References

Response
We thank Drs Shahar, McGovern, and Sprafka for their interest in our paper in which we demonstrated, inter alia, that low doses of aspirin may not be as efficacious as higher doses.1 Our sample population was indeed matched, and Shahar et al are correct in pointing out that analysis for data obtained according to a matched design should have been performed. However, it is possible to ignore matching when the stratification is conditionally independent of the risk factors, given disease status.2 In any case, the odds ratios reported in our paper are very close to those for matched-paired analysis (Table) and the \( \chi^2 \) test for significance of change did not reveal any difference in statistical significance. Similar results were obtained for evaluation of risks (for the corresponding factors) computed from the estimates of logistic regression, while no potential interaction was observed. In fact, as can be seen in the Table, the conclusions remain the same regardless of the method of analysis. As for the analysis of dose effect, we indeed calculated the relative risks mentioned by Shahar et al, but considered the analysis for trend a more straightforward approach.

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References

Coagulation-Fibrinolysis Abnormalities in Poststroke Patients

To the Editor:
In their recent study, Tohgi et al1 found that markers of coagulation-fibrinolysis are increased in poststroke patients. They also suggested that plasminogen activator inhibitor-1 (PAI-1) levels are reduced in poststroke patients who receive antiplatelet medication. In selecting patients with small subcortical strokes for their study, the authors identified patients with a high prevalence of diabetes and hypertension. We are concerned that the demographic features of the patient and control groups are not homogeneous, and may explain some of the differences they found.

We examined differences between the patients and control subjects using the numbers from Table 1 (although the number of patients with risk factors differs slightly from that in "Subjects and Methods"). Eighty-nine of 153 (58%) poststroke patients were hypertensive, compared with 14 of 69 control subjects (20%); this difference is very significant (\( P<.001, \chi^2 \) test). A similarly high proportion—32 of 153 (21%)—of patients were diabetic, compared with 0 of 69 control subjects (\( P<.001, \chi^2 \) test). Both hypertension3 and diabetes4 have been associated with elevated levels of PAI-1. We suggest that the elevation in coagulation factors in poststroke patients in this study may be due to certain stroke risk factors.

Although there are no statistically significant differences between the treatment groups, the numbers are small and the groups are not homogeneous. Differences in cholesterol and triglyceride levels may also contribute to differences in levels of coagulation-fibrinolytic markers.5,6 In addition, we do not know why patients were assigned to receive aspirin, ticlopidine, or no treatment. We would be cautious about drawing the conclusion that antiplatelet medication lowers PAI-1 levels on the basis of this nonrandomized study.

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References

Response
We would like to thank Dr Öztürk and colleagues for their comments on our article.1 We agree that our study did not establish the significance of activated coagulation-fibrinolysis as a risk marker for stroke that is independent from conventional risk factors. To do so, we would have had to compare stroke patients with subjects without stroke matched for every risk factor.

In our study the incidence of diabetes was not significantly higher in patients taking antiplatelet medication than in those not taking it. Our conclusion, therefore, was that PAI-1 levels were significantly lower in aspirin- or ticlopidine-treated patients despite their slightly higher incidence of diabetes. We could not assign patients to treatment groups completely randomly because we had to consider history of gastrointestinal ulcers and tolerance...
of aspirin and ticlopidine before continuing long-term treatment. Our patients, however, were homogeneous in terms of infarct size and clinical severity.

As Dr Öztürk and colleagues state, further studies based on a large number of patients (with more appropriate controls) are necessary to determine the significance of the coagulation-fibrinolysis markers for stroke and stroke recurrence and the effects of antiplatelet medication on the markers.

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Reference

Apolipoprotein E e4 Allele Frequency in Vascular Dementia and Alzheimer's Disease

To the Editor:

The association of the apo E allele with vascular disease has been repeatedly reported, and it should not be surprising that it is a risk factor for cerebrovascular or Alzheimer's disease. 1-3-4 raising questions about the specificity of the e4 allele as a risk factor for cerebral vascular or Alzheimer's disease. 2

We assessed apo E allele frequencies in 51 elderly control subjects, 23 subjects with vascular dementia, 6 and 93 patients with Alzheimer's disease compared with 10% to 16% of control subjects.1-3-4 The specificity of the linkage between the apolipoprotein E (apo E) polymorphism and Alzheimer's disease has been repeatedly reported, and it should not be surprising that it is a risk factor for cerebrovascular or Alzheimer's disease. 1-3-4 raising questions about the specificity of the e4 allele as a risk factor for cerebral vascular or Alzheimer's disease. 2

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The specificity of the linkage between the apolipoprotein E (apo E) e4 allele and Alzheimer's disease is indeed a very important issue. In a study by Saunders et al there were no differences in e4

<table>
<thead>
<tr>
<th>Population</th>
<th>n</th>
<th>No. of Alleles</th>
<th>Age*</th>
<th>e2†</th>
<th>e3†</th>
<th>e4†</th>
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<tr>
<td>Control subjects</td>
<td></td>
<td></td>
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<tr>
<td>Elderly</td>
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<td>102</td>
<td>69.2</td>
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<td>704</td>
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<td>.54</td>
<td>.46</td>
</tr>
</tbody>
</table>

*Mean (standard deviation); †Frequency (standard error).
‡Data taken from Gabelli et al.7
§P=.0005 on z-test for difference with controls.

References

Response

The specificity of the linkage between the apolipoprotein E (apo E) e4 allele and Alzheimer's disease is indeed a very important issue. In a study by Saunders et al there were no differences in e4
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