Letters to the Editor

mended by the manufacturers of the Liaison calcitonin assay; however, the upper limit for healthy females is twice the manufacturer’s recommended value of 5.5 ng/L. Thirteen percent of healthy male volunteers and 54% of healthy female volunteers had basal calcitonin concentrations that exceeded the manufacturer’s recommended upper reference limit. When a basal calcitonin diagnostic limit of 10 ng/L was used to indicate the need for further assessment with the PGT (1), 48% of healthy males and 19% of healthy females had a basal calcitonin value greater than this limit. After pentagastrin stimulation, 1 individual had a peak stimulated calcitonin value >100 ng/L (basal, 16.6 ng/L; peak, 110 ng/L).

Our data show an upper reference limit for males that is almost twice that for females. This result is supported by postmortem studies demonstrating that men have twice the number of C cells than females (5). Therefore, the validity of applying a single diagnostic limit for basal and stimulated calcitonin for both males and females remains questionable.

The information gained from this study is insufficient to make any definite recommendation regarding changes to the currently used cutoff limits for stimulated calcitonin concentrations, and further studies are needed. This study offers strong evidence, however, to suggest that the current diagnostic limits of >10 ng/L for basal concentrations are too low when the Liaison assay is used. Extrapolating these cutoffs obtained with the Cisbio assay to the Liaison assay has the potential to lead to unnecessary thyroid biopsies. Thus, our data support calls for a revision of the diagnostic limits for basal serum calcitonin with the Liaison assay (4).

References


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Lack of Transferability of Results between Procalcitonin Assays

To the Editor:

In a recent issue of Clinical Chemistry, De Wolf et al. described an evaluation of the new Procalcitonin (PCT) assay from Roche, performed according to CLSI (Clinical and Laboratory Standards Institute) recommendations, compared with the widely accepted PCT assay on the Brahms Kryptor analyzer (Brahms) (1). We recently carried out an analogous study on a Cobas e411 (Roche Diagnostics) (2) and reached some different conclusions. We found no transferable results between the Elecsys Brahms PCT (Cobas) and PCT-TRACE (Kryptor) when we

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compared 152 samples from the same number of different patients. A regression analysis demonstrated the heteroscedasticity of the results as well as the lack of normality of the residuals. Passing-Bablock nonparametric analysis showed a proportional tendency toward lower PCT concentrations on the Cobas than the Kryptor analyzer. The regression equation was: PCT Cobas = −0.0024 + 0.8586 PCT Kryptor (intercept 95% CI, −0.0061 to 0.0051; slope 95% CI, 0.84–0.87). We created a folder empirical cumulative distribution plot (mountain plot) to compare both methods, following the CLSI-EP21A recommendation for situations in which differences do not follow a gaussian distribution. The mountain plot was not fully included among the specification lines, the graph was biased toward positive differences between methods, and an outlier was detected (2). Less than 95% of the differences were included within the tolerance limits (defined by the 2.5th and 97.5th percentiles, respectively), and on the basis of these results we concluded that there was not transferability between both methods. Because the same analytical handling conditions were followed in both studies, this point could not explain the discrepant results. A similar range of concentrations were compared in both studies, but a different percentage of low concentration samples were assayed (70% of the PCT values were ≤0.25 µg/L in the study by de Wolf et al. compared to 28% in our study), probably due to the fact that de Wolf et al. included only patients with lower respiratory tract infections, whereas we also included patients with sepsis who were hospitalized in the intensive care unit. In our study the tendency toward lower values on the Cobas analyzer was confirmed over the entire measuring range. With regard to concordance between the 2 assays, de Wolf et al. found 99% and 98% at cutoff values of 0.25 µg/L and 0.5 µg/L, respectively, whereas we found a slightly lower grade of concordance of 97% and 94% for the same cutoff values.

It is beyond the scope of this communication to state whether a reappraisal of the cutoff is necessary, because this was not a clinically based study. However, if the present lack of transferability is confirmed in the clinical management of the patients, it would be interesting to open up further discussion about the best cutoff points of the new Elecsys Brahms PCT method, not on the basis of calculated predictions but rather clinical findings.

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In Reply

Prieto and Alvarez point out a lack of transferability between the PCT assay for use on a routine immunochemistry analyzer family and the PCT assay on the Brahms Kryptor analyzer.

Compared to our study, the study by these authors revealed a more pronounced tendency toward lower concentrations on the Cobas analyzer. This was especially true when PCT values covering the entire concentration range were included (0 to >50 µg/L). The regression lines were: y = 0.86x − 0.002 and y = 0.95x − 0.09 for their and our study, respectively. Besides interlaboratory differences in sample handling and calibration procedures, the use of different orthogonal regression methods likely contributed to the difference in proportional bias. The same holds true for the inclusion by Prieto and Alvarez of more high-concentration PCT samples, which acted as leverage points on the regression line.

In our study, we focused on the PCT range relevant for diagnostic purposes. Concordance at the clinical cutoff points (0.25 and 0.5 µg/L) was high in both the study by Prieto and Alvarez (97% and 94%) and our study (99% and 98%). We performed a Bland-Altman difference analysis within the clinically important interval. The distribution of the differences (Fig. 1) demonstrates a mean bias of −0.02 µg/L that is randomly