Modern Management of Hypertension

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Declaration of full disclosure: No conflict of interest

Blood Pressure and Risk

- Risk of Cardiovascular Disease (CVD) is linear to Systolic Blood Pressure (SBP) level. Starts at relatively low BP’s (118 mm Hg)

- Risk doubles for every 20/10 mm Hg

- 120-139/80-89 is “pre-hypertension” and merits lifestyle modifications
Current Status of Hypertension

• Prevalence 29.1%; Blacks 42.1%
• About 75.6% treated; 51.8% controlled (<140/90)
• Risk for poor control: Latinos, Blacks, age 18-44 and ≥80, <300% poverty, < college degree
• Better control: Any insurance, ≥2 visits, and a usual source of care

Hypertension Control by Cardiovascular Disease and Risk: NHANES, 2003-04

<table>
<thead>
<tr>
<th>Condition</th>
<th>%HTN</th>
<th>%Rx</th>
<th>% Not Controlled</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average Risk</td>
<td>34</td>
<td>66</td>
<td>35</td>
</tr>
<tr>
<td>Diabetes</td>
<td>85</td>
<td>96</td>
<td>54</td>
</tr>
<tr>
<td>Chronic Kidney Disease</td>
<td>83</td>
<td>95</td>
<td>53</td>
</tr>
<tr>
<td>CHF</td>
<td>86</td>
<td>98</td>
<td>50</td>
</tr>
<tr>
<td>Cardiovascular Dis</td>
<td>85</td>
<td>95</td>
<td>51</td>
</tr>
<tr>
<td>Framingham Score ≥10</td>
<td>77</td>
<td>68</td>
<td>59</td>
</tr>
</tbody>
</table>

MMWR 2012; NCHS 2013
Bertoia ML, Hypertension 2011
Racial Differences in Impact of Elevated BP

- 27,748 patients followed for 4.5 years
- 715 strokes
- SBP 10 mm Hg: 8% increase for whites and 24% for blacks
- HR = 2.38 for stage 1 HTN, age 45-64

- Should blacks be treated more intensively?


Accurate BP Measurement

1) Seated for 5 minutes in chair
2) Arms bared and supported
3) No cigs, coffee; no talking
4) Correct fitting cuff for arm (small cuff results in elevated BP: 3/2 mm Hg - 12/8 mm Hg)
5) First appearance of sound is SBP; disappearance is DBP
6) Two or more reading in 2 minutes averaged
7) Two visits to define HTN
Treatment Based on What Blood Pressure Measurement?

- Office clinician measures are standard, used in trials
- Home BP measurement leads to less intensive drug Rx & BP control. Identifies “white-coat” HTN
- Ambulatory monitor measures higher correlation with CVD

Clinic, Home and Ambulatory BP in Diagnosis of Hypertension

- Systematic review comparing measures in initial diagnosis
- 20 studies with 5683 patients, compared to ambulatory monitor daytime mean ≥135/85

<table>
<thead>
<tr>
<th>Measure</th>
<th>Definition</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Home</td>
<td>135/85 mean</td>
<td>85.7%</td>
<td>62.4%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>+LR = 2.28</td>
<td>–LR= 0.23</td>
</tr>
<tr>
<td>Clinic</td>
<td>140/90 mean</td>
<td>74.6%</td>
<td>74.6%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>+LR = 2.94</td>
<td>+LR = 0.34</td>
</tr>
</tbody>
</table>

Individual Lifestyle Modifications for Hypertension Control

• Weight loss if overweight: 5-20 mm Hg/10-kg weight loss
• Limit alcohol to ≤ 1 oz/day: 2-4 mm Hg
• Reduce sodium intake to ≤100 meq/d (2.4 g Na): 2-8 mm Hg in SBP
• DASH Diet: 6 mm alone; 14 mm plus Na
• Physical activity 30 min/day: 4-9 mm Hg
• Habitual caffeine consumption not associated with risk of HTN

Joint National Commission 8 (JNC 8)

Three questions:
1) Does Rx at specific BP thresholds improve outcomes?
2) Does Rx to a specific BP goal improve outcomes?
3) Do various meds differ on outcomes?

Nine recommendations
Recommendations for Management of Hypertension

Recommendation 1
≥60 years:

- Lower BP at SBP ≥150 mm Hg or DBP ≥90 mm Hg
- Treat to a goal SBP <150 mm Hg and goal DBP <90 mm Hg.

Strong Recommendation – Grade A (but not unanimous)

Recommendation 1

- Evidence from 6 studies of patients over age 60, treated to goal ≤150/90: HYVET, Syst-Eur, SHEP, JATOS, VALISH, CARDIO-SIS

- Some evidence (lower quality) comparing ≤160 to ≤140 and ≤150 to ≤140 showing no additional benefit
Hypertension in the Very Elderly Trial (HYVET)

- 3845 patients ≥ 80 y, 2 years
- >160 mm Hg – goal of 150/80 mm Hg BP=173/91
- Indapamide SR 1.5 mg vs. placebo
  Added perindopril if needed

Beckett NS, NEJM 2008; 358: 1887-1898

HYVET Study Results

<table>
<thead>
<tr>
<th>End Point</th>
<th>Meds</th>
<th>Placebo</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke</td>
<td>12.4</td>
<td>17.7</td>
<td>0.64 (0.46 -0.95)</td>
</tr>
<tr>
<td>CVA Death</td>
<td>6.5</td>
<td>10.7</td>
<td>0.55 (0.33 -0.93)</td>
</tr>
<tr>
<td>CHF</td>
<td>5.3</td>
<td>14.8</td>
<td>0.28 (0.17 -0.48)</td>
</tr>
<tr>
<td>CV Death</td>
<td>23.9</td>
<td>30.7</td>
<td>0.73 (0.55 -0.97)</td>
</tr>
<tr>
<td>Any Death</td>
<td>47.2</td>
<td>59.6</td>
<td>0.72 (0.59-0.88)</td>
</tr>
</tbody>
</table>

Beckett NS, NEJM 2008; 358: 1887-1898
HYVET Conclusions and Implications

• Benefits appear at 1 year of Rx
• NNT = 20 to prevent one stroke
• NNT = 10 to prevent one CHF
• Never too old to treat SBP > 160
• Goal does not have to be < 140

73 yo woman. BP=148/88. No Diabetes, Kidney normal. Otherwise well. On non-drug therapy. The next best step is:

1) Continue current therapy
2) Begin hydrochlorothiazide
3) Begin ace inhibitor
4) Begin calcium channel blocker
5) Begin beta blocker
73 yo woman. BP=148/88. No Diabetes, Kidney normal. Otherwise well. On non-drug therapy. The next best step is:

1) Continue current therapy
2) Begin hydrochlorothiazide
3) Begin ace inhibitor
4) Begin calcium channel blocker
5) Begin beta blocker

Recommendations for Management of Hypertension

Corollary Recommendation
≥60 years:

♣ If treatment results in lower SBP (eg, <140 mm Hg) and is well tolerated treatment does not need to be adjusted.

Expert Opinion – Grade E
Recommendations for Management of Hypertension

Recommendation 2
<60 years:
- Treat to lower BP at DBP $\geq 90$ mm Hg
- Treat to a goal DBP $<90$ mm Hg.

30-59 years, Strong Recommendation – Grade A
18-29 years, Expert Opinion – Grade E

Recommendation 3
<60 years:
- Treat to lower BP at SBP $\geq 140$ mm Hg
- Treat to a goal SBP $<140$ mm Hg.

(Expert Opinion – Grade E)
Recommendations for Management of Hypertension

Recommendation 4
≥18 years with chronic kidney disease (CKD) (GFR < 60 or proteinuria >30 mg alb/g creat):
- Treat to lower SBP ≥140 mm Hg or DBP ≥90 mm Hg
- Treat to goal SBP <140 mm Hg and goal DBP <90 mm Hg.

Expert Opinion – Grade E

Recommendation 5
≥18 years with diabetes, treat to lower BP at SBP ≥140 mm Hg or DBP ≥90 mm Hg
- Treat to a goal SBP <140 mm Hg and goal DBP <90 mm Hg.

Expert Opinion – Grade E
**Intensive BP Control in Type 2 DM: ACCORD**

- RCT of 4733 patients with type 2 DM
- Compare BP less than 120 mm Hg vs 140

<table>
<thead>
<tr>
<th></th>
<th>120</th>
<th>140</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>BP</td>
<td>119</td>
<td>133</td>
<td></td>
</tr>
<tr>
<td>CV events plus death</td>
<td>1.87%</td>
<td>2.09%</td>
<td>.20</td>
</tr>
<tr>
<td>Mortality</td>
<td>1.28%</td>
<td>1.19%</td>
<td>.55</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.32%</td>
<td>0.53%</td>
<td>.01</td>
</tr>
<tr>
<td>Adverse events</td>
<td>3.3%</td>
<td>1.3%</td>
<td>.001</td>
</tr>
</tbody>
</table>

- In type 2 DM: treating to 120 mm Hg did not reduce the rate of composite fatal and non-fatal CV events

**Recommendations for Management of Hypertension**

**Recommendation 6**

Nonblack population, including diabetes:

Initial treatment:
- ✔ Thiazide-type diuretic
- ✔ Calcium channel blocker (CCB)
- ✔ Angiotensin-converting enzyme inhibitor (ACEI)
- ✔ Angiotensin receptor blocker (ARB).

(Moderate Recommendation – Grade B)
Thiazide Diuretics

- Very effective for systolic BP
- Do not increase sudden death
- Most effective in LVH regression
- Lipid effects are short lasting (1 y)
- Hyperglycemia only in high doses
- Still effective in early chronic kidney disease (to GFR 40-45)
- Erectile dysfunction in 20%
- More effective in Blacks and older

### Efficacy of HCTZ

Messerli FH, et al. JACC 2011; 57: 590-600

<table>
<thead>
<tr>
<th>Medication Class</th>
<th>Decrease in mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCTZ 12.5 -25 mg</td>
<td>6.5/4.5</td>
</tr>
<tr>
<td>HCTZ 50 mg</td>
<td>12.0/5.4</td>
</tr>
<tr>
<td>ACE-I</td>
<td>12.9/7.7</td>
</tr>
<tr>
<td>ARB</td>
<td>13.3/7.8</td>
</tr>
<tr>
<td>CCB</td>
<td>11.0/8.1</td>
</tr>
<tr>
<td>Beta Blockers</td>
<td>11.2/8.5</td>
</tr>
</tbody>
</table>
Beta Blockers

- Most effective as mono-therapy in younger persons and whites
- Adverse effects: no clear depression or sexual dysfunction, but + fatigue
- Glucose elevation with A1C increase by 0.2%
- No lasting effect on lipids
- Less efficacy in stroke prevention among those older than 60 years

Atenolol in hypertension: is it a wise choice?

No benefit to prevent MI or All-cause mortality

Bo Carlberg, LANCET 2004, Vol 364
**ACE–I or ARB**

- 30% reduction of ESRD (dialysis) and of doubling of serum creatinine; optimal with GFR 30-60, proteinuria
- Not better tolerated than other drugs
- Regression of LVH not more than other drugs–SBP reduction
- Elevates K+
- Do not use in women < 50 y
- Works less well in Blacks as 1 drug
- Best choice in diabetes (in non-blacks)
- Don’t combine

**Calcium Channel Blockers**

- Effective in Blacks and elderly
- Effective in preventing CV events
- No increase risk of cancer
- Short acting CCB may be harmful
- Effective in systolic hypertension
- Better outcomes in latest trials
ACCOMPLISH
Calcium Blockers Combined with ACE

• Comparison of combinations: ACE-I + HCTZ vs. ACE-I + amlodipine. 3 yrs

• RCT, 11,506 patients, ≥ 65 y, 60% men, 83% White, 60% diabetes, BMI = 31

• Outcomes: CV death, MI, stroke, hospitalization for angina, resuscitation after cardiac arrest, CABG or PCI

• Funded by Novartis: USA and 4 N Europe

Jamerson K, NEJM 2008; 359:2417-28

ACCOMPLISH Results

<table>
<thead>
<tr>
<th>Primary Outcomes</th>
<th>Benazepril + Amlodipine N=5744</th>
<th>Benazepril + HCTZ N=5762</th>
<th>Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Events</td>
<td>552 (9.6%)</td>
<td>679 (11.8%)</td>
<td>0.80 (0.72-0.90)</td>
</tr>
<tr>
<td>CV Death</td>
<td>107 (1.9%)</td>
<td>134 (2.3%)</td>
<td>0.80 (0.62-1.03)</td>
</tr>
<tr>
<td>All MI</td>
<td>125 (2.2%)</td>
<td>159 (2.8%)</td>
<td>0.78 (0.62-0.99)</td>
</tr>
<tr>
<td>All Strokes</td>
<td>112 (1.9%)</td>
<td>133 (2.3%)</td>
<td>0.84 (0.65-1.08)</td>
</tr>
<tr>
<td>Revasc procedure</td>
<td>334 (5.8%)</td>
<td>386 (6.7%)</td>
<td>0.86 (0.74-1.00)</td>
</tr>
</tbody>
</table>
ACCOMPLISH Conclusions

- Combination of CCB and ACE was superior to ACE/HCTZ
- BP differences of 1 mm only
- Different populations may matter
- Chlorthalidone vs. HCTZ?
- Recommendation to change practice in highest risk patients – ACE and CCB may have special benefits

53 yo African-American woman, BP=148/88. Has Diabetes Type 2, Kidney normal. Otherwise well. On non-drug therapy. The next best step is:

1) Continue current therapy
2) Begin hydrochlorothiazide
3) Begin ace inhibitor
4) Begin calcium channel blocker
5) Begin angiotensin receptor blocker
53 yo African-American woman, BP=148/88. Has Diabetes Type 2, Kidney normal. Otherwise well. On non-drug therapy. The next best step is:

1) Continue current therapy
2) Begin hydrochlorothiazide
3) Begin ace inhibitor
4) Begin calcium channel blocker
5) Begin angiotensin receptor blocker

Recommendations for Management of Hypertension

Recommendation 7
Black population, including diabetes:

Initial treatment:
✓ Thiazide-type diuretic
✓ Calcium Channel Blocker (CCB)

General black population: Moderate Rec – Grade B
Black patients with diabetes: Weak Rec – Grade C
Recommendations for Management of Hypertension

Recommendation 8
≥18 years with CKD, initial (or add-on) treatment:

❖ ACEI or ARB to improve kidney outcomes.

❖ For all CKD patients with HTN regardless of race or diabetes

Moderate Recommendation – Grade B

Recommendation 9
❖ If goal BP not reached within 1 month, increase the dose of the initial drug or add a second drug from one of the classes in recommendation 6 (thiazide-type diuretic, CCB, ACEI, or ARB).

❖ Assess BP and adjust the treatment regimen until goal is reached.

❖ If goal cannot be reached with 2 drugs, add and titrate a third drug from the list provided.

JAMA 2014;311(5):507-520.
Recommendations for Management of Hypertension

Recommendation 9

- Do not use and ACE and an ARB in the same patient.

- If goal cannot be reached using the drugs in rec 6 drugs from other classes can be used.

- Referral to a specialist may be indicated

- Expert Opinion – Grade E

Evidence-based Medications

ACE inhibitors
- Captopril
- Enalapril
- Lisinopril

Angiotensin receptor blockers
- Eprosartan
- Candesartan
- Losartan
- Valsartan
- Irbesartan
Evidence-based Medications

Beta blockers
  Atenolol, Metoprolol
Calcium channel blockers
  Amlodipine, Diltiazem ER, Nitrendipine
Thiazide-type diuretics
  Bendroflumethiazide, Chlorthalidone, Hydrochlorothiazide, Indapamide

Strategies to Dose BP Meds

1) One drug, titrate to max, add second
2) One drug, add second before max of initial
3) Two drugs at same time, separate or as combo
Resistant Hypertension

- Not reaching goal BP despite three medications from different classes (including one diuretic)
- Adherence is number one cause
- Avoid NSAID, decongestants, speed
- Other causes not common

What About Other Drugs?

- Spironolactone
- Beta blockers
- CNS sympatholytics: Clonidine
- Methyldopa: Little reason to use
- Alpha-1 blockers: OK but inferior as single drug and tachyphylaxis
- Labetalol good 5th or 6th choice
- Direct vasodilators - hydralazine or minoxidil - need more diuretics
- Peripheral adrenergic antagonists
**British Management of Hypertension**

- If BP 140/90 in office, use ambulatory monitor to confirm
- Estimate CV risk, evaluate for target organ effects (LVH, CKD, retinopathy)
- Treat stage 1 with meds only if target organ damage, known CVD, diabetes, 10-year CV risk ≥ 20%
- Offer meds to all at any age with stage 2 (>155/95) independent of other effects

Krause, BMJ 2011
Kaiser Northern California HTN Program

- 80% control

Key elements

- Patient registry
- Sharing of performance metrics
- Evidence-based guidelines
- Medical assistant/pharmacist visits
- Single pill combination therapy

Jaffe, JAMA 2013

Key Points of JNC 8

1) ≥60 yo: goal ≤150
2) Others <140/<90 (including DM, CKD, race/ethnicity)
3) Non blacks: thiazide, CCB, ACEI, ARB
4) Blacks: thiazide, CCB
5) CKD: ACEI or ARB
Other Take Home Points

- Most patients will need two or more drugs to achieve goal SBP
- Control only occurs with motivated patients who trust their clinician

One Other Key Point

Take the BP accurately yourself, and record it in the medical record.