care unit with a 44% prevalence of IMI cases vs the corresponding reference group and in a worst-case situation with 30-40% severe skeletal muscle injuries added to the reference group. As mentioned in our discussion (2), we might have added to our target group any higher number of AMI cases, as confirmed by the WHO criteria, and might thus have attained any—but clinically irrelevant—specificity. Moreover, if we had evaluated clinical specificity against a reference group of exclusively healthy blood donors, we would have obtained an apparent increased specificity of 99-100%, even while lowering the discriminator to 0.10 μg/L. However, this high specificity would not be clinically relevant because the reference group in a coronary care unit (CCU) is patients suspected of having AMI and not healthy blood donors.

An analytically still more sensitive and cardiосpecific S-TNT assay is currently being developed. This may be expected to permit use of a lower discriminator, leading to increased clinical sensitivity but retaining present or better clinical specificity. In our opinion, we have yet to see the best performance of S-TNT as a marker of ischemic myocardial injury.

References

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The authors of the cited report respond:

To the Editor:

The simple explanation for the different cutoff values used in the recent reports (1, 2) is that they relied on (a) different versions of the troponin T (TnT) assay with different analytical sensitivities and (b) different operational definitions of myocardial ischemia. In comparing the results of the new TnT assay with the generally accepted standard classification of coronary artery disease (WHO criteria for acute myocardial infarction (AMI) and myocardial ischemia), we followed the standard procedure in evaluating a new analyte. In contrast to what Gerhardt et al. claim above, we also tested various discriminators in the differentiation of non-AMI and AMI (subsequently verified according to WHO criteria) in emergency room patients presenting with chest pain. In these patients 0.5 μg/L proved to be the best discriminator as well (see receiver-operating characteristics curve published in reference 1). Gerhardt et al. (2), by contrast, evaluated the TnT assay against a new classification of myocardial ischemia.

References

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Chelation with Ferric Ions May Prevent Extraction of 2-Hydroxdesipramine from Whole Blood

To the Editor:

Recent clinical studies suggest that the hydroxy metabolites of tricyclic antidepressants (TCAs) may be responsible, in part, for the therapeutic and toxicological effects reported after administration of these agents (1, 2). Chromatographic assays have been developed to accurately quantify the concentration of TCAs and their hydroxy metabolites in plasma, urine, and cerebrospinal fluid (3). In attempting to develop an HPLC assay for desipramine and 2-hydroxidesipramine (DMI-OH) in whole blood, we observed poor recoveries of DMI-OH. This report summarizes our efforts to understand the reasons for the poor recoveries, and our unsuccessful attempts to rectify the problem.

Extraction of DMI-OH from 1-mL blood samples is initiated by adding 1 mL of water to hemolyze the erythrocytes. The sample is then alkalized with 1.5 mol/L sodium hydroxide and extracted with 5 mL of a mixture of ethyl acetate/hexane/isooamyl alcohol (50/49/1 by vol). The organic supernate is subsequently back-extracted with 0.1 mol/L hydrochloric acid. For chromatographic analysis we used a 0.05 mol/L potassium dihydrogen phosphate/acetonitrile (79/21 by vol) mobile phase at a flow rate of 2 mL/min with a C₁₈ column (Waters, Milford, MA) and monitored the eluent at 240 nm. The internal standard used was 10-hydroxy-nortriptyline (NT-OH). The recoveries for DMI-OH and NT-OH after whole-blood extraction were 4% and 87%, respectively (Table 1). We found these results surprising because both DMI-OH and NT-OH are structurally similar and would therefore be expected to have comparable recoveries.

References