HK Core Cardiology Certificate Course (Module 4)
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Cardiac Amyloidosis and Restrictive Cardiomyopathy

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Restrictive Cardiomyopathy (RCM)

- Least common type of cardiomyopathy
- Increased stiffness of myocardium – impaired diastolic filling
- Ventricular volumes normal / reduced
- Wall thickness normal / mildly increased
- Systolic function – typically preserved

Differential diagnosis

- Restrictive cardiomyopathy (RCM)
- Constrictive pericarditis

Causes of RCM

- 50% - infiltration by amyloidosis
- Unknown

Causes of diastolic abnormalities

- Infiltration
- Myocardial fibrosis
- Endomyocardial fibrosis

Classification of RCM

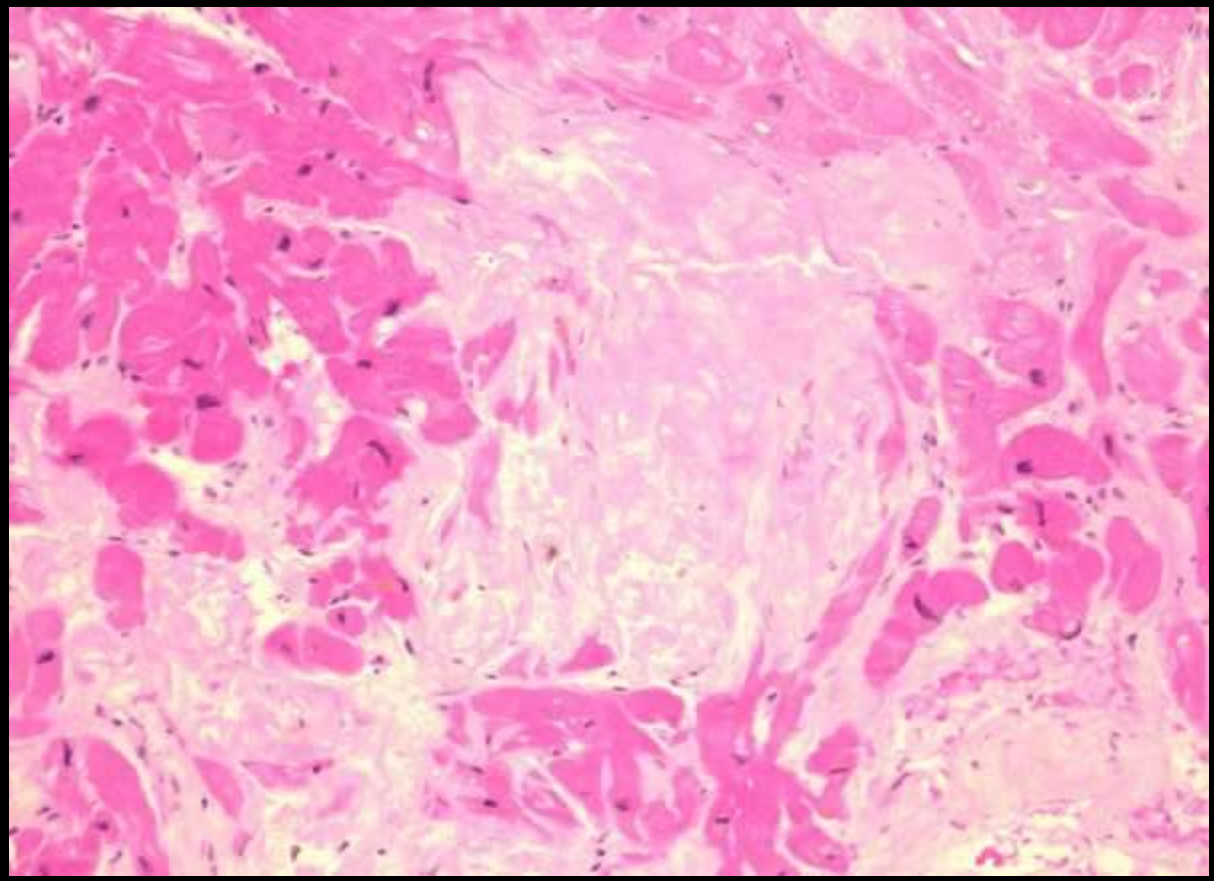
- Infiltrative
  - Amyloidosis
  - Sarcoidosis
- Storage disease
  - Hemochromatosis
  - Glycogen storage disease
  - Fabry disease
- Noninfiltrative
  - Scleroderma
  - Diabetic cardiomyopathy
  - Idiopathic
- Endomyocardial
  - Endomyocardial fibrosis
  - Hypereosinophilic syndrome
  - Carcinoid syndrome
  - Metastatic cancer
  - Radiation
  - Drugs - anthracycline, serotonin, ergotamine

Symptoms

- Volume overload
- Arrhythmia
- Reduced cardiac output
- Angina
- Sudden cardiac death

Cardiac amyloidosis

- Extracellular deposition of insoluble fibrils with beta pleated sheet configuration
- Can occur in multiple organs – heart, kidney, liver, nervous system, lung, skin, eyes



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Cardiac Amyloid

- Myocardium (thick and rubbery)
- Atria
- Pericardium (effusion)
- Endocardium (AV valve dysfunction, intracardiac thrombosis)
- Microvascular involvement (ischemia and infarct) – epicardial vessels spared
- Conduction system abnormalities (BBB, AV block)
- Severe SA node fibrosis (30%)

Cardiac amyloidosis - Types

- AL amyloidosis: Light chain amyloidosis most common

  MGUS (monoclonal gammopathy)

  Multiple myeloma with plasma cell burden 5-10% (lambda > kappa light chain)
- ATTR – mutant: Hereditary cardiac amyloidosis due to mutation in transthyretin

  ATTR – wild: Senile systemic amyloidosis – age > 80
- AA amyloidosis: Secondary – chronic inflammatory disorder (reversible)
- $A\beta_2M$ - dialysis

Cardiac amyloidosis - Prognosis

- Poor
- Median survival 13 months
- If CHF – survival 6 months

Cardiac amyloidosis – Lab Ix setting of CHF

- Elevated troponin T
- NT-proBNP – high sensitivity with cardiac involvement with AL amyloidosis

  Surrogate marker of myocardial amyloid burden

Cardiac amyloidosis – Diagnosis Setting

- Setting of heart failure
- ECG low voltage
- Echo thickened heart
- MRI
- Nuclear scan

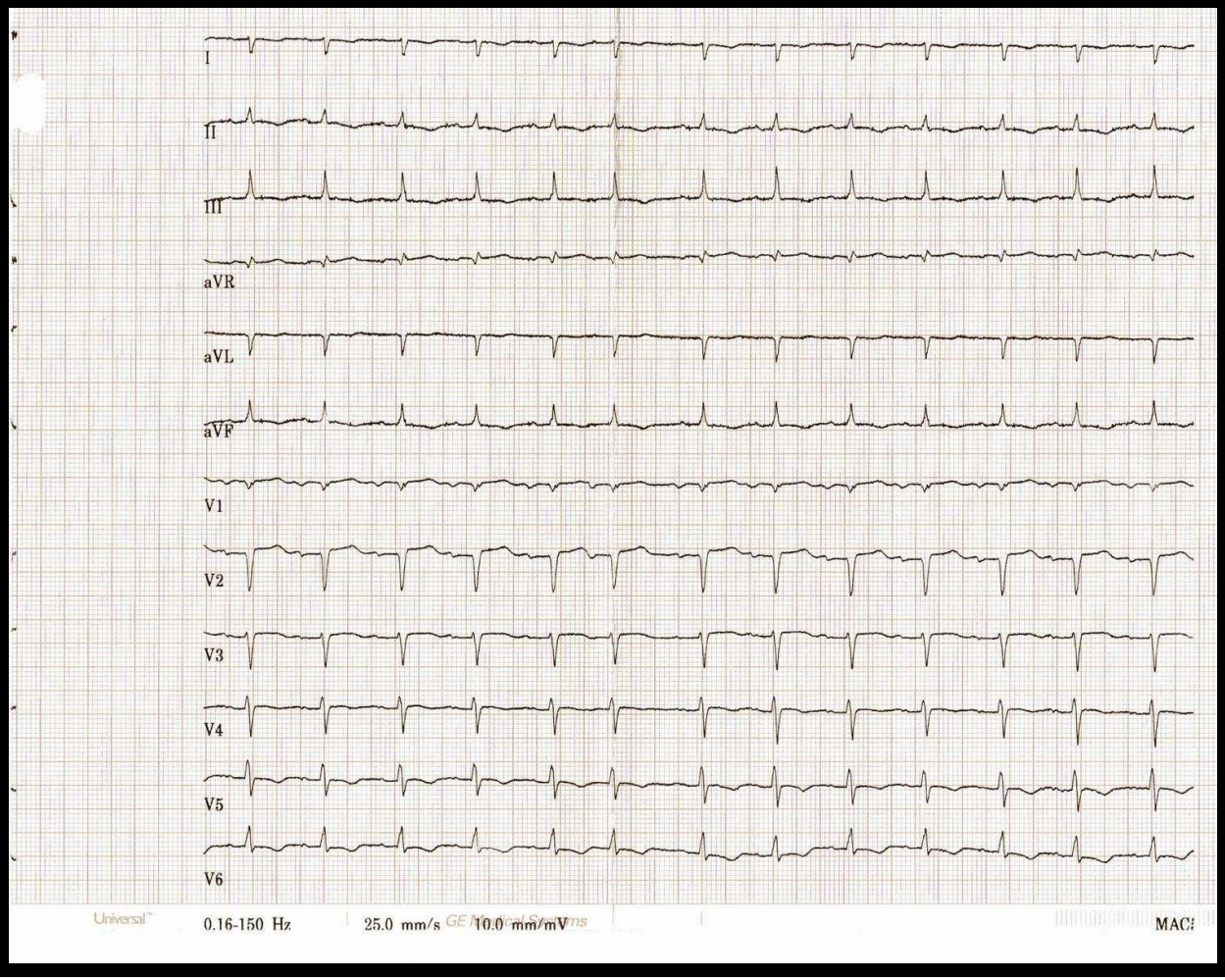
ECG Findings

- Large P wave – biatrial enlargement
- Conduction delay (high grade AV block – sarcoidosis, amyloid)
- Various ST and T segment changes
- Ventricular tachycardia (esp in sarcoidosis)
- Atrial tachyarrhythmia
- Classical low QRS voltage
- Pseudo-infarct pattern

- 276 systemic amyloidosis
  cardiac amyloidosis = 189
  control = 87
- Low voltage (QRS < 0.5mV) 54.5% vs 20.7% p<0.001
- Pseudo-infarct pattern – 40.2% vs 4.6% P <0.001
- AV block – 14.8% vs 1.1% p < 0.001
- Atrial arrhythmia – 15.9% vs 3.4% p = 0.003

Most common ECG abnormality – low voltage +/- pseudoinfarct

Cheng et al – Noninvasive Electrocardiol 2013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Cardiac amyloidosis – Diagnosis Setting

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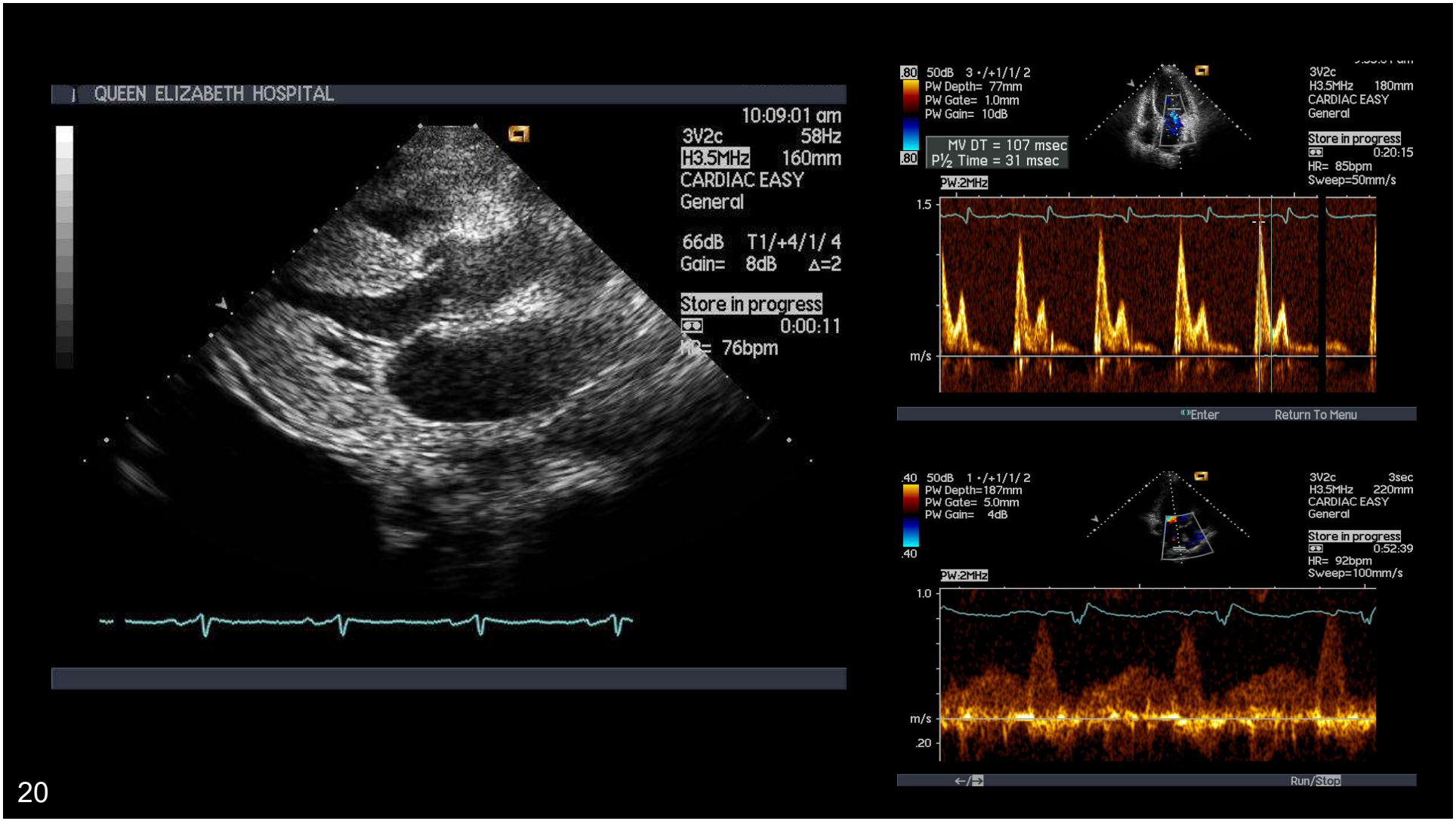
Cardiac amyloidosis – Echo

- LV thickening
  - > 1.98cm + low voltage ECG – 72% sensitive + 91% specific
  - LV wall – granular or sparkling appearance (poor sensitivity 26%)
- Normal or small LV size
- Preserved LVEF
- Diastolic dysfunction – E/e' > 12.3 (69.7% sensitivity, 83.3% specificity) → parameter for serial FU
- RV dilatation (poor prognosis)
- TAPSE (tricupsid annular plane systolic excursion) < 14mm – poor prognosis
- LA enlargement
- Small pericardial effusion, thickened AV valves, thickened interatrial septum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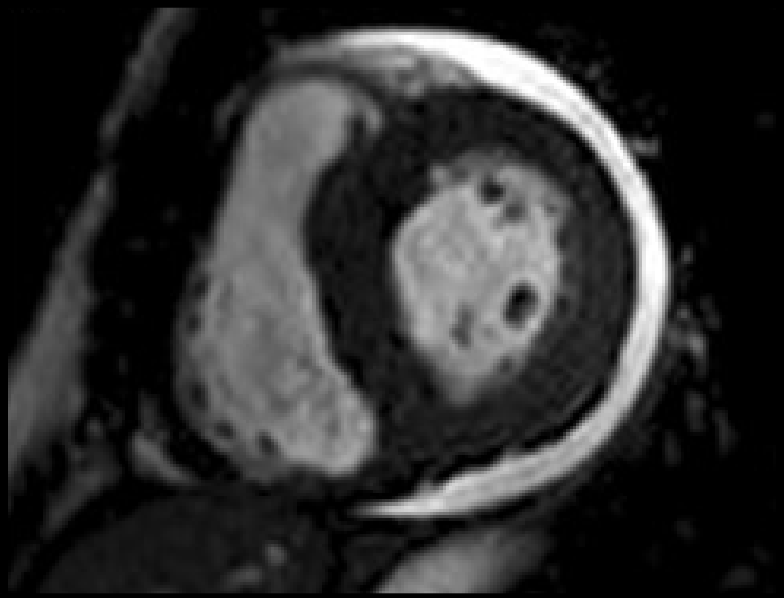
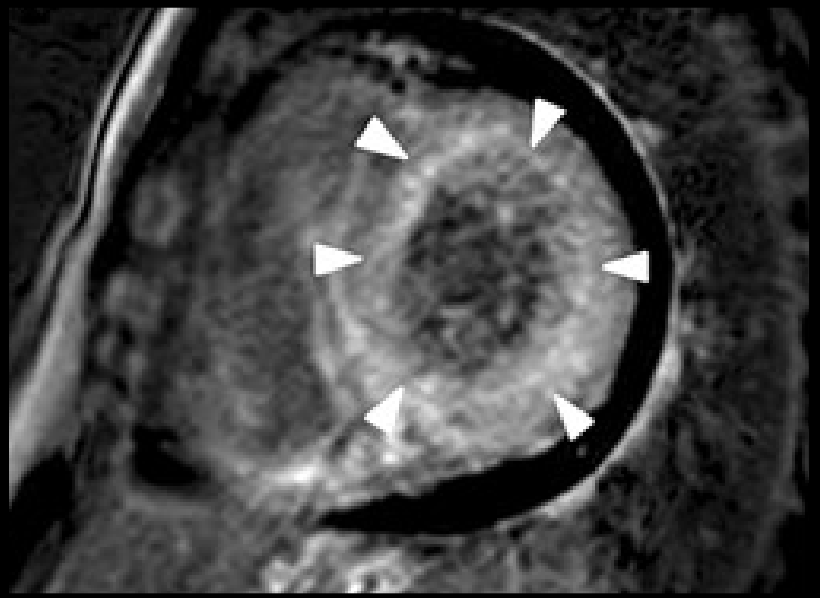
Cardiac amyloidosis – Diagnosis Setting

- Setting of heart failure
- ECG low voltage
- Echo thickened heart
- MRI
  - Global subendocardial enhancement
  - Left atrial LGE – extent correlates with diastolic dysfunction
- Nuclear scan

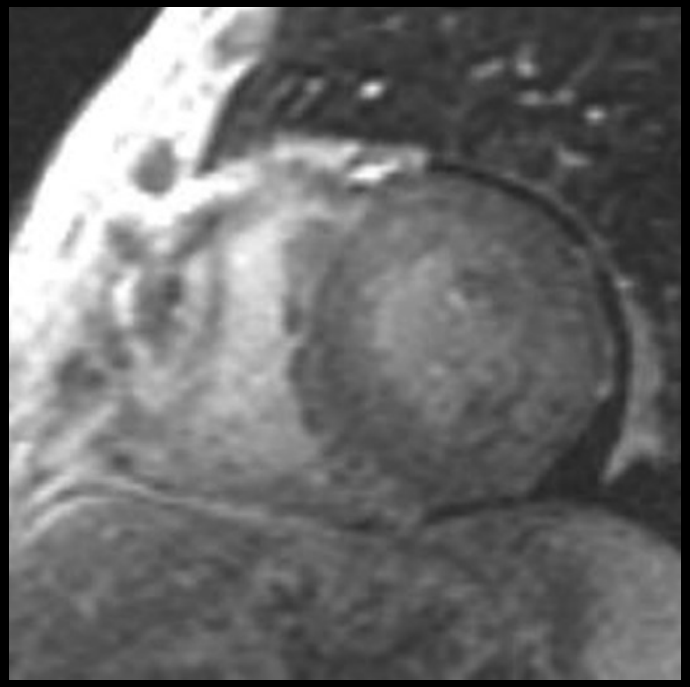
Postgadolinium delayed enhancement images show widespread enhancement

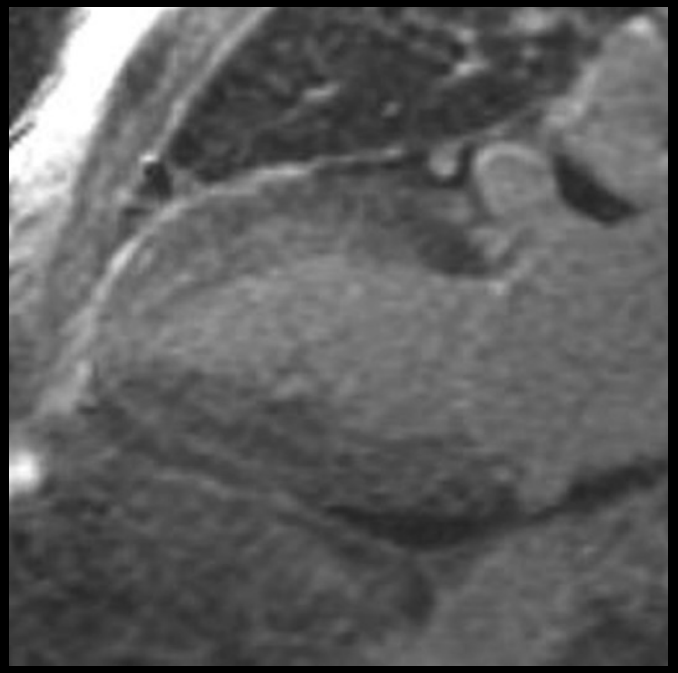




T2-weighted image showing diffuse hypertrophy of the left ventricular muscle

Postgadolinium delayed enhancement images show widespread enhancement (SAX and 2C Long axis view)





Cardiac amyloidosis – Diagnosis Setting

- Setting of heart failure
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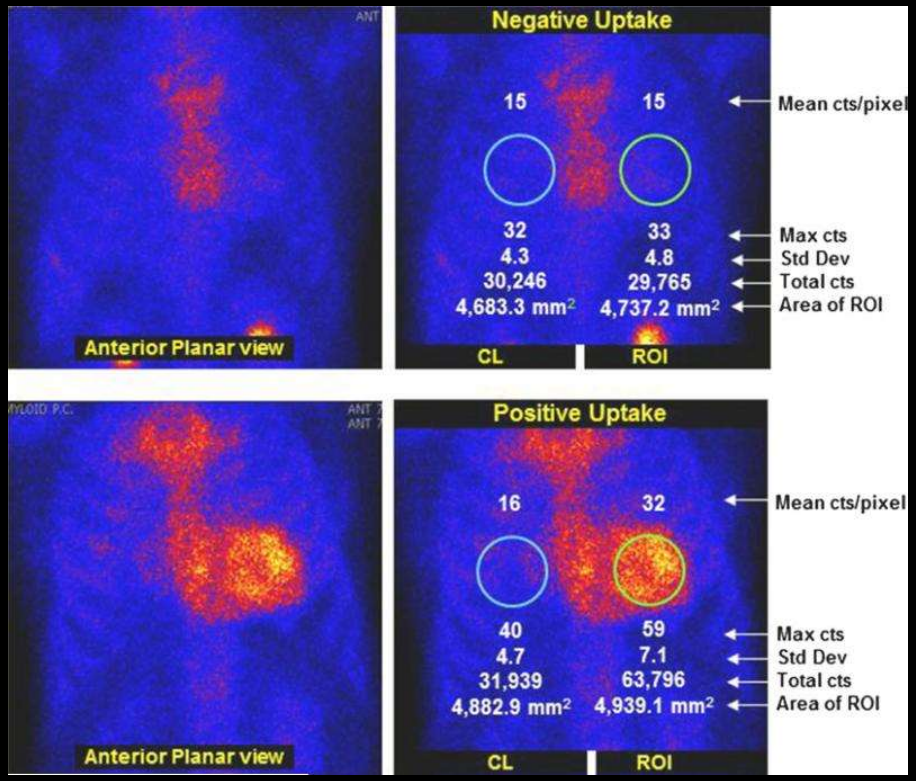
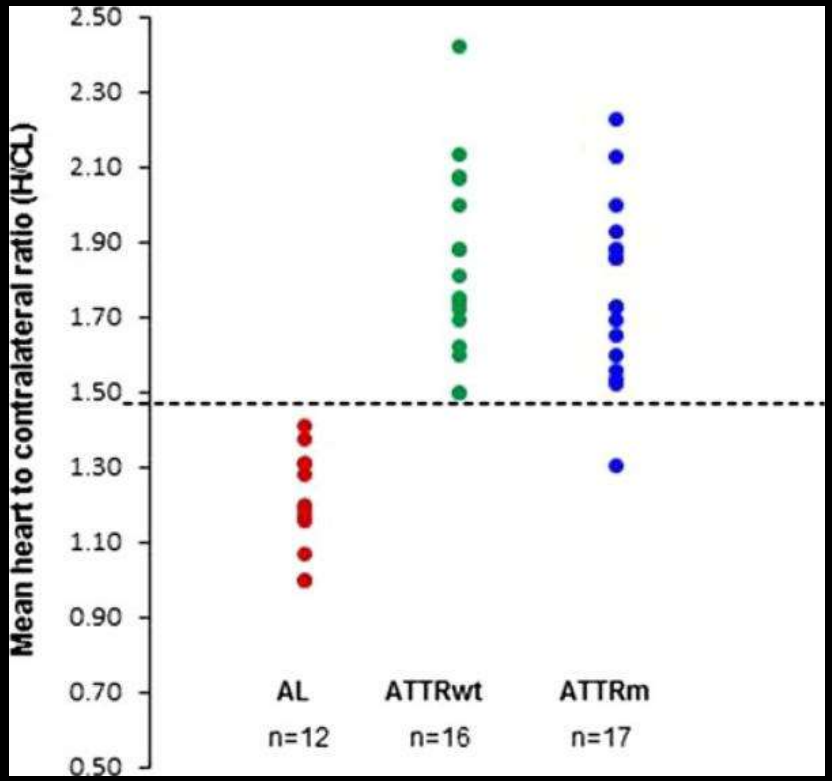
  Global subendocardial enhancement

  Left atrial LGE – extent correlates with diastolic dysfunction
- Nuclear scan – technectium pyrophosphate (TTR amyloidosis)

Differentiating AL from ATTR amyloidosis by Tc99m-PYP SPECT imaging has been proven to be very sensitive and specific method (about 90% both) for detecting ATTR amyloidosis, but not AL amyloidosis





ATTR cardiac amyloid had significantly higher semi-quantitative uptake than the AL cohort

Cardiac amyloidosis – type of amyloid

- Urine for protein
- Serum and urine immunofixation (AL amyloidosis)
- Free light chain assay (to quantify + FU response to Px)
- Bone marrow (% of plasma cells)
- Blood for TTR mutation (transthyretin protein)
  if negative for TTR – then most likely is ATTR – wild

Cardiac amyloidosis – Tissue diagnosis

- Easiest way – abdominal fat under LA (amyloid not always found)
- Endomyocardial biopsy

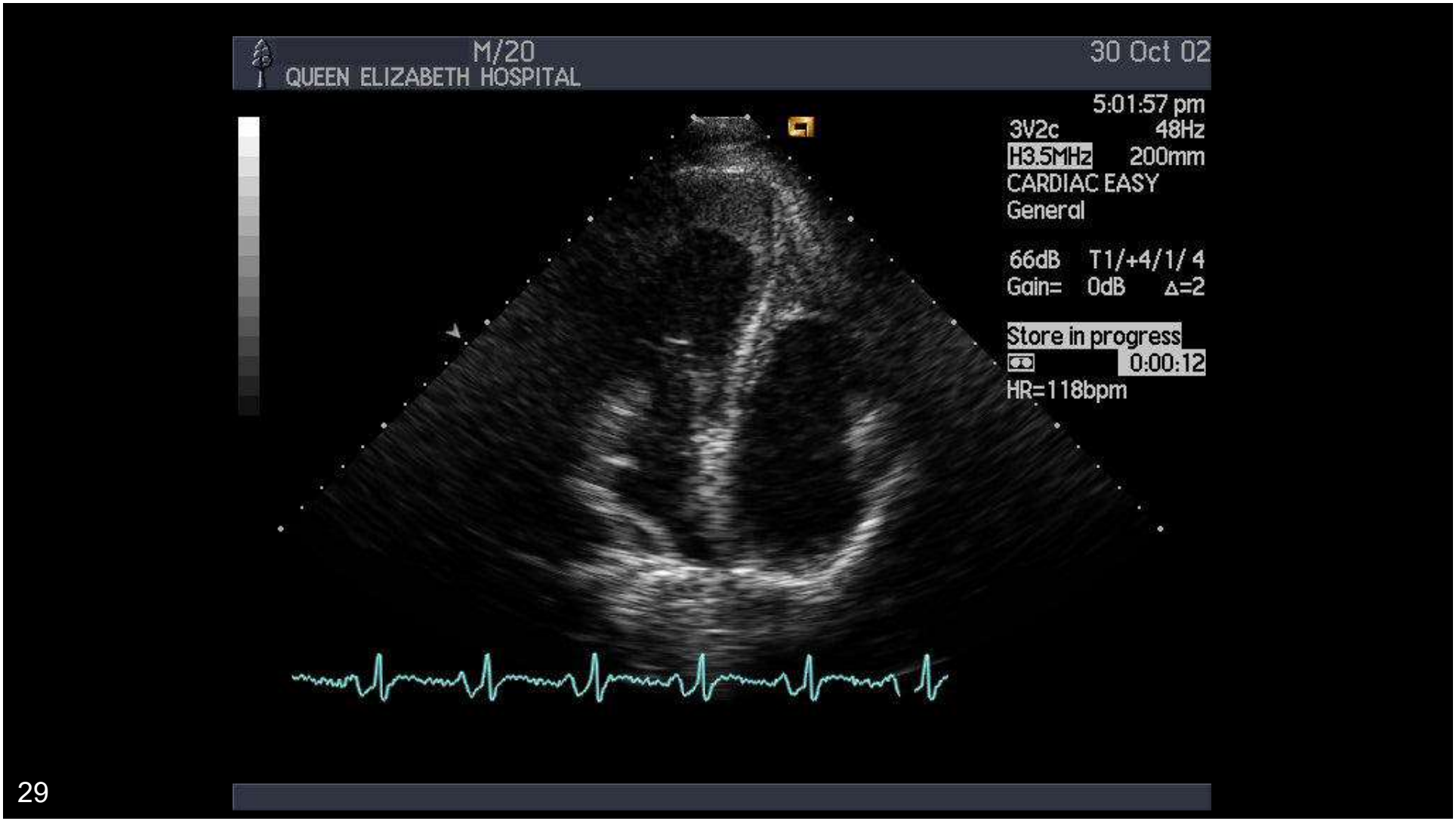
Cardiac amyloidosis – Treatment

- No cure

  limit further production of amyloid protein

  Specific treatments depend on the type of amyloidosis
- AL amyloidosis - same chemotherapy that treat multiple myeloma

  Autologous blood stem cell transplant (ASCT) - high-dose chemotherapy + not too advance disease
- AA amyloidosis - underlying condition (e.g antiinflammatory for RA)
- Hereditary amyloidosis - Liver transplantation
- Dialysis-related amyloidosis - changing mode of dialysis or kidney transplant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Endomyocardial disease (EMD)

2 forms

- tropical – endomyocardial fibrosis
- Temperate zones – The Hypereosinophilic Syndrome (Loffler Endocarditis)

3 different phases of EMD

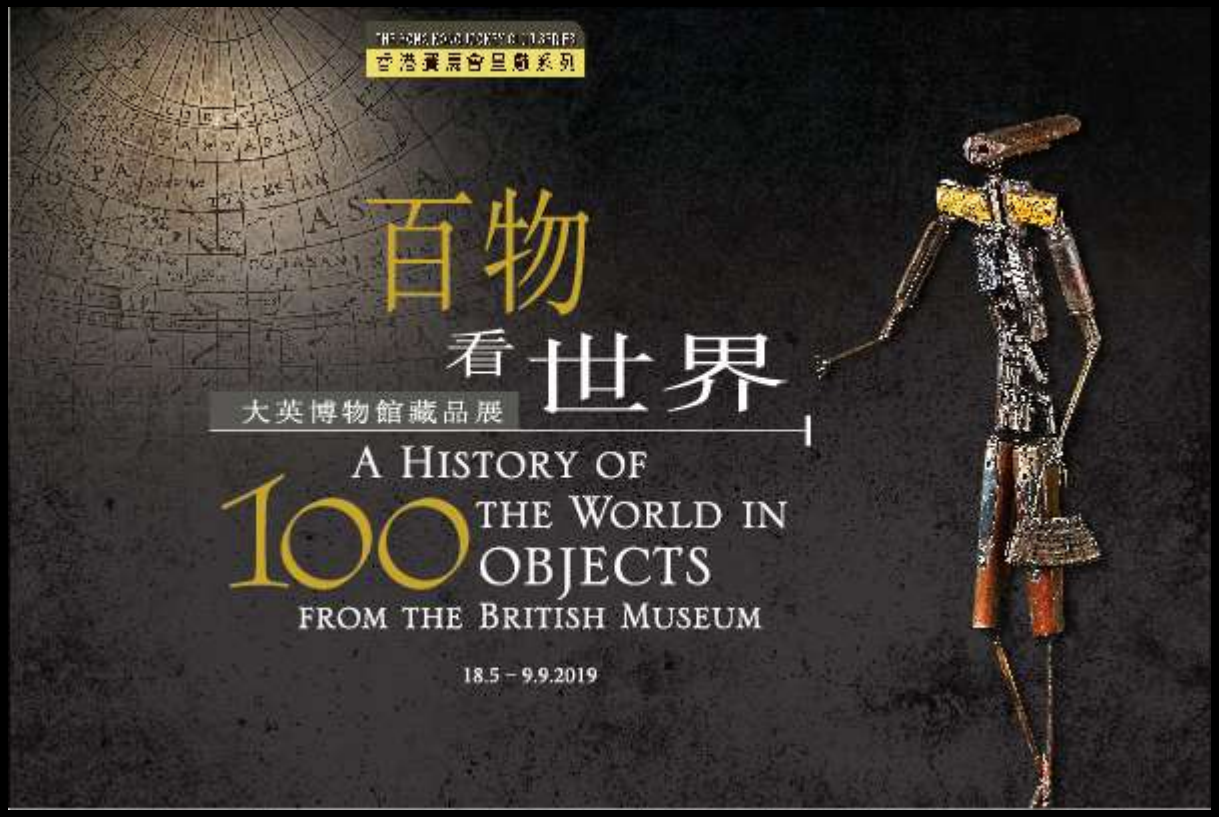
- 1st phase with hypereosinophilia – lasts for few months → necrotic phase with intense myocarditis and arteritis
- Thrombotic stage (~ a year after initial presentation) layer of thrombus replaces inflammatory myocardium
- Late fibrotic phase - final healing by fibrosis

Role of Eosinophils

- ? Cardiotoxic substance released by degranulated eosinophils
- ? Direct myocardium infiltration
- in necrotic phase mainly
- Eosinophilia usually resolved by thrombotic / fibrotic phase

Echo findings in EMF

- Thrombi adherent to apical LV + RV myocardium
- LV wall (inferior + basal) thickening
- Pericardial effusion frequent
- Restrictive filling (usually present lately)
- MR TR (retraction or adherence of MV TV)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