Constrictive/Restrictive Cardiomyopathies: Diagnosis and Management Update; Radiation Induced Heart Disease

Alexander (Sandy) Dick, MD
Outline

• Pericardial Constriction
  – Diagnosis: Imaging, Hemodynamics
  – Outcomes

• Restrictive Cardiomyopathy
  – Diagnosis: Imaging

• Radiation Induced Heart Disease
  – Incidence
  – Imaging follow-up
Case

- Afib, global LV dysfunction LVEF 40-45%
- 6 month Hx of increasing dyspnea NYHA Class III. Significant peripheral edema.
General Principles

• Both constrictive pericarditis and restrictive cardiomyopathy represent disorders of impaired diastolic filling.

• In constriction, filling is limited by a non-compliant, rigid pericardium that restricts cardiac volumes.

• In restriction, filling is impaired by stiff myocardium.

• Presentation of these two conditions may be similar (RHF), but therapy is very different.
Pathophysiological Differences

Constriction
- Myocardial compliance is normal
- No impedance to early diastolic filling
- Total cardiac volume is fixed by the pericardium
- Atria are able to empty into the ventricles, though at higher pressure
- Marked respiratory effect on LV and RV filling

Restriction
- Abnormal myocardial compliance
- Impedance to filling increases throughout diastole
- Pericardium is compliant
- Septum is non-compliant
- Atrial enlargement and pulmonary HTN is common
- Minimal respiratory effect on LV and RV filling
Etiology of Pericardial Constriction

- 3 series for total >400 patients with constriction proven at surgery
  - Idiopathic/viral 42-49%
  - Post cardiac surgery 11-37%
  - Post radiation therapy 9-31%
  - Connective tissue 3-7%
  - Bacterial 3-6%
  - Misc 1-10%
Risk Constriction post Acute Pericarditis

- 500 consecutive cases
- All causes 1.8%
  - Idiopathic/viral <0.5%
  - Connective tissue/injury 2.8%
  - Neoplastic 4.0%
  - TB 20%
  - Purulent 33%
- Reversible 15%

Imazio, Circ 2011: 1124; 1270-75
Echocardiographic parameters in constrictive pericarditis and restrictive cardiomyopathy

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Constrictive pericarditis</th>
<th>Restrictive cardiomyopathy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Septal bounce</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>MV inflow respiratory variation</td>
<td>$\geq 25%$</td>
<td>None</td>
</tr>
<tr>
<td>TV inflow respiratory variation</td>
<td>$&gt;40%$</td>
<td>None</td>
</tr>
<tr>
<td>MVDT</td>
<td>Short</td>
<td>$&lt;160$ ms</td>
</tr>
<tr>
<td>Hepatic vein reversal</td>
<td>Diastolic reversal with expiration</td>
<td>No change</td>
</tr>
<tr>
<td>IVRT</td>
<td>Decrease during expiration Increase during inspiration</td>
<td>No change</td>
</tr>
<tr>
<td>TR duration</td>
<td>Increase</td>
<td>No change</td>
</tr>
<tr>
<td>E:e'</td>
<td>$&lt;8–10$</td>
<td>$&gt;15$</td>
</tr>
<tr>
<td>Myocardial mechanics with strain image</td>
<td>Normal longitudinal strain Decrease net-twist angle</td>
<td>Decrease longitudinal strain Normal net-twist angle</td>
</tr>
</tbody>
</table>
# Echo Studies

<table>
<thead>
<tr>
<th>Author (year)</th>
<th>CP patients (n/total)</th>
<th>Age (mean ± SD)</th>
<th>Parameter</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oh et al. (1994)</td>
<td>25/28</td>
<td>55 ± 15</td>
<td>MV inflow respiratory variation ≥25%</td>
<td>86</td>
<td>67</td>
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<tr>
<td>Rajagopalan et al. (2001)</td>
<td>19/30</td>
<td>56 ± 13</td>
<td>Mitral color M mode propagation &gt;100 cm/s</td>
<td>84</td>
<td>91</td>
</tr>
<tr>
<td>Rajagopalan et al. (2001)</td>
<td>19/30</td>
<td>56 ± 13</td>
<td>Respiratory variation of pulmonary venous peak diastolic flow &gt;18%</td>
<td>79</td>
<td>91</td>
</tr>
<tr>
<td>Sengupta et al. (2005)</td>
<td>40/60</td>
<td>24 ± 12</td>
<td>Biphasic diastolic septal motion TDI/color TDI</td>
<td>82</td>
<td>100</td>
</tr>
<tr>
<td>Voelkel et al. (1978)</td>
<td>12/22</td>
<td>56 ± 10</td>
<td>LVPW flattening M mode</td>
<td>92</td>
<td>100</td>
</tr>
<tr>
<td>von Bibra et al. (1989)</td>
<td>25/38</td>
<td>51 ± 11</td>
<td>Dilated hepatic veins</td>
<td>68</td>
<td>100</td>
</tr>
<tr>
<td>Choi et al. (2007)</td>
<td>17/44</td>
<td>55 ± 12</td>
<td>Septal E:e’ &gt;8</td>
<td>70</td>
<td>100</td>
</tr>
<tr>
<td>Rajagopalan et al. (2001)</td>
<td>19/30</td>
<td>56 ± 13</td>
<td>Lateral E:e’ ≥8</td>
<td>89</td>
<td>100</td>
</tr>
<tr>
<td>Sengupta et al. (2008)</td>
<td>26/46</td>
<td>56 ± 13</td>
<td>Septal and lateral E:e’ &gt;5</td>
<td>92</td>
<td>90</td>
</tr>
</tbody>
</table>
LV RV Strain

Kusunose, Circ Card Imag, 2013
Reality

- Echo report: “Echo findings not diagnostic of pericardial constriction. However if the clinical suspicion is high, suggest CT/MRI or hemodynamic study.”
Normal Pericardium
Pericardial Thickening
Constrictive Pericarditis in 26 Patients With Histologically Normal Pericardial Thickness, Circ 2003; 108:1852-1857
CT Pericardial Calcification
Effusive constrictive
Fibroblasts (Movat stain)

Chronic Inflammation

Granulation Tissue

Neovascularization

Zurick, JACC Image, 2011, 1180-91
LGE Intensity and CRP Predicts Reversibility

## Hemodynamics of Constriction
### Traditional Criteria

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
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<tr>
<td><strong>Traditional</strong></td>
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<td></td>
</tr>
<tr>
<td>1. LVEDP-RVEDP ≤5 mmHg</td>
<td>60</td>
<td>38</td>
<td>4</td>
<td>57</td>
</tr>
<tr>
<td>2. RVEDP/RVSP &gt; 1/3</td>
<td>93</td>
<td>38</td>
<td>52</td>
<td>89</td>
</tr>
<tr>
<td>3. PASP &lt;55mmHg</td>
<td>93</td>
<td>24</td>
<td>47</td>
<td>25</td>
</tr>
<tr>
<td>4. LV rapid filling wave ≥ 7mmHg</td>
<td>93</td>
<td>57</td>
<td>61</td>
<td>92</td>
</tr>
<tr>
<td>5. Respiratory change in RAP &lt;3 mmHg</td>
<td>93</td>
<td>48</td>
<td>58</td>
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Respiratory Influences
3. In severe constrictive pericarditis, changes in intrathoracic pressure is not communicated to the pericardial space.

- CVP and RAP do not ↓, and may actually ↑ with inspiration (Kussmaul)

- Interdependence of ventricular filling – on inspiration, intrathoracic pressure and pulmonary venous pressure ↓, but LA pressure does not. A reduced pulmonary veins to LA gradient results in decreased flow into the LA and LV. Decreased LV filling allows for more RV filling (compliant septum), leading to increased flow across the TV
  ↓ LV Stroke volume, ↑ RV Stroke volume
Hemodynamics of Constriction
Dynamic Respiratory Criteria

1. PCWP- LV respiratory difference ≥ 5mmHg.

2. RV/LV interdependence (ie. RV - LV discordance), systolic area index >1.1.
1. PCWP-LV respiratory change ≥ 5mmHg

Hatle LK, et. al.

Circ. 1989;79357-370
2. RV/LV interdependence

LV and RV are discordant = CONSTRUCTION
2. RV/LV interdependence

LV and RV are concordant = RESTRICTION
Systolic Area Index > 1.1

- Systolic area index

\[
\begin{align*}
\text{RV area/LV area in inspiration} \\
\text{RV area /LV area in expiration}
\end{align*}
\]

\[>1.1 \text{ is consistent with constriction}\]

Talreja, JACC 2008: 315-19
Restriction
Constriction
<table>
<thead>
<tr>
<th>Criteria FOR CONSTRUCTION</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
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<td></td>
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<td></td>
</tr>
<tr>
<td>1. PCWP/LV respiratory gradient ≥ 5mmHg</td>
<td>93</td>
<td>81</td>
<td>78</td>
<td>94</td>
</tr>
<tr>
<td>2. LV/RV Interdependence</td>
<td>100</td>
<td>95</td>
<td>94</td>
<td>100</td>
</tr>
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</table>
Pericardectomy
Retrospective Studies

- Ling Circulation 1999;100: 1380–86.
- Cameron Am Heart J 1987;113:354–60.
Pericardectomy

• 313 patients 1936 -1990, the overall mortality was 14%
  – NYHA IV 46%; III 10%; I and II 1%)

• 135 patients 1985 -1995 the 30-day perioperative mortality 6%
  – 10 yr follow-up independent predictors of late survival were age, NYHA class and previous radiation
Pericardectomy

• Perioperative mortality of 5–7.6% in recent studies
  – Most frequent cause of death low output HF failure, as described in
• Idiopathic constrictive pericarditis had the best prognosis with 7-year Kaplan-Meier survival of 88%, post-surgical constrictive pericarditis with 66% and post-radiation constrictive pericarditis with 27%.
Restriction
Amyloid

Sarcoid

Myocarditis

Peripheral Eosinophilia
Iron Overload
So Where Should CMR Fit into Practice?

“Every patient with undiagnosed cardiomyopathy deserves one good CMR exam!”


“Every patient with heart failure should have a CMR exam!”

European Heart Failure Guidelines, 2012.
Radiation Induced Heart Disease
Relative risks of RIHD in cancer survivors

<table>
<thead>
<tr>
<th>Types</th>
<th>Hodgkin’s disease relative risk</th>
<th>Breast cancer relative risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>RIHD</td>
<td>&gt;6.3</td>
<td>2–5.9</td>
</tr>
<tr>
<td>Ischaemic heart disease</td>
<td>4.2–6.7</td>
<td>1–2.3</td>
</tr>
<tr>
<td>Cardiac death</td>
<td>2.2–12.7</td>
<td>0.9–2</td>
</tr>
</tbody>
</table>

Consensus RIHD Follow-up Imaging, Eur Hrt J, 2013
Risk factors of RIHD

- Anterior or left chest irradiation location
- High cumulative dose of radiation (> 30 Gy)
- Younger patients (< 50 years)
- High dose of radiation fractions (> 2 Gy/day)
- Presence and extent of tumour in or next to the heart
- Lack of shielding
- Concomitant chemotherapy (the anthracyclines considerably increase the risk)
- Cardiovascular risk factors (i.e. diabetes mellitus, smoking, overweight, ≥ moderate hypertension, hypercholesterolaemia)
- Pre-existing cardiovascular disease

Consensus RIHD Follow-up Imaging, Eur Hrt J, 2013
CHEST RADIATION EXPOSURE

Macrovascular injury accelerates age-related atherosclerosis, leading to coronary artery disease (years/decades post RT)

- Reduces myocardial capillary density (within months post RT)
- Valve endothelial injury and dysfunction
  - Leaflet fibrosis, thickening, shortening and calcification
  - Valve regurgitation and/or stenosis

Microvascular injury

- Reduces flow to a myocardial territory
- Reduced collateral flow/vascular reserve (often subclinical)

MYOCARDIAL ISCHEMIA

REGIONAL WALL MOTION ABNORMALITIES

PROGRESSIVE MYOCARDIAL FIBROSIS

PERICARDIAL EFFUSION/CONSTRICION

PROGRESSIVE DECLINE IN LV SYSTOLIC AND DIASTOLIC FUNCTION

CONCOMITANT CARDIOTOXIC CHEMOTHERAPY

LV VOLUME/PRESSURE OVERLOAD

ASYMPTOMATIC STAGE

OVERT HEART FAILURE
Radiation Induced Osteogenesis AV

<table>
<thead>
<tr>
<th>Condition</th>
<th>Acute</th>
<th>Chronic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pericarditis</td>
<td>Acute and delayed acute effusion predicts late CP</td>
<td>20% within 2yrs 4-20% CP (dose dependent)</td>
</tr>
<tr>
<td>Cardiomyopathy</td>
<td>Acute myocarditis Mild dysfunction</td>
<td>Diffuse fibrosis (&gt;30Gy) Restrictive</td>
</tr>
<tr>
<td>Valve Disease</td>
<td>None</td>
<td>Regurg &gt; Stenosis 1% 10yrs, 5% 15yrs &gt;20yrs 15% Mod AR, AS</td>
</tr>
<tr>
<td>CAD</td>
<td>Perfusion defect 47%</td>
<td>Accelerated at young age Latent &gt;10yrs Ostial involvement RR MI death 2.2 - 8.8</td>
</tr>
<tr>
<td>Carotid</td>
<td>None</td>
<td>Incidence 7.4%</td>
</tr>
<tr>
<td>Other vascular</td>
<td>None</td>
<td>Porcelain aorta</td>
</tr>
</tbody>
</table>
Baseline pre-radiation comprehensive Echocardiography → CHEST RADIATION EXPOSURE → Yearly targeted clinical history and physical examination → Screen for modifiable risk factors

Search for signs and symptoms suggestive of:
- Pericardial effusion/constriction
- Valvular heart disease
- LV dysfunction/heart failure
- Coronary artery disease
- Carotid artery disease
- Conduction system disease

Correct risk factors → Asymptomatic

Screening Echocardiography
- 5 years after exposure in high risk patients
- 10 years after exposure in the others

Functional non-invasive stress test for CAD detection (5 to 10 years after exposure in high risk patients)

Re-assess every 5 years

New murmur → Echocardiography

Signs/symptoms of heart failure
- Angina

Neurological signs/symptoms
- Carotid US

CMR if suspicion of pericardial constriction