### Commentary

Are polymorphisms in the ACE gene a potent genetic risk factor for restenosis?

The three forms of the gene for the human angiotensin converting enzyme (ACE) are determined by the insertion (I) or deletion (D) of an extra sequence in the DNA code. These forms are DD (two deletions), ID (one deletion), and II (no deletion). People who inherit the DD form of the gene have higher concentrations of circulating ACE than those who have the ID or two insertions. Because ACE, through the activation of angiotensin II, is a potent stimulator of vascular smooth muscle proliferation it is possible that those who inherit the DD form of the gene are at a higher risk of restenosis after angioplasty. A recent study by Ohishi et al suggests that this may be so.² Eighty two consecutive patients with myocardial infarction who had successful emergency coronary angioplasty within 24 hours of the onset of infarction were studied. All had follow-up angiography 3–6 months later. Restenosis was defined as a lesion producing more than a 50% reduction in lumen diameter at the angioplasty site. A method based on the polymeric chain reaction was used to detect the ACE gene polymorphism in DNA extracted from peripheral leucocytes. The DD genotype was found in 37 (45%) patients compared with 16 (15%) of 102 controls. A higher frequency of the DD genotype in those with acute infarction has been reported by others.¹ The results of the restenosis study, which are summarised in the table, show that compared with the ID and II genotypes, the DD genotype was more frequent in patients who had restenosis than in patients without restenosis. The odds ratio, an estimate of relative risk of restenosis between patients with the DD genotype and those with ID or II genotypes, was 4:1. Thus the study suggests that the DD genotype of ACE is a potent risk factor for restenosis after emergency angioplasty.²

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Restenosis</th>
<th>No restenosis</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>DD (%)</td>
<td>21 (56%)</td>
<td>8 (24%)</td>
<td>29 (100)</td>
</tr>
<tr>
<td>ID or II (%)</td>
<td>11 (24-4)</td>
<td>36 (75.6)</td>
<td>47 (100)</td>
</tr>
</tbody>
</table>

χ² = 8.91 (P = 0.0028)

The implications of the study, if the results are confirmed in a larger series of patients and different geographic populations, are important. First, it may be necessary to characterise the ACE genotype in patients undergoing angioplasty to identify those patients who are at higher risk of restenosis. Treatment with ACE inhibitors may benefit this group. In addition the numerous studies that have assessed the role of different risk factors for restenosis after coronary angioplasty may need re-evaluation. The results of large trials, such as the MERCATOR study, designed to test the hypothesis that ACE inhibition may prevent restenosis in patients after balloon angioplasty, may require re-analysis.

Certain factors in the study reported by Ohishi et al may have influenced the results. The angiographic analysis was by visual means alone, the definition of restenosis arbitrary, and the study group small and selected. Moreover, because only Japanese patients were studied, it is possible that ethnic differences could have had a role. In addition, though the frequency of the DD genotype was significantly higher in patients with restenosis, many patients without restenosis also had the DD genotype.

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