Treatment of Hypertension and Hyperlipidemia Board Review

Hypertension:Who Should be treated?

- Patients with out-of-office daytime blood pressure ≥135 mmHg systolic or ≥85 mmHg diastolic (or an average office blood pressure ≥140 mmHg systolic or ≥90 mmHg diastolic if out-of-office readings are not available)
- Patients with an out-of-office blood pressure (mean home or daytime ambulatory) ≥130 mmHg systolic or ≥80 mmHg diastolic (or, if out-of-office readings are unavailable, the average of appropriately measured office readings ≥130 mmHg systolic or ≥80 mmHg diastolic) who have one or more of the following features: CV disease, DM, CKD, 10 year CV risk > 10%
- 2017 AHA/ACC Blood pressure guidelines. Hypertension. 2018;71(6):e13. Epub 2017 Nov 13.

SPRINT >75 YEARS INTENSIVE TARGET BENEFIT SUMMARY

- • 34% lower rate of fatal and nonfatal major CVD events
- • 33% lower rate of death from any cause
- • Benefits similar regardless of frailty status
- • Intensive therapy is cost-effective
- Therapy was well tolerated –patient reported physical and mental function
- • Time to benefit is acceptably short
- N Engl J Med. 2015; 373:2103–2116.

- 1) A 68 yo man with hypertension is seen in follow up. His BP in clinic is 150/96 P 80 . BP's last year were all 130/80 or less. He gets multiple home readings which are all over 150 systolic and 90 diastolic. PMH: Hypertension, Depression, prediabetes, bilateral collar bone fractures (6 weeks ago) Medications: Lisinopril 20 mg, chlorthalidone 25 mg
- What is the most likely cause for his worsening HTN?

A) Renal artery stenosis
B) Hyperaldosteronism
C) Pheochromocytoma
D) Medication use
E) Cushing syndrome

Common Causes of Secondary Hypertension

- Sleep Apnea
- NSAID use (most important in patients on ACEI/ARBS/Diuretics)
- Other Medications- OCP, Venlafaxine, licorice
- Recreational drugs- amphetamines, cocaine
- ETOH

Pearls on When to Think of Rare Causes of Secondary HTN

- Fibromuscular dysplasia- 90% in women, some have carotid disease
- Renal artery stenosis (atherosclerosis)- flash pulmonary edema, sudden worsening of renal function with treatment, worsening htn in patient with known atherosclerosis
- Pheochromocytoma- headache/sweating/tachycardia/orthostatic hypotension/hypertension during procedures/surgery/after receiving meds

- 2)A 47 yo woman presents for follow up for elevated BP. She had a BP of 160/90 at her last clinic visit. Her average BP of 20 home readings is 158/92. What do you recommend for treatment?
- A) Lifestyle modifications
- B) Chlorthalidone
- C) Lisinopril
- D) Metoprolol
- E) Telmisartan/amlodipine

Lifestyle Modifications that Have Evidence of Benefit for HTN

- Dietary salt restriction
- Potassium supplementation
- Weight loss
- DASH diet
- Limit alcohol
- Exercise

Initial Treatment of Hypertension

- Initial combination antihypertensive therapy with two first-line agents of different classes is suggested in any patient whose blood pressure is more than 20 mmHg systolic or 10 mmHg diastolic above their goal blood pressure

- 2017 AHA/ACC Blood pressure guidelines. Hypertension. 2018;71(6):e13. Epub 2017 Nov 13.
- Cochrane Database Syst Rev. 2020;2(2):CD010316.

3) A 60 yo woman presents for follow-up of hypertension. She has been taking medication (Lisinopril) for the past 3 months. Her most recent outside blood pressure readings are 156/94, 150/96, 158/92. PMH: Type 2 DM, GERD, depression. Meds: Lisinopril 20mg qd, Omeprazole 20mg qd, Sertraline 50 mg qd, Metformin 500 mg bid.

What do you recommend?

A) No changes in therapy

B) Increase Lisinopril to 20 mg bid

C) Add Metoprolol XL100 mg

D) Add Amlodipine 5mg qd

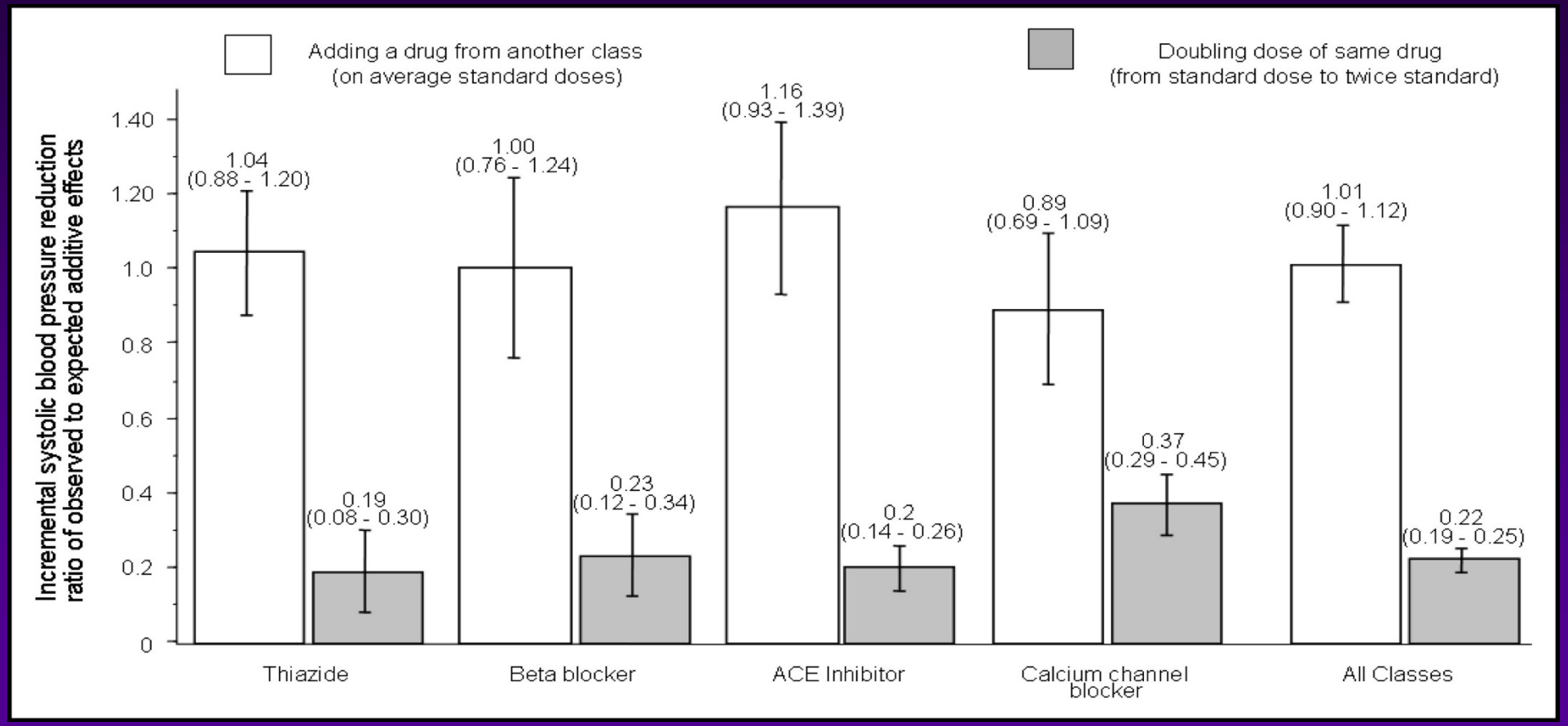
Double the dose or add a second agent?

Titrate single drug vs combo?

- Meta-analysis of 11,000 patients from 42 trials comparing single dose with up titration vs switch to combo therapy

Am J Med 2009;122:290-300

Adding a second agent is about 5-fold more effective



Am J Med 2009;122:290-300

Based on RCTs of HTN, at least 75% of patients will require combination therapy to achieve BP targets

Am J Hypertens 2010;4:42-50

Combination Therapy

- Low doses of thiazide can be very effective in combination with ACE inhibitors (12.5 mg of thiazide)
- Thiazide ACE combination can be further enhanced by moderate dietary salt restriction
- ACE/Amlodipine combination may have CV benefits slightly better than ACE/diuretic in high risk diabetic paients

Combination of ARB + Diuretic

- Azilsartan + chlorthalidone SBP -35.1
- Azilsartan + hydrochlorothiazide -29.5

- P<.001

- Am J Med 2012 ;25:1229

4) A 58 yo man is seen for treatment of hypertension. He has not ever had good control of his hypertension since treatment was started 2 years ago. He has been taking her medications faithfully. Meds: Amlodipine, Atenolol , Clonidine, and Losartan . On exam BP is 200/106 P-55.Labs- BUN 30, Cr 2.0, Na 137, K 4.0. ECG- LVH

What would you recommend?

A) Increase amlodipine from 10mg a day to 10mg BID

B) Increase losartan from 50mg BID to 100mg BID

C) Add hydrochlorathiazide 12.5 mg qd

D) Add hydrochlorathiazide 25 mg qd

E) Add furosemide 40 mg BID

Most Common Cause of Resistant Hypertension is Nonadherance

- In a study of patients referred for renal denervation therapy for refractory /resistant hypertension, blood levels measured of antihypertensive drugs patients were prescribed
- In 80% of patients, fewer medications were detected than prescribed

- Hypertension. 2017;69(4):678.

- 5)A 55 yo woman presents with persistent hypertension. She has been taking clorthalidone, lisinopril, amlodipine and metoprolol. BP today is 158/96. Outside readings are similar (160/96, 154/94, 166/98).
- Labs: Na 134 K 4.2 Bun 12 Cr 1.0
- What do you recommend?

A) Replace clorthalidone with furosemide
B) Add Diltiazem
C) Add Clonidine
D) Add Spironolactone
E) Switch amlodipine to minoxidil

Primary Hyperaldosteronism

- Most common cause of secondary hypertension in Hypertension clinics (up 25%)
- Estimated to be present in 5-10% of patients with hypertension
- Surprisingly, >50% of patients DO NOT have hypokalemia- Classic board presentation would be patient with hypertension, hypokalemia and alkalosis
- Work up- Plasma renin activity and aldosterone concentration, CT scan in patients with positive results*

Adding Spironolactone for Refractory Hypertension

- Average blood pressure reduction of 17-20/4-9 mmHg, with the largest reductions seen in patients with SBP >150 mmHg at baseline (1,2).
- In a study of 175 patients with refractory hypertension on a mean of 4 blood pressure medications, addition of spironolactone resulted in a lowering of blood pressure by an average of 16/9 mmHg, with about half of the patients on the medication achieving a goal blood pressure of < 140/90 mmHg (3).
- 1) Cochrane DB Syst Rev 2010 Aug 4;8:CD008169
- 2) J Hum Hypertens 2015;29:159-166
- 3) Hypertension 2010;55:147-152

Aldosterone, Hypertension and Antihypertensive Therapy

- Community based cohort with (477) and without HTN (1073), plasma aldosterone levels were measured
- In those with hypertension, number of antihypertensive drugs were recorded
- Subjects with HTN had higher aldosterone leves (6.4) than those who did not have HTN (4.1)
- The more antihypertensive drugs that patients were on, the higher the aldosterone level (0 drugs=4.8, 1=6.4, 2=7.1, 3=7.9, p=.002)

- Mayo Clinic Proc 2018; 93(8): 980-990.

- 6)A 64yo woman presents for follow up. She has a PMH of osteopenia (T -2.3 at her hip) and GERD. She has had 3 outside BP readings of 160/90, 158/88, and 164/92 . Today in clinic her BP is 158/86. Her BP a year ago was 154/88. Meds: Omeprazole and Vitamin D.
- Which would be the best treatment recommendation?
- A) Monitor BP, no therapy
- B) Chlorthalidone
- C) Lisinopril
- D) Metoprolol
- E) Diltiazem

Benefit of Thiazide Diuretics for Calcium

- Meta-analysis of 5 trials with 756 patients enrolled
- Serum calcium levels higher in thiazide treated patients (Difference +.33, 95%CI .16-.50)
- Urinary calcium lower in thiazide treated patients (- .35, 95% CI -.52- -.17)

- Drug Des Devel Ther. 2018 Nov 14;12:3929-3935.

Thiazide Diuretic Usage and Risk of Fracture

- Eleven eligible cohort studies involving 2,193,160 participants were included for analysis
- Thiazide diuretic users, as compared with non-users, had a significant 14% reduction in the risk of all fractures (relative risk [RR], 0.86; 95% confidence interval [CI], 0.80-0.93; p = 0.009) and an 18% reduction in the risk of hip fracture (RR, 0.82; 95%CI, 0.80-0.93; p = 0.009)
- Osteoporos Int. 2018 Jul;29(7):1515-1524.

- 7)A 48 yo woman with hypertension presents for annual follow up. Her last lipids were checked 5 years ago (TC 190, LDL 125, HDL 45, Tri-100). Meds: Nifedipine and chlorthalidone. Exam: BP 140/60 P 80 chest – clear
- Cardiac- nl S1S2 no M. Ext- 2+ edema
- Lab- TC 255 LDL 170 HDL 40 Tri 160
- What is appropriate next step?

A) Start pravastatin
B) Start atorvastatin
C) Start ezetimide
D) Check CMP,Ua and TSH
E) Check BMP, estrogen

Secondary Hyperlipidemia

Increased LDL

- Hypothyroidism
- Nephrotic Syndrome
- Cholestatic liver disease

- 8)A 61 yo man with hyperlipidemia,

Type 2 DM, and a family history of early MI had a hospitalization for unstable angina and received a coronary stent last week. He is taking 40 mg of pravastatin , clopidogrel, asa, and metformin. Labs: A1c 6.5%,

- TC 210, HDL 45, LDL 119, TG 183

Most appropriate treatment?

A) Pravastatin 80 mg
B) Atorvastatin 80 mg
C) Atorvastatin 80 mg + Niacin 1000mg
D) Niacin 1000mg

- 9)70 yo woman presents for primary care visit. She has no symptoms. PMH: hypertension, GERD. nonsmoker
- PE: BP 120/70 P 66
- Labs: HBA1C 5.2, Bun 10 Cr 1.1 TC 190 LDL 135 HDL 42
- What do you recommend?

A) Diet and exercise , recheck cholesterol
B) Fenofibrate
C) Pravastatin 40 mg
D) Atorvastatin 80 mg
E) No intervention

Using AHA Cardiac Risk Calculator

- Risk of MI/Stroke 11.5% over next 10 years
- Recommendation: Low to Moderate intensity statin (Pravastatin 40mg/Atorvastatin 20 mg)
- In general, if 65 with 1 or more risk factors, will have > 7.5% risk over 10 years

USPSTF Recommendation

- The USPSTF recommends initiating use of low- to moderate-dose statins in adults aged 40 to 75 years without a history of CVD who have 1 or more CVD risk factors (dyslipidemia, diabetes, hypertension, or smoking) and a calculated 10-year CVD event risk of 10% or greater (B recommendation).

- JAMA. 2016 Nov 15;316(19):1997-2007.

10)While undergoing evaluation following a hysterectomy, a 50 yo is noted to have TC 245, HDL 56, TG 645. She has an A1c of 5.6%. PMH: Migraine, hypertension. Her exam is normal and her medications include propranolol, hydrochlorothiazide, and oral estrogen.

What do you recommend now?

A. No change in therapy.
B. Add niacin.
C. Add gemfibrozil.
D. Replace propranolol and oral estrogen.

Audience Response
next slide

Elevated Triglycerides

- Moderate elevation (300-800)- non fasting state, medications- estrogen(less with transdermal), b blockers, protease inhibitors, Isotretinoin, clozapine, olanzapine, hypothyroidism, insulin resistance
- Severe Elevation (>885)- Familial hypertriglyceridemia, medications (PI, Clozapine/olanzapine)

Ezetimibe

- 2nd line lowering
- Inhibits cholesterol absorption at brush border
- Lowers LDL by 15–25%
- Approved for use alone or with statin or fenofibrate
- Increased risk of statin induced myopathy
- Avoid use with gemfibrozil

Bile Acid Sequestrants (Resins)

- Cholestyramine, colestipol
- May increase TG
- Slightly ↑ HDL
- Lower LDL by 10–25%
- Adjuvant in combination with statins, rarely used now
- Side effects: Nausea, vomiting, bloating

Niacin

- Blocks LDL synthesis
- ↓ LDL by 5–25%
- ↑ HDL by 15–35%
  ↓ TG by 20–50%
- Flushing, hyperuricemia, hepatotoxicity
- No effect on mortality
- No benefit when added to statin
- Really no role

Fibrates

- Gemfibrozil
  - ↓ TG by 50%
  - ↑ HDL by 15%
  - ↓ LDL
- Fenofibrate best combination with a statin (less drug interactions)
  - ↓ VLDL
  - Reduce TG by 50%

  Only appropriate use is to lower triglycerides- not indicated for CV protection

Marine Omega-3 Fatty Acids

- Icosapent ethyl (E-EPA)- prescription drug, used in patients with high triglycerides and highest CV risk
- Omega-3 fatty acid ethyl esters (EPA and DHA)- in patients without CV risk
- Major concern is risk for Afib

- 11)A 68 yo man presents for follow up after recent MI. He has had 4 prior MI's over the past 12 years. He has had a 3 vessel CABG, and 2 stents placed. He quit smoking after his 1st MI 12 years ago. BP ranges from 110-130/ 55-65.

Medications: Irbesartan 300 mg , ASA 81 mg, Atorvastatin 80 mg , ezetimibe 10. Labs: TC 150 HDL 36 LDL 78 Trigly 200. What is the best treatment to reduce his risk of reinfarction?

A) Add chlorthalidone
B) Add Niacin
C) Add Evolocumab
D) Add Fenofibrate

PCSK9 inhibitors

- Indicated for Homozygous or heterozygous familial hypercholesterolemia
- Statin intolerant patients at high cardiovascular risk
- Very high risk patients with CVD unable to achieve LDL <70 with maximal statin/ezetimibe

- 12)A 66 yo woman is discharged from the hospital after an MI. Her discharge medications include atorvastatin 40 mg, lisinopril 20 mg, ASA 81 mg and clopidogrel 75mg. At her follow up appt she mentions that she has muscle pain and stiffness in both legs and her back. Labs: TSH 2.0 Vitamin D 40 . She stops the atorvastatin for 2 weeks with resolution of her symptoms
- What do you recommend?
- A) Restart atorvastatin
- B) Start Rosuvastatin twice a week
- C) Start Ezetimibe
- D) Start a PCSK9 inhibitor

Nocebo Effect and SAMS

- 60 patients with a hx of SAMS were entered into the trial
- The patients received four bottles containing atorvastatin at a dose of 20 mg, four bottles containing placebo, and four empty bottles; each bottle was to be used for a 1-month period according to a random sequence.
- The mean symptom intensity was 8.0 during no-tablet months (95% CI, 4.7 to 11.3),15.4 during placebo months (95% CI, 12.1 to18.7; P<0.001 for the comparison with no-tablet months), and 16.3 during statin months (95%CI, 13.0 to 19.6; P<0.001 for the comparison with no-tablet months and P=0.39 for the comparison with placebo months) .
- N Engl J Med 2020; 383;22

SAMS- How Good is Rechallenge?

- Retrospective study of 118 patients referred to a lipid clinic as being statin intolerant (muscle symptoms on 2 or more statins)
- Patients were either rechallenged with the same statin, a different statin or non statin therapy
- Tolerability 71% same statin, 53% statin switch and 57% non statin therapy
- Can J Card 2017;33:666-673

Approach to Management of Myalgias on Statins

- Check CK ,TSH, Vitamin D
- Review for drug interactions- especially ca channel bl
- Stop statin, when symptoms disappear restart statin at lower dose (up to 70% success with same statin rechallenge*) or change statin (30-40% success*)
- Can switch to intermittent potent statin
- Ezetimibe or PCSK9 inhibitor in appropriate patients

• . 2023 Apr 13;388(15):1353-1364.
• . 2023 Apr 13;388(15):1353-1364.

Bempedoic Acid in Statin Intolerant Patients

- 13,970 statin intolerant patients enrolled , in a double blind, randomized placebo controlled trial
- Randomized to Bempedoic acid or placebo
- The incidence of a primary end-point event was significantly lower with bempedoic acid than with placebo. HR, 0.87; 95% CI, 0.79 to 0.96; P = 0.004), as were the incidences of a composite of death from cardiovascular causes, nonfatal stroke, or nonfatal myocardial infarction HR, 0.85; 95% CI, 0.76 to 0.96; P = 0.006)
- Side effects- Gout, gall stones, tendon rupture
- N Engl J Med. 2023 Apr 13;388(15):1353-1364.

Bempedoic Acid Side Effects

- Increased Uric Acid- gout- 3.1% vs 2.1 % placebo
- Increased risk of cholelithiasis 2.1% vs 1.1 %
- Black box warning tendon rupture

- J Am Heart Assoc, 2019. 8(7): p. e011662.

ANSWERS

1) D-Medication use
2) E-Telmisartan/amlodipine
3) D-Add amlodipine
4) E- Add furosemide
5) D-Add spironolactone
6) D-chlorthalidone
7) D-Check CMP,Ua, TSH
8) B-Atorvastatin 80 mg
9) C-Pravastatin 40 mg
10) D- Replace propranolol and oral estrogen
11) C- Add evolocumab
12) A-Restart Atorvastatin