To the Editor:

McPherson et al recently reported (in the journal Science) the association of 2 single nucleotide polymorphisms (rs10757274 and rs2383206) with coronary heart disease (CHD). After their report, we examined the possible association of these 2 gene variants with atherothrombotic events using a prospective, nested, matched case-control design among initially healthy US white men participating in the Physicians’ Health Study. The baseline characteristics of the sample participants used have been described elsewhere. Genotypes were determined on 335 myocardial infarction (MI) case-control pairs, and 254 ischemic stroke (IsST) case-control pairs; all matched on age ±2 years, smoking status, and time of follow-up. Our observed allele frequencies were similar to those reported by McPherson et al: the rs10757274 G-allele frequencies were 0.467, 0.430, 0.508, and 0.506 for MI-controls, MI-cases, IsST-controls, and IsST-cases, respectively; and the rs2383206 G-allele frequencies were 0.565, 0.599, 0.537, and 0.534 for MI-controls, MI-cases, IsST-controls, and IsST-cases, respectively. Overall, we found little evidence of association between the rs10757274 variant and incident MI or IsST (Table). By contrast, although statistically nonsignificant, the magnitude and direction of the effect estimate for rs2383206 with risk of MI were similar to the CHD risk estimates reported by McPherson et al. These data highlight the complexity of genetic association studies designed to dissect heritable patterns in common human disorders.

Table. Conditional Logistic Regression Analysis

<table>
<thead>
<tr>
<th>Variant</th>
<th>Crude OR; 95% CI; P</th>
<th>Adjusted OR; 95% CI; P</th>
<th>Crude OR; 95% CI; P</th>
<th>Adjusted OR; 95% CI; P</th>
</tr>
</thead>
<tbody>
<tr>
<td>rs10757274</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AA</td>
<td>Reference</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AG</td>
<td>0.840; 0.580–1.217; 0.36</td>
<td>0.765; 0.511–1.145; 0.19</td>
<td>0.949; 0.599–1.503; 0.82</td>
<td>1.046; 0.644–1.697; 0.86</td>
</tr>
<tr>
<td>GG</td>
<td>0.723; 0.457–1.144; 0.17</td>
<td>0.645; 0.392–1.062; 0.08</td>
<td>1.029; 0.619–1.712; 0.91</td>
<td>1.157; 0.668–2.003; 0.60</td>
</tr>
<tr>
<td>rs2383206</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>AG</td>
<td>1.127; 0.737–1.724; 0.58</td>
<td>1.106; 0.706–1.735; 0.66</td>
<td>1.093; 0.691–1.727; 0.70</td>
<td>1.005; 0.614–1.646; 0.98</td>
</tr>
<tr>
<td>GG</td>
<td>1.303; 0.831–2.045; 0.25</td>
<td>1.449; 0.895–2.347; 0.13</td>
<td>0.909; 0.550–1.501; 0.71</td>
<td>0.842; 0.490–1.449; 0.53</td>
</tr>
</tbody>
</table>

OR indicates odds ratio; Crude: conditional on age, smoking status and time of follow-up; Adjusted, further adjusting for randomized treatment assignment, BMI, history of hypertension, and presence or absence of diabetes.

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Disclosures

None.

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Robert Y.L. Zee and Paul M Ridker

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