CMR Manifestations of cardiac amyloidosis
The term *amyloid*, popularized by Rudolf Virchow in 1854, is derived from the Greek word for starch.
Diagnosis
Effusions and ascites

• Signs of HFpEF (amyloidosis)

• Heart failure TX

• Ascites without pleural effusions
Hypertrophy in Cardiac amyloidosis
• Symmetric, asymmetric

• Concentric LVH: 59%

• Eccentric LVH or concentric remodeling in 33%

• Normal geometry in 8%

• RVH is frequent
Rare Morphology

• A few cases with a dilated cardiomyopathy phenotype
• Occasionally patients have outflow tract obstruction.
EF

• EF may be normal even into the late phase
• Poor measure of systolic function in patients with concentric remodeling.
• Long axis biventricular function reduces early, mainly at the level of the basal segments.
• The reduction, in many cases to effectively zero longitudinal function,
• is associated with small cavity size, decreased stroke volume and reduced cardiac output.
• The indexed stroke volume, usually severely reduced, is therefore a better measure of systolic function than the ejection fraction, and we would recommend scrutinising it in reports of possible cardiac amyloid.
Atria
CMR shows that much of the apparent atrial thickening in amyloidosis is interatrial fat.

Valvular disease in cardiac amyloidosis seems no more prevalent than in other people of similar age.

AF definitely occurs,

In later phases, AF, particularly coarse or flutter-like fibrillation may be observed and thrombi may be seen in the LAA.

Smoke in the LA also occurs in patients in sinus rhythm.
• not common in cardiomyopathy in adult life (although late onset HCM is well known),

• rapid changes over months in WT and function, should place AL amyloidosis high on the DDx.
Tissue Characterization
Late Gadolinium Enhancement
LGE T1

Normal Myocardium  Myocardial Infarction  Cardiac Amyloidosis  Cardiac Amyloidosis
TI Scout
There are three patterns associated with LGE imaging using PSIR:

- No LGE
- Subendocardial LGE
- Transmural LGE

AL

ATTR
• LGE more specific and sensitive than echo or CMR functional

• Early finding without hypertrophy

• Amyloid protein (subendocardium 42.4%, subepicardium 17.6%) is the cause of the enhancement

• Minor diffuse fibrosis (1.3%).
• Gadolinium is relatively contraindicated in patients with severe renal failure

• LGE quantification

• Total abnormal myocardium: false-negative
- Contraindication of GD
- Markers of systolic and diastolic function, mass and
- Prognostic and early disease markers
- Elevated before LVH, LGE or blood biomarkers
- High diagnostic accuracy when the pre-test probability is high
- Limitation
  - 2. Secondly: edema + amyloid
  - 3. different CMR systems and sequences have different normal ranges
Native T1 in the hypertrophic phenotype

Hypertension  HCM  AS

Amyloid

Normal range

Sado DM et al. Circ Cardiovasc Imaging 2013
FIGURE 5  Diagnostic Algorithm in Patients With Suspected Cardiac Amyloidosis

Suspected Cardiac Amyloidosis

Non-contrast CMR

Native T1 ≤1036 ms (z-score 0.4)

No Cardiac Amyloidosis

Native T1 ≥1036 ms (z-score 0.4) ≤1164 ms (z-score 3.5)

Consider giving contrast

Native T1 >1164 ms (z-score 3.5)

Cardiac Amyloidosis

Baggiano A, JACC CVI 2019
Histological correlation shows that edema is part of acute cardiac amyloidosis (particularly AL) and is linked to prognosis.
T2 in AL and ATTR

Error Bars: 95% CI

- p<0.01
- p=1.00
- p<0.001

Mean T2 (ms)

- AL NO TREATMENT
- AL TREATED
- ATTR
- Healthy Volunteers
ECV

- A measure of the free water in the myocardium
- An ECV > 40% in remote myocardium
- The normal range: 22% to 28%
- Focal scar or edema: up to 70%
- ECV elevations are early, before LGE and conventional clinical testing
ECV of the Spleen and Liver

Spleen ECV 0.29
Liver ECV 0.26

Spleen ECV 0.78
Liver ECV 0.70
AS vs Amyloidosis
Echocardiography

CMR

certainty of probable amyloidosis
adds value to the Mayo classification
LGE can be pathognomonic
increased specificity and sensitivity

Probability of Amyloidosis
CMR methods to distinguish types of cardiac amyloidosis:

• ATTR disproportionately increased LV mass and IVST, larger atrial area, smaller cavity volumes and lower EF (within the normal range) than AL amyloid, despite similar NYHA class and NT-pro BNP levels.
• LGE more extensive in ATTR than AL patients, but, this may be a survivor bias – with transmural LGE in AL associated with swift death.

• RV LGE in most ATTR amyloid cases, but in only a majority with AL amyloid.

• Apparent relative (compensatory) hypertrophy response in ATTR not present in AL, highlighting that amyloidosis is not just an interstitial disease.
Prognostic ability
CMR Imaging With Rapid Visual T1 Assessment Predicts Mortality in Patients Suspected of Cardiac Amyloidosis

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London, Ontario, Canada; Durham, North Carolina; and Houston, Texas

Delayed Hyper-Enhancement Magnetic Resonance Imaging Provides Incremental Diagnostic and Prognostic Utility in Suspected Cardiac Amyloidosis

Bethany A. Austin, MD,* W. H. Wilson Tang, MD,* E. Rene Rodriguez, MD,† Carmela Tan, MD,‡ Scott D. Flamm, MD,¶ David O. Taylor, MD,* Randall C. Starling, MD, MPH,* Milind Y. Desai, MD*†
Cleveland, Ohio
• Presence of LGE is predictive of prognosis in virtually all the cardiac pathologies, except for amyloidosis

• Magnitude

• PSIR-LGE clarifying the role of LGE

• T1 and ECV aids risk-stratifying patients with AL
ECV and prognosis in AL and ATTR amyloidosis

ECV in ATTR amyloidosis

ECV ≤ 0.58

ECV ≥ 0.58

Cumulative survival

Follow-up (months)

ECV in AL amyloidosis

ECV ≥ 0.45

ECV < 0.45

Cumulative Survival Probability

Months of Follow-Up
Prognosis

Survival Function for T2 in all AL patients

- AL Amyloidosis
- T2=55ms
- T2<35ms
Tracking changes with treatment
Surrogate endpoints in drug development

- Detection of biological effect (beneficial and off target)
- Dose ranging.
- No imaging modality has been shown to track changes. But T1 mapping has high potential
- LV mass: myocyte volume (beneficial) + infiltration volume (adverse), changes over time are not large compared to measurement error.
- Changes in function (stroke volume index rather than EF) have similar problems, with the additional confounder of deterioration in function associated with occurrence of atrial fibrillation rather than disease progression.
1. infiltration (amyloid burden, ECV)
2. possibly edema (native T1)
3. myocyte response (intracellular volume)
4. Disease stage

Richer understanding of the pathophysiological of the response to treatment
ECV sufficiently robust.
After Tafamidis Tx

LGE-CMR 2014

LGE-CMR 2019

A

B

C

D
**Haematological response:**
- Complete response (CR): normal FLC levels with normal kappa/lambda ratio and negative serum and urine immunofixation
- Very good partial response (VGPR): reduction in the dFLC to <40 mg/L
- Partial response (PR): >50% reduction in dFLC
- No response (NR): less than PR

**CMR response:**
- Regression: absolute decrease of at least 5% in ECV or visual reduction in LGE
- Stable: <5% absolute change in ECV and no visual changes in LGE
- Progression: absolute increase of at least 5% in ECV or visual increase in LGE

**CMR response:**
- 66% patients achieved CR or VGPR
- 34% patients achieved PR or NR

**CMR response:**
- 32% patients → Regression (lower ECV or LGE)
- 49% patients → Stable (no changes in ECV or LGE)
- 19% patients → Progression (higher ECV or LGE)

Amyloid regression was detectable only in 1 patient 6 months after chemotherapy.

Amyloid progression was present in 30% of patients: ~50% of amyloid progression occurred in a CR or VGPR patients.
Prospective study on patients EAMS programme

Patisiran: n=16
Controls: n=16

0 → 3 weekly patisiran infusions → 12 months

Blood biomarkers, 6MWT, Echocardiogram, Cardiac MRI

Blood biomarkers, 6MWT, Echocardiogram, Cardiac MRI

Cardiac Structure:
- IVSd
- PWTd
- LVM
- LVEDD
- LVEDDind
- WT
- LVEDV
- LVEDVind
- RWT
- LAA
- LAAind
- RAA
- RAAlind

Cardiac systolic function:
- SV
- SVind
- EF
- MCF
- MAPSE
- TAPSE
- TAPSE/PASP
- S’ tricuspid

Strain:
- LS
- SABr
- RALS

Cardiac diastolic function:
- SV
- E/A
- E’ Lat
- E’ Sept
- E/E’ Latc

Valves:
- PASP
- Significant MR
- Significant TR
- Severe AS

Echocardiography:
- Structure
- Systole
- Diastole
- Valves
- Strain

CMR with multiparametric:
- Cine
- Native T1
- ECV
- T2
- LGE

Functional:
- 6MWT

Blood Biomarkers:
- BNP

Activate Wir
Go to specific section

Patisiran was typically associated with a reduction in ECV (adjusted mean difference between groups -6.2% [95% CI -9.5% to -3.0%]; p=0.001)

No significant changes from baseline to 1 year
Conclusion:

- *Clinical impact of imaging:*
  - diagnosis (disease substrate),
  - measure myocardial process
- *Prognostic ability*
- *Track treatment changes*
Thank You