MANAGEMENT OF HYPERTENSION

- Definitions
- Epidemiology
- Measurements
- Evaluation
- Post Guideline Mania (Choosing the BP target)
- Treatment

DISCLOSURES:
SPRINT Investigator (SPRINT ASK follow up completed 5/2018)
DETERMINANTS AND INTERACTIONS IN PRIMARY HTN

Carey RM et al
*J of the Am Coll Cardiol.* 2018;72 (11): 1278-1293
HYPERTENSION

• 54% strokes
• 47% of ischemic heart disease
• 13.5% premature deaths
• 6% disability-adjusted life years
• SBP >115 and DBP >75 linearly associated with ↑CV events
<table>
<thead>
<tr>
<th>Definitions</th>
<th>Office-Based BP (mm Hg)</th>
<th>24-Hour mean Ambulatory BP (mm Hg)</th>
<th>Self-Recorded BP (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt;120/80</td>
<td>&lt;115/75</td>
<td>&lt;120/80</td>
</tr>
<tr>
<td>Elevated BP</td>
<td>120-129/&lt;80</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>HTN, Stage 1</td>
<td>130-139/80-89</td>
<td>≥125/75</td>
<td>≥130/80</td>
</tr>
<tr>
<td>HTN, Stage 2</td>
<td>≥140/90</td>
<td>≥130/80</td>
<td>≥135/85</td>
</tr>
<tr>
<td>White Coat HTN</td>
<td>≥130/80</td>
<td>&lt;125/75</td>
<td>&lt;130/80</td>
</tr>
<tr>
<td>Masked HTN</td>
<td>&lt;130/80</td>
<td>≥125/75</td>
<td>≥130/80</td>
</tr>
</tbody>
</table>

**Resistant HTN:** Rx 3 different categories including diuretic, not at target.
BP MEASUREMENT - PROPER TECHNIQUE

• Quiet environment, seated, back support, feet on floor, 5 min of rest
• Remote from tobacco, caffeine, exercise, medication,
• Arm supported, cuff at heart level; arm bare
• Bladder portion large enough to encircle 80% of upper arm
• Two measurements at least 30 seconds apart
• SBP higher, DBP lower in distal arteries
Office BP (automated preferred) for screening
Drug Initiation/titration based on ABPM or HBPM
HBPM in almost all, similar to daytime ABPM
Evidence: HBPM managing, improving BP
Available, low cost, good acceptance
7-day HBPM, AM, PM
  minimum 4 days
  exclude first day
ABPM

- Day BP every 15 to 20 min; night BP every 30 to 60 min
- Normal
  
  day average <130/80
  night average <110/65
  24-hour average <125/75
  Night dipping – night BP 15% < day BP
- HTN by ABPM associated with risk of CV death vs home, office
- Non dipping associated with LVH
- High night BP “reverse” strongly associated with CV death
RCT: UNOBSERVED VS OTHER CLINIC BPS

EVALUATION AFTER HTN DIAGNOSED

• History
  - family hx
  - drugs
  - CVD risk

• Physical examination
  - accurate BP in both arms
  - abdominal bruit, enlarged thyroid
  - potential end-organ targets
EVALUATION AFTER HTN DIAGNOSED

- Lab
  - renal function
  - fasting BS
  - fasting lipid
  - serum Ca, K
  - urinalysis
  - Urine albumin/creatinine
  - EKG (echo if LBBB, known heart disease, white coat HTN)
  - aldosterone-plasma renin ratio (hypokalemia, BP > 160/100, resistant HTN)
FEATURES OF SECONDARY HTN

• Age of onset < 20 or > 50
• BP > 180/110
• Organ damage
• Findings suggestive of secondary HTN
  - unprovoked hypokalemia
  - abdominal bruit
  - variable pressures with sweating, tachycardia, tremor
  - Cr > 1.5 mg/dL
• Poor response to generally effective therapy
• Controlled HTN now resistant in setting of compliance
SECONDARY HYPERTENSION

- CKD
- Renal Vascular Hypertension
  - FMD (young female, IR Intervention)
  - ASVD (medical management)
- Hyperaldosteronism
  - hypokalemia, BP > 160/100, resistant HTN
  - aldo(ng/dL), renin(ng/ml/hr)
    - dx if ratio > 25 with aldo > 15 ng/dL
- Pheochromocytoma
  - triad of episodic headache, sweating, and tachycardia associated with coincident↑ in BP
ACC/AHA 2017 HIGH BP GUIDELINES

• 11 organizations
• 116 recommendations
  Class of recommendation
  Level of Evidence
• 448 evidence tables
• Peer Review
  5 ACC/AHA officials
  9 partners
  38 expert global content reviewers
“THE NEW BP GUIDELINES”
ACC/AHA Guidelines vs JNC 7

• Focus on overall 10-yr CV risk
• Changes definition for diagnosis of HTN; makes it a goal
• Goal to minimize CV risk
• Strongly endorses HBPM
• Underscores need for correct measurements
• Expands on importance of lifestyle modification
• Acknowledges sleep disorders
• Based largely on SPRINT
“THE NEW BP GUIDELINES” ACC/AHA

• Elevated BP or stage 1 HTN
  - Lifestyle Modification if 10 yr CVD risk < 10%
• Stage 1 HTN
  - AHT if 10 yr CVD risk ≥ 10%

• ≥ 65 yrs old, high comorbidity, limited life time
  - Clinical judgment
  - Patient preference
  - Team approach: risk/benefit of ↓ BP, target, AHT choice

• Target SBP < 130/80
  - Community-dwelling patients ≥ 65 yrs old
  - DM, CKD, stable CVD, CHF
CONSEQUENCE OF ACC/AHA GUIDELINES

• Cutoff change from $\geq 140/90$ to $\geq 130/80$ ↑ prevalence from 32% to 46%

• 1. 9% ↑ in initiating drug compared to previous guidelines

• 22 % US adults: lifestyle modification
“THE NEW BP GUIDELINES”
ACP and AAFP Joint Practice Guideline for SBP targets for > 60 yr olds

• Start or intensify treatment for persistent SBP $\geq 150$
  - Target SBP $\leq 150$ to ↓ stroke, cardiac events, death (strong evidence)

• Hx of stroke, TIA or CVD risk, consider starting or ↑ AHT if SBP $\geq 140$
  - ↓ stroke risk, cardiac events (weak evidence)

• Based on “high value medicine”
  - Benefit with acceptable harms and costs
WHAT TO DO
RCTs (post hoc/secondary/meta analyses), observational studies, guidelines, populations, individuals

63 year old women
BP 148/86
STROKE RISK BY GUIDELINE: 63 Y/O BP 148/86

- TARGETS (AHT #)
  - ACC/AHA 130/80 (1)
  - ESH/ESC 140/80 (2)
  - ACP/AAFP 150/90 (0)

- Absolute risk of stroke mortality
  - 5% ACC/AHA target
  - 8% ESH/ESC target
  - 14% ACP/AAFP target

DETERMINING A BP GOAL

• Risk vs benefit understanding by patient
• Consider CV risk (CKD not in calculators)
• Consider frailty, comorbidities
• Consider drug-drug interactions
• Guidelines will continue to evolve
• Individualize
• Post guideline science
LONG TERM RISK ASSOCIATED WITH STAGE 1 HTN

- 21,441 (China)
- Recruited 1992-2004
- Age 35-64
- No CVD at baseline
- Follow-up: mean 13 yrs
- Followed until 1/2014
LONG TERM RISK ASSOCIATED WITH STAGE 1 HTN
AGE 35-59 VS AGE ≥ 60

- 34-59 yrs n=19,285; ≥ 60 yrs n = 2,156

- Higher risk in younger suggests incremental risk over time when risk factors left untreated

- Strong argument to support aggressive and early treatment

AHA/ACA 2017 APPLIED TO REGARDS (REasons for Geographic And Racial Differences in Stroke)

- N= 29,218
- Mean age 64
- Recruited 2003-2007
- Followed until 2014
- Divided into yes AHT, no AHT

Colantonio LD et al. *J of the Am Coll Cardiol.* 2018;72(11): 1187-1197
REGARDS: CV EVENTS

<table>
<thead>
<tr>
<th>BLOOD PRESSURE</th>
<th>CV EVENTS (per 1000 person-yrs)</th>
<th>ALL CAUSE MORTALITY (per 1000 person-yrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOT TAKING AHT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 140 or ≥ 90</td>
<td>22.7</td>
<td>32.9</td>
</tr>
<tr>
<td>130 to &lt; 140 or 80 to &lt; 90</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AHT Recommended</td>
<td>20.5</td>
<td>29.6</td>
</tr>
<tr>
<td>AHT Not Recommended</td>
<td>3.4</td>
<td>4.8</td>
</tr>
<tr>
<td>TAKING AHT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 140 or ≥ 90</td>
<td>33.6</td>
<td>42.5</td>
</tr>
<tr>
<td>130 to &lt; 140 or 80 to &lt; 90</td>
<td></td>
<td></td>
</tr>
<tr>
<td>↑ AHT Recommended</td>
<td>22.4</td>
<td>29.9</td>
</tr>
<tr>
<td>↑ AHT Not Recommended</td>
<td>3.8</td>
<td>5.6</td>
</tr>
</tbody>
</table>

- 4094 CV events (stroke, MI, CHF)
- AHA/ACC guidelines: direct drug initiation/↑ to high CVD risk patients

Colantonio LD et al. *J of the Am Coll Cardiol.* 2018;72(11): 1187-1197
COST EFFECTIVENESS: INTENSIVE VS. STANDARD BP CONTROL IN SPRINT

- Simulation models
- Cost effective <$50,000 per QALY
- Base case
  - Cost $47,000 per QALY gained
  - Probability cost-effective 54%
- Best-case (adherence and treatment effects persist)
  - Cost $28,000 per QALY gained
  - Probability cost-effective 79%

ADVERSE AND SERIOUS ADVERSE EVENTS IN SPRINT

Total number of serious adverse events similar in two arms of trial

<table>
<thead>
<tr>
<th>Variable</th>
<th>Intensive Treatment (N = 4678)</th>
<th>Standard Treatment (N = 4683)</th>
<th>Hazard Ratio</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of serious adverse events</td>
<td>1793 (38.3)</td>
<td>1736 (37.1)</td>
<td>1.04</td>
<td>0.25</td>
</tr>
<tr>
<td>Emergency department visit or serious adverse event</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypotension</td>
<td>158 (3.4)</td>
<td>93 (2.0)</td>
<td>1.70</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Syncope</td>
<td>163 (3.5)</td>
<td>113 (2.4)</td>
<td>1.44</td>
<td>0.003</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>104 (2.2)</td>
<td>83 (1.8)</td>
<td>1.25</td>
<td>0.13</td>
</tr>
<tr>
<td>Electrolyte abnormality</td>
<td>177 (3.8)</td>
<td>129 (2.8)</td>
<td>1.38</td>
<td>0.006</td>
</tr>
<tr>
<td>Injurious fall†</td>
<td>334 (7.1)</td>
<td>332 (7.1)</td>
<td>1.00</td>
<td>0.97</td>
</tr>
<tr>
<td>Acute kidney injury or acute renal failure‡</td>
<td>204 (4.4)</td>
<td>120 (2.6)</td>
<td>1.71</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

SPRINT ELIGIBILITY APPLIED TO NHANES

- Prevent 179,600 deaths/yr
- Prevent 46,100 cases of CHF/yr
- Careful patient selection and implementation

BASELINE DPB AND EFFECT OF INTENSIVE SBP GOAL
The Notorious J Curve

- Studies of achieved BP suggest J-curve relationship of DBP with CV events
- Intensive treatment benefit still realized with low levels of DBP in SPRINT
- BP lowering: go slow
SPRINT
ELDERLY
OUTCOME, SYNCOPE, HYPOTENSION & FALLS IN SPRINT NOT MODIFIED BY AGE

• Primary composite outcome HR, 0.66 [95% CI, 0.51–0.85]

• All-cause mortality HR, 0.67 [95% CI, 0.49–0.91]

• Syncope, Low BP, falls (In. vs Std.)
  - absolute risk increased in elderly
  - relative risk no different from young

PREVALENCE RATES OF INJURIOUS FALLS AND SYNCOPE SPRINT VS. THE IRISH LONGITUDINAL STUDY ON AGING (TILDA) PARTICIPANTS ≥75 YEARS OLDER

- External validity?
- TILDA- self report
- Rates: TILDA 5 x SPRINT
- Falls not considered in Bress et al cost analysis (no difference in treatment arms)
- SAEs would have to be 7 x higher in SPRINT a lower value (> $100,000 QALY)
- Individualize

Sexton DJ et al. JAMA IM. 2017: 177,(9);1385-1387
SPRINT AND THE KIDNEY

AKI
Incident CKD
CKD Subgroup
AKI MORE COMMON IN INTENSIVE ARM

Stage 1 (>0.3 mg/dl ↑ in Cr or 1.5-2.0 fold ↑ in Cr)
Stage 2 (>2.0 – 3.0 fold ↑ in Cr)
Stage 3 (>3.0 fold ↑ in Cr, or dialysis)

N = 219
N = 129

RECOVERY FROM AKI BY STAGE
(>90% partial, complete)

eGFR IN SPRINT

- 4.71 mL/min/1.73 m² lower eGFR at 42 mo in intensive arm
- Hemodynamic effect

CUMULATIVE INCIDENCE OF INCIDENT CKD IN SPRINT

- pre-specified incident CKD defined as >30% decrease in eGFR to <60 ml/min/1.73 m²);

- HR [95% CI] 3.54 [2.50, 5.02] \(P < 0.001\)

- % Absolute ↑ risk -3 yrs [95% CI] 2.6 [1.9,3.3]

- Reclassification: 6 standard vs 20 intensive (no ESRD)

SPRINT IN CKD PATIENTS (stay tuned)

- Primary outcome not modified by CKD
- Differences from 6 month baseline in eGFR between groups not clinically significant
- Biomarkers of parenchyma damage supportive of hemodynamic effect

TYPE 2 DIABETES
ACCORD REVISITED
HYPERTENSION

• How low to go (RCTs internal validity, ? external validity)

ACCORD
  Negative except for stroke
  Underpowered Older with high CVD burden
  Complicated DM long standing, poor control

SPRINT
  Stopped early because of benefit (MIND, Kidney results 2019)
  Measurements
  SAEs
  Exportability to practice ?
  Cost
SPRINT ELIGIBILITY APPLIED TO ACCORD STANDARD GLYCEMIC COHORT

SPRINT Primary Endpoint
composite of MI, ACS, stroke, acute decompensated CHF, or CV mortality

ACCORD Primary Endpoint
non fatal MI, non fatal stroke, CV mortality

INTENSIVE N=652
STANDARD N=632

Buckley LF et al. *Diabetes Care* 2017;40:1733–1738
ACCORD AND THE KIDNEY

• Slopes similar to SPRINT
• Larger changes in eGFR

INTENSIVE SBP CONTROL AND INCIDENT CKD: SPRINT vs. ACCORD

TREATMENT OF HTN

• Life style modification using behavioral and motivational strategies
  - vegetables, fruits, whole grains, legumes, low-fat dairy
  - sweets, red meat, saturated/total fat
  - Weight reduction
  - Exercise
  - dietary potassium
  - limit alcohol
  - tobacco cessation
SALT AND DASH

• Sodium reduction lowers BP over 4 weeks, and possibly beyond 4 weeks
• DASH diet lowers BP quickly

CVD RISK FACTORS COMMON IN PATIENTS WITH HYPERTENSION

MODIFIABLE RISK FACTORS

• Current cigarette smoking, secondhand smoking
• Diabetes mellitus
• Dyslipidemia/high cholesterol
• Overweight/obesity
• Physical inactivity/low fitness
• Unhealthy diet

RELATIVELY FIXED RISK FACTORS

• CKD
• Family history
• Increased age
• Low socioeconomic/educational status
• Male sex
• Obstructive sleep apnea
• Psychosocial stress

2017 ACC/AHA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults
CLASSES OF ANTIHYPERTENSIVES

- Angiotensin Converting Enzyme (ACE) Inhibitors / Angiotensin Receptor Blockers (ARBs) / Direct Renin Inhibitors (DRI)
- Diuretics: Thiazides / Loop
- Calcium Channel Blockers
  - Beta-Blockers
  - Central Adrenergic Inhibitors e.g. clonidine
  - Peripheral Alpha blockers: e.g. prazosin
- Aldosterone blockade (mineralocorticoid receptor antagonists (MRA))
- Vasodilators: e.g. minoxidil, hydralazine
- Anti-anxiety Rx
AHT TREATMENT OF HTN

• Drugs with longer t^{1/2} (chlorthalidone, amlodipine, lisinopril, telmisartan)
• Aim for 24 hr control
• Consider night time dosing
• Recognize
  Contraindications
  Side effects
  Drug-drug interactions
• Compelling indications
  DM with proteinuria: ACEI or ARB
  Beta Blocker post MI
  CKD stage 4,5: thiazides loose potency, require loop diuretics
AHT TREATMENT OF HTN

• Combination AHT when BP >20/10 mm Hg above goal
• Moderate dose of 2 AHT more successful achieving BP, vs 1 agent at max dose
  
  Minimizes side effect

• Avoiding Cardiovascular Events in Combination Therapy in Patients Living with Systolic HTN (ACCOMPLISH) trial
  
  ACEI and CCB vs. ACEI and thiazide ↓ CV eventa

• ACEI/ARB/DRI combination contraindicated
AHT TREATMENT OF HTN IN BLACKS

- Two or more drugs to achieve BP <130/80
- Initial RX: thiazide or CCB (including Diabetics)
- Have less BP lowering with equivalent ACEI dose vs. whites
- ACEI vs. CCBs have 50% higher rate of stroke
- Thiazide vs ACE inhibitor ↓ CV events
Clinician’s Flow Chart for Management of HTN

Use team-based care

Measure office BP accurately

Confirm diagnosis with HBPM

Detect white coat HTN, masked HTN by using ABPM and HBPM

Evaluate for secondary HTN

Identify target organ damage

Introduce lifestyle interventions

Identify and discuss treatment goals

Use ASCVD risk estimation to guide BP threshold for AHT drugs

Align treatment options with comorbidities

Consider age, race, ethnicity, sex, special circumstances in AHT
<table>
<thead>
<tr>
<th>Step</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initiate AHT pharmacological therapy</td>
<td>(once a day, pill burden, side effects, interactions)</td>
</tr>
<tr>
<td>Insure appropriate follow-up</td>
<td>(q mo until at goal, then q 3 mo)</td>
</tr>
<tr>
<td>Use team-based care</td>
<td></td>
</tr>
<tr>
<td>Connect patient to clinician via telehealth, social media, texting</td>
<td></td>
</tr>
<tr>
<td>Detect and reverse nonadherence</td>
<td></td>
</tr>
<tr>
<td>Detect white coat effect or masked uncontrolled HTN</td>
<td></td>
</tr>
<tr>
<td>Use health information technology for remote monitoring/self-monitoring</td>
<td></td>
</tr>
</tbody>
</table>

Modified 2017 ACC/AHA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults