stolic dysfunction as determined by echocardiography. All attending physicians/cardiologists were blinded to the BNP results.

To determine the diagnostic accuracy of the two assays for CHF, we performed ROC plot analysis, and areas under the curve (AUC) were calculated for both BNP assays. Comparisons between AUC were assessed according to the method of Hanley and McNeil (10). Cutoff values for the two methods were determined at the 90% sensitivity criterion derived directly from the ROC curves. Statistical analysis for the clinical evaluation was performed with the MedCalc 7.2.1.0 package (MedCalc Software) and the software N (IDV). All probabilities were two-tailed, and P values <0.05 were regarded as statistically significant.

Of the 100 patients enrolled in the clinical study, 49 were classified as having dyspnea attributable to CHF, and 51 were classified as having dyspnea attributable to other reasons. The reasons for dyspnea in these 51 patients were as follows: chronic obstructive pulmonary disease (n = 21), pneumonia (n = 10), bronchitis/asthma (n = 5), malignancy of the lung (n = 1), musculoskeletal chest pain (n = 4), hypertension (n = 2), cardiac troponin-negative ACS (n = 2), tachycardia/arrhythmia (n = 2), and other causes (n = 4), such as pulmonary embolism, interstitial lung disease, or anemia. In distinguishing between patients with (n = 49) and patients without CHF (n = 51), the AUC (SE) were 0.938 (0.025) for the AxSYM BNP assay (95% CI, 0.872–0.977) and 0.932 (0.027) for the ADVIA Centaur assay (95% CI, 0.863–0.972; Fig. 1C). AUC were not significantly different for the two BNP assays [difference (SE) of AUC, 0.007 (0.006); 95% CI, −0.005 to 0.019; P = 0.265]. A power calculation showed that the power of this analysis was >99%. On the basis of the ROC curves, the cutoff values with a 90% sensitivity for CHF were 137 ng/L for the AxSYM BNP method [95% CI for sensitivity, 78–97%; specificity, 78% (95% CI, 65–89%)] and 110 ng/L for the ADVIA Centaur BNP method [95% CI for sensitivity, 78–97%; specificity, 78% (95% CI, 65–89%)].

In conclusion, we demonstrated a considerable proportional difference between results obtained with the AxSYM and ADVIA Centaur BNP assays. Given the limitations of low enrollments, our preliminary clinical study suggests that both assays provide comparable diagnostic information for the diagnosis of CHF in an emergency setting. Further studies are needed to clarify additional analytical issues concerning the AxSYM BNP assay (including sample stability data and reference intervals by age and gender) and to expand the database for the clinical relevance of this assay with respect to diagnostic and prognostic issues as well as its potential role in guiding medical treatment of CHF patients.

References
might be occurring with the Dade Dimension RxL analyzer because of the high frequency of negative anion-gap calculations in samples from patients with metabolic alkalosis. Reviews of external quality assurance data for Dade Dimension RxL analyzers showed measured chloride concentrations in samples with above-normal bicarbonate that were higher than the values obtained with other instruments.

We evaluated the effect of increasing concentrations of bicarbonate on chloride measured by six different analyzers in two sets of experiments, using an aqueous and a plasma matrix. In the first set, a human lithium-heparin-plasma pool was prepared with a bicarbonate concentration of 10 mmol/L and a chloride concentration of 109 mmol/L. These values were the means of the results obtained on the six different analyzers. From this pool we prepared four other samples by adding various amounts of sodium bicarbonate (sodium bicarbonate, 8.4 g in 100 mL; Pharmacia & Upjohn), giving final bicarbonate concentrations ranging from 10 mmol/L (pH 7.49) to 44 mmol/L (pH 7.69). In the second set, we prepared a sodium chloride solution of 107 mmol/L by adding 0.619 g of sodium chloride to deionized water to a final volume of 100 mL. We then prepared eight samples with bicarbonate concentrations ranging up to 50 mmol/L by adding the same sodium bicarbonate solution used in the first set. The samples were then analyzed for chloride and bicarbonate on the six different analytical systems with the manufacturers’ standard methods. To demonstrate that any changes were not attributable to the pH changes on addition of bicarbonate, we prepared a pooled plasma to which sodium hydroxide was added, increasing the pH from 7.58 to 8.40. The measured chloride concentration remained constant at 105 mmol/L.

The results (Table 1) show a clear linear increase in chloride with increasing bicarbonate in all except the Vitros analyzer. The effect is much greater in the Dade Dimension RxL.

Table 1. Slopes for the differences between observed and expected chloride concentrations (y axis) with increasing bicarbonate concentration (x axis) for two sets of samples (pooled plasma and aqueous samples) measured with various analytical systems.

<table>
<thead>
<tr>
<th>Analyzer</th>
<th>Plasma samples</th>
<th>Aqueous samples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ortho Diagnostics Vitros</td>
<td>0.001</td>
<td>−0.037</td>
</tr>
<tr>
<td>Bayer 865 Rapidlab</td>
<td>0.105</td>
<td>0.084</td>
</tr>
<tr>
<td>Roche Integra</td>
<td>0.093</td>
<td>0.100</td>
</tr>
<tr>
<td>Bayer Advia 1650</td>
<td>0.093</td>
<td>0.113</td>
</tr>
<tr>
<td>Hitachi Modular</td>
<td>0.081</td>
<td>0.235</td>
</tr>
<tr>
<td>Dade Dimension RxL</td>
<td>0.349</td>
<td>0.436</td>
</tr>
</tbody>
</table>

The slopes of the other four analyzers were similar and were the same for the two specimen sets. This indicates that, in four of the analyzers, the apparent chloride will increase by ~3 mmol/L if bicarbonate increases by 30 mmol/L and will increase by ~10 mmol/L in the Dade Dimension RxL analyzer.

It is difficult to comment on the bicarbonate concentration at which the chloride value is unaffected because of the between-analyzer variability, but it would be expected to be in the region of the bicarbonate concentration of the calibrators. There is a fundamental difference in chloride methods between the affected analyzers and the Vitros. The Vitros has an ion-selective electrode based on a silver/silver chloride electrode, whereas the others use an electrode based on a quaternary nitrogen compound. These results clearly establish that the problem of bicarbonate interference in ion-selective chloride electrodes is still present in modern analyzers and is of a degree that dramatically distorts the quantitative evaluation of the acid/base balance. This could disguise the presence of a renal tubular acidosis in an acidic patient or a coexistent unmeasured anion in a patient with metabolic alkalosis.

This problem with most current chloride methods is unacceptable and needs correction. An immediate corrective measure is possible by introduction of an on-board equation modifying the measured chloride value based on the linear relationship between the magnitude of interference and the bicarbonate concentration. However, the best corrective action would be for manufacturers to correct the problem present in quaternary ammonium-based ion-selective chloride methods.

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References

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