concentration from monitoring devices used to assay finger-puncture whole blood. Monitoring device data allowed participants to readily modify their therapy so as to more closely approximate euglycemia.

Although much has been published on self-monitoring of blood glucose and the various instruments and procedures used for measurement, relatively few studies have provided information about the performance of these systems in high altitude or simulated high-altitude environments [2–6]. Some of these reports have indicated that environmental effects, including altitude, could change the apparent performance of the systems. A monitoring system response as low as ~34% from the reference method response has been reported [3]. Because of these reports, many healthcare professionals and patients in locations of high altitude have inquired about the performance of these systems in their environment. Further, the US Food and Drug Administration suggests that new devices be tested in real or simulated high-altitude environments as part of the application package that device manufacturers must use when applying for a 510(k) premarket notification of a new or enhanced system for monitoring blood glucose. Therefore, it is important to understand how these systems work at high elevations.

Here, we report the results of an investigation into the environmental altitude effects of the Accu-Chek® Advantage® blood glucose monitoring system (Boehringer Mannheim Corp., Indianapolis, IN). Our investigation included accuracy data collected for assays performed at 2668 m with capillary blood from 143 diabetic donors, and precision data collected for assays performed at 213, 2668, and 3665 m with blood, manufacturer's control solutions, and Sugar-Chek® whole-blood glucose product (Streck Labs., Omaha, NE). This evaluation typifies how the system will be used by patients and assessed by clinicians in high-altitude environments.

We had the opportunity to test a large patient population (n = 143) of children and young adults at an American Diabetes Association-sponsored camp in Colorado. The camp was located at an elevation of 2668 m above sea level. All participants and their parents or legal guardians signed consent forms approved by the Institutional Review Board of The Children's Hospital, Denver, CO. The accuracy of the system was assessed by comparison with a Somogyi-like [7–9] hexokinase-based assay of deproteinized whole blood. The whole blood to be assayed with the comparison method was