High dose lisinopril was more effective than low dose for reducing combined mortality and cardiovascular events in congestive heart failure


QUESTION: In patients with congestive heart failure (CHF), is high dose lisinopril more effective than low dose lisinopril for reducing mortality and admission to hospital rates?

Design
Randomised (allocation concealment unclear*), blinded (patients, investigators, and outcome assessors)* controlled trial with 3 year follow up.

Setting
287 hospitals in 19 countries.

Patients
3793 patients were screened, and 3164 (mean age 63.6 y, 80% men) were studied. Inclusion criteria were New York Heart Association class II, III, or IV CHF, despite use of diuretics for ≥2 months, and left ventricular ejection fraction ≤30%. Exclusion criteria were recent revascularisation procedure or ischaemic event, history of ventricular tachycardia, intolerance to angiotensin converting enzyme (ACE) inhibitors, serum creatinine levels >2.5 mg/dl, or non-cardiac disorders that could limit survival. Follow up was 100%.

Intervention
Patients received their usual CHF medications and were allocated to lisinopril, 2.5 or 5.0 mg/day (n = 1596), or 30 mg/day (n = 1568).

Main outcome measures
All cause mortality. Secondary endpoints were cardiovascular (CV) mortality and 5 combined endpoints.

Main results
The groups did not differ for all cause mortality (42.5% for high dose v 44.9% for low dose lisinopril, p = 0.13) or CV mortality (37.2% v 40.2%, p = 0.07). Patients in the high dose group had lower rates of all cause mortality combined with all cause admissions to hospital (p = 0.002), CV admissions to hospital (p = 0.04), or CHF admissions to hospital (p < 0.001) and lower rates of CV mortality plus CV admissions to hospital (p = 0.03) (table) than did patients in the low dose lisinopril group.

Conclusion
High dose lisinopril was more effective than low dose lisinopril for reducing the combined endpoints of all cause mortality combined with either all admissions to hospital, CV admissions to hospital, or CHF admissions to hospital and CV mortality plus CV admissions to hospital for patients with CHF.

*See glossary.

**Table 1**

<table>
<thead>
<tr>
<th>Outcomes at 3 years</th>
<th>High dose</th>
<th>Low dose</th>
<th>Hazard ratio (95% CI)</th>
<th>NNT (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality plus admission to hospital</td>
<td>79.7%</td>
<td>83.8%</td>
<td>0.88 (0.82 to 0.96)</td>
<td>26 (16 to 82)</td>
</tr>
<tr>
<td>Mortality plus CV admission to hospital</td>
<td>71.1%</td>
<td>74.1%</td>
<td>0.92 (0.84 to 0.99)</td>
<td>34 (17 to 284)</td>
</tr>
<tr>
<td>Mortality plus CHF admission to hospital</td>
<td>55.1%</td>
<td>60.4%</td>
<td>0.85 (0.78 to 0.93)</td>
<td>17 (12 to 37)</td>
</tr>
<tr>
<td>CV mortality plus CV admission to hospital</td>
<td>69.4%</td>
<td>72.7%</td>
<td>0.91 (0.84 to 0.99)</td>
<td>30 (16 to 281)</td>
</tr>
</tbody>
</table>

†CV = cardiovascular. Other abbreviations defined in glossary; NNT and its CI calculated by using hazard ratios provided in article.