plasma samples of $-11.4\%$...", but Fig. 1B shows the opposite, with a mean bias of $+14.5\%$ and a scatter of $+10$ to $+100\%$ higher values in seven samples having a cTnI value of $-1.0 \mu g/L$, the clinically most important concentrations. Perhaps the authors inverted the factors (plasma – serum values in the text and serum – plasma values in the figure), but they did so without any reason, and this fact markedly clouds the data presentation. Finally, the same scale should be used for the $x$ axis in all of the graphs to permit a direct comparison of the results obtained with the two assay generations.

More importantly, the authors make improper use of the recommendations reported in the quoted letter by Dewitte et al. (3) and in the corresponding response by Altman and Bland (4). The reference to the method comparison issue is questionable, the anticoagulant problem being indeed an interference (and preanalytical) issue (5). Nevertheless, the original suggestion by the previous authors was to take logarithms of the original data or, alternatively, the percentage bias, both of which give similar information (4). Accordingly, reporting the data as the percentage difference on the $y$ axis and serum cTnI concentrations on the $x$ axis is the correct and more transparent approach to evaluate possible anticoagulant effects on cTnI assays and the variability among samples (6).

Another limitation of the study is that at least two samples used in the second experiments had cTnI concentrations $<0.02 \mu g/L$, the detection limit of the assay (7). The use of samples having undetectable cTnI concentrations makes calculation of the sample difference impossible. This could have significantly biased the results obtained with the second-generation assay. Finally, Dorizzi et al. (2) do not provide any information on the time of sampling after hospital admission (or onset of chest pain) of the patients studied, the assay cutoff value(s), or the analytical imprecision at the cutoff value(s) (8).

Time-dependent losses of troponin immunoreactivity have clearly been shown in heparin plasma by previous authors (9).

In conclusion, the study by Dorizzi et al. (2) shows that the data obtained with the second-generation Dimension assay are significantly different from those obtained previously with the first-generation assay; the scatter was very different (although they do not indicate standard errors of estimates), and the statistical test (and the 95% confidence interval of the mean bias) evaluating the serum/plasma difference reached significance for the second-generation assay. Thus, the data presented by these authors do not support their claim that “heparinized plasma and serum samples appear interchangeable in cTnI measurement with the second-generation Dimension RxL”.

References

To the Editor:
S-100B protein is a 21-kDa dimeric protein from the S-100 calcium-binding protein family that contains at least one $\beta$ subunit. S-100B is expressed by cells of neuroectodermal origin, particularly cerebral glial cells (astrocytes), and in several tumor processes, including malignant melanocytic lesions (1). Although S-100B is localized primarily in the intracellular compartment, it is physiologically detectable in biological fluids (cerebrospinal fluid, serum, and urine). Measurement of S-100B has been proposed as a biological marker of brain damage, e.g., head injury, cerebral hypoxia, and stroke (2), and of malignant melanoma (3). Serum S-100B values in healthy individuals range from 0.02 to 0.15 $\mu g/L$, as determined by immunoluminometric analytical methods. Although studies are controversial, S-100B concentrations in biological fluids appear to be age- and sex-dependent (4–7). No information is available regarding potential differences according to the race or ethnicity of individuals.

Here we report the results of a study to determine the influence of race on serum S-100B concentrations. Blood samples were taken from 136 healthy individuals, divided into three groups according to race: black (B), Asian (A), and Caucasian (C). All individuals gave informed consent for participation in the study. The three groups did not differ significantly in sample size ($n = 46, 44$, and $46$ for groups B, A, and C, respectively), mean (SD) age $[45 (11), 49 (13), 46 (13)],$
and 49 (14 years; not significant), or M/F ratio (28/18, 25/19, and 24/22 for groups B, A, and C, respectively). Blood was collected in Vacutainer® Tubes and centrifuged within 2 h (1000g for 10 min); serum samples were then frozen at −20 °C until assayed (within 2 months). S-100B concentrations were determined with an immunoluminometric sandwich assay on a LIASON analyzer (DiaSorin Laboratories) with the manufacturer’s reagents. All determinations were performed in duplicate.

The results of these analyses are shown in Fig. 1. Mean (SD) values for serum S-100B were significantly higher in groups B and A compared with group C (0.14 (0.08), 0.11 (0.08), and 0.07 (0.03) μg/L for groups B, A, and C, respectively; P < 0.001). Median values also showed similar differences between the groups: 0.12, 0.09, and 0.06 μg/L for groups B, A, and C, respectively (P < 0.001 between B and C and between A and C). Serum S-100B concentrations did not differ significantly between groups B and A, although a trend to statistical significance was noted (P = 0.064). Finally, the number of healthy individuals having a serum S-100B concentration above the recognized pathologic cutoff value (0.15 μg/L) was 14 of 46 (30%), 9 of 44 (20%), and 1 of 46 (2%) for groups B, A, and C, respectively.

Our data indicate that healthy black and Asian individuals have higher serum S-100B concentrations than do Caucasians. We hypothesize that these differences in serum S-100B according to skin color may be related to increased expression of this protein by healthy melanocytes in blacks and, to a lesser extent, in Asians, compared with Caucasians. Melanocytes from black individuals have been shown to have a higher metabolic activity than those from Caucasians, including increased melamin synthesis (8). To our knowledge, there are no in vitro experimental data available regarding S-100B protein expression and release according to the origin of melanocytes (i.e., black, Asian, or Caucasian individuals); we believe that the S-100B protein subunit might be more highly expressed in black and oriental races and that this higher expression could explain the higher concentrations of circulating S-100B observed in healthy black and Asian individuals. In vitro experimental data are also lacking for determining the involvement of S-100B expression and release by healthy melanocytes in the physiologic serum concentrations of this protein, especially with respect to skin color. Our results clearly indicate that the racial origin of patients should be taken into account when interpreting serum S-100 concentrations as an indicator of brain damage or malignant melanoma.

References

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