Aortic Aneurysmal Regression of Dilation: Value of Ace-inhibition on RisK

Do ACE inhibitors slow the growth rate of small AAA independent of blood pressure lowering?

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The AARDVARK trial

- No disclosures
- 14 hospitals in England
- Patients with AAA 3.0-5.4cm & systolic BP ≤150 mm Hg
- Patients randomised to perindopril or amlodipine or placebo
- Patients followed up at 3-6m intervals using ultrasonography (external diameter) for 2 years

AARDVARK: multicentre randomised trial

- Primary outcome: AAA growth rate over 2 years
- Secondary outcomes: Time to 5.5cm diameter/referral for surgery/rupture, drug intolerance & compliance.
- Power: 90% power at the 5% level to detect a 38% reduction in growth rate associated with an ACE inhibitor versus placebo

Trial outcomes & sample size estimation

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Perindopril 10mg (75 patients)</th>
<th>Amlodipine 5mg (75 patients)</th>
<th>Placebo (75 patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>71.6 (6.9)</td>
<td>71.5 (6.7)</td>
<td>70.7 (7.5)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>71 (97%)</td>
<td>66 (92%)</td>
<td>74 (94%)</td>
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<tr>
<td>Systolic BP (mmHg)</td>
<td>131 (12)</td>
<td>132 (13)</td>
<td>131 (12)</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>77 (8)</td>
<td>78 (7)</td>
<td>78 (8)</td>
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<tr>
<td>AAA diameter (cm)</td>
<td>4.05 (0.65)</td>
<td>4.03 (0.69)</td>
<td>4.06 (0.67)</td>
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<tr>
<td>Diabetes, n (%)</td>
<td>2 (2.7%)</td>
<td>6 (8.3%)</td>
<td>8 (10.1%)</td>
</tr>
<tr>
<td>Current smokers, n (%)</td>
<td>21 (29%)</td>
<td>18 (25%)</td>
<td>17 (22%)</td>
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<tr>
<td>Pack years current smokers</td>
<td>33.1 (24.0)</td>
<td>29.3 (17.3)</td>
<td>32.9 (28.0)</td>
</tr>
<tr>
<td>Statin/anti-platelet use</td>
<td>73%/51%</td>
<td>63%/46%</td>
<td>61%/33%</td>
</tr>
</tbody>
</table>

Baseline Characteristics

Aneurysm growth rate

- Multilevel modelling estimates of annual diameter growth [mm]/y(SE):
  - Perindopril: 1.77 (0.2)
  - Amlodipine: 1.81 (0.2)
  - Placebo: 1.68 (0.2)
- Comparison of slopes of regression of modelled growth over time:
  - Perindopril vs placebo: P=0.78
  - Perindopril vs amlodipine: P=0.89
  - Placebo vs amlodipine: P=0.92
- Exclusion of patients with diabetes and adjustment for baseline age, sex, smoking and statin use also gave similar results.

Flow of patients through the trial

- Reasons for not completing: 7 deaths, 26 AAA repairs and 30 withdrawals
- Total attrition rate at 24 months = 4% (data from only one visit)
- Trial drug compliance >80% throughout
Time to reach 5.5 cm/referral for surgery

Kaplan-Meier estimates

After 2 years
Events (no ruptures): Systolic pressure change
Perindopril = 10  -5.0mm Hg
Amlodipine = 11  -2.8mm Hg
Placebo = 11+ 2.5mm Hg

- We were unable to demonstrate a significant impact of the ACE-inhibitor perindopril, compared with either placebo or amlodipine, on the growth rate of small AAAs over a 2-year period.

- In this population (small AAA + BP <150mmHg), differential BP lowering did not affect AAA growth.

Conclusions