

Hypertension: JNC-8 and beyond

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Disclosure

- No real or potential conflict of interest to disclose
- No off-label, experimental or investigational use of drugs or devices will be presented.

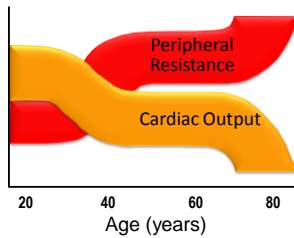
Objectives

- Upon completion of the learning activity the participant will be able to:
 - Describe the clinical consequences of hypertension.
 - Identify the recommended use of antihypertensive medications per current recommendation for adults and elders.
 - Discuss recommendations for antihypertensive therapy with select comorbid conditions.

Evidence-based Guideline for the Management of High BP in Adults: Report from the Panel Members Appointed to the Eighth Joint National Committee (JNC-8)

The Eighth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. JAMA. Doi: 10.1001/jama.2013.284427

$BP = HR \text{ (Heart Rate)} \times SV \text{ (Stroke Volume)} \times PR \text{ (Peripheral Resistance, Also Known as Peripheral Vascular Resistance \{PVR\})}$



Definition of Hypertension



Definition of HTN unchanged from through JNC-1, JNC-2, JNC-3, JNC-4, JNC-5, JNC-6, JNC-7, JNC-8 (one exception)

HTN: A Complex Disease with a Core Defect of Vascular Dysfunction that Leads to Select Target Organ Damage (TOD)

Treating HTN Goal=Reach BP goal while minimizing risk of HTN TOD

HTN TOD



- Brain
 - Stroke
 - 35–40% rate reduction with HTN treatment
 - Vascular (multi-infarct) dementia

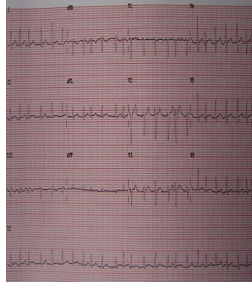
HTN TOD (continued)

- Eye
 - HTN retinopathy with risk of blindness



Hypertension TOD Atrial Fibrillation

- HTN=Major AF development risk factor
 - New onset of AF approx. 2% per year age ≥ 65 years
 - Evidence that HTN control prevents its development/recurrence



Establishing the Diagnosis of HTN

Key to Effective Practice An Accurate BP Measurement

- ≥ 2 measurements per visit
 - Auscultatory method preferred
- Patient seated comfortably for ≥ 5 minutes with back supported, feet on floor, arm supported in horizontal position
- BP cuff at heart level
 - Technique for home or clinic

Key to Effective Practice
An Accurate BP Measurement
(continued)

- BP cuff size
 - Covers more than 80% of upper arm
 - Cuff’s bladder approximately 40% of arm circumference
 - Use of too small cuff can lead to a falsely elevated BP
 - Source: <http://hyper.ahajournals.org/content/24/6/786.abstract>

Key to Effective Practice
An Accurate BP Measurement
(continued)

- Additional measure
 - Measured with patient standing for 1–3 minutes to evaluate for postural hypotension or hypertension

What about lifestyle modification in treatment of hypertension?

AHA/ACC Guideline on Lifestyle Management to Reduce Cardiovascular Risk:
A Report of the American College of Cardiology/American Heart Association Task Force on Practice of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

Available at
<http://circ.ahajournals.org/content/early/2013/11/11/01.cir.000.0437740.48606.d1.citation>

Advise adults who would benefit from BP lowering to:

- Preferable diet
 - Vegetables, fruits, and whole grains; includes low-fat dairy products, poultry, fish, legumes
 - Nontropical vegetable oils and nuts
 - Limits intake of sweets, sugar-sweetened beverages, and red meats

Advise adults who would benefit from BP lowering to:
(continued)

- Engage in aerobic physical activity
 - 3 to 4 sessions a week
 - Lasting on average 40 minutes per session
 - Involving moderate-to-vigorous intensity physical activity

What is the effect of different levels of dietary sodium intake on BP?

- In adults 30 to 80 years of age with or without HTN, counseling to reduce sodium intake by an average 1,150 mg/day reduces BP by 3–4/1–2 mm Hg.

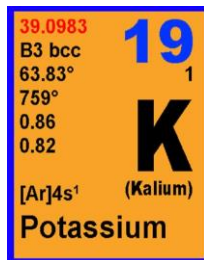


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22

What is the effect of dietary intake of potassium on BP and CVD outcomes?

- There is insufficient evidence to determine whether increasing dietary potassium intake lowers BP.



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23

What is the effect of dietary intake of potassium on BP and CVD outcomes? (continued)

- In observational studies with appropriate adjustments (BP, sodium intake, etc.), higher dietary potassium intake is associated with lower stroke risk.

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24

What is the effect of dietary intake of potassium on BP and CVD outcomes? (continued)

- There is insufficient evidence to determine whether there is an association between dietary potassium intake and CHD, HF, and cardiovascular mortality.

When to initiate pharmacologic therapy, establishing treatment goals per JNC-8

Applying Classification of Recommendation and Level of Evidence

ESTIMATE OF CERTAINTY (PRECISION) OF TREATMENT EFFECT	SIZE OF TREATMENT EFFECT			
	CLASS I Benefit >>> Risk Procedure/Treatment SHOULD be performed/administered	CLASS IIa Benefit >> Risk Additional studies with focused objectives needed IT IS REASONABLE to perform procedure/administer treatment	CLASS IIb Benefit > Risk Additional studies with broad objectives needed; additional rigidity data would be helpful Procedure/Treatment MAY BE CONSIDERED	CLASS III No Benefit or Harm Treatment is not useful, ineffective, or may be harmful Use of Procedure/Treatment is not recommended
LEVEL A Multiple populations evaluated? Data derived from multiple randomized clinical trials or meta-analyses	<ul style="list-style-type: none"> Recommendation that procedure or treatment is useful/effective Sufficient evidence from multiple randomized trials or meta-analyses 	<ul style="list-style-type: none"> Recommendation in favor of treatment or procedure being useful/effective Some conflicting evidence from multiple randomized trials or meta-analyses 	<ul style="list-style-type: none"> Recommendation's usefulness/efficacy less well established Some conflicting evidence from multiple randomized trials or meta-analyses 	<ul style="list-style-type: none"> Recommendation that procedure or treatment is not useful/ineffective and may be harmful Sufficient evidence from multiple randomized trials or meta-analyses
LEVEL B Limited populations evaluated? Data derived from a single randomized trial or nonrandomized studies	<ul style="list-style-type: none"> Recommendation that procedure or treatment is useful/effective Evidence from single randomized trial or nonrandomized studies 	<ul style="list-style-type: none"> Recommendation in favor of treatment or procedure being useful/effective Some conflicting evidence from single randomized trial or nonrandomized studies 	<ul style="list-style-type: none"> Recommendation's usefulness/efficacy less well established Some conflicting evidence from single randomized trial or nonrandomized studies 	<ul style="list-style-type: none"> Recommendation that procedure or treatment is not useful/ineffective and may be harmful Evidence from single randomized trial or nonrandomized studies
LEVEL C Very limited populations evaluated? Only consensus opinion of experts, case studies, or standard of care	<ul style="list-style-type: none"> Recommendation that procedure or treatment is useful/effective Only expert opinion, case studies, or standard of care 	<ul style="list-style-type: none"> Recommendation in favor of treatment or procedure being useful/effective Only emerging expert opinion, case studies, or standard of care 	<ul style="list-style-type: none"> Recommendation's usefulness/efficacy less well established Only emerging expert opinion, case studies, or standard of care 	<ul style="list-style-type: none"> Recommendation that procedure or treatment is not useful/ineffective and may be harmful Only expert opinion, case studies, or standard of care
Suggested phrases for writing recommendations	should be recommended or indicated to use/not-use/continue/stop	is reasonable to use/not-use/continue/stop or not well established	may/might be considered or reasonable usefulness/ineffectiveness is unknown/unclear/balanced or not well established	COB III is not recommended
Comparative effectiveness phrases	Treatment/strategy A is preferred to treatment B or treatment A should be chosen over treatment B	Treatment/strategy A is probably preferred to treatment B or it is reasonable to choose treatment A over treatment B	COB II is not indicated	COB IV is not indicated

A recommendation with Level of Evidence B or C does not imply that the recommendation is weak. Many important clinical questions addressed in the guidelines do not lend themselves to clinical trials. Even when randomized trials are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective. *Data available from clinical trials or registries about the usefulness/efficacy in different subpopulations, such as sex, race, history of diabetes, history of prior myocardial infarction, history of heart failure, and prior aspirin use.

Recommendations for Management of Hypertension

- General population age < 60 years
 - Initiate pharmacologic treatment to lower BP at DBP 90 mm Hg and treat to a goal DBP < 90 mm Hg, lower BP at SBP 140 mm Hg and treat to a goal SBP < 140 mm Hg.
 - Grade A evidence for ages 30–59 years, Grade E evidence for ages 18–29 years

Recommendations for Management of Hypertension (continued)

- General population age ≥ 60 years (cont.)
 - Threshold to start meds = 150/90 mm Hg (Grade A)
 - BP goal with treatment goal SBP < 150 mm Hg and goal DBP < 90 mm Hg (Grade A)
 - Yields reduction in stroke, HF, CHD

Recommendations for Management of Hypertension (continued)

- Diabetes mellitus age ≥ 18 years
 - Start pharmacologic treatment to lower BP at SBP 140 mm Hg or DBP 90 mm Hg and treat to this goal
 - Expert opinion – Grade E
 - Insufficient evidence to support a lower threshold (or goal) based on outcomes

Recommendations for Management of Hypertension

(continued)

- Chronic kidney disease (CKD) age \geq 18 years
 - Start pharmacologic treatment to lower BP at SBP 140 mm Hg or DBP 90 mm Hg, treat to goal SBP<140 mmHg and goal DBP<90 mm Hg
 - Expert opinion – Grade E

Are there benefits of additional lowering BP?

- In adults age<60 years
 - DBP 90 mm Hg based on evidence that DBP<85 or 80 mm Hg=No additional benefit noted
- In adults age \geq 60 years
 - Lowering to <140/<90 mm Hg showed no additional benefit, compared to 140–160 or 140–149 mm Hg

What if already at lower BP with current therapy?

- In general population
 - Treatment is well tolerated without adverse effects to QoL (quality of life).
- Treatment does not need to be adjusted.
 - Expert opinion – Grade E

JNC-7 vs. JNC-8: Medication Recommendations

- JNC-7
 - 5 drug classes to be considered as initial therapy, thiazide-type diuretics as initial therapy for most patients without compelling indication for another class, dose ranges mentioned
- JNC-8
 - 4 specific medication classes and doses based on RCT evidence, racial, CKD, and diabetic subgroups, created table of drugs and doses used in the outcome trials

How many medications?

When BP is >20/10 mm Hg above goal, consideration should be given to starting with 2 drugs.

References

Blood Pressure Reduction, Persistence and Costs in the Evaluation of Antihypertensive Drug Therapy, available at <http://www.cardiab.com/content/8/1/18>

Combination Therapy Versus Monotherapy in Reducing Blood Pressure: Meta-analysis on 11,000 participants from 42 trials, available at www.ncbi.nlm.nih.gov/pubmed/19272490

The Major AntiHTN Drug Groups

- ACEI, ARB
- CCB
- Thiazide-like diuretics
 - Thiazide diuretics (HCTZ)
chlorthalidone, indapamide

The Major AntiHTN Drug Groups (continued)

- Why these drug classes?
 - Comparable outcomes, particularly in general population
 - Grade B evidence (moderate amount)
 - Lower overall death rates
 - Improved CV (with exception of heart failure), cerebrovascular, renal outcomes

Ethnic Differences in Cardiovascular Drug Response: Potential Contribution of Pharmacogenetics

Drug category	Mean BP reduction (SBP/DBP)		White-Black difference
	Whites	Blacks	
Diuretics	11.5/9.1	15.0/10.7	-3.5/-1.5
CCBs	15.3/12.6	16.9/13.3	-2.4/-0.6
β-blockers	11.7/11.3	5.9/9.5	6.0/2.9
ACEI/ARB	12.8/11.4	8.5/8.0	4.6/3.0

Source: www.ncbi.nlm.nih.gov/pmc/articles/PMC2730023/table/T2/

Effect of Adding BP Medications vs. Increasing Single Drug

- “Comparison of our results with those of a published meta-analysis of different doses of the same drug showed that doubling the dose of 1 drug had approximately one fifth of the equivalent incremental effect (0.22 [95% CI, 0.19–0.25]).”

– Source: <http://www.ncbi.nlm.nih.gov/pubmed/19272490>

Medication

Comment

Thiazide-like diuretics
Examples- HCTZ, chlorthalidone, indapamide
• MOA- Low volume sodium depletion that leads to PVR reduction
BP=HR x SV x PVR↓

Thiazide diuretic use is an independent risk factor of T2DM development.

Monitor for K+, Na+, Mg+ depletion. Calcium sparing. Elders particularly sensitive to hyponatremia induced by thiazide diuretic use.

Thiazide-type Diuretics

Antihypertensive medication	Initial daily dose, mg	Target dose in RCTs, mg/d	No. of doses per day
Chlorthalidone (Hygroton®)	12.5	12.5–25	1
Hydrochlorothiazide (HydroDiuril®)	12.5–25	25–100 ^a	1–2
Indapamide (Lozol®)	1.25	1.25–2.5	1

^aCurrent recommended evidence-based dose that balances efficacy and safety is 25–50 mg daily.

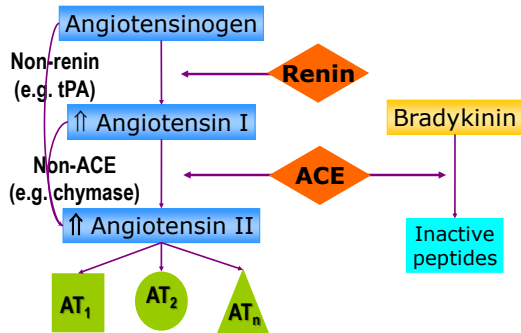
Thiazide Diuretic Use

- Less effective when $GFR < 30 \text{ mL/min/1.73 m}^2$
 - Loop diuretics will likely remain effective.
- Be vigilant for evidence of overdiuresis in older adult.
 - Postural hypotension
 - BUN: Cr ratio ≥ 20
 - Hyponatremia

K⁺ Monitoring with Diuretic Use

- Thiazide without K⁺ sparing medication
 - K⁺ usually at its lowest point 1 mo after starting or adjusting dose
- Loop without K⁺ sparing medication
 - K⁺ wasting typically
 - Dose dependent
 - Worse in first weeks of use
 - Check at least weekly for first month

Renin-angiotensin Cascade What works where?



Medication	Comments
Angiotensin converting enzyme inhibitors (ACEI) ACEI examples- Lisinopril, enalapril, all with -pril suffix Angiotensin receptor blockers (ARB) ARB examples- Losartan, telmisartan, all with -sartan suffix	Adjust dose in renal insufficiency. Do not use in presence of bilateral renal artery stenosis. Hyperkalemia risk, especially with inadequate fluid intake, excessive diuresis, when used with aldosterone antagonist.

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Medication	Comments
MOA- Attenuate angiotensin II (Ag II, a potent vasoconstrictor that stimulates adrenal catecholamine release) effect by minimizing its production (ACEI) or blocking its action (ARB) BP=HR x SV x PVR ↓ (without increase in HR, SV)	ACEI-induced cough- Can use ARB as alternative. Angioedema risk with ACEI use, less so with ARB use Do not use during pregnancy (category D).

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ACE Inhibitors

Antihypertensive medication	Initial daily dose, mg/d	Target dose in RCTs reviewed, mg/d	No. of doses per day
Captopril	50	150-200	2
Enalapril	5	20	1-2
Lisinopril	10	40	1

Abbreviations: ACE, angiotensin-converting enzyme; RCT, randomized controlled trial.

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Angiotensin Receptor Blockers

Antihypertensive medication	Initial daily dose, mg	Target dose in RCTs reviewed, mg	No. of doses per day
Eprosartan	400	600–800	1–2
Candesartan	4	12–32	1
Losartan	50	100	1–2
Valsartan	40–80	160–320	1
Irbesartan	75	300	1

Abbreviations: ACE, angiotensin-converting enzyme; RCT, randomized controlled trial.

Monitoring K⁺ in Person on ACEI/ARB with CKD

- Check K⁺ and SCr within 1 to 2 weeks of initiation (1 week in elderly) and after dosage increases.
- Recheck in 3 to 4 weeks if stable, then 1–2 times per year or as dictated by patient comorbidities or status change.

Per JNC-8

- “ACEI or ARB improves kidney outcomes for patients with CKD. This recommendation applies to CKD patients with and without proteinuria, as studies using ACEIs or ARBs showed evidence of improved kidney outcomes in both groups.”



Medication	Comment
Calcium channel blockers (CCB) Dihydropyridine (DHP) examples- Amlodipine, felodipine, others, all with -ipine suffix NonDHP CCB examples- Diltiazem, verapamil • MOA- Causes vasodilatation BP=HR x SV x PVR↓	Use with caution in presence of heart failure, renal or hepatic impairment. NonDPH=CYP4503A4 inhibitors, potential for drug-drug interaction

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Calcium Channel Blockers

Antihypertensive medication	Initial daily dose, mg	Target dose in RCTs reviewed, mg	No. of doses per day
Amlodipine	2.5	10	1
Diltiazem extended release	120-180	360	1

Abbreviations: ACE, angiotensin-converting enzyme; RCT, randomized controlled trial.
 *Current recommended evidence-based dose that balances efficacy and safety is 25-50 mg daily.

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What does this mean in practice?

- 58-year-old African-American man with T2DM, HTN and dyslipidemia, BP=170/105 mm Hg
 - Clear need for 2+ meds
 - JNC-7=Thiazide, ACEI, CCB
 - BP goal ≤130/<80 mm Hg
 - JNC-8=Thiazide, ACEI, CCB
 - BP goal ≤140/<90 mm Hg

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What does this all mean in practice? (continued)

- 66-year-old woman of European ancestry with HTN, BP=162/92 mm Hg
 - Possible control with 1 med
- JNC-7=Thiazide as 1st line, BB, ACEI, CCB as 2d line
 - Goal BP<140/<90 mm Hg
- JNC-8=Thiazide, ACEI, CCB
 - BP goal≤150/<90 mm Hg

Beta blockers as a 4th line therapy?

Meta-analysis Results Beta Blockers in Uncomplicated HTN

- Stroke
 - Significantly higher with beta blockers than with other antiHTN (relative risk, 1.16; 95% CI, 1.04–1.30)
 - Most problematic w/ atenolol than w/ other non-beta blocker antiHTN (RR, 1.26; 95% CI, 1.15–1.38)
 - Lindholm LH et al. Should beta blockers remain first choice in the treatment of primary hypertension? A meta-analysis. *Lancet* 2005 Oct 29; 366:1545-53.

Beta Blockers

Antihypertensive medication	Initial daily dose, mg	Target dose in RCTs reviewed, mg	No. of doses per day
Atenolol	25-50	100	1-2
Metoprolol	50	100-200	1-2

Abbreviations: ACE, angiotensin-converting enzyme; RCT, randomized controlled trial.
^aCurrent recommended evidence-based dose that balances efficacy and safety is 25-50 mg daily.

Aldosterone antagonist as a 4th line drug?

Medication

Comment

Aldosterone antagonist
 Examples: Spironolactone (Aldactone[®]), eplerenone (Inspra[®])
 •MOA: Block effects of aldosterone, therefore better regulating of Na⁺ and water homeostasis and maintenance of intravascular volume
BP=HR x SV x PVR↓

Hyperkalemia risk, particularly w/ ACEI, ARB use or volume depletion, including excessive diuresis. Most often used in heart failure treatment. Gynecomastia risk with prolonged use
 Use with caution in renal impairment, especially when GFR<30 mL/min/1.73 m²

Anticipated BP Response with Spironolactone Use

- SBP reduction
– 22 mm Hg
- DBP reduction
– 10 mm Hg
- Average dose
– 25 mg per day

You start a patient...

- ...on spironolactone who is also on an angiotensin-converting enzyme inhibitor. You advise the patient to return in 4 weeks to check which of the following laboratory parameters?

Why not check the labs sooner?

- A. Sodium
- B. Calcium
- C. Potassium
- D. Chloride

Why not check the labs sooner?

- A. Sodium
- B. Calcium
- C. Potassium
- D. Chloride

Per JNC-8

Medications that are Not Mentioned

- Centrally-acting agents
 - Clonidine, methyldopa
- Direct renin inhibitor
 - Aliskiren

Hypertension in the Elderly

ACCF/AHA

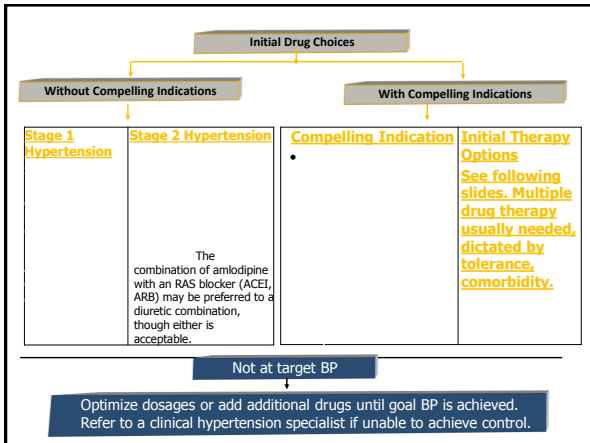
Expert Consensus Document

available at <http://content.onlinejacc.org/article.aspx?articleid=1146473>

Developed in collaboration with the American Academy of Neurology, Association of Black Cardiologists, American Geriatrics Society, American Society of Hypertension, American Society of Nephrology, American Society for Preventive Cardiology, and the European Society of Hypertension

Hypertension in the Elderly Therapeutic Options

- Per ACCF/AHA
 - Diuretics, ACEI, calcium antagonists, beta blockers
 - All shown benefit on CV outcomes in randomized trials among elderly cohorts
 - Specific agents choice dictated by efficacy, tolerability, comorbidities, and cost

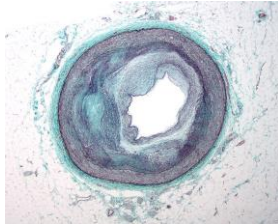


Compelling Indications for Use of Select Meds in Elder w/HTN

- Heart failure
 - Thiazide diuretic, beta blocker, ACEI, ARB, CCB, aldosterone antagonist
- Post myocardial infarction
 - Beta blocker, ACEI, ARB, aldosterone antagonist

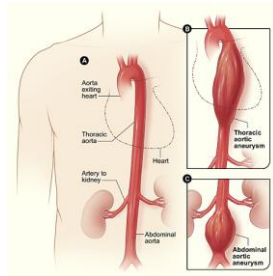
Compelling Indications for Use of Select Meds in Elder w/HTN (continued)

- CAD or high CVD risk
 - Thiazide diuretic, beta blocker, ACEI, CCB
- Angina pectoris
 - Beta blocker, CCB



Compelling Indications for Use of Select Meds in Elder w/HTN (continued)

- Aortopathy/aortic aneurysm
 - Thiazide diuretic, beta blocker, ACEI, CCB

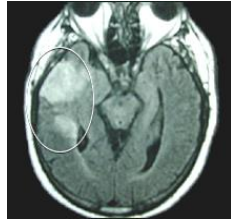


Compelling Indications for Use of Select Meds in Elder w/HTN (continued)

- Diabetes mellitus
 - Thiazide diuretic, beta blocker, ACEI, ARB, CCB
- Chronic kidney disease
 - ACEI, ARB

Compelling Indications for Use of Select Meds in Elder w/HTN (continued)

- Recurrent stroke prevention
 - Thiazide diuretic, ACEI, ARB, CCB



Postural Hypotension in Older Adult: Major Etiology

- Age-related changes
- Low circulating volume
 - Overdiuresis
 - Poor oral intake
- Use of medications with vasodilating capability

Postural Hypotension

AKA Orthostatic Hypotension or Orthostasis

- Defined
 - Abnormal fall in blood pressure, ≥ 20 mm Hg systolic, ≥ 10 mm Hg diastolic or both, within three minutes of standing upright
- Usually associated with symptoms

Postural Hypotension

AKA Orthostatic Hypotension or Orthostasis (continued)

- Origin of postural hypotension
 - Age-associated reduction in baroreflex function
 - Increase in venous insufficiency
- Risk for falls, syncope, CV events

Postural Hypotension

AKA Orthostatic Hypotension or Orthostasis (continued)

- Postural hypotension symptoms
 - Faintness, light-headedness
 - Dizziness
 - Confusion
 - Blurred vision
- Occur within seconds to a few minutes of standing and resolve rapidly on lying down

Antihypertensive Treatment-related Adverse Effects

- The high prevalence of both CV and non-CV comorbidities among the older adults dictates need for great vigilance to avoid treatment-related adverse effects such as
 - Electrolyte disturbances
 - Renal dysfunction
 - Excessive orthostatic BP decline

Difficulty in HTN Control Possible Contributors

- Use of select medications
 - NSAIDs in dose-dependent manner
 - Partial reversal of antiHTN effect of beta blockers (most potent), diuretics, ACEI, ARB but not CCB
 - Use associated w/renal impairment, sodium retention, decreased GFR, edema, hyperkalemia, and/or papillary necrosis

Difficulty in HTN Control Possible Contributors (continued)

- Use of select medications (cont.)
 - Cyclooxygenase-2 (COX-2) inhibitors
 - An NSAID form
 - Systemic corticosteroids
 - Mechanism similar to NSAIDs, as much 15 mm Hg rise within 24 h of starting medication
 - Certain DMARDs
 - Cyclosporine, leflunomide

Conclusion

End of Presentation

Thank you for your time and attention.

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