Combining Serum Carbohydrate-Deficient Transferrin and Hair Ethyl Glucuronide to Provide Optimal Information on Alcohol Use

To the Editor:

Weykamp et al. recently reported on their efforts toward the harmonization of carbohydrate-deficient transferrin (CDT) measurements in serum (1). Alcohol biomarkers play a key role in the identification of alcohol abuse, a chronic disorder with enormous health and legal implications. CDT is a widely used biomarker for the detection of excessive alcohol use that has a high diagnostic sensitivity and specificity and cannot be compared to traditional biomarkers such as alanine and aspartate aminotransferase, γ-glutamyl transferase, and blood count indices (mean corpuscular volume) (2). However, CDT’s diagnostic ability depends on many factors including sex, age, metabolic diseases, and mutant transferrins (3). Although used widely in clinical practice, CDT has a half-life of about 10 days and, therefore, estimates the excessive use of alcohol only over the past month rather than the length of the disorder. When such extensive efforts are directed to harmonize measurements for CDT throughout labora-

Table 1. Differences between patients with CKD stage <3 and 3 and correlates of CKD 3 in 2 different regression models.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>CKD stage &lt;3</th>
<th>CKD stage 3</th>
<th>P</th>
<th>Adjusted OR (95% CI)</th>
<th>P</th>
<th>Adjusted OR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>333 (82.8%)</td>
<td>69 (17.2%)</td>
<td>0.418</td>
<td>1.00</td>
<td>0.493</td>
<td>1.00</td>
<td>0.493</td>
</tr>
<tr>
<td>Female</td>
<td>460 (84.4%)</td>
<td>85 (15.6%)</td>
<td>0.418</td>
<td>0.86 (0.55–1.33)</td>
<td>0.493</td>
<td>0.86 (0.55–1.33)</td>
<td>0.493</td>
</tr>
<tr>
<td>White</td>
<td>575 (81.0%)</td>
<td>135 (19.0%)</td>
<td>&lt;0.001</td>
<td>1.00</td>
<td>0.119</td>
<td>1.00</td>
<td>0.119</td>
</tr>
<tr>
<td>South Asian</td>
<td>218 (92.0%)</td>
<td>19 (8.0%)</td>
<td>&lt;0.001</td>
<td>0.63 (0.36–1.12)</td>
<td>0.119</td>
<td>0.63 (0.36–1.12)</td>
<td>0.119</td>
</tr>
<tr>
<td>Age (years)</td>
<td>51.8 (17.1)</td>
<td>71.7 (13.9)</td>
<td>&lt;0.001</td>
<td>1.08 (1.06–1.09)</td>
<td>&lt;0.001</td>
<td>1.08 (1.06–1.10)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hemoglobin (g/dl)</td>
<td>14.2 (1.5)</td>
<td>13.9 (1.4)</td>
<td>&lt;0.01</td>
<td>0.94 (0.80–1.11)</td>
<td>0.448</td>
<td>0.94 (0.80–1.11)</td>
<td>0.448</td>
</tr>
<tr>
<td>Fasting glucose (mmol/L)</td>
<td>5.2 (0.9)</td>
<td>5.4 (0.8)</td>
<td>&lt;0.01</td>
<td>1.03 (0.81–1.32)</td>
<td>0.796</td>
<td>1.03 (0.81–1.32)</td>
<td>0.796</td>
</tr>
<tr>
<td>Fructosamine (mmol/L)</td>
<td>225.8 (23.3)</td>
<td>233.7 (22.4)</td>
<td>&lt;0.001</td>
<td>1.00 (0.99–1.02)</td>
<td>0.460</td>
<td>1.01 (1.00–1.02)</td>
<td>0.058</td>
</tr>
<tr>
<td>Hb A1c (mol/mol)</td>
<td>39.8 (6.5)</td>
<td>41.6 (5.8)</td>
<td>&lt;0.01</td>
<td>0.98 (0.94–1.01)</td>
<td>0.264</td>
<td>0.99 (0.91–1.08)</td>
<td>0.870</td>
</tr>
<tr>
<td>Albumin (g/dl)</td>
<td>4.54 (0.3)</td>
<td>4.42 (0.3)</td>
<td>&lt;0.001</td>
<td>0.99 (0.91–1.08)</td>
<td>0.870</td>
<td>0.99 (0.91–1.08)</td>
<td>0.870</td>
</tr>
<tr>
<td>Glycation gap (mmol/mol)</td>
<td>0.13 (6.9)</td>
<td>0.01 (6.8)</td>
<td>0.848</td>
<td>0.98 (0.94–1.02)</td>
<td>0.264</td>
<td>0.98 (0.94–1.02)</td>
<td>0.264</td>
</tr>
</tbody>
</table>

* Data are n (%) or mean (SD) unless noted otherwise.

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ories, questions arise whether this really is the best way forward, in terms of both time and finances.

In recent years, much research has been directed toward direct markers of alcohol use, since these markers are less sensitive to variables not related to alcohol consumption than traditional biomarkers. Examples include the alcohol metabolites ethyl glucuronide (EtG), ethyl sulfate, fatty acid ethyl esters, and phosphatidylethanol. Of these, EtG is the most widely used and accumulates in hair, where it remains incorporated for months to years according to hair length (4), providing the possibility of identifying the duration of alcohol consumption. This is of utmost importance in liver transplant patients, for example, where abstinence from alcohol is the norm for receiving a graft (5). Hair EtG measurements have good correlation with the amount of alcohol used over the past month and the chronicity of the intake in the past few months to years. In this case, we should focus on a metabolite of ethanol as a more accurate biomarker, preferentially one that can also detect the chronicity of the alcohol use.

We agree that harmonization of measurements should take place for a better interpretation of laboratory results in general, but we would like to emphasize that time, finances, and effort should be according to the scientific and clinical utility of the biomarker. We believe that CDT in serum could be combined with hair EtG to provide optimal information, in terms of both alcohol intake over the prior month and the chronicity of the intake in the past few months to years. In this case, we should focus on a metabolite of ethanol as a more accurate biomarker, preferentially one that can also detect the chronicity of the alcohol use.

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