To the Editor:

In their report earlier this year, McLaurin et al. reproduced the finding of increased cardiac troponin T (cTnT) concentrations in dialysis patients [1]. Using the first-generation cTnT assay, they observed an increased serum concentration of cTnT in 17 of 24 patients. The prevalence of an increased cTnT concentration in the blood of dialysis patients was somewhat lower when the second-generation cTnT assay was used, but higher than the prevalence of an increased concentration of cardiac troponin I (cTnI). Because none of the patients had clinically apparent cardiac ischemia (although most had hypertension or other cardiac risk factors, and 2 had echocardiographically documented hypertensive heart disease), the increased cTnT concentrations were interpreted as “false positive.” The authors suggested this might be related to the extracardiac expression of cTnT, which they believed to have demonstrated in skeletal muscle biopsies from 4 of 5 dialysis patients.

However, there was no apparent correlation between the immunoblot detection of a protein band comigrating with cTnT and the serum concentration of cTnT. Despite detection of a protein with similar migration properties as cTnT in the immunoblot, the blood samples of patients shown in lanes 4 and 5 (of their Fig. 2) did not reveal an increased serum troponin T concentration in either the first- or second-generation cTnT assay. The patients whose samples were shown in lanes 7 and 9 had only a minor increase of cTnT concentration in blood by the first-generation assay, but not by the second-generation assay. McLaurin et al. used an anti-cTnT antibody with “a minor cross-reactivity with some human skeletal muscle troponin T isoforms.” As shown in the immunoblot, the reactivity of this antibody varied greatly between the different muscle specimens of the different patients. The Western blot analysis revealed that this antibody reacts not only with cTnT but also with many different myofibrillar proteins.

In our opinion, therefore, it is premature to attribute the increased cTnT concentration in the serum of a substantial subgroup of dialysis patients to the expression of cTnT in skeletal muscle on the basis of these immunoblot data. Indeed, the data of McLaurin et al. do not exclude the possibility that subclinical cardiac injury combined with the high sensitivity of the cTnT assay may account for the increased steady-state serum concentration of cTnT, especially given the high prevalence of cardiac risk factors in addition to end-stage renal disease in this relatively young dialysis population.

Reference


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Two authors of the report referred to reply:

To the Editor:

Haller and Katus make several points we wish to comment on. First, without definitive clinical, electrocardiogram, or echocardiogram evidence of myocardial injury, then by definition an increased serum cTnT, a specific marker of myocardial injury, is deemed a false-positive result. Further, the finding of an increased serum cTnT was also shown not to have prognostic value in the 6-month follow-up of our renal disease patients [1]; however, the population studied was small in number.

Second, the Western blot analysis demonstrated cTnT expression in the skeletal muscle biopsies of renal disease patients. We agree that the findings are qualitative, in that the antibodies used did demonstrate minor cross-reactivity with other myofibrillar proteins that migrated to different molecular-mass locations on the gels.
However, our findings are in agreement with our previously published studies demonstrating cTnT expression in skeletal muscle from muscular dystrophy and polymyositis patients [2]. Our discussion [1] cites these findings as “a possible source of abnormally elevated cTnT” in renal disease patients. What needs to be determined is whether the cTnT form expressed in these adults’ diseased muscles is the adult cardiac, fetal cardiac, or regenerative cardiac isoform [3]. To help clarify these concerns, we would need access to the monoclonal anti-cTnT antibodies used in the second-generation Boehringer Mannheim cTnT immunoassay so we could perform similar Western blot experiments on our stored blots.

Finally, we do not disagree that the possibility does exist that subclinical myocardial injury may account for the increased serum cTnT concentrations. In our renal disease population with several cardiac risk factors, we plan to continue to follow these patients over the next several years. Nonetheless, our data continue to demonstrate significant differences in increases of serum cTnT and cTnI in patients with renal failure. However, cTnI demonstrates substantially fewer increases that are unexplained in terms of the clinical information gathered.

References


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Effect of Plasma Replacement Therapy on Determinations of Urine Protein Concentration

To the Editor:

Total protein concentration in urine is currently analyzed in our laboratory by a colorimetric method—Py- rogallol Red (PR)–molybdate com- plex [1]—adapted to a Cobas Integra analyzer (Cobas Integra Total Protein Urine/CSF 07.5723.3; Roche). We quantify specific urinary proteins by the following immunochemical methods: turbidimetry for urinary al- bumin (Cobas Integra) and nephe- lometry for IgG, α₁-microglobulin, and light chains of immunoglobulins (BNAII; Behring).

We recently observed discrepancies between results obtained for some urine samples, in that the total protein concentration was increased and did not agree with the sum of the concentrations of individual urine proteins such as albumin, IgG, α₁-microglobulin, and light chains of immunoglobulins. These urines also tested negative for myoglobin and hemoglobin. When we then determined the urine total protein concentration of the discrepant samples with the Coomassie Brilliant Blue (CBB) method [2] adapted to a Cobas Fara II (Roche) analyzer, this total protein concentration (CBB) did agree with the sum of the specific proteins, for a given urine. We thus thought it likely a substance or drug was present that positively interfered with determination of total protein by the PR method but had no effect on the CBB method.

A careful review of the clinical an- amneses revealed that the discrepant urines came from patients receiving replacement plasma therapy for hemodynamic instability. Interestingly, all of these patients were adminis- tered a plasma substitute commonly used in Spain: Hemoce® (Behring- werke). Hemoce contains polypeptide polymers (average molecular mass 35 kDa) obtained from gelatin. Supplied as a 35 g/L colloidal solution, it is mostly (75%) excreted through the kidneys via glomerular filtration.

Subsequently, several dilutions of the Hemoce preparation were ana- lysed by various methods: the biuret method in a Hitachi 747 analyzer, the PR method in a Cobas Integra ana- lyzer, a modified biuret method [3] in a Vitros 250 analyzer, and the CBB method in a Cobas Fara analyzer.

Fig. 1. Protein concentrations of Hemoce dilutions measured by different methods.

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