Hypertension Update 2016

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Disclosures: None

Systolic & Diastolic Blood Pressure by Age


Hypertension in the Elderly: Key Questions

• How is it defined and measured?
• Is it dangerous? [Recent data on cognition.]
• Can BP be reduced safely in the very old?
• Does treatment reduce morbidity [Dementia & Disability] and mortality in the very old?
• How low should we go? [Controversial guidelines from JNC 8, new data from SPRINT]
• What treatment should we use?

Definition of Hypertension

• Healthy Elderly
  > 140/90

• Frail Elderly
  > 150/90

  • Systolic Hypertension
  > 160/ <90

Pitfalls of BP Measurement

• Pseudohypertension (Osler’s Maneuver)
• Auscultatory Gap
• Cuff size (bladder = 80% of arm circumference)
• Rounding bias and digit preference
• BP Variability (Feature of HTN):
  – Orthostatic hypotension
  – Postprandial hypotension
  – Atrial Fibrillation
  – “White Coat Hypertension,” Ambulatory BP monitor

Is Hypertension Dangerous in Elderly Patients?

• Meta-analysis of 61 prospective studies involving 120,000 deaths in one million participants showed increased IHD and Stroke mortality with increasing age, across all levels of systolic and diastolic BP.

• Hypertension is also associated with cognitive and functional decline in elderly people
Can BP be Reduced Safely in Very Elderly Patients?

- Numerous clinical trials in selected elderly populations show that BP can be lowered safely with similar side effects as placebo.
- HYVET: No difference in adverse effects in Sx ≥ 80 yrs.
- Lingeriing concerns:
  - Trial exclusion criteria
  - Orthostatic hypotension
  - Decreased cerebral perfusion
  - J-shaped relation between BP and mortality

Effect of 6 Months of BP Control on Cerebral Blood Flow

Lipsitz, et. al., Hypertension, 2003

Low BP and Worse Survival in a Finnish Population over age 85

Rastas, JAGS, 2006

Risk of Death, MI or Stroke by Age and Achieved BP (on verapamil or atenolol) in 22,576 INVEST Subjects with CAD.

Denardo, AJM, 2010

Does antihypertensive therapy reduce morbidity and mortality in the very old?

<table>
<thead>
<tr>
<th>Trial</th>
<th>No.</th>
<th>Age</th>
<th>Entry BP</th>
<th>Stroke</th>
<th>CAD</th>
<th>CHF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Austral.</td>
<td>582</td>
<td>60-69</td>
<td>165/101</td>
<td>33</td>
<td>18</td>
<td>--</td>
</tr>
<tr>
<td>EWPHE</td>
<td>840</td>
<td>&gt;60</td>
<td>182/101</td>
<td>36</td>
<td>20</td>
<td>22</td>
</tr>
<tr>
<td>Coope &amp; Warrender</td>
<td>884</td>
<td>60-79</td>
<td>197/100</td>
<td>42*</td>
<td>0.03</td>
<td>32</td>
</tr>
<tr>
<td>STOP</td>
<td>1627</td>
<td>70-84</td>
<td>195/102</td>
<td>47*</td>
<td>13</td>
<td>51*</td>
</tr>
<tr>
<td>MRC</td>
<td>4396</td>
<td>65-74</td>
<td>185/91</td>
<td>25*</td>
<td>19</td>
<td>--</td>
</tr>
<tr>
<td>SHEP</td>
<td>4736</td>
<td>60-80</td>
<td>170/77</td>
<td>33*</td>
<td>27*</td>
<td>55*</td>
</tr>
<tr>
<td>HDFP</td>
<td>2374</td>
<td>60-69</td>
<td>170/101</td>
<td>44*</td>
<td>15*</td>
<td>--</td>
</tr>
<tr>
<td>Syst-Ear</td>
<td>4695</td>
<td>&gt;60</td>
<td>174/86</td>
<td>42*</td>
<td>30</td>
<td>29</td>
</tr>
</tbody>
</table>

Denardo, AJM, 2010

Effects of Therapy in Older Patients with Hypertension (% risk reduction, *p<.05)
Meta-analysis of 1670 Hypertensive Pts. > age 80 from 7 trials

From Elliott, Hypertension 2004; 44: 800

2008: Hypertension in the Very Elderly Trial (HYVET)

- Randomized, placebo-controlled, double-blinded
- Indapamide ± perindopril vs. placebo
- N=3,845, age 83 years, median follow-up 1.8 years
- Generally healthy, very old adults with stage 2 HTN
  - Baseline CVD 12%, Stroke 7%, MI 3%, and HF 3%
  - Prematurely terminated due to ↓stroke and mortality


HYVET: BP Control Over Time


HYVET Results

<table>
<thead>
<tr>
<th>End Point</th>
<th>% (Number) Events</th>
<th>Hazard Ratio (unadj)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active</td>
<td>Placebo</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroke death</td>
<td>6.5 (27)</td>
<td>10.7 (42)</td>
<td>0.61 (0.38–0.99)</td>
</tr>
<tr>
<td>Any death</td>
<td>47.2 (196)</td>
<td>59.6 (235)</td>
<td>0.79 (0.65–0.95)</td>
</tr>
<tr>
<td>Any CHF</td>
<td>5.3 (22)</td>
<td>14.8 (57)</td>
<td>0.36 (0.22–0.58)</td>
</tr>
<tr>
<td>CV Events</td>
<td>33.7 (138)</td>
<td>50.6 (193)</td>
<td>0.66 (0.53–0.82)</td>
</tr>
</tbody>
</table>


Does Antihypertensive Therapy Prevent Dementia? Randomized Trials

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Age</th>
<th>Treatment</th>
<th>Follow-up</th>
<th>% Dementia Reduction</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>SHEP</td>
<td>4756</td>
<td>72</td>
<td>Chlorthal +/- atenolol or reserpine</td>
<td>4.5 yrs.</td>
<td>10%</td>
<td>NS</td>
</tr>
<tr>
<td>SYST-EUR</td>
<td>2418</td>
<td>70</td>
<td>Nitrindipine +/- BB +/- HCTZ</td>
<td>2.0 yrs.</td>
<td>50% (8-76%)</td>
<td>0.05</td>
</tr>
<tr>
<td>PROGRESS</td>
<td>6105</td>
<td>64</td>
<td>Perindopril +/- indapamide</td>
<td>4.0 yrs.</td>
<td>12% (-4-28%)</td>
<td>0.20</td>
</tr>
<tr>
<td>SCOPE</td>
<td>4937</td>
<td>76</td>
<td>Candesartan +/- diuretic</td>
<td>3.7 yrs.</td>
<td>7% increase</td>
<td>&gt;0.2</td>
</tr>
<tr>
<td>HYVET</td>
<td>3336</td>
<td>84</td>
<td>Indapamide +/- Perindopril</td>
<td>2.2 yrs.</td>
<td>14% (-9-23%)</td>
<td>0.20</td>
</tr>
<tr>
<td>PRoFESS</td>
<td>20332</td>
<td>66</td>
<td>Telmisartan</td>
<td>2.4 yrs.</td>
<td>0%</td>
<td>0.48</td>
</tr>
</tbody>
</table>

How Low Do We Go? JNC-8 Recommendations

“In the general population aged ≥ 60 years, initiate pharmacologic treatment to lower BP at SBP ≥ 150 mm Hg or DBP ≥ 90 mm Hg and treat to a goal SBP <150 mm Hg and goal DBP <90 mm Hg.” (Strong Recommendation – Grade A)

Caveats: Doesn’t account for heterogeneity in older population: Healthy people aged 60-75 may benefit from lower goals; frail seniors may require higher.
Systolic BP Intervention Trial
Randomized controlled clinical trial to examine effect of more intensive high blood pressure treatment strategy than is currently recommended (standard treatment)

Target Systolic BP
- Intensive Treatment
  - Goal SBP < 120 mm Hg
- Standard Treatment
  - Goal SBP < 140 mm Hg

SPRINT Research Group, NEJM, 2015, Presented at GSA 215

Major Inclusion Criteria
- ≥50 years old
- SBP: 130 – 180 mm Hg, on up to 4 antihypertensive meds
- Additional cardiovascular disease (CVD) risk
  - Clinical or subclinical CVD (excluding stroke)
  - Chronic kidney disease (CKD), defined as eGFR 20 – <60 ml/min/1.73m² based on MDRD equation
  - Framingham Risk Score for 10-year CVD risk ≥ 15%
  - Age ≥ 75 years

At least one of these risk factors

Major Exclusion Criteria
- Stroke
- Diabetes mellitus
- Polycystic kidney disease
- Congestive heart failure (symptoms or EF < 35%)
- Proteinuria >1g/dl
- CKD with eGFR < 20 mL/min/1.73m² (MDRD)
- Adherence concerns


Systolic Blood Pressure in the Two Treatment Groups over the Course of the Trial (Median 3.26 yrs.)

Primary Outcome and Death from Any Cause
- NNT = 61
- NNT = 90

Forest Plot of Primary Outcome According to Subgroups
Kaplan-Meier Curves for SPRINT Primary Outcome and All-Cause Mortality in Participants 75 and older

HR: 0.67 95% CI (0.51 to 0.86)
NNT = 28 at 3.26 years

Kaplan-Meier Curves for SPRINT Primary Outcome by Frailty Status

HR: 0.23 95% CI: 0.23 to 0.95
HR: 0.63 95% CI: 0.43 to 0.92
HR: 0.68 95% CI: 0.45 to 1.02

Kaplan-Meier Curves for SPRINT Primary Outcome by Gait Speed

HR: 0.65 95% CI: 0.41 to 1.02
HR: 0.68 95% CI: 0.48 to 0.95

Serious Adverse Events (SAE) and Conditions of Interest During Follow-up for Participants 75 Years and Older at Randomization

<table>
<thead>
<tr>
<th>Conditions of Interest</th>
<th>Intensive Events %/yr</th>
<th>Standard Events %/yr</th>
<th>HR</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypotension</td>
<td>36</td>
<td>24</td>
<td>1.55</td>
<td>0.038</td>
</tr>
<tr>
<td>Syncope</td>
<td>46</td>
<td>37</td>
<td>1.50</td>
<td>0.309</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>41</td>
<td>43</td>
<td>1.10</td>
<td>0.650</td>
</tr>
<tr>
<td>Electrolyte abnormality</td>
<td>58</td>
<td>41</td>
<td>1.47</td>
<td>0.061</td>
</tr>
<tr>
<td>Injurious Fall</td>
<td>78</td>
<td>79</td>
<td>1.01</td>
<td>0.575</td>
</tr>
<tr>
<td>Acute Kidney Injury or Acute Renal Failure</td>
<td>75 2.0</td>
<td>54 1.4</td>
<td>1.40</td>
<td>0.051</td>
</tr>
</tbody>
</table>

Number of Participants with a Monitored Clinical Measure During Follow-up

<table>
<thead>
<tr>
<th>Measure</th>
<th>Intensive Events %/yr</th>
<th>Standard Events %/yr</th>
<th>HR</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium&lt;130 mmol/L</td>
<td>66</td>
<td>44</td>
<td>1.51</td>
<td>0.034</td>
</tr>
<tr>
<td>Sodium&gt;150 mmol/L</td>
<td>1</td>
<td>&lt;0.1</td>
<td>-</td>
<td>0.290</td>
</tr>
<tr>
<td>Potassium&lt;3 mmol/L</td>
<td>17</td>
<td>11</td>
<td>1.50</td>
<td>0.303</td>
</tr>
<tr>
<td>Potassium&gt;5.5 mmol/L</td>
<td>68</td>
<td>64</td>
<td>1.01</td>
<td>0.975</td>
</tr>
<tr>
<td>Orthostatic hypotension</td>
<td>277</td>
<td>288</td>
<td>0.90</td>
<td>0.243</td>
</tr>
<tr>
<td>Orthostatic hypotension with dizziness</td>
<td>25</td>
<td>17</td>
<td>1.44</td>
<td>0.252</td>
</tr>
</tbody>
</table>

How low do you go? Systolic BP

- **Most Seniors:** Most trials showing benefit achieved 20+ mm Hg SBP reduction, or SBP < 150 mmHg. SPRINT suggests better outcomes in CVD pts at SBP < 120 mmHg.
- **Diabetics:** ACCORD: DM-2 pts, aged 62 ±7: more adverse events and similar CV events for SBP < 120, but fewer strokes. JNC 8 recommends < 140/90.
- **Frail:** Conflicting data. Balance aggressive Rx against risks of multiple medications and co-morbidities.
- **Suggestions:** 120-130 if tolerated, < 150 at age ≥80; <140 in DM; <160 in frail elderly with co-morbidity.
**How Low Do You Go? DBP**

- **Most Seniors**: Not addressed in SPRINT (achieved 69 and 76 mmHg). HOT study: Fewest CV events @ 83, lowest CV mortality @ 87 mmHg.
- **Diabetics**: 51% reduction in major CV events if DBP ≤ 80, compared to ≤ 90.
- **Frail**: Lower Mortality with DBP ≥ 90 in Slow Walkers (<0.8 m/sec) (Odden Arch IM, 2012), but good outcomes at <80 in SPRINT.

**Summary**: Most patients do OK at 70-90 mmHg. Frail patients may have better survival at higher DBP.

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**Management of Hypertension**

- Consider secondary causes: NSAIDs, Steroids, Sleep apnea, Hyperthyroid, Hyperaldosteronism.
- First, non-pharmacologic Rx: Salt restriction, wt. loss
- Then, pharmacologic therapy
- For refractory HTN
  - Assess compliance
  - Use a diuretic
  - Evaluate for renal artery stenosis

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**Pharmacologic Treatment**

- **Diuretics**:
  - proven effective, chlorthalidone more potent, watch K+
  - Aldactone in CHF
  - may be slightly less effective than amlodipine when combined with ACEI in high risk pts.
- **Beta-blockers**:
  - CAD
  - May be less effective (LIFE study: BB<ARB in patients with LVH).

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**Pharmacologic Treatment 2**

- **ACE inhibitors and ARBs**: CHF, DM, stroke, MI
- **Ca-channel blockers**:
  - Use long-acting, avoid 1st generation if LV dysfxn.
  - Amlodipine + ACEI for high risk pts (ACCOMPLISH).
  - More effective in African Americans than ACE, ARB, BB
- **Central sympatholytics**: depression, patch available
- **Alpha-blockers**: urinary outlet obstruction, increased risk of syncope and OH

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**Summary**

- Hypertension is common, dangerous, and safely treatable in elderly people.
- Hypertension increases the risk of hypotension, cognitive, & functional decline in pts <85.
- The treatment of hypertension reduces cardiovascular morbidity and mortality without excessive side effects in patients aged 80-85.
- Treatment of non-frail pts. may improve cerebral blood flow and reduce the incidence of dementia.

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**References**

- James PA, et. al., 2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults: Report From the Panel Members Appointed to the Eighth Joint National Committee (JNC 8). JAMA online, 2013
- SPRINT Research Group, A randomized trial of intensive versus standard blood-pressure control, NEJM online, 2015.