The ideal blood pressure: assessment of fixed and variant targets over time in clinical trial and routine clinical practice

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Session contents

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Rationale

• High blood pressure is a leading risk factor of the global burden of disease (GBD 2016).
• SPRINT results showed great survival benefits of intensive treatment of systolic blood pressure (SPRINT 2015).
• Different updated American and United Kingdom clinical guidelines.

Source: UAB 2015
Research question

• What are the survival prospects and renal side effects of intensive treatment of systolic blood pressure to <120 mmHg versus standard treatment to <140 mmHg in the US clinical trial SPRINT in comparison to similar hypertensive patients managed in routine primary care in the UK?

Study design of SPRINT

• SPRINT: US randomised control trial.
  – Sample of people aged 50 to 90 with systolic blood pressure of 130-180 mmHg and increased risk of cardiovascular disease, and no history of cancer, dementia, diabetes, heart failure, or stroke.
  – Randomly assigned intensive treatment of lowering systolic blood pressure to <120 mmHg or standard treatment to <140 mmHg.
  – Our additional exclusion criteria: history of chronic kidney disease at baseline, not prescribed antihypertensive drugs at trial entry, or not reached the target blood pressure in six months.
Study design of THIN

• THIN: UK primary care database.
  – Patients selected whose systolic blood pressure reduced from 141-180 mmHg (baseline) to either 121-140 mmHg (standard treatment) or 70-120 mmHg (intensive treatment) within six months.
  – Same selection criteria as SPRINT plus:
    • diagnosis of hypertension at baseline or at least one ongoing antihypertensive drug prescription in the month prior to the baseline, and
    • change in antihypertensive treatment in the month prior to the dropped blood pressure.
Methodology

• Outcomes: time to all-cause mortality and time to chronic kidney disease (eGFR to <60 ml/min/1.73m²)
• Exposures: intensive treatment (SBP target <120 mmHg) vs standard treatment (SBP target <140 mmHg); number of antihypertensive drugs; and change in number of drugs.
• Confounders: sex, age, ethnicity (SPRINT only), deprivation (THIN only), systolic blood pressure (SBP), cardiovascular disease, aspirin, statin, smoking status, body mass index, and clinical site.
• Regression: standard Cox’s.
  – Tested for competing risks adaption, which provided similar results.
  – Tested for interactions between treatment type and other factors.
  – Tested for time-dependent effects.
## Results: cohorts’ characteristics

<table>
<thead>
<tr>
<th></th>
<th>SPRINT</th>
<th>THIN_spr</th>
<th>THIN_ext</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study period</td>
<td>2010-15</td>
<td>2010-15</td>
<td>2005-17</td>
</tr>
<tr>
<td>Sample size</td>
<td>4,165</td>
<td>8,361</td>
<td>54,683</td>
</tr>
<tr>
<td>Exposure intensive treatment (SBP&lt;120 mmHg)</td>
<td>45%</td>
<td>43%</td>
<td>36%</td>
</tr>
<tr>
<td>Outcome death</td>
<td>3%</td>
<td>3%</td>
<td>12%</td>
</tr>
<tr>
<td>Outcome chronic kidney disease</td>
<td>3%</td>
<td>4%</td>
<td>15%</td>
</tr>
</tbody>
</table>
Results: systolic blood pressure

*Standard treatment of systolic blood pressure <140 mmHg.
†Intensive treatment of systolic blood pressure <120 mmHg.
Results: regression models

- Adjusted effects of antihypertensive treatment associated with the hazard of all-cause mortality.

<table>
<thead>
<tr>
<th>Factor</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antihypertensive treatment</td>
<td>Standard</td>
</tr>
<tr>
<td></td>
<td>Intensive &lt;1 yr</td>
</tr>
<tr>
<td></td>
<td>Intensive &gt;=1 yr</td>
</tr>
<tr>
<td>Number of antihyp. drugs at</td>
<td>0/1 drug</td>
</tr>
<tr>
<td>baseline</td>
<td>2+ drugs</td>
</tr>
<tr>
<td>Change in number of</td>
<td>Same/less</td>
</tr>
<tr>
<td>antihyp. drugs at entry</td>
<td>More</td>
</tr>
</tbody>
</table>

Standard SBP < 140 mmHg vs intensive SBP < 120 mmHg
Discussion

• Study found intensive treatment associated with survival benefits in SPRINT, but survival harms in THIN, which were time-dependent.

• Study found intensive treatment associated with increased hazard of chronic kidney disease, where the hazards were higher in SPRINT and dependent on number of drugs in THIN. (Results not shown.)

• Possible explanations for different results:
  – how blood pressure was measured, and
  – stable/unstable follow-up blood pressure.
Recommendations

• Study suggests that the optimal systolic blood pressure is <140 mmHg in hypertensive patients treated in routine clinical practice.

• However, lowering systolic blood pressure to <120 mmHg might be beneficial in some selective and closely monitored group of patients.
References


• National Institute for Health and Care Excellence. Hypertension in Adults: Diagnosis and Management (CG127). 2011.


Any questions?

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