New Clinical Trends in Geriatric Medicine

April 8, 2016
Amanda Lathia, MD, MPhil
Staff, Center for Geriatric Medicine
Objectives

• Review current guidelines for blood pressure (BP) control in older adults
  - Critique the newest evidence in BP goals
• Discuss diabetes management in older adults
• Define chronic kidney impairment
• Describe appropriate medication prescribing in kidney disease
THE PRESSURE IS ON:

Defining optimal blood pressure (BP) goals in older adults
Case 1- Ms. A

- 82 yo black woman
- Community dwelling, independent
- History of HTN, CAD, mild memory loss
- Home BP range: 140s-160s/70s-90s
- BP in office: 147/82
- On HCTZ
- eGFR >60 mg/dl
Case 2- Mr. T

- 75 yo Caucasian man
- Lives with daughter
- History of BPH, HTN, stroke, a-fib
- On metoprolol for rate control
- Dependent in activities of daily living
- 3 falls in past 6 months, + weight loss
- eGFR 40 mg/dl
- BP in office is 156/89
Would you treat their HTN?

- Case 1
- Case 2

- Is there clinical trial evidence?
- What do the guidelines say?
Timeline BP treatment in ≥ 60

1960s-1980s
- SHEP
- SYST-EUR

Trials show benefit of HTN Rx, but few include ≥ 60 yo

1990-2000s
- HYVET

Rx of adults ≥ 60 to mean SBP in 140s reduced stroke and MI

2005-2014
- JATOS
- VALISH

Rx SBP mean SBP 144 in nonfrail ≥ 80 reduced all cause mortality and HF

2015
- SPRINT

Rx SBP < 140 in adults 70-85 yrs no difference in CVD, renal disease (underpowered)

Potential benefit of intensive BP control (goal SBP <120) in ≥ 50 yo

Saklayen MG, Front Cardiovasc Med, 2016
Kovell LC, J Am Heart Assoc, 2015
JNC 7 - 2003

- BP treatment goals:
  - <140/90 in adults ≥18
  - < 130/80 in adults with diabetes or chronic kidney disease

Chobanian AV, *Hypertension*, 2003
Timeline BP treatment in ≥ 60

1960s-1980s
Trials show benefit of diastolic HTN Rx, but few include ≥ 60 yo

1990-2000s
Rx of adults ≥ 60 to mean SBP in 140s reduced stroke and MI
Rx SBP mean SBP 144 in nonfrail ≥ 80 reduced all cause mortality and HF

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2015
Potential benefit of intensive BP control (goal SBP <120) in ≥ 50 yo

SHEP SYST-EUR
HYVET
JATOS VALISH
SPRINT

JNC 7 2003
JNC 8 2014

Saklayen MG, Front Cardiovasc Med, 2016
Kovell LC, J Am Heart Assoc, 2015
JNC 8 Guidelines 2014

- Changed the goals of HTN management:
  - <140/90 in adults < 60
  - < 150/90 in adults ≥ 60
  - < 140/90 in adults with DM or CKD
- Rational: lack of evidence of benefit for SBP < 140 compared to SBP 140 to 150 in VALISH and JATOS trials

James, PA, JAMA, 2014
Guideline based BP goals in adults without DM or CKD

<table>
<thead>
<tr>
<th>Guideline</th>
<th>Age &lt; 60</th>
<th>Age 60-79</th>
<th>Age 80+</th>
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</thead>
<tbody>
<tr>
<td>JNC 7 – 2003</td>
<td>&lt;140/90</td>
<td>&lt;140/90</td>
<td>&lt;140/90</td>
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<tr>
<td>JNC 8 - 2014</td>
<td>&lt;140/90</td>
<td>&lt;150/90</td>
<td>&lt;150/90</td>
</tr>
<tr>
<td>American Heart Assoc – 2011</td>
<td>&lt;140/90</td>
<td>&lt;140/90</td>
<td>&lt;150/90</td>
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<tr>
<td>European – 2013</td>
<td>&lt;140/90</td>
<td>&lt;140/90</td>
<td>&lt;150/90</td>
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<tr>
<td>Canadian – 2014</td>
<td>&lt;140/90</td>
<td>&lt;140/90</td>
<td>&lt;150/90</td>
</tr>
</tbody>
</table>

Kovell LC, *J Am Heart Assoc*, 2015
JNC 8 Controversy

- JATOS and VALISH underpowered
- Panel didn’t include FEVER trial:
  - 9800 Chinese subjects
  - Ages 50-79, mean age 62
  - Reducing BP < 140/90
  - Decreased risk of stroke, CV events, and death
- JNC 8 guidelines:
  - Potential loss of mortality and CVD benefit in adults 60-79
MORE FUEL TO THE FIRE:
The Systolic Blood Pressure Intervention Trial (SPRINT)
SPRINT - Overview

- Funded by the NIH
- Multi-center, randomized, controlled trial
- 9361 subjects enrolled Nov 2010-Mar 2013
- Intervention:
  - SBP target of $< 120$ mm Hg
- Standard treatment group:
  - SBP target of $135 – 139$ mm Hg

SPRINT- Subjects

- Age ≥ 50
  - mean age 67.9 years
- SBP 130 to 180 mm Hg
  - mean BP 140/78 at baseline
- Increased cardiovascular risk
  - Age ≥ 75 years (28% of subjects)
  - Cardiovascular disease (CVD)
  - Chronic kidney disease (CKD)
  - Framingham 10-yr risk score ≥ 15%

SPRINT- Exclusions

• Prior history of:
  - Diabetes
  - Stroke or TIA
  - End stage renal disease or eGFR < 20 ml/min
  - Proteinuria, polycystic kidney disease, glomerulonephritis
  - Secondary HTN
  - Organ transplant

SPRINT- Exclusions Cont’d

- 1 minute standing SBP < 110
- Unintentional weight loss > 10% past 6 mo
- Symptomatic CHF past 6 mo or LVEF <35%
- Cardiovascular event past 3 mo
- Life expectancy < 3 years
- Factors limiting adherence
  - (cognitive impairment, substance abuse, residence in nursing home, psych or behavioral conditions)

SPRINT outcomes

- **Primary:**
  - composite of MI, acute coronary syndrome (ACS), stroke, acute decompensated HF, or death from CV causes

- **Secondary:**
  - Each of the composite events individually
  - Death from any cause
  - Primary outcome or death any cause

SPRINT - Results

- Mean SBP and # meds at 1 year:
  - 121.4 mm Hg, 2.8 meds (intensive)
  - 136.2 mm Hg, 1.8 meds (standard)
- Median follow up of 3.26 years
- Intervention ended early in August 2015

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Intensive treatment (N=4678) # patients (%)</th>
<th>Standard Treatment (N=4683) # patients (%)</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary</td>
<td>243 (5.2)</td>
<td>319 (6.8)</td>
<td>0.75 (0.64-0.89)</td>
<td>&lt;0.001</td>
<td>61</td>
</tr>
<tr>
<td>Secondary: MI</td>
<td>97 (2.1)</td>
<td>116 (2.5)</td>
<td>0.83 (0.64-1.09)</td>
<td>0.19</td>
<td></td>
</tr>
<tr>
<td>ACS</td>
<td>40 (0.9)</td>
<td>40 (0.9)</td>
<td>1.00 (0.64-1.55)</td>
<td>0.99</td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td>62 (1.3)</td>
<td>70 (1.5)</td>
<td>0.89 (0.63-1.25)</td>
<td>0.50</td>
<td></td>
</tr>
<tr>
<td>Heart failure</td>
<td>62 (1.3)</td>
<td>100 (2.1)</td>
<td>0.62 (0.45-0.84)</td>
<td>0.002</td>
<td></td>
</tr>
<tr>
<td>Death from CV</td>
<td>37 (0.8)</td>
<td>65 (1.4)</td>
<td>0.57 (0.38-0.85)</td>
<td>0.005</td>
<td>90</td>
</tr>
<tr>
<td>Death any cause</td>
<td>155 (3.3)</td>
<td>210 (4.5)</td>
<td>0.73 (0.60-0.90)</td>
<td>0.003</td>
<td>162</td>
</tr>
</tbody>
</table>

• CKD at baseline:
  - No difference in renal outcomes
• No CKD at baseline
  - Intervention group increased decline in GFR (p < 0.001)
• Subgroup analysis:
  - Significant reduction in primary outcome
    • Age ≥ 75, Male, non-black, no baseline CKD or CVD, baseline SBP ≤ 132
SPRINT- Adverse Effects

- Significantly greater in intensive treatment group
  - Hypotension
  - Syncope
  - Electrolyte abnormality
    - Na+ < 130, Na+ >150, K+ < 3.0
  - Acute kidney injury
- No significant difference in bradycardia, injurious falls

SPRINT- Summary

- In non-frail adults \( \geq 50 \), without diabetes or eGFR < 20
- Lower BP targets may decrease risk of heart failure and death
Potential Consequences of Lower BP targets

• Increased risk for:
  - hypotension, syncope, electrolyte abnormalities, and acute kidney injury
• Increased mortality
Mortality Risk Across the Spectrum of BPs

- Retrospective cohort study
- Adults ≥ 18 yo treated for hypertension
- Between 2006-2010
- 398,419 subjects (30% with DM)
- Mean age 64
- Risk of death or ESRD in BP categories
- Lowest risk at BP of 137/71
  - SBP 130-139
  - DBP 60-79

Sim J, J Am Coll Cardiol, 2014
SBP and Mortality/ESRD Risk

Sim J, J Am Coll Cardiol, 2014
WHAT ABOUT THOSE WITH SUGAR:

BP Management and Diabetes
ACCORD BP Trial

- Action to Control Cardiovascular Risk in Diabetes trial
- 4733 ≥ 40 yo with type 2 DM, SBP 130-180
- Mean 62 yo, BP 139/78, HbA1c 8.3%
- Creatinine < 1.5 mg/dl
- SBP treatment groups
  - Intensive: goal <120, mean 119 mm Hg
  - Standard: goal < 140, mean 134 mm Hg

ACCORD Study Group, N Engl J Med, 201
ACCORD BP- Results

- Decreased rate of stroke in intensive group
- No significant difference in:
  - Nonfatal MI or stroke or CVD death
  - Nonfatal MI, heart failure
  - Death from any cause or CVD cause
- Treating SBP to goal of $< 120$ mm Hg:
  - Increased adverse effects from meds, hypokalemia, creatinine elevations
  - Decreased macroalbuminuria

REVIEW OF CASES
Case 1- Ms. A

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Take Home Points

• Individualized approach
• Based on comorbidities, functional status, goals of care
• For adults 60-79, consider goal of <140/90
  - Possibly SBP <130 if no DM, stroke, or frailty and if no side effects
• For adults ≥ 80, consider goal of < 150/90 or higher if frail
MORE SUGAR PLEASE:

Diabetes management in older adults
Choosing Wisely

- American Geriatrics Society
- Recommends:
  - Avoiding medication to achieve hemoglobin A1c (HbA1c) < 7.5% in most older adults
  - Moderate control generally better
Rationale for Looser Blood Sugar Control

- To achieve decrease in MI and death in middle aged adults
  - Requires 10 to 19 years of treatment to HbA1c < 7.0%
- Older adults less likely to benefit from intensive control
  - Less likely newly diagnosed
  - Limited life expectancy (LE)
- Harm more likely

ADVANCE Trial

- 11,000 subjects from 20 countries
- Mean age 66 yo, mean A1c 7.5
- Intensive treatment with sulfonylurea to mean HbA1c of 6.5% compared to 7.3%
- Decreased macroalbuminuria
- No differences in MI, CV events, retinopathy, neuropathy, or all-cause mortality
- Increased hypoglycemia

ACCORD Trial

- 10,251 adults, mean 62 yo, HbA1c 8.1%
- Intensive treatment for 3.5 years to mean HbA1c 6.4% versus 7.5%
  - No difference in nonfatal MI/stroke or CV mortality
  - Increased risk:
    - Death (5.0% versus 4.0%, p = 0.04)
    - Hypoglycemia (11% versus 4%)
    - Weight gain

Hypoglycemia

- Risk factors:
  - Age
  - Comorbidities
  - Polypharmacy
- Leads to falls, injuries, hospitalization

Individualized HbA1c Goals

- Healthy, few comorbidities, LE > 10 yrs, newly diagnosed
  - 7.0-7.5%
- Moderate comorbidities, LE 5-10 yrs
  - 7.5-8.0%
- Multiple comorbidities, functional/cognitive impairments, LE < 5 years
  - 8.0-9.0%

Recommendations from Beers 2015

- Avoid long acting sulfonylureas
  - Glyburide, chlorpropamide
  - Higher risk of hypoglycemia
- Avoid sole use of sliding scale insulin
  - Higher risk of hypoglycemia without improvement in hyperglycemia
  - Regardless of care setting
DON’T FORGET THE KIDNEYS:

CKD and Medication Prescribing in older adults
CKD- Definition

- Presence of kidney damage for at least 3 months
  - eGFR of < 60 mL/min/1.73 m²
  - Proteinuria > 30mg/day (albumin)

<table>
<thead>
<tr>
<th>GFR Stage</th>
<th>GFR</th>
<th>Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>3a</td>
<td>45-59</td>
<td>Mild to moderate</td>
</tr>
<tr>
<td>3b</td>
<td>30-44</td>
<td>Moderate to severe</td>
</tr>
<tr>
<td>4</td>
<td>15-29</td>
<td>Severe</td>
</tr>
<tr>
<td>5</td>
<td>&lt;15</td>
<td>Kidney failure</td>
</tr>
</tbody>
</table>
CKD- Risk Factors

- Age >65
- Male sex
- DM, HTN, Heart failure, CVD
- Proteinuria
- Acute kidney injury episodes
- Elevated uric acid
- Smoking
- Medications
- Obesity
Estimates of Creatinine Clearance

- Modification of Diet in Renal Disease (MDRD)
- Cock-croft Gault
- CKD- Epi
MDRD

- Used by most laboratories
- Derived from Caucasian subjects, mean age 51, without diabetes
- Doesn’t include age in equation
- Overestimates GFR in older adults
- Less accurate in obesity and normal GFRs
Cockcroft-Gault

- Includes age and weight
- Uses ideal body weight
- Less accurate in obesity
- Developed prior to use of standardized creatinine assays
- Lower estimates of GFR in adults > 70 yo
- May be safer for drug dosing in older adults
CKD-Epi

• Developed to more accurately estimate GFR in patients with normal or mildly reduced GFRs
Drug Prescribing in CKD

- Consider using Cockcroft gault for drug dosing in adults > 70 yo
- Beers Criteria 2015:
  - Avoid NSAIDs if GFR < 30 ml/min
- Start low and go slow
Cleveland Clinic

Every life deserves world class care.
References


References


Timeline HTN trials in ≥ 60 yo

- **1991, 1997**: SHEP/Syst-Eur
  - Rx SBP < 160 in US and European adults ≥ 60 reduced stroke, MI, and HF
- **2005**: FEVER
  - Rx SBP < 140 in Chinese adults with mean age 62 reduced stroke, CVD, and mortality
- **2005**: HYVET
  - Rx SBP to mean SBP 144 in nonfrail adults ≥ 80 reduced all cause mortality and HF
- **2008**: JATOS
  - Rx SBP < 140 in Japanese adults 65-85 yrs showed no difference in CVD and renal disease (underpowered)
- **2010**: VALISH
  - Rx SBP to < 140 in adults 70-85 yrs showed no difference in CVD and renal disease (underpowered)
- **2015**: SPRINT
  - Rx SBP to target < 120 in adults > 50 at risk of CVD without stroke or DM reduced

Kovell LC, *J Am Heart Assoc*, 2015