Coumadin alone or aspirin plus coumadin reduced coronary events and death after acute myocardial infarction or unstable angina


QUESTION: In patients who have had acute myocardial infarction (MI) or unstable angina, is high intensity coumadin or aspirin plus moderate intensity coumadin more effective than aspirin alone for reducing coronary events and all cause mortality?

Patients
999 patients who had had acute MI (88%) or unstable angina (13%) within the preceding 8 weeks. Exclusion criteria included planned revascularization or recent intra coronary stenting, thrombocytopenia, anaemia, and history of stroke. Follow up was 95% (mean age 61 y, 77% men).

Intervention
Patients were allocated to phenprocoumon or acenocoumarol with target international normalized ratio (INR) of 3.0 to 4.0 (coumadin group, n=330); aspirin, 80 mg/day, plus phenprocoumon or acenocoumarol with target INR of 2.9 to 2.5 (combination group, n=333); or aspirin, 80 mg/day (aspirin group, n=366).

Main outcome measures
The primary outcome was a composite of all cause mortality, MI, or stroke. The major secondary outcome was bleeding.

Main results
Analysis was by intention to treat. The incidence of the composite outcome of all cause mortality, MI, or stroke was lower in the coumadin and combination groups than in the aspirin group (table). The incidence of minor bleeding was greater in the combination group than in the aspirin group (table). The groups did not differ for major bleeding (table).

Conclusion
In patients who have had acute myocardial infarction or unstable angina, high intensity coumadin alone or aspirin plus moderate-intensity coumadin was more effective than aspirin alone for reducing coronary events and all cause mortality.

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COMMENTARY
Clinical interest in coumadin therapy after MI declined in the 1990s after several studies showed no benefit over aspirin. Therefore, recent guidelines recommend the use of aspirin and other antiplatelet therapies (eg, clopidogrel) at discharge for patients with acute coronary syndromes (ACSs).

The ASPECT-2 study by van Es et al and 2 other recent trials suggest that long term coumadin therapy compared with aspirin improves outcomes in patients after ACS. In ASPECT-2, fewer patients in both the aspirin plus coumadin group (hazard ratio 0.59, 95% CI 0.27 to 0.92) and the coumadin alone group (hazard ratio 0.55, CI 0.30 to 1.00) reached the primary end point (death, MI, or stroke) than in those in the aspirin group after 12 months. The benefits from coumadin therapy were further supported by secondary analyses showing lower rates of death, vascular death, MI, unstable angina, stroke, and revascularisation in patients receiving coumadin or aspirin plus coumadin therapy than in those receiving aspirin alone. However, the aspirin plus coumadin group had a 2 fold higher rate of major bleeding, and a 3 fold higher rate of minor bleeding than the aspirin alone group.

Clinical application of the ASPECT-2 findings and widespread use of coumadin therapy after ACS are doubtful in contemporary cardiovascular practice. In ASPECT-2, aspirin plus coumarin was more effective than aspirin alone for reducing coronary events and all cause mortality.

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<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Event rates</th>
<th>RRR (95% CI)</th>
<th>NNT (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composite end point</td>
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<tr>
<td>Coumadin v aspirin</td>
<td>5% v 9%</td>
<td>43% (1 to 68)</td>
<td>26 (13 to 2740)</td>
</tr>
<tr>
<td>Combination v aspirin</td>
<td>5% v 9%</td>
<td>48% (7 to 71)</td>
<td>23 (12 to 184)</td>
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<tr>
<td>Major bleeding</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Coumadin v aspirin</td>
<td>1% v 1%</td>
<td>3% (-76 to 345)</td>
<td>Not significant</td>
</tr>
<tr>
<td>Combination v aspirin</td>
<td>2% v 1%</td>
<td>136% (-32 to 733)</td>
<td>Not significant</td>
</tr>
<tr>
<td>Minor bleeding</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Coumadin v aspirin</td>
<td>8% v 5%</td>
<td>68% (-7 to 205)</td>
<td>Not significant</td>
</tr>
<tr>
<td>Combination v aspirin</td>
<td>15% v 5%</td>
<td>216% (86 to 442)</td>
<td>10 (7 to 17)</td>
</tr>
</tbody>
</table>

†Composite end point = all cause mortality, myocardial infarction, or stroke. Abbreviations defined in glossary; RRI, RRR, NNT, NNH, and CI calculated from data in article.