Hypertension: When to Look for a Secondary Cause?

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Disclosures

• Cook Medical – Honoraria/training
Background

• The treatment of hypertension is the most common reason for office visits of adults to clinicians in the United States and for use of prescription drugs

• The National Health and Nutrition Examination Survey (NHANES) conducted from 2005 to 2008 estimated that approximately 29-31% of adults in the US have hypertension

• Extrapolating from this data, approximately 76.4 million Americans over the age of 20 have hypertension

• Data from the NHANES has also suggests that as many as 8% of US adults have undiagnosed hypertension
Global Burden of Hypertension is Substantial and Growing

- Global Prevalence in 2000: 26.4% (972M)
- Global Prevalence in 2025: 29.2% (1,560M)

- Total Hypertensive Population in 2000: 972M
- Total Hypertensive Population in 2025: 1,560M
Hypertension and risk of death from stroke and heart disease

Systolic BP / Diastolic BP (mmHg)

CV mortality risk doubles for every 20 mmHg increase in systolic blood pressure.$^1$,$^2$
Background

• Essential hypertension is the cause of the vast majority of cases of arterial hypertension.
• Approximately 5 to 10 percent of adults with hypertension have secondary hypertension.
• Secondary hypertension is defined as increased systemic blood pressure due to an identifiable cause.
Background

• Secondary forms are less common and screening for them can be expensive and laborious.
• Not cost effective to perform complete evaluations for all secondary causes in every patient.
• Early detection and treatment are important to minimize/prevent irreversible changes in the systemic vasculature which may give rise to persistent hypertension with a poor long-term outcome.
So When!?

LOOK for a secondary cause of hypertension while evaluating ALL patients with hypertension

But only TEST for secondary hypertension if indicated based on this comprehensive evaluation
Initial Evaluation

• Rule out pseudoresistance prior to screening
• Consider drugs or interfering substances as cause
• Examine for signs and symptoms in the history and physical exam suggestive of specific secondary causes, if present proceed with directed testing only
• In the absence of identifiable signs and symptoms, screen and test for secondary hypertension more broadly based on the presence of suggestive clinical characteristics
Suggestive Clinical Characteristics

- An acute rise in blood pressure in a patient with previously stable values
- Age < 30 years old in a non-obese patient with a negative family history and no other risk factors
- Proven age of onset before puberty
- Resistant hypertension (140/90 mmHg despite three antihypertensive drugs including a diuretic)
- Severe hypertension (180/110 mmHg) or hypertensive emergencies, particularly if onset after age of 55 years
- Non-dipping or reverse dipping during 24h ambulatory BP monitoring
- Presence of target organ damage (i.e. LVH, hypertensive retinopathy, etc.)
Secondary Hypertension or Pseudoresistance?

- Improper blood pressure measurement
- Heavily calcified or arteriosclerotic arteries that are difficult to compress
- “White coat” effect
- Poor patient adherence
  - Medication side effects
  - Complicated dosing
  - Inadequate patient education
  - Cost of medication
- Inadequate dosing or inappropriate combination therapy
- Physician inertia (failure to change or increase dose regimens while not at goal)

“I’m going to take your blood pressure, so try to relax and not think about what a high reading might mean for your chances of living a long, healthy life.”
Secondary Hypertension: Drugs, etc

- Immunosuppressive agents
- NSAIDS/COX-2 Inhibitors
- Estrogens/BCP
- Decongestants
- Diet pills
- Anti-depressants
- Mineralocorticoids
- Licorice
- Anabolic steroids
- Cocaine
- Amphetamine
- Alcohol
- Angiogenesis drugs
## Causes of Secondary Hypertension

<table>
<thead>
<tr>
<th>Disease</th>
<th>HTN Referral Center¹</th>
<th>Japanese General Outpatient Clinic²</th>
<th>Kaiser Northern CA / Colorado Systems³</th>
<th>REACH Registry⁴</th>
</tr>
</thead>
<tbody>
<tr>
<td>Common</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drugs</td>
<td>No estimate provided</td>
<td>No estimate provided</td>
<td>Etoh 3.6%, Smoking 10.2%, Elicit drugs 13.9%</td>
<td>13.6% NSAIDS</td>
</tr>
<tr>
<td>Obstructive Sleep Apnea</td>
<td>No estimate provided</td>
<td>No estimate provided</td>
<td>2.0%</td>
<td>No estimate provided</td>
</tr>
<tr>
<td>Renal disease</td>
<td>1.8% (8.0% with atherosclerosis)</td>
<td>excluded</td>
<td>5.2%</td>
<td>40.1% (GFR &lt; 60)</td>
</tr>
<tr>
<td>Primary aldosteronism</td>
<td>1.4%</td>
<td>6.0%</td>
<td>No estimate provided</td>
<td>No estimate provided</td>
</tr>
<tr>
<td>Renal artery stenosis</td>
<td>3.1% (9.5% with atherosclerosis)</td>
<td>0.5%</td>
<td>No estimate provided</td>
<td>No estimate provided</td>
</tr>
<tr>
<td>Hypo/Hyperthyroidism</td>
<td>3.0%</td>
<td>No estimate provided</td>
<td>No estimate provided</td>
<td>No estimate provided</td>
</tr>
<tr>
<td>Uncommon</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pheochromocytoma</td>
<td>0.3%</td>
<td>0.6%</td>
<td>No estimate provided</td>
<td>No estimate provided</td>
</tr>
<tr>
<td>Cushing’s disease</td>
<td>0.5%</td>
<td>2.1%</td>
<td>No estimate provided</td>
<td>No estimate provided</td>
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<tr>
<td>Hyperparathyroidism</td>
<td>No estimate provided</td>
<td>No estimate provided</td>
<td>No estimate provided</td>
<td>No estimate provided</td>
</tr>
<tr>
<td>Aortic coarctation</td>
<td>No estimate provided</td>
<td>No estimate provided</td>
<td>No estimate provided</td>
<td>No estimate provided</td>
</tr>
</tbody>
</table>

4 Kumbani et al. Resistant hypertension: a frequent and ominous finding among hypertensive patients with atherothrombosis. European Heart Journal (2013) 34, 1204-1214
Secondary Hypertension: OSA

• Prevalence of 2%-30%, increases with age, plateau between age 55-65
• Mechanism includes increased sympathetic nerve activity, alterations of the renin–angiotensin–aldosterone system and endothelial dysfunction as a result of recurrent nocturnal hypoxemia
• Signs and symptoms
  - Obesity, macroglossia, apneic episodes/snoring
    Increased neck circumference, edema, somnolence
• Screen with Epworth Sleepiness Scale
• Diagnosis by Polysomnography
Secondary Hypertension: Renal Artery Stenosis

- Prevalence of 2-20%
- Consider FMD in young adults/women and atherosclerotic disease in older adults
- Signs and symptoms
  - Hypertension before age 30
  - Severe hypertension after age 55
  - Accelerated hypertension
  - New azotemia/worsening renal function after ACE
  - Atrophic kidney or size discrepancy of 1.5 cm
  - Flash pulmonary edema
- Screening and diagnosis with CTA, MRA, duplex ultrasonography
Secondary Hypertension: Primary Hyperaldosteronism

• Prevalence of 6-23%
• Signs and symptoms
  - Hypokalemia, unprovoked or with diuretic
  - Severe or resistant hypertension
  - Family history of hyperaldosteronism
  - Adrenal “incidentaloma” (2% prevalence)
• Screen with aldosterone/renin ratio, Na+ loading
• Diagnosis with imaging CT/MR + adrenal vein sampling
Secondary Hypertension: Renal parenchymal disease

• Prevalence of 2-10%
• Most common cause of secondary hypertension in children and also a common cause in adults.
• Signs and symptoms
  - Loss of adequate BP control
  - Diabetes, Smoking
  - Generalized atherosclerosis
  - Previous renal failure/nocturia
  - Edema, loss of muscle mass
• Screen with urinalysis, serum creatinine
• Diagnosis with renal ultrasound
Secondary Hypertension: Cushings Syndrome

• Prevalence of < 1%, typical age range 25-45 years
• Affects women 3 to 8 times more than men
• Sign and symptoms
  - Obesity
  - Facial plethora
  - Buffalo hump
  - Hirsutism
  - Purple striae
  - Hypertension very common > 80%
• Diagnosis by positive results in at least two of the following tests:
  – 24 hour urinary cortisol (3 times upper limit)
  – Low dose dexamethasone suppression test
  – Late evening salivary cortisol
• Specificity of these tests is 84-96% in obese pts with + features
Secondary Hypertension: Pheochromocytoma

• Prevalence of <1%, age on onset < 40 years old
• Associated with familial endocrinopathies, malignant in 10%
• Sign and symptoms
  - Hyperadrenergic spells (paroxysmal hypertension, pounding headache, perspiration, palpitations, palor)
  - Severe or resistant hypertension
  - Family history
  - Onset < 20 years old
  - Incidentaloma
• Screen with plasma metanephrines, 24 hour urine for catecholamines, metanephrines, vma
• Confirmatory imaging with CT or MRI, MIBG
Secondary Hypertension: Thyroid disease

- Prevalence of 1-3%
- Thyroid hormone affects cardiac output and SVR
- Hypothyroidism can cause an elevation in diastolic blood pressure, hyperthyroidism can cause an isolated elevation of systolic blood pressure, leading to a widened pulse pressure.
- Signs and symptoms
  - Hyperthyroidism - palpitations, weight loss, heat intolerance, exophthalmos, tachycardia
  - Hypothyroidism – bradycardia, weight gain, fatigue, muscle weakness
- Screening and diagnosis with thyroid-stimulating hormone measurement
Secondary Hypertension: Aortic coarctation

- Prevalence of <1%
- Aortic coarctation is the second most common cause of hypertension in children and young adults.
- It is characterized by constriction of the lumen of the aorta usually near the ligamentum arteriosum.
- Signs and symptoms
  - headache, cold feet, nose bleeds, claudication
  - arterial hypertension in the presence of weak femoral pulses
- Screening and diagnosis with LE blood pressure measurement, echocardiography, CT, MRI
Conclusion

• Secondary hypertension is defined as increased systemic blood pressure due to an identifiable cause.

• Early detection and treatment are important to minimize/prevent irreversible changes in the systemic vasculature which may give rise to persistent hypertension with a poor long-term outcome.

• The initial evaluation of ALL patients with hypertension should include consideration of the possibility of secondary hypertension.

• Examine for signs and symptoms of secondary hypertension to direct testing but in the absence of these, screen and test for secondary hypertension based on the presence of suggestive clinical clues.
Thank You!!

“No, it’s not water. You seem to be retaining food.”