Influence of PON1 Polymorphisms on the Association between Serum Paraoxonase 1 and Homocysteinemia in a General Population

To the Editor:

Homocysteine (Hcy)-induced vascular impairment may be partially mediated by the production of Hcy thiolactone (HTL). This compound acylates side-chain lysine groups in proteins and alters protein structure and function. HTL is formed under conditions of high Hcy resulting from insufficient remethylation of Hcy to methionine; however, HTL is not a reliable marker of plasma total Hcy (tHcy). In healthy volunteers, it contributes only 0.14%–0.28% of tHcy, has a half-life of 1 h, and is below the detection limit in approximately one half of volunteers (1).

Paraoxonase 1 (PON1) is a hydrolase associated with HDL that is thought to degrade lipid peroxides and HTL (2). Decreased PON1 activity has been associated with atherosclerosis (3). Hepatic expression of the PON1 gene is down-regulated in hyperhomocysteinemic mice (4); it is plausible, therefore, that the proatherogenic effects of Hcy may involve diminished serum PON1 activity, leading to impaired antioxidant function and decreased capacity to degrade HTL. In support of this hypothesis, an inverse relationship between PON1 and Hcy in hospital patients was reported recently (5).

We observed the following means: tHcy 8.9 (8.7–9.2) μmol/L; HDL 1.53 (1.49–1.57) mmol/L; PON1 activity, 411 (396–426) U/L; PON1 concentration, 96.5 (88.8–104.2) mg/L. Bivariate analysis showed no significant relationship between tHcy and PON1 activity (r = −0.089; P = 0.07) or between tHcy and PON1 concentration (r = 0.075; P = 0.15). The correlation was unchanged after exclusion of 12 participants with tHcy greater than the mean + 2 SD (r = −0.089; P = 0.08). However, persons in the highest tHcy tertile had significantly lower PON1 activity than the remaining participants [388 (362–414) vs 422 (404–441) U/L; P < 0.05]. There was no significant difference between PON1 concentra-

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Table 1. Effect of tHcy and other confounding factors on PON1 activity and concentration.*

<table>
<thead>
<tr>
<th></th>
<th>PON1 activity</th>
<th>PON1 concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 μmol/L increase in tHcy</td>
<td>-2.3</td>
<td>-3.1</td>
</tr>
<tr>
<td>1 mmol/L increase in HDL</td>
<td>16.9</td>
<td>-16.5</td>
</tr>
<tr>
<td>PON1&lt;sup&gt;3&lt;/sup&gt;R2 RR genotype</td>
<td>77</td>
<td>-2</td>
</tr>
<tr>
<td>PON1&lt;sup&gt;5&lt;/sup&gt;a MM genotype</td>
<td>-33</td>
<td>5.7</td>
</tr>
<tr>
<td>PON1&lt;sup&gt;-107&lt;/sup&gt; TT genotype</td>
<td>-16</td>
<td>-2</td>
</tr>
<tr>
<td>F</td>
<td>48.475</td>
<td>1.002</td>
</tr>
<tr>
<td>P</td>
<td>&lt;0.001</td>
<td>NS</td>
</tr>
</tbody>
</table>

*Multiple linear regression analysis. Models are adjusted for body mass index and sex. The table shows the percentage changes in PON1 activity and concentration for the indicated predictor. In the case of PON1 polymorphisms, the table shows the effect of being homozygotic.

<sup>b</sup> P <0.001.
<sup>c</sup> P <0.05.
<sup>d</sup> NS, not significant.

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**References**


**Tumor M2 Pyruvate Kinase as a Stool Marker for Colorectal Cancer: Stability at Room Temperature and Implications for Application in the Screening Setting**

Colorectal cancer (CRC) remains the third most common malignancy worldwide (1, 2). To improve noninvasive screening for CRC, various stool tests have been described based on tumor-associated markers (3). Among these is a test for fecal tumor M2 pyruvate kinase (M2-PK) activity...