No Conflicts of Interests
Non ischemic cardiomyopathies

*Functional impairment
- Dilated cardiomyopathy (DCM)
- Hypertrophic Cardiomyopathy (HCM)
- Restrictive Cardiomyopathy (RCM)
- Arrhythmogenic Right Ventricular (ARVC)
- Unclassified (Non compaction)

etiology
- idiopathic
- specific
  - valvular
  - hypertensive
  - Inflammatory/metabolic
  - Muscular dystrophies

Restrictive Cardiomyopathy

- The World Health Organization (WHO) defines RCM as a myocardial disease characterized by restrictive filling and reduced diastolic volume of either or both ventricles with normal or near-normal systolic function and wall thickness.
- Heterogeneous group of heart muscle disease that, in common have heart failure.
- The hallmark of the restrictive cardiomyopathies is abnormal diastolic function; the ventricular walls are excessively rigid and impede ventricular filling.
Restrictive Cardiomyopathy
Exclusion “Guidelines”

- LV end-diastolic dimensions ≥ 7 cm
- Myocardial wall thickness ≥ 1.7 cm
- LV end-diastolic volume ≥ 150 mL/m²
- LV ejection fraction < 20%
Restrictive Cardiomyopathy Classification

- **Idiopathic**
- **Myocardial**
  1. Noninfiltrative
     - Idiopathic
     - Scleroderma
  2. Infiltrative
     - Amyloid
     - Sarcoid
     - Gaucher disease
     - Hurler disease
- **Storage Disease**
  - Hemochromatosis
  - Fabry disease
  - Glycogen storage
- **Endomyocardial**
  - endomyocardial fibrosis
  - Hyperesinophilic synd
  - Carcinoid
  - metastatic malignancies
  - radiation, anthracycline
Symptoms

- Gradual worsening of symptoms of left heart failure.
- Fatigue and weakness are results of the decreased stroke volume.
- Distention of the abdomen and bilateral swollen feet (right heart failure).
- Angina like chest pains are observed only in patients with amyloidosis.
- Palpitations (atrial fibrillation), which are common in idiopathic RCM.
- As many as one third of patients with idiopathic RCM may present with thromboembolic complications.
- Syncopes may be present.
- Conduction disturbances particularly are common in infiltrative RCM.
- Regarding etiology, some patients may have a prior history of radiation therapy, heart transplantation, chemotherapy, or a systemic disease.
Restrictive Cardiomyopathy

Signs

CVS Exam

- The pulse is low volume, consistent with decreased stroke volume.
- High JVP with diastolic collapse (Friedreich's sign).
- JVP with rapid X and Y descents, but the most prominent wave is the Y descent (atrium emptying into the “stiff” ventricle).
- Elevation of JVP with inspiration (Kussmaul's sign).
Restrictive Cardiomyopathy

Signs

- S4 in early disease (forceful atrial contraction against a stiff ventricle).
- S3 in advanced disease.
- Murmurs due to mitral and tricuspid valve regurgitation may be present.
Restrictive Cardiomyopathy

Signs

Resp. Exam.
- Reduced breath sounds because of pleural effusion
- Crepitations due to left heart failure

Abd. Exam.
- In advanced cases, liver may be palpable and pulsatile.
Restrictive Cardiomyopathy

Investigations

- **CXR**
  - Pulmonary venous congestion. The cardiac silhouette can be normal (familial) or show cardiomegaly and/or atrial enlargement.

- **ECG**
  - Usually has low-voltage and ST segment and T wave abnormalities.

- **Echocardiogram**
  - Symmetrical myocardial thickening and often a normal systolic ejection fraction, but impaired ventricular filling.
RESTRICTIVE CARDIOMYOPATHY
DIFFERENTIAL DIAGNOSIS

Constrictive Pericarditis

- Pericardial calcification on x-ray, which occurs in constrictive pericarditis, is absent.
- Right ventricular transvenous endomyocardial biopsy (by revealing myocardial infiltration or fibrosis in restrictive cardiomyopathy)
- CT scan or MRI (by demonstrating a thickened pericardium in constrictive pericarditis).
# Clinical features of constrictive pericarditis and restrictive cardiomyopathy

<table>
<thead>
<tr>
<th>Clinical Features</th>
<th>Constrictive Pericarditis</th>
<th>Restrictive Cardiomyopathy</th>
</tr>
</thead>
<tbody>
<tr>
<td>History</td>
<td>Prior history of pericarditis or condition that causes pericardial disease</td>
<td>History of systemic disease (e.g., amyloidosis, hemochromatosis)</td>
</tr>
<tr>
<td>General examination</td>
<td></td>
<td>Peripheral stigmata of systemic disease</td>
</tr>
<tr>
<td>Systemic examination - Heart sounds</td>
<td>Pericardial knock, high-frequency sound</td>
<td>Presence of loud diastolic filling sound $S_3$, Low-frequency sound</td>
</tr>
<tr>
<td>Murmurs</td>
<td>No murmurs</td>
<td>Murmurs of mitral and tricuspid insufficiency</td>
</tr>
<tr>
<td>Prior chest x-ray</td>
<td>Pericardial calcification</td>
<td>Normal results of prior chest x-ray</td>
</tr>
</tbody>
</table>
Restrictive Cardiomyopathy

- The characteristic feature of RCM is decreased diastolic ventricular compliance ("myocardial stiffness") resulting in impaired diastolic ventricular filling with preserved or near-normal systolic contraction.

- The hallmark signs of restrictive cardiomyopathy on cine MR images are: biatrial enlargement, small or normal sized ventricles, preserved systolic ventricular contraction.

- Typical findings of constrictive pericarditis, namely abnormal diastolic septal motion and irregular thickening of the pericardium, are absent in restrictive cardiomyopathy.
Restrictive Cardiomyopathy
TREATMENT & PROGNOSIS

- No specific treatment. Cardiac failure and embolic manifestations should be treated. Cardiac transplantation should be considered in some severe cases, especially the idiopathic variety. In primary amyloidosis, combination therapy with melphalan plus prednisolone with or without colchicine may improve survival.
SUSPECTED CARDIAC AMYLOIDOSIS
(E.g. heart failure with typical echocardiogram)

Careful physical exam seeking other potential organ involvement e.g. proteinuria, periorbital purpura.

Biopsy of selected cardiac or non-cardiac tissue

Biopsy positive:
AMYLOIDOSIS CONFIRMED

Where feasible, special stains such as immunogold

Special stains unavailable
Serum and urine IFE, FLC assay,
Bone marrow biopsy

One or (usually) more positive

All negative

Genetic testing for mutant TTR or ApoA1

Positive

Negative

Familial
Probably SSA
Therapy as below

Amyloid type confirmed

TTR

AL amyloidosis

Genetic testing for mutant TTR

Quantify light chains (as baseline for follow-up) and exclude concomitant myeloma

Positive

Familial amyloidosis
Supportive therapy.
Assess for liver transplant and need for cardiac transplant.

Negative

SSA
Supportive therapy.

AL amyloidosis
Chemotherapy and supportive therapy.
EKG
ECHO B

Diameters and function conserved

Thickness of IVS (granular)

Thickness of valves
DOPPLER ECHO

RESTRICTIVE FILLING PATTERN
RIGHT VENTRICULAR IMPORTANCE IN PROGNOSIS OF AMYLOID

Stefano Ghio, European Journal of Heart Failure 9 (2007) 808–813
CARDIAC MRI
CMR of Non Ischemic Cardiomyopathy

- Evaluation of cardiac chambers – morphology
- Evaluation of cardiac function
- Delayed myocardial enhancement
- Evaluation of myocardial edema, fat
- Evaluation of flow: Velocity-encoded cine MRI
- Coronary MR angiography - optional
MRI

Sensitivity of 80% & specificity of 94%.
Positive Predictive V 92% & negative of 82%

Vogelsberg et al. CMRI in Cardiac Amyloidosis, JACC Vol. 51, No. 10, 2008
CARDIAC MRI

Diffuse or subendo-cardial enhancement
MRI LATE ENHANCEMENT
Myocardial Iron Deposition

- May be secondary to hereditary hemochromatosis, hemolytic anemias like thalassemia, or chronic liver disease.
- Changes the magnetic susceptibility of myocardium → reduces T2* time.
- T2* weighted imaging is most sensitive to detect myocardial iron deposition.
- T2* time can be estimated from a signal decay curve which is generated from multiple signals obtained at increasing ECHO times after the excitation pulse.
The myocardium is of low signal when compared to skeletal muscle.
Sarcoidosis

- Sarcoidosis is a multisystem granulomatous disorder of unknown etiology.

- Most common findings on cine MR images are those of dilated cardiomyopathy, particularly LV dilation, LV wall thinning, diffuse hypokinesis with decreased LV ejection fraction.

- The very important MRI finding is patchy pattern of delayed enhancement.
Sarcoidosis

Short axis

Short axis DE

4 chamber

4 chamber DE
RESTRICTIVE CARDIOMYOPATHY

Follow up

- Cardiac catheterization and haemodynamic studies help distinction from constrictive pericarditis.

- Endomyocardial biopsy in contrast with other cardiomyopathies is often useful in this condition and may permit a specific diagnosis such as amyloidosis to be made.
Constrictive - Restrictive Pattern

“Square-Root Sign” or “Dip-and-Plateau”
### ENDOMYOCARDIAL BIOPSY

<table>
<thead>
<tr>
<th>Scenario Number</th>
<th>Clinical Scenario</th>
<th>Class of Recommendation</th>
<th>Level of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>New-onset heart failure of &lt;2 weeks’ duration associated with a normal-sized or dilated left ventricle and hemodynamic compromise</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>2</td>
<td>New-onset heart failure of 2 weeks’ to 3 months’ duration associated with a dilated left ventricle and new ventricular arrhythmias, second- or third-degree heart block, or failure to respond to usual care within 1 to 2 weeks</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>3</td>
<td>Heart failure of &gt;3 months’ duration associated with a dilated left ventricle and new ventricular arrhythmias, second- or third-degree heart block, or failure to respond to usual care within 1 to 2 weeks</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>4</td>
<td>Heart failure associated with a DCM of any duration associated with suspected allergic reaction and/or arrhythmias or second- or third-degree heart block, that responds to usual care within 1 to 2 weeks</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>11</td>
<td>Heart failure associated with unexplained HCM</td>
<td>IIb</td>
<td>C</td>
</tr>
<tr>
<td>12</td>
<td>Suspected ARVD/C</td>
<td>IIb</td>
<td>C</td>
</tr>
<tr>
<td>13</td>
<td>Unexplained ventricular arrhythmias</td>
<td>IIb</td>
<td>C</td>
</tr>
<tr>
<td>14</td>
<td>Unexplained atrial fibrillation</td>
<td>III</td>
<td>C</td>
</tr>
</tbody>
</table>

6- HF for restrictive cardiomyopathy  

Cooper et al Endomyocardiocoral Biopsy in Cardiovascular Disease, *Circulation November 6, 2007*
Restrictive Cardiomyopathy Treatment

- The goal of treatment in RCM is to reduce symptoms by lowering elevated filling pressures without significantly reducing the cardiac output.
### Diagnosis and Management of the Cardiac Amyloidoses, *Circulation* 2005;112;2047-2060

<table>
<thead>
<tr>
<th>Nomenclature</th>
<th>Precursor of Amyloid Fibril</th>
<th>Organ Involvement</th>
<th>Treatment</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>AL</td>
<td>Immunoglobulin light chain</td>
<td>Heart, Kidney, Liver</td>
<td>Chemotherapy</td>
<td>Plasma cell dyscrasia related to (but usually not associated with) multiple myeloma</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Peripheral/autonomic nerves, Soft tissue</td>
<td></td>
<td>Heart disease occurs in 1/3 to 1/2 of AL patients; heart failure tends to progress rapidly and has a very poor prognosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Gastrointestinal system</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ATTR (familial)</td>
<td>Mutant transthyretin</td>
<td>Peripheral/autonomic nerve, Heart</td>
<td>Liver transplantation</td>
<td>Autosomal dominant; amyloid derived from a mixture of mutant and wild-type TTR; if present before, cardiac amyloid may progress despite liver transplantation</td>
</tr>
<tr>
<td>AApoA1</td>
<td>Mutant apolipoprotein</td>
<td>Kidney, Heart</td>
<td>? Liver transplantation</td>
<td>Kidney disease is the commonest presentation; heart involvement rare</td>
</tr>
<tr>
<td>Senile systemic amyloid</td>
<td>Wild-type transthyretin</td>
<td>Heart</td>
<td>Supportive</td>
<td>Almost exclusively found in elderly men; slowly progressive symptoms</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>? New pharmacological strategies to stabilize the TTR.</td>
<td></td>
</tr>
<tr>
<td>AA</td>
<td>Serum amyloid A</td>
<td>Kidney (rarely)</td>
<td>Treat underlying inflammatory process</td>
<td>Heart disease rare and, if present, rarely clinically significant</td>
</tr>
<tr>
<td>AANP</td>
<td>Atrial natriuretic peptide</td>
<td>Localized to the atrium</td>
<td>None required</td>
<td>Very common; may increase risk of atrial fibrillation and/or be deposited in greater amounts in the fibrillating atrium</td>
</tr>
</tbody>
</table>

**Summary of the Main Forms of Amyloidosis That Affect the Heart**
"The docs just install the artificial heart.
We at Al's garage do the maintenance on the battery."
PROGNOSIS

- Patients with cardiac amyloidosis have a worse prognosis than those with other forms of the disease, and the disease often recurs after transplantation. Liver transplantation may be effective in familial amyloidosis (due to production of mutant prealbumin) and may lead to reversal of the cardiac abnormalities.
CONCLUSIONES (I)
Applications of echo/CMR

- Early diagnosis
- Predict outcomes with treatment
- Monitor response to treatment
CONCLUSIONES (II)

- Persists an inconvenient to classify CM in four major groups, because an overlap between anatomic and functional characteristics.

- As genetic classification of CM continues, the boundaries of the various types of CM may be better determined.

- CM have a familial nature and it is important to screen family members.

- As causes and pathophysiology of CM are better understood, in the future the term “idiopathic” may no longer be sustainable.
THANK YOU