Vasodilatory β-blockade: Clinical Implications and Pleiotropic Effects

Tuesday, September 23, 2008
Dallas, TX

Unraveling Their Heterogeneity to Understand β-blockers

C. Venkata Ram, MD
UT Southwestern Medical Center at Dallas
Dallas, TX

Treating Hypertension in Clinical Practice: Interrupting the Continuum of Global Cardiovascular Risk

Henry A. Punzi, MD, FCP
Trinity Hypertension Research Institute
Texas Women’s University
Dallas, TX
Session 6: Vasodilatory β-blockade: Clinical Implications and Pleiotropic Effects

Learning Objectives
- Outline the evolution and heterogeneity of beta-blockers, the most utilized class of cardiovascular agents, with a focus on recent meta-analyses about the efficacy of these agents.
- Identify the clinical and pleiotropic differences between older-generation and newer beta-blockers, and describe how newer formulations may aid in the control of complicated hypertension and elevated cardiovascular risk in primary care practice.

Faculty
C. Venkata Ram, MD
UT Southwestern Medical Center at Dallas
Dallas, Texas

C. Venkata S. Ram, MD, is professor of internal medicine at the University of Texas Southwestern Medical Center in Dallas. Dr Ram has also served as director of clinical research and education, Dallas Nephrology Associates; governor-designate, American Society of Hypertension, Texas Chapter; director, Hypertension Clinic, St. Paul Medical Center, Dallas, Texas; and director, Texas Blood Pressure Institute, Dallas, Texas. He is a member of the American Heart Association, American College of Cardiology, American College of Clinical Pharmacology, International Society of Hypertension, American Society of Hypertension and several other associations.

Dr Ram has focused his professional career on the management of hypertension. He has served as the deputy editor for the Journal of Human Hypertension and the American Journal of Cardiovascular Drugs. Dr Ram has authored a book and more than 240 articles on the treatment of hypertension.

Henry A. Punzi, MD, FCP
Medical Director, Trinity Hypertension Research Institute
Clinical Professor, Texas Women’s University
Dallas, Texas

Henry A. Punzi, MD, FCP, is in private practice and performs clinical research at the Trinity Hypertension Research Institute in Carrollton, Texas. Dr Punzi has been a clinical associate professor at Texas Women’s University in Denton, Texas, and an attending physician of internal medicine at Trinity Medical Center, in Carrollton, Texas.

Dr Punzi has been a fellow of the American College of Clinical Pharmacology, a member of the Council for High Blood Pressure Research of the American Heart Association, the American Society of Hypertension, and the American Society for Clinical Pharmacology and Therapeutics. Dr Punzi has been the principal investigator in more than 60 cardiovascular clinical trials and has published numerous articles in medical journals. In addition to writing 4 book chapters, Dr Punzi has written a book on hypertension and served as series editor for 3 volumes of Clinical Cardiovascular Therapeutics.

Faculty Financial Disclosure Statements
The presenting faculty reported the following:
Dr Ram is a member of speaker’s bureaus for Pfizer Inc.; Novartis Pharmaceuticals Corporation; GSX; Forest Pharmaceuticals, Inc.; Bristol-Myers Squibb; and Daiichi Sankyo, Inc.
Dr Punzi receives study grants from Abbott and Forest Pharmaceuticals, Inc. He is also a consultant for Forest Pharmaceuticals, Inc.

Education Partner Financial Disclosure Statements
The content collaborators at Strategic Medical Initiatives have reported that they have a relationship for various therapeutic areas and educational programs with Daiichi Sankyo, Inc.; Dey Pharmaceuticals; Forest Pharmaceuticals, Inc.; the American Society of Hypertension; and Ophthotech.
### Drug List

<table>
<thead>
<tr>
<th>Generic</th>
<th>Trade</th>
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</thead>
<tbody>
<tr>
<td>acebutolol</td>
<td>Sectral</td>
</tr>
<tr>
<td>atenolol</td>
<td>Tenormin</td>
</tr>
<tr>
<td>bisoprolol</td>
<td>Zebeta</td>
</tr>
<tr>
<td>carvedilol</td>
<td>Coreg</td>
</tr>
<tr>
<td>labetalol</td>
<td>Normodyne</td>
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<td>Investigational</td>
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<tr>
<td>bucindolol</td>
<td></td>
</tr>
<tr>
<td>celiprolol</td>
<td></td>
</tr>
<tr>
<td>dilevalol</td>
<td></td>
</tr>
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</table>

### Suggested Reading List


Tzemos N, Lim PO, MacDonald TM. Nebivolol reverses endothelial dysfunction in essential hypertension. *Circulation*. 2001;104:511-514.


Vasodilatory β-blockade: Clinical Implications and Pleiotropic Effects

Tuesday, September 23, 2008
Dallas, TX

Meeting Agenda and Learning Objectives

30 minutes  Unraveling Their Heterogeneity to Understand β-blockers
C. Venkata Ram, MD

30 minutes  Treating Hypertension in Clinical Practice: Interrupting the Continuum of Global Cardiovascular Risk
Henry A. Punzi, MD, FACP

15 minutes  Questions and Answers

Learning Objectives

• Outline the evolution and heterogeneity of beta blockers, the most utilized class of cardiovascular agents, with a focus on recent meta-analyses about the efficacy of these agents.
• Identify the clinical and pleotropic differences between older generation and newer beta blockers, and describe how newer formulations may aid in the control of complicated hypertension and elevated cardiovascular risk in primary care practice.

Unraveling Their Heterogeneity to Understand β-blockers

C. Venkata Ram, MD
UT Southwestern Medical Center at Dallas
Dallas, Texas

Hypertension* Prevalence Increases With Age (NHANES 1999-2004)

*Defined as systolic/diastolic blood pressure ≥ 140/90 mm Hg.
NHANES=National Health and Nutrition Examination Survey.

Awareness, Treatment, and Control Rates by Race/Ethnicity

NHANES 2003–2004

Age adjusted.
NHANES=National Health and Nutrition Examination Survey; hypertension=average BP ≥140/90 mm Hg, or patient was taking antihypertensive medications.

Ischemic Heart Disease Rates by SBP, DBP, and Age

CI=confidence interval; DBP=diastolic blood pressure; IHD=ischemic heart disease; SBP=systolic blood pressure.
The Role of Beta-blockers in the JNC 7 Algorithm for Blood Pressure Control

ARS Question
Do you believe that beta-blockers are still a safe and effective first-line treatment in hypertension?

1. Yes
2. No

JNC 7 Compelling Indications

Diuretic Beta-blocker ACEI ARB CCB AA
Heart failure ✓ ✓ ✓ ✓ ✓
Post-MI ✓ ✓ ✓ ✓ ✓
High CAD risk ✓ ✓ ✓ ✓ ✓
Diabetes ✓ ✓ ✓ ✓ ✓
Chronic kidney disease ✓ ✓
Recurrent stroke prevention ✓ ✓

Clinical Outcome Data With Beta-blockers

Total Mortality
22% to 23% reduction in total mortality in patients with hypertension or post-MI

CV Endpoints
27% to 38% reduction in sudden CV death or fatal/nonfatal stroke

Heart Failure
32% to 65% improvement in probability of event-free survival

Diabetes
Comparable cardiovascular profile in clinical endpoints related to diabetes (vs ACE-I)

Evidence for Beta-blockers in Secondary Prevention

MAPHY: Beta-blockers in Primary Prevention

Mortality and CV death rates for beta-blockers and thiazide diuretics in MAPHY study.

Risk reduction=65%
Placebo
Carvedilol

Risk reduction=34%
Placebo
Bisoprolol
Metoprolol

COPERNICUS

Risk reduction=55%
Placebo
Carvedilol

Risk reduction=38%
Placebo
CR/XL
Metoprolol

References:
Meta-analysis of Beta-blockers in Hypertension

- Meta-analysis of randomized, controlled trials of treatment of primary hypertension
  - Beta-blocker as first-line therapy in ≥50% of all patients in one treatment group
  - Outcome data for all-cause mortality, CV morbidity, or both
- 13 trials (n=105,951) comparing beta-blockers with other antihypertensive therapies
- 7 trials (n=27,433) comparing beta-blockers with placebo or no therapy
- Data analyzed for all beta-blockers, non-atenolol beta-blockers, mixed beta-blockers and diuretics, and atenolol

Meta-analysis of Beta-blockers in Hypertension: Outcome Data for Atenolol vs Non-beta-blocker Antihypertensive Therapy

<table>
<thead>
<tr>
<th>Event</th>
<th>Atenolol vs Non-beta-blocker</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke</td>
<td>1.26 (1.15-1.38)</td>
</tr>
<tr>
<td>MI</td>
<td>1.05 (0.91-1.21)</td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>1.08 (1.02-1.14)</td>
</tr>
</tbody>
</table>

Meta-analysis of Beta-blockers in Hypertension: Outcome Data for Non-atenolol Beta-blockers vs Non-beta-blocker Antihypertensive Therapy

<table>
<thead>
<tr>
<th>Event</th>
<th>Non-atenolol Beta-blockers vs Non-beta-blocker</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke</td>
<td>1.20 (0.30-4.71)</td>
</tr>
<tr>
<td>MI</td>
<td>0.86 (0.67-1.11)</td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>0.89 (0.70-1.12)</td>
</tr>
</tbody>
</table>

ARS Question

In your opinion, is the increased risk of certain cardiovascular events associated with beta-blockers a class effect?

1. Yes
2. No
The Evolution of Beta-blockers

<table>
<thead>
<tr>
<th>Year</th>
<th>Non-Selective</th>
<th>Selective</th>
<th>Non-Selective</th>
<th>Selective</th>
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<tbody>
<tr>
<td>1960s</td>
<td>propranolol</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1970s</td>
<td>atenolol</td>
<td>metoprolol</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1980s-1990s</td>
<td>carvedilol</td>
<td>labetalol</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2007</td>
<td>nebivolol</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Main Factors Contributing to Heterogeneity Within the Beta-blocker Class

- β₁/β₂ Selectivity
- Vasodilating Properties
  - Side effects
  - Metabolic profile
  - Efficacy

Pharmacologic Properties of Beta-blockers

<table>
<thead>
<tr>
<th>β-blocker</th>
<th>ISA</th>
<th>Selectivity</th>
<th>Vasodilation</th>
<th>Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acebutolol</td>
<td>+</td>
<td>Cardioselective</td>
<td>No</td>
<td>q4bid</td>
</tr>
<tr>
<td>Atenolol</td>
<td>-</td>
<td>Cardioselective</td>
<td>No</td>
<td>qd</td>
</tr>
<tr>
<td>Metoprolol</td>
<td>-</td>
<td>Cardioselective</td>
<td>No</td>
<td>qd</td>
</tr>
<tr>
<td>Nebivolol*</td>
<td>-</td>
<td>Nonselective</td>
<td>Yes</td>
<td>qd</td>
</tr>
<tr>
<td>Carvedilol</td>
<td>-</td>
<td>Nonselective</td>
<td>Yes</td>
<td>bid</td>
</tr>
<tr>
<td>Labetalol</td>
<td>+</td>
<td>Nonselective</td>
<td>Yes</td>
<td>bid</td>
</tr>
<tr>
<td>Timolol</td>
<td>-</td>
<td>Nonselective</td>
<td>No</td>
<td>bid</td>
</tr>
</tbody>
</table>

Various Mechanisms of Action of Vasodilating Beta-blockers

- β₁-receptor blockade: labetalol, carvedilol, and (likely) bucindolol
  - β₁-receptors located in smooth muscle, heart
  - When stimulated, cause contraction
- β₂-agonism: dilevalol*, celiprolol†
  - β₂-receptors located in bronchi, blood vessels, gut
  - When stimulated, cause vasodilation
- Increase in NO bioavailability: nebivolol
  - Pathways located in blood vessel walls
  - When stimulated, increases release/activity of NO, and vasodilation

Sympathetic Nervous System and HTN

Rationale for Dual α,β Blockade in HTN

HYPERTENSION

Potential Benefits of Combined α and β-Blockade

- β₁ receptors
- β₂ receptors
- α₁ receptors

Cardiotoxicity
**Effects of Nebivolol and Atenolol on Endothelial-Mediated Vasodilation**


**Effects of Nebivolol and Atenolol on NO in White and African American Endothelium**


**Effect of Beta-blockers on NO Release in Endothelial Cells of Black Americans**

*P<0.05 vs control; n=5-7.


**ARS Question**

The potential clinical advantages of vasodilatory beta-blockers are due to what factors?

1. Pleiotropic effects beyond beta-blockade
2. β-blockade
3. Increases in nitric oxide bioavailability
4. All of the above

**Summary**

- Beta-blockers remain an essential component of cardiovascular pharmacotherapy
- Beta-blockers are highly heterogeneous
  - Most notable recent advance is development of vasodilating beta-blockers
- Vasodilating beta-blockers may have important clinical advantages

**Treating Hypertension in Clinical Practice: Interrupting the Continuum of Global Cardiovascular Risk**

Henry A. Punzi, MD, FCP
Trinity Hypertension Research Institute
Texas Women’s University
Dallas, TX
ARS Question
How would you describe the patients in your practice who you treat with a beta-blocker (ie, what are their characteristics)?

1. General Hypertension (uncomplicated hypertension, patients requiring multiple medications to attain BP goal, elevated heart rate)
2. Hypertension with Cardiovascular Disease Risk (obese, smokers, elderly, hyperlipidemia, diabetes, physically inactive)
3. Compelling Indications (heart failure, post-MI, angina)

ARS Question
What are the issues with traditional beta-blockers that may prevent you from using them in certain patients?

1. 24-hour BP control with QD dosing (atenolol, metoprolol tartrate, carvedilol)
2. Tolerability (fatigue, sexual dysfunction, cold extremities, orthostatic hypotension)
3. Hard to treat patients (Black patients, obese patients)
4. Additional considerations (effects on metabolic parameters)
5. All of the above

ARS Question
If adverse events were not a concern with traditional beta-blockers, in which patients would you use these agents more frequently?

1. Younger patients
2. Male patients
3. Elderly patients
4. Patients with peripheral vascular disease
5. Earlier use in treatment regimen
6. Increased use across all patient types

The Cardiovascular Continuum: Targeting Mechanisms and Mediators

Maladaptive Cardiovascular Remodeling

Endothelial Dysfunction → Tissue Injury (MI, stroke) → Pathological remodeling → Target-organ damage (HF, renal disease) → End-stage organ failure → Death

Risk factors: Diabetes, hypertension

Vascular disease → Vascular dysfunction

Development and Progression of CVD

Risk factors → Age, gender, smoking, obesity, cholesterol, BP, glucose → Endothelial dysfunction → Compensatory responses:

1. Oxidative stress
2. Inflammation
3. Cell migration/proliferation
4. Monocyte/platelet adhesion
5. Platelet aggregation

Hypertension, Dyslipidemia, Diabetes, Smoking → CV Disease

Progression From Cardiovascular Risk Factors to Cardiovascular Disease

Adapted from Pepine CJ. Am J Cardiol. 2001;88(suppl 1):5K-9K.


Adapted from Dzau V, Braunwald E. Am Heart J. 1991;121:1244-1263.

Correlation Between Endothelial Function and Hypertension


Blood flow (mL/min/100 mL forearm volume)

<table>
<thead>
<tr>
<th>Acetylcholine (μg/min)</th>
<th>Base</th>
<th>Normotensives</th>
<th>Hypertensives</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.5</td>
<td>28</td>
<td>20</td>
<td>12</td>
</tr>
<tr>
<td>15</td>
<td>4</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>30</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

Acetylcholine (μg/100 mL/min)

Forearm blood flow (mL/100 mL forearm tissue/min)

<table>
<thead>
<tr>
<th>Base</th>
<th>Normotensives</th>
<th>Hypertensives</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.15</td>
<td>7.5</td>
<td>15.0</td>
</tr>
<tr>
<td>0.45</td>
<td>15.0</td>
<td>30.0</td>
</tr>
<tr>
<td>1.5</td>
<td>30.0</td>
<td>60.0</td>
</tr>
<tr>
<td>4.5</td>
<td>60.0</td>
<td>90.0</td>
</tr>
<tr>
<td>15</td>
<td>90.0</td>
<td>120.0</td>
</tr>
</tbody>
</table>

Endothelial Dysfunction Predicts CV Events in Hypertensive Patients


Follow-up (mo) | Event-free survival
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0.2</td>
</tr>
<tr>
<td>12</td>
<td>0.4</td>
</tr>
<tr>
<td>24</td>
<td>0.6</td>
</tr>
<tr>
<td>36</td>
<td>0.8</td>
</tr>
<tr>
<td>48</td>
<td>1.0</td>
</tr>
<tr>
<td>60</td>
<td>0.4</td>
</tr>
<tr>
<td>72</td>
<td>0.2</td>
</tr>
<tr>
<td>84</td>
<td>0.0</td>
</tr>
</tbody>
</table>

FBF= forearm blood flow.

More than 50% have ≥ 2 CV risk factors

CV=cardiovascular; HDL=high-density lipoprotein; LDL=low-density lipoprotein; LVH=left ventricular hypertrophy; TG=triglycerides.

Kannel WB. Am J Hypertens. 2000:13:3S-10S.

Benefits of Beta-blockade

• Beta-blockers are of proven benefit in many patients with hypertension and concomitant conditions, including:
  - Heart failure
  - Post-myocardial infarction
  - High CV risk
  - Diabetes


Carvedilol And Metoprolol in Patients with Hypertension: Diastolic and Systolic BP

<table>
<thead>
<tr>
<th>Change from baseline in trough BP (mm Hg)</th>
<th>Carvedilol</th>
<th>Metoprolol succinate*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diastolic</td>
<td>25 mg/d: -3.5</td>
<td>-4.0 to -7.0 across doses</td>
</tr>
<tr>
<td></td>
<td>50 mg/d: -5.5</td>
<td>across doses</td>
</tr>
<tr>
<td>Systolic</td>
<td>25 mg/d: -7.5</td>
<td>-6.0 to -8.0 across doses</td>
</tr>
<tr>
<td></td>
<td>50 mg/d: -9.0</td>
<td>across doses</td>
</tr>
</tbody>
</table>

*Placebo corrected.

Nebivolol in Patients With Hypertension: Diastolic and Systolic BP

**P** < 0.001 vs placebo.

BP = sitting blood pressure; DBP = sitting diastolic blood pressure; SBP = sitting systolic blood pressure.


### Hypertension in African-Americans
- Increased prevalence and severity
- Increased complication rate
  - 1.8 X risk for fatal stroke
  - 1.5 X risk for CHD mortality
  - 4.2 X risk for ESRD
  - 2 X risk for HF
- Volume-dependent hypertension
- Reduced BP response to beta-blockers
- Reduced bioavailability of endothelial-derived NO

### Efficacy Of Carvedilol and Acebutolol in Black Patients: Diastolic and Systolic BP

*P* < 0.005 vs baseline; †*P* < 0.05 vs baseline.


### Nebivolol in Black Patients: Diastolic and Systolic BP

*P* = 0.05 vs placebo. BP = sitting blood pressure; DBP = sitting diastolic blood pressure; SBP = sitting systolic blood pressure.


### Classic β-blocker Side Effects
- Fatigue
- Reduced exercise capacity
- Raynaud’s phenomenon
- Cold extremities
- Erectile dysfunction
- Bronchospasm
- Sinus bradycardia
- A-V block
- Metabolic effects

### Side Effects Commonly Associated with β-Blockers

<table>
<thead>
<tr>
<th>Adverse Event %</th>
<th>Nebivolol 5 mg–40 mg (n=1977)*</th>
<th>Carvedilol</th>
<th>Metoprolol Succinate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>4.0 to 8.6 across doses</td>
<td>11.5 to 20.0 across doses</td>
<td>7.5 to 15.0 across studies</td>
</tr>
<tr>
<td>Fatigue</td>
<td>3.6</td>
<td>5 to rates in PRO group</td>
<td>8.5% to 14.0 across studies</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>1.9</td>
<td>5 to rates in PRO group</td>
<td>4.7 to 7.5 across studies</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>0.8</td>
<td>2.5</td>
<td>16.9</td>
</tr>
<tr>
<td>Erectile Dysfunction</td>
<td>0.6†</td>
<td>13.5</td>
<td>4.0</td>
</tr>
<tr>
<td>Depression</td>
<td>0.3</td>
<td>&gt;5.1 to ≤5</td>
<td>4.0</td>
</tr>
</tbody>
</table>

GEMINI: Hemoglobin A1c

Treatment Difference
Carvedilol vs
Metoprolol tartrate
-0.13% (-0.22, -0.04)
P=0.004

Mean HbA1c (%)
Carvedilol (n=454)
Metoprolol tartrate (n=657)

1111 patients (90%) were evaluable for efficacy, having both a valid baseline and at least one on-therapy HbA1c assessment.


Effect of β-Blockers on Insulin Sensitivity in Patients with Hypertension

Difference between vasodilating and nonvasodilating β-blockers is approximately 30%, (similar to effects of insulin-sensitizers)

Effect of β-Blockade on Mortality in Mild-to-Advanced HF


Hemodynamic Effects of Nebivolol in Patients with Hypertension

Nebivolol1
Carvedilol2
Pindolol2
Atenolol2
Metoprolol2
Propranolol2

COPERNICUS

Effect of β-Blockade on Mortality and CV Hospitalizations

SENIORS Primary Endpoint: All-cause Mortality and CV Hospitalizations

Nebivolol
Placebo

Mortality: 34% 35%

Effect of β-Blockade on Mortality and CV Hospitalizations

RRR: -14%
ARR: -4.2%
P=0.039

Summary

- Vasodilatory beta-blockers may offer advantages over older, non-vasodilating agents
- These potential advantages include efficacy in populations not usually responsive to beta-blockers, such as Black patients, obese patients, patients with diabetes, women, and the elderly
- Vasodilating beta-blockers also may result in lower rates of AEs typically associated with beta-blockers
- The hemodynamic profiles of these agents may enhance the documented benefits of beta-blockers in terms of reducing CV morbidity and mortality

Case Study

Presentation

- 54-year-old African-American male with hypertension
- Previous medical history: benign
  - Specifically denying diabetes, hyperlipidemia, or known vascular disease
- Denies alcohol or tobacco use
- Has been told his BP was borderline on exams over the past 10 years
- Family history: positive for hypertension and diabetes
- Current medications: none

Physical Examination and Labs

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height (in)</td>
<td>5'11</td>
</tr>
<tr>
<td>Weight (lbs)</td>
<td>243</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>34</td>
</tr>
<tr>
<td>Abdominal Circumference (in)</td>
<td>42</td>
</tr>
<tr>
<td>BP (mm Hg)</td>
<td>165/96</td>
</tr>
<tr>
<td>RR (bpm)</td>
<td>88 and regular</td>
</tr>
<tr>
<td>FBS (mg/dL)</td>
<td>105</td>
</tr>
<tr>
<td>Creatinine</td>
<td>1.3</td>
</tr>
<tr>
<td>eGFR</td>
<td>74</td>
</tr>
<tr>
<td>K⁺</td>
<td>4.1</td>
</tr>
<tr>
<td>Alb/creat (mg/g creat)</td>
<td>17</td>
</tr>
<tr>
<td>Lipids</td>
<td></td>
</tr>
<tr>
<td>Total C</td>
<td>197</td>
</tr>
<tr>
<td>LDL-C</td>
<td>128</td>
</tr>
<tr>
<td>HDL-C</td>
<td>23</td>
</tr>
<tr>
<td>TG</td>
<td>218</td>
</tr>
</tbody>
</table>

- Fundi: Grade II K-W change (no hemorrhages or exudates)
- Neck: normal thyroid, carotid pulses 2+, no bruits
- Cardiac exam: regular rate, ⊕S4, no murmurs, gallops, rubs
- Abdomen: centrally obese, no bruits
- ECG: increased R-wave voltage with ST flattening c/w LVH

Risk Considerations

- African American
- Male
- Family history of hypertension and diabetes
- 5 metabolic syndrome risk factors: abdominal obesity, hypertension, low HDL, high TG, + IFG
- ECG-LVH with strain pattern

ARS Question

What is this patient's goal BP?

1. <140/90 mm Hg
2. <140/80 mm Hg
3. <130/85 mm Hg
4. <130/80 mm Hg
5. <120/80 mm Hg
ARS Question
What treatment do you recommend for this patient?
1. Anti-hypertension monotherapy, lifestyle changes, with follow-up appointment after 1 month
2. Anti-hypertension monotherapy, lifestyle changes, with follow-up appointment after 3 months
3. Combination anti-hypertension therapy, lifestyle changes, with follow-up appointment after 2 weeks
4. None of the above

Follow-up
• Patient returns in 2 weeks
• BP: 142/88 mm Hg

ARS Question
Which fixed-dose combination would you begin with?
1. ACE inhibitor/diuretic
2. ARB/diuretic
3. Beta-blocker/diuretic
4. Dihydropyridine type CCB/ACE inhibitor
5. Non-dihydropyridine type CCB/ACE inhibitor
6. Dihydropyridine type CCB/ARB

ARS Question
What treatment adjustments would you make?
1. Initiate vasodilating beta-blocker therapy
2. Initiate CCB therapy
3. Initiate α-blocker therapy
4. Initiate aldosterone antagonist therapy
5. None of the above