Treating Hypertension in the Context of Cardiometabolic Risk

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Hypertensive Metabolic Cardiac Kidney Phenotype

ABCs of Diabetes Control
(Stark Casagrande DC 2/15/13)

HYPERTENSION
- Average systolic or diastolic blood pressure above 95th percentile for age and sex on at least three occasions
- Defined as >=140/90 in American adults
- About 28% of all North American adults have hypertension
- Higher prevalence in U.S. blacks (40%) 
- With suggested targets of 130/80 in diabetes, hypertension is even more common

Hypertension Control
- Controlling high blood pressure has been a national priority in the U.S.
- Healthy People 2010 goal was met
- Hypertension control (<140/<90) improved from 27% in 1988-1994 to 50% in 2007-8
- USRDS: Improved hypertension in CKD population
- European Society for Hypertension Task Force: No compelling evidence of 130/80 mm Hg goal in diabetes
- ADA: Goals 140/80 in most cases
- JNC 8 due soon

Framingham Risk Assessment Calculator
- Hypertension
- Lipid abnormalities
  - Elevated total cholesterol
  - Elevated low density cholesterol
  - Low high-density cholesterol
- Diabetes mellitus
- Smoking
- Family history of premature coronary artery disease
  - First-degree male relative with event before age 55
  - First-degree female relative with event before age 65
- Age (men >=45, women >=55)
- Male gender

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Risk of CV Events According to Blood Pressure

<table>
<thead>
<tr>
<th>SBP, mmHg</th>
<th>HR (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Office</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;120</td>
<td>1.0 (Ref)</td>
<td>.25</td>
</tr>
<tr>
<td>120-129</td>
<td>1.04 (0.98-1.07)</td>
<td>.05</td>
</tr>
<tr>
<td>130-139</td>
<td>1.06 (0.99-1.13)</td>
<td>.1</td>
</tr>
<tr>
<td>140-149</td>
<td>1.11 (1.04-1.18)</td>
<td>.01</td>
</tr>
<tr>
<td>&gt;150</td>
<td>1.14 (1.06-1.23)</td>
<td>.001</td>
</tr>
<tr>
<td>Diastolic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;80</td>
<td>1.0 (Ref)</td>
<td>.69</td>
</tr>
<tr>
<td>80-89</td>
<td>1.10 (0.89-1.37)</td>
<td>.98</td>
</tr>
<tr>
<td>90-99</td>
<td>1.23 (1.00-1.51)</td>
<td>.05</td>
</tr>
<tr>
<td>100-109</td>
<td>1.30 (1.02-1.65)</td>
<td>.03</td>
</tr>
<tr>
<td>&gt;110</td>
<td>1.59 (1.24-2.04)</td>
<td>.001</td>
</tr>
</tbody>
</table>

Minutolo Arch Intern Med 2011; 171: 1090

Risk of CV Events and Renal Death According to Blood Pressure Success

Estimated Effects of Population-wide Shifts in Systolic BP Distributions on Mortality

Office Blood Pressure

- Considered to be the most accurate
- Usually only taken 1-3 times/year
- White Coat Hypertension may confound data
- Office BP machines are usually accurate but need to be calibrated on a routine basis.

Home Blood Pressure MonitoringPredicts Events Better than Office Measurements

- Detailed Recording
- Very Helpful for Diagnosing White Coat Hypertension
- Discover Unrecognized Hypertension
- Dippers versus Non-dippers

24 Hour Ambulatory Blood Pressure
Non-Dippers have Higher Mortality

Hypertension in Diabetes Mellitus
- Causality is multifactorial
- Type 1 diabetes:
  - Strongly associated with diabetic nephropathy
  - Genetic predisposition – increased red blood cell sodium-lithium countertransport activity – increased peripheral resistance
  - Insulin may suppress insulin release
- Type 2 diabetes:
  - Coexists with other cardiometabolic risk factors
  - Insulin resistance, hyperinsulinemia
  - Increased proximal tubule sodium resorption

Hypertension and Diabetes

**TABLE 57.1. Metabolic Disorders Associated with Hypertension and Diabetes**

<table>
<thead>
<tr>
<th>Central obesity</th>
<th>Microalbuminuria</th>
<th>Low HDL cholesterol levels</th>
<th>High triglyceride levels</th>
<th>High TC/HDL cholesterol ratio</th>
<th>Cigarette smoking</th>
<th>Hypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased BP</td>
<td>Increased BP</td>
<td>Increased BP</td>
<td>Increased BP</td>
<td>Increased BP</td>
<td>Increased BP</td>
<td>Increased BP</td>
</tr>
<tr>
<td>Increased aortic stiffness</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

HOT Diabetic Subgroup
Reduction in Cardiovascular Events


P=0.005

<table>
<thead>
<tr>
<th>Target diastolic BP (mmHg)</th>
<th>Achieved systolic BP (mmHg)</th>
<th>Achieved diastolic BP (mmHg)</th>
<th># of patients</th>
<th>Reduction in events*</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 90</td>
<td>137.7</td>
<td>59.2</td>
<td>501</td>
<td>0.01</td>
</tr>
<tr>
<td>≤ 85</td>
<td>141.4</td>
<td>63.3</td>
<td>501</td>
<td>0.01</td>
</tr>
<tr>
<td>≤ 80</td>
<td>139.7</td>
<td>81.1</td>
<td>501</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Mean of all blood pressures for all study patients in BP subgroups from 6 months of follow-up to end of study.

*Includes all myocardial infarction, all strokes, and all other cardiovascular deaths


ACCORD Blood Pressures

ACCORD Blood Pressure Outcomes - Improvement for Stroke Outcomes

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Intensive Therapy (mmHg)</th>
<th>Standard Therapy (mmHg)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic</td>
<td>129.1</td>
<td>138.8</td>
<td>0.008</td>
</tr>
<tr>
<td>Diastolic</td>
<td>76.5</td>
<td>79.0</td>
<td>0.002</td>
</tr>
<tr>
<td>Total</td>
<td>86.9</td>
<td>91.3</td>
<td>0.003</td>
</tr>
</tbody>
</table>


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**ACCORD Trial:** No benefit of Tight BP Control on Cardiovascular Outcomes

![Graph showing comparison of primary outcomes](image)

New England Journal of Medicine 362:1575-1585; 2010

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**Intensive BP Control (systolic <130) did Not Improve Cardiovascular Outcomes**

**INVEST Study (Diabetes)**

![Graph showing adjusted risk of all-cause mortality](image)

Cooper-DeHoff RM et al JAMA 304: 61-68 (2010)

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**Low Blood Pressures Appear to Increase Cardiovascular Mortality**

![Graph showing adjusted risk of all-cause mortality](image)

Cooper-DeHoff RM et al JAMA 304: 61-68 (2010)

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**Mathematical Analysis Suggests that Systolic Blood Pressure <120 Does Not Improve Outcomes Except for Stroke**

![Table showing analysis](image)


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**Prevalence of Hypertension in Diabetic Kidney Disease**

![Table showing prevalence](image)
Prevalence of CKD in Framingham Risk for Developing Coronary Heart Disease

(Weiner Am J Med 2007; 120: 552)

CKD Stages and Treatable CVD Risk Factors*

<table>
<thead>
<tr>
<th>Stage</th>
<th>Percent of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
</tr>
<tr>
<td>4-5</td>
<td></td>
</tr>
</tbody>
</table>

*Smoking, BMI ≥ 30 kg/m², total cholesterol ≥ 240 mg/dL, systolic blood pressure ≥ 140 mm Hg or diastolic blood pressure ≥ 90 mm Hg, hemoglobin < 12 g/dL in females and < 13 g/dL in males, C-reactive protein ≥ 1 mg/dL, homocysteine > 11 µmol/L, and urinary albumin/creatinine ratio ≥ 30 mg/g.

Effect of Blood Pressure Control on CKD Progression

CV Events/Mortality and eGFR KDIGO

Microalbuminuria and Cardiovascular Death

(Cardiovascular Risk Factors in CKD

- CKD-specific factors
  - Vascular calcification
  - Hyperphosphatemia
  - Elevated Ccr
  - Phosphorus Product
  - Hypertension

- Traditional: modifiable
  - Smoking
  - Hypertension
  - Hyperglycemia
  - Hyperlipidemia

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Joslin Diabetes Center
Primary Care Congress for Cardiometabolic Health 2013
Treating Hypertension in the Context of Cardiometabolic Risk

Physiology of CKD and CV Risk (white-traditional RF, shaded-nontraditional RF)

Guidelines Hypertension/CKD/DM

Blood Pressure Treatment

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<th>Drug class</th>
<th>Special considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diuretic</td>
<td>Edema common in diabetic nephropathy; thiazides not effective in renal insufficiency</td>
</tr>
<tr>
<td>Angiotensin-converting enzyme (ACE) inhibitor</td>
<td>Treatment of choice; reduce proteinuria and protect from progression; risk of hyperkalemia and worsening renal function; no adverse effects on glucose or lipid levels; avoid in renal failure</td>
</tr>
<tr>
<td>Angiotensin receptor blocker</td>
<td>Alternative to ACE inhibitor</td>
</tr>
<tr>
<td>Calcium-channel blocker</td>
<td>May use in combination with ACE inhibitor; variable effects on diabetic nephropathy</td>
</tr>
<tr>
<td>ß-Blocker</td>
<td>No long-term data on diabetic nephropathy; increased risk of diabetes; may mask warning signs of hypoglycemia</td>
</tr>
<tr>
<td>α-Blocker</td>
<td>Neutral effect on proteinuria; orthostatic hypotension; neutral on lipids and glucose intolerance; recent concern about congestive heart failure</td>
</tr>
</tbody>
</table>

Impact of Cardiovascular Disease on Antihypertensive Choices

Table 4: Special considerations in the selection of antihypertensive medications for Salt Intake and Hypertension

<table>
<thead>
<tr>
<th>Drug class</th>
<th>Special considerations</th>
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Salt Intake and Hypertension

Progress in Cardiovascular Diseases 52:363, 2010

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Diet and Hypertension:  
American Heart Association Recommendations

<table>
<thead>
<tr>
<th>Lifestyle Modification</th>
<th>Recommendation</th>
<th>Expected systolic BP reduction (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight loss</td>
<td>For overweight or obese persons, lose weight, ideally attaining a BMI &lt;25 kg/m²; for non-overweight persons, maintain a BMI &lt;25 kg/m².</td>
<td>5-10 mmHg per 1 kg weight lost</td>
</tr>
<tr>
<td>Reduced salt intake</td>
<td>Lower salt (sodium chloride) intake as much as possible, ideally to &lt;65 mmol sodium (corresponding to &lt;2.5 g of sodium or 5.6 g sodium chloride).</td>
<td>2-8 mmHg</td>
</tr>
<tr>
<td>DASH-type dietary pattern</td>
<td>Consume a diet rich in fruits and vegetables (8-10 servings/day), rich in low-fat dairy products (2-3 servings/day), and limited in saturated fat and cholesterol.</td>
<td>2-4 mmHg</td>
</tr>
<tr>
<td>Increased potassium intake</td>
<td>Increase potassium intake to 150 mmol (4.7 g), which is also provided in DASH-type dietary pattern.</td>
<td>2-4 mmHg</td>
</tr>
<tr>
<td>Limitation of alcohol intake</td>
<td>For those who drink alcohol, consume 2 alcoholic drinks/day (men) and 1 alcoholic drink/day (women).</td>
<td>2-4 mmHg</td>
</tr>
</tbody>
</table>

ACEI/ARB treatment on CKD Outcomes

- Hermida CD 2011;34: 1270
- Type 2 DM
- Prospective, randomized
- All meds in AM vs. some bedtime treatment

Time of BP Meds and Cardiovascular Risk

Recommendations

- AN INTEGRATED APPROACH
- Use Home Blood Pressure Monitoring
- Consider Patient Compliance
- Dosing Schedule
- Number of Medications
- Cost
- EDUCATION: Discuss pathophysiology with patients
- Exercise, weight loss, diet, smoking cessation, and salt restriction are paramount
- Select Medications Based on Comorbidities
  - Cardiovascular Disease
    - Beta Blockers
    - ACE Inhibitors
    - Aldosterone Antagonists
  - Kidney Disease
    - RAAS System inhibitors
    - Non-dihydropyridine Calcium Channel Blockers
Question 1: The risk of cardiovascular disease in increased significantly with:

- CKD
- Microalbuminuria
- Both
- Neither

Question 2: Cardiovascular risk factors in CKD include:

- Traditional risk factors
- CKD-specific risk factors
- Both
- Neither

Question 3. The blood pressure measurement that has been shown to best predict development of complications of hypertension is:

1. Home blood pressure
2. Office blood pressure
3. 24-hour blood pressure monitoring
4. Arterial line blood pressure measurement