Infiltrative and Restrictive Cardiomyopathy: Recognition by Echo

Gerard P. Aurigemma MD, FASE, FAHA, FACC
University of Massachusetts Medical School
<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Clinical Findings</th>
<th>Biomarkers</th>
<th>ECG</th>
<th>X-Ray/CT</th>
<th>Echo/Doppler</th>
<th>CMR</th>
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<td>Pericardial calcification†</td>
<td>Septal bounce, high e', exaggerated respiratory flow variability*</td>
<td>Pericardial thickening, ventricular interdependence, pericardial late enhancement†</td>
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<td>Pericardial fibrosis/inflammation, normal myocardium</td>
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*Highly sensitive findings with low specificity. †Highly specific findings with low sensitivity. ‡Findings that are both highly sensitive and specific.

CMR = cardiac magnetic resonance; CPK = creatine phosphokinase; CT = computed tomography; e' = tissue Doppler early myocardial velocity; ECG = electrocardiogram; Echo = echocardiography; EMF = endomyocardial fibrosis; H/O = history of; LV = left ventricle/ventriclear; LVH = left ventricular hypertrophy; LVOT = left ventricular outflow tract; PRKAG2 = protein kinase AMP-activated noncatalytic subunit gamma 2; RCM = restrictive cardiomyopathy.
Peak Systolic Strain

| GLSP_LAX  | -8.4 % | GLPS_Avg  | -9.2 % |
| GLPS_A4C  | -8.7 % | AVC_Auto  | 281 msec |
| GLPS_A2C  | -10.4 % | HR_ApLAX  | 91.4 bpm |
City of Worcester, MA
Mobile Strain Screening Program
Restrictive Cardiomyopathy in Clinical Practice 2017
80 year old man with DOE and new onset AF
74 year old man s/p TAVR Still has HF
88 year old initial visit at TAVR clinic
58 year old with dizziness and presyncopal symptoms
19 year old with chest pain and dyspnea
Restrictive Cardiomyopathy

- Least common of the cardiomyopathies
- The cardiac chambers cannot stretch normally = stiff/noncompliant
- Filling at normal pressure is limited
- Normal LV and RV chamber size
- Atrial enlargement – reflects increased ventricular filling pressures/atrial pressure
Pathophysiology

- Rigid Myocardium
- Diastolic ventricular pressure
  - Venous congestion
    - Jugular vein distention
    - Hepatomegaly and ascites
    - Peripheral edema
- Ventricular filling
  - CO
    - Weakness
    - Fatigue
90\% \times \text{small EDV} = \text{small SV}
Rise in PCWP

Flat stroke volume response to exercise

Kitzman Circulation 1991
Case 1

- 80 year old male with mild AS, COPD not on O2 who presented with DOE x 1 month.
- new Afib that was rate controlled.
- Sudden dyspnea after CXR
The ‘Transducer of Truth’
TTE
4 years ago

Now
- RA 6 mmHg
- RV 26/9 mmHg
- PA 27/11/16 mmHg
- PCWP 14 mmHg
- Fick CO 3.82, CI 2.16
$^{99m}$Tc-Pyrophosphate Scintigraphy for Differentiating Light-Chain Cardiac Amyloidosis From the Transthyretin-Related Familial and Senile Cardiac Amyloidoses

Sabahat Bokhari, MD; Adam Castaño, MD; Ted Pozniakoff, BS, RT(N)(R); Susan Deslisle, MS; Farhana Latif, MD; Mathew S. Maurer, MD
Whole Body Scan

- Degenerative change in the right shoulder, otherwise normal scan.
Amyloidosis

**Light Chain (AL)**

- Fibrills composed of light chain Ig.
- Produced by clonal population of plasma cells.
- Treatment with chemotherapy.

**Transthyretin related (ATTR)**

- Familial (ATTRm)
- Wild/Senile type (ATTRwt)
- Mutation of the TTR protein
- ATTRm all ages
- ATTRwt mostly old age
# How to Use Imaging

## How to Image Cardiac Amyloidosis

Rodney H. Falk, MD; Candida C. Quarta, MD; Sharmila Dorbala, MD, MPH

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<td>Results from amyloid infiltration of interstitial space and may relate to amyloid burden</td>
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<td>Decreased LV end-diastolic volumes</td>
<td>Leads to reduced stroke volume despite near-normal LVEF</td>
</tr>
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<td>Typically preserved or mildly reduced LVEF</td>
<td>LVEF may decrease in end-stage disease</td>
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<td>High E/A ratio</td>
<td>Is seen because of restrictive pathophysiology, but a reduced amplitude A wave may suggest poor atrial function and higher risk of thrombus formation*</td>
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<td>Shortened mitral E deceleration time (restrictive filling pattern)</td>
<td>High E/e’ suggests increased left atrial pressures</td>
</tr>
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<td>High E/e’ ratio</td>
<td>A common feature. Also imaged on CMR</td>
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<td>Increased left and right atrial volumes and reduced atrial function</td>
<td>Atrial strain can be significantly reduced</td>
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<td>LS in the left ventricle is impaired and worse at the base and mid-ventricular regions when compared with the apex^4</td>
<td>Specific patterns of LV LS may differentiate amyloid from aortic stenosis and hypertrophic cardiomyopathy^7,8</td>
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<td>RV thickening, reduced RV myocardial velocities on tissue Doppler imaging, and reduced RV LS^5,6</td>
<td>TAPSE and RV LS are early indicators of cardiac involvement in patients with systemic AL amyloidosis^6,8</td>
</tr>
<tr>
<td>Reduced tricuspid annular plane excursion despite normal RV end-diastolic dimension^5,6</td>
<td>RV LS may be an independent predictor of cardiac death^5</td>
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<td>Valve thickening</td>
<td>Nonspecific</td>
</tr>
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<td>Pericardial effusion</td>
<td>Nonspecific</td>
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<tr>
<td>Atrial septal thickening</td>
<td>A characteristic feature of cardiac amyloidosis</td>
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<td>A less common feature but need to distinguish from hypertrophic cardiomyopathy</td>
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AL indicates amyloid light-chain; CMR, cardiac magnetic resonance; LS, longitudinal strain; LV, left ventricular; LVEF, LV ejection fraction; RV, right ventricular; and TAPSE, tricuspid annular plane excursion.

^Hypertrophic cardiomyopathy, hypertensive heart disease with or without renal failure, Anderson Fabry’s disease, mucopolysaccharidosis, Friedreich ataxia.
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Conclusions: Among older adults undergoing TAVR 16% of patients (92% of which were men) had ATTR-CA by 99mTc-PYP scan with a phenotype of severe concentric left ventricular hypertrophy and low flow AS. Ongoing study in larger population will determine the implications of such findings with regard to outcomes.
74 year old man
s/p TAVR
Still has HF
88 year old initial visit at TAVR clinic
Strain Images

LVEF: GLS (6:1)
15.0 MCI TC99M PYP
PYP CARDIAC AMYLOID STUDY

IMAGED 70 MINUTES POST INJECTION
4 Questions

• Can you tell types apart?
• Why the gradient?
• Is wall thickness all due to amyloid deposition?
• Do they benefit from TAVR?
• GLS correlates with WT
• TTRwt had worst GLS but best outcome
• Light chain toxicity in AL might be important mechanism
LVEF: GLS (6:1)
## Cardiomyopathies

### Echo Parameters for Differential Diagnosis in Cardiac Amyloidosis

A Head-to-Head Comparison of Deformation and Nondeformation Parameters

Efstathios D. Pagourelis, MD, PhD; Oana Mirea, MD, PhD; Jürgen Duchenne, MSc; Johan Van Cleemput, MD, PhD; Michel Delforge, MD, PhD; Jan Bogaert, MD, PhD; Tatyana Kuznetsova, MD, PhD; Jens-Uwe Voigt, MD, PhD

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### Table 4. Bootstrapped ROC Curve Characteristics and Cut-Off Points of Deformation Echo Parameters for Differential Diagnosis of Amyloidosis

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<tr>
<th>Variable</th>
<th>AUC</th>
<th>95% CI</th>
<th>P Value</th>
<th>Cutoff</th>
<th>95% CI</th>
<th>Sens, %</th>
<th>95% CI</th>
<th>Spec, %</th>
<th>95% CI</th>
<th>+LR</th>
<th>95% CI</th>
<th>-LR</th>
<th>95% CI</th>
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<tr>
<td>GLS, %</td>
<td>0.85</td>
<td>0.77–0.89</td>
<td>&lt;0.0001</td>
<td>&gt;−15.1</td>
<td>&gt;−16.7 to &gt;−13.1</td>
<td>87.5</td>
<td>73–96</td>
<td>71.7</td>
<td>59–83</td>
<td>3.09</td>
<td>2–4.7</td>
<td>0.17</td>
<td>0.08–0.4</td>
</tr>
<tr>
<td>GCS, %</td>
<td>0.83</td>
<td>0.73–0.90</td>
<td>&lt;0.0001</td>
<td>≤−18.3</td>
<td>&gt;−22.2 to &gt;−17.4</td>
<td>86.2</td>
<td>68.3–96.1</td>
<td>57.1</td>
<td>43.2–70.3</td>
<td>2.01</td>
<td>1.4–2.8</td>
<td>0.24</td>
<td>0.09–0.6</td>
</tr>
<tr>
<td>GRS, %</td>
<td>0.82</td>
<td>0.72–0.90</td>
<td>&lt;0.0001</td>
<td>≤9.01</td>
<td>≤5.33 to ≤9.78</td>
<td>65.5</td>
<td>45.7–82.1</td>
<td>89.3</td>
<td>78–96</td>
<td>6.1</td>
<td>2.7–13.6</td>
<td>0.39</td>
<td>0.2–0.6</td>
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<tr>
<td>EFSR</td>
<td><strong>0.95</strong></td>
<td><strong>0.89–0.984</strong></td>
<td>&lt;0.0001</td>
<td>&gt;4.1</td>
<td>&gt;3.6 to &gt;4.1</td>
<td>89.7</td>
<td>75.8–97.1</td>
<td>91.7</td>
<td>81.6–97.2</td>
<td>10.8</td>
<td>4.6–25.1</td>
<td>0.11</td>
<td>0.04–0.3</td>
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<td>RELAPS</td>
<td>0.78</td>
<td>0.68–0.86</td>
<td>&lt;0.0001</td>
<td>&gt;0.87</td>
<td>&gt;0.79 to &gt;1</td>
<td>62.5</td>
<td>43.8–77.3</td>
<td>85</td>
<td>73.4–92.9</td>
<td>4.17</td>
<td>2.2–8</td>
<td>0.44</td>
<td>0.3–0.7</td>
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<td></td>
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<td>&gt;1.0*</td>
<td>...</td>
<td>37.5</td>
<td>22.7–54.2</td>
<td>93.3</td>
<td>83.8–98.2</td>
<td>5.63</td>
<td>2.1–15.7</td>
<td>0.67</td>
<td>0.5–0.9</td>
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<td>SAB</td>
<td>0.67</td>
<td>0.57–0.76</td>
<td>0.0024</td>
<td>&gt;3.1</td>
<td>&gt;1.7 to &gt;3.7</td>
<td>47.5</td>
<td>31.5–63.9</td>
<td>86.7</td>
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<td>&gt;2.1*</td>
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<td>48.3–79.4</td>
<td>53</td>
<td>41.6–67.9</td>
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Case 2

- 43 year old man
- Excessive EtOH usage
- Abdominal discomfort
- Now DOE
- + troponin
EKG
Case The Attorney

58 year old with dizziness and presyncopal symptoms

left leg pain, numbness and swelling in both lower extremities.
Fabry’s Disease

- Fabry Disease
- Anderson-Fabry Disease
- α-galactosidase A deficiency
- Leukocyte levels
- Angiokeratosis
- X-linked recessive
- Affects predominantly males
- Affects homozygous females
Fabry Disease Cardiac Manifestations

- Left ventricular hypertrophy
- Hypertrophic cardiomyopathy, generally symmetric.
- Conduction defects: Short PR interval, Qt prolongation often with RBBB, tachyarrythmias, SCD.
- Aortic root dilatation
- Aortic and mitral valve insufficiency
- Ischemic disease, either due to endothelial dysfunction, microvasculature dysfunction or secondary to severe LV hypertrophy.
19 year old with chest pain and dyspnea