Hypertensive Heart Disease

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HEART FAILURE
A COMPANION TO BRAUNWALD'S HEART DISEASE
3rd Edition

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G. MICHAEL FELKER

CEDARS-SINAI HEART INSTITUTE
HYPERTENSION CENTER
ASH Certified Comprehensive Center
Impact

- >1 billion hypertensive world-wide
- >70 million hypertensives in the US (29%)
- Hypertension is underdiagnosed and undertreated \( \rightarrow \) Hypertensive Heart

Case: 72 yom with isolated systolic hypertension and exertional dyspnea

- Treated for many years with Atenolol and HCTZ.
- Normal kidney function
- No known CAD
- Diet-controlled DM
- Clinic BP 156/72
- Increasing shortness of breath x 2 months
Case: 72 yom with isolated systolic hypertension and exertional dyspnea
Case: 72 yom with isolated systolic hypertension and exertional dyspnea

ECG
- No/borderline criteria for LVH on ECG
- Non-pathologic Q-wave in III and aVF

Echo:
- Mild concentric LVH on Echo
- Preserved LVEF
- Minimal hypokinesis in inferolateral wall
**Case:** 72 yom with isolated systolic hypertension and exertional dyspnea
Causes, Course and Complications of Hypertensive Heart Disease

- Genetic predisposition?
- Obesity
- Diabetes
- Smoking
- CKD

Hypertension

- Smoking
- Dyslipidemia
- Diabetes
- Genetic Predisposition

LVH

- AFIB
- SCD

Diastolic dysfunction

Systolic dysfunction

CHF

MI
A heterogeneous disease

• Structural remodeling from pressure overload (LVH)
• Development of ischemic heart disease as “optional” intermediate step
• Congestive heart failure
  – “Diastolic heart failure” - HFpEF
  – “Systolic heart failure” - HFrEF
Prevalence of LVH

- Dallas Heart Study
  9.4% by cardiac MRI (NT&HTN)
- Multi-Ethnic Study of Atherosclerosis (MESA)
  11% by cardiac MRI
- Among hypertensives
  ~40% by echo
  ~1 to 40% by ECG
Epidemiology-Ethnic differences

- **Dallas Heart Study:**
  - Black Americans 1.8x more LVH

- **Hypertension Genetic Epidemiology Network**
  - Black Americans 2.5x more LVH

- **MESA** and other population-based studies suggest:
  - Hispanics may have a similarly greater risk for LVH
  - Both in Hispanics and Black, greater increases in LV mass is a response to pressure overload—not inherent—thus preventable
Risk factors for LVH

- Office/ambulatory BP
- Men > women
- Ethnicity
- Smoking
- Obesity
- OSA
- CKD (even mild)
- Black race and CKD: 70% LVH!!

Diagnosis
<table>
<thead>
<tr>
<th>ECG criteria</th>
<th>Diagnostic cut-off</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>R in aVL</td>
<td>≥ 1.1 mV</td>
<td>11</td>
<td>97</td>
</tr>
<tr>
<td>Sokolow-Lyon voltage</td>
<td>≥ 3.5 mV</td>
<td>13</td>
<td>93</td>
</tr>
<tr>
<td>S in V₄ + R in V₅ or V₆</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cornell voltage</td>
<td>&gt;2.8 mV (men)</td>
<td>19</td>
<td>97</td>
</tr>
<tr>
<td>S in V₃ + R in aVL</td>
<td>&gt;2.0 mV (women)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Romhilt-Estes score</td>
<td>total of ≥5 points</td>
<td>16</td>
<td>96</td>
</tr>
<tr>
<td>Components:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Any of these:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>R or S in limb leads ≥20;</td>
<td>1 point</td>
<td></td>
<td></td>
</tr>
<tr>
<td>S in V1 or V2 ≥30;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>R in V5 or V6 ≥30</td>
<td>3 points</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. ST-T vector opposite to QRS</td>
<td>3 points</td>
<td></td>
<td></td>
</tr>
<tr>
<td>with digitalis</td>
<td>2 points</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ST-T vector opposite to QRS</td>
<td>1 point</td>
<td></td>
<td></td>
</tr>
<tr>
<td>without digitalis</td>
<td>1 point</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. left atrial enlargement in V1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Left axis deviation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. QRS duration ≥0.09 s</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. Intrinsicoid deflection in V₅</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>or V₆ &gt;0.05 s</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perugia criteria</td>
<td>≥1 of the following criteria</td>
<td>36</td>
<td>90</td>
</tr>
<tr>
<td>Components:</td>
<td>≥1 of the following criteria</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. S in V₃ + R in aVL</td>
<td>&gt;2.4 mV (men)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. LV strain (ST-T vector opposite to QRS)</td>
<td>&gt;2.0 mV (women) present ≥5 points</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Diagnosis-ECHO
Diagnosis-Echo

Linear measurements: septum or inferolateral wall in diastole > 1.0 cm
Left ventricular mass = \(0.8 \times (1.04 \times \left[\left(LVIDd + PWTd + SWTd\right)^3 - (LVIDd)^3\right]) + 0.6 \text{ g}\)

<table>
<thead>
<tr>
<th>Severity</th>
<th>LVMI in men, g/m²</th>
<th>LVMI in women, g/m²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild LVH</td>
<td>103 to 116</td>
<td>89 to 100</td>
</tr>
<tr>
<td>Moderate LVH</td>
<td>117 to 130</td>
<td>101 to 112</td>
</tr>
<tr>
<td>Severe LVH</td>
<td>≥131</td>
<td>≥113</td>
</tr>
</tbody>
</table>

Cardiac MRI: 2x as precise and 93% less interstudy variability, but has limitations
Relative wall thickness
(2x PWT/LVEDD)

Concentric LV Remodeling

Concentric LVH

Normal LV

Eccentric LVH

Men: 111 g/m²
Women: 106 g/m²

Left ventricular mass index

Pathomechanisms

LVH=Increases of:

- Cardiomyocyte proteins
- Fibroblasts
- Endothelial cells
- Extracellular matrix

*Lack of proportional increase of microvasculature is key (similar in HCM)*

Pathomechanisms of LVH

• Hemodynamic burden:
  – 24-hour ABPM better than office
  – Lifetime burden (Blacks)

• Neurohormonal stimulation
  – Angiotensin II → G-protein mediated myocyte protein and fibroblast (collagen) stimulation
  – Aldosterone: “Aldosterone escape”
  – Endothelin-1

Mazzolai L et al. Hypertension 1998;31:1324-1330
Genetic determinants of LVH

• Twin-studies demonstrate *heritability* of LV mass between ~0.2
• Corin (splice enzyme for ANP and BNP) reduces LVH and mutations have been found exclusively in Blacks (6-12% prevalence) and was associated with LVH
• Bradykinin-2 (9bp receptor)
• ACE polymorphisms associated with LVH

Post WS et al. *Hypertension* 1997;30:1025-1028
COMPLICATIONS OF HYPERTENSIVE HEART DISEASE
Hypertensive Heart Disease Classification

- **Class I**: Subclinical diastolic dysfunction without LVH: Asymptomatic patients with abnormal left ventricular relaxation/stiffness by Doppler echocardiography, a common finding in individuals >65 years

- **Class II**: LVH
  - IIA: with normal functional capacity (NYHA class I)
  - IIB: with abnormal functional capacity (NYHA class >2)

- **Class III**: Heart failure with preserved ejection fraction (HFpEF)

- **Class IV**: Heart failure with reduced ejection fraction (HFrEF)
HFpEF “Cardiogeriatric Syndrome”

- CHF-admissions tripled 1979 to 2004
- Age>65 → 80% of HF admissions
- HF most expensive DRG diagnosis $$$$$
- Most frequent diagnosis for 30-day readmissions

**Advances:** decrease in LOS, decreases in hospital admission rates **BUT**

**Forecast:** in an aging population, hypertensive heart disease and resulting heart failure will continue to be a major societal burden

HFpEF-Risk≈LVH Risk

- Older Age
- Female gender
- HTN
- DM
- Obesity
- CKD
- CAD
HFpEF—it’s not only the heart

Treatment of HFpEF

- No effective Rx (mortality)
  - Irbesartan
  - Candesartan
  - Perindopril
  - spironolactone
- Spironolactone
  - may reduce HF admissions
- Stem cells?

CHARM-Preserved. Lancet 2003;362:777-781
PEP-CHF. Eur Heart J 2006;27:2338-2345
Treatment of HFrEF

- BB, RAAS blocker, aldo blocker, Bidil, devices,…
- Cardiovascular Health Study
  - Increased LV mass index strongly predicted decreased LVEF over 5 year follow up (independent of age, BP, DM or CAD)
  - Elevated BNP and hs-Troponin levels may identify high risk groups for development of low LVEF and death
  - Reduction of LV mass with medical therapies also improves systolic LV function
Ischemic Heart Disease

• HTN and LVH are potent risk factors for CAD (Framingham, CARDIA)
• LVH increases the risk for unstable (vs. stable) CAD
• Microvascular ischemia is a hallmark of hypertensive heart disease and is more common in women
• Aggressive risk factor modification is key in the prevention of CAD in patients with LVH
Atrial fibrillation

- Most common supraventricular arrhythmia
- 0.1% in <55y and >10% in 80+y
- Linked to SBP, LVH, systolic and diastolic function, obesity (OSA!!) and DM
- HTN is most prevalent modifiable RF for AF
- Pressure overload, atrial fibrosis, angiotensin II, oxidative stress are causative
- AF increases risk for SCD in LVH
- ARB may or may not prevent AFIB

+CHARM substudy. Am Heart J 2006;152:86-92
+ValHeFT substudy. Am Heart J 2005;149:548-557
Mortality

- Framingham: 50 g increase of LV mass
  - SCD: RR 1.45
  - all-cause mortality: Men: RR 1.49, Women: RR 2.01

- LIFE-study:

Devereux RB et al. *JAMA* 2004;292:2350-2356.
Treatment of LVH

• Premise: treating risk factors for LVH is key but some medical therapies may specifically target LVH regression

Treatment of LVH

Treatment of LVH

- ARBs: 13% (95% CI 8% to 18%)
- CCB: 11% (95% CI 9% to 13%)
- ACE-inhibitors: 10 % (95% CI 8% to 12%)
- Diuretics: 8% (95% CI 5% to 10%)
- Beta blockers by 6% (95% CI 3% to 8 %)

Summary

- Hypertensive heart disease ≈ LVH+/-CAD
- Identify high risk populations: Blacks, CKD
- Important prognosticator and therapeutic target
- High risk! Aggressive CV risk factor modification!
- Treat to avoid HFpEF, HFrEF, CAD, AFIB, death
- For LVH regression, ARB may be most effective, beta blockers least
- Recent data (SPRINT) suggests that more aggressive treatment of HTN is beneficial