Diagnostic and Screening Strategies —and Pitfalls—in Cardiac Amyloidosis

ACC Cardiac Amyloidosis Roundtable, October 2021
Martha Grogan, MD
Director, Cardiac Amyloid Clinic
Mayo Clinic, Rochester MN

Disclosures

Research grants (clinical trials, funding to institution, site PI): Alnylam, Eidos, Pfizer, Prothena

Consulting/Advisory Boards (Alnylam, Prothena: funding to institution, no personal compensation)

@MarthaGrogan1

66 Year-Old Male with Exertional Dyspnea

- CAD: previous stents; No HTN
- 1 yr. ago - Dyspnea while hiking

  cath: mild CAD
- 6 mo. ago: progressive dyspnea,

  NT BNP ~2200 pg/ml ↓ to 500 after lasix (20 mg)
- 3 mo. ago - Renal infarct

  30 day monitor – no AF
- Echo: severe increase wall thickness (18 mm), EF 55%, strain -11%, RVSP 60 mmHg; MRI c/w amyloid, +LAA thrombus
- Serum protein electrophoresis: no monoclonal protein
- PYP scan: *markedly positive*

  H/CL ratio 2.4 at 1 hr, (positive . 1.3)

  SPECT + uptake in myocardium
- Creatinine 1.4 mg/dl
- NT BNP = 7257 pg/ml
- Trop T = 119 ng/l
- Peak V02 = 12.5 ml/kg-min (42% predicted)

66 Year-Old Male with Echo and MRI c/w amyloid

You recommend:

1. Tafamidis
2. Diflunisal
3. Patisiran
4. Heart transplant
5. Something else

66 Year-Old Male with Exertional Dyspnea

- CAD: previous stents; No HTN
- 1 yr. ago - Dyspnea while hiking

  cath: mild CAD
- 6 mo. ago: progressive dyspnea,

  NT BNP ~2200 pg/ml ↓ to 500 after lasix (20 mg)
- 3 mo. ago - Renal infarct

  30 day monitor – no AF
- Echo: severe increase wall thickness (18 mm), EF 55%, strain -11%, RVSP 60 mmHg; MRI c/w amyloid, +LAA thrombus

- **Serum protein electrophoresis: no monoclonal protein**
- PYP scan: ***markedly positive***

  H/CL ratio 2.4 at 1 hr, (positive . 1.3)

  SPECT + uptake in myocardium
- Creatinine 1.4 mg/dl
- NT BNP = 7257 pg/ml
- Trop T = 119 ng/l
- Diagnosis: ATTRwt,
- Prescribed tafamidis

66 Year-Old Male with Echo and MRI c/w amyloid

You recommend:

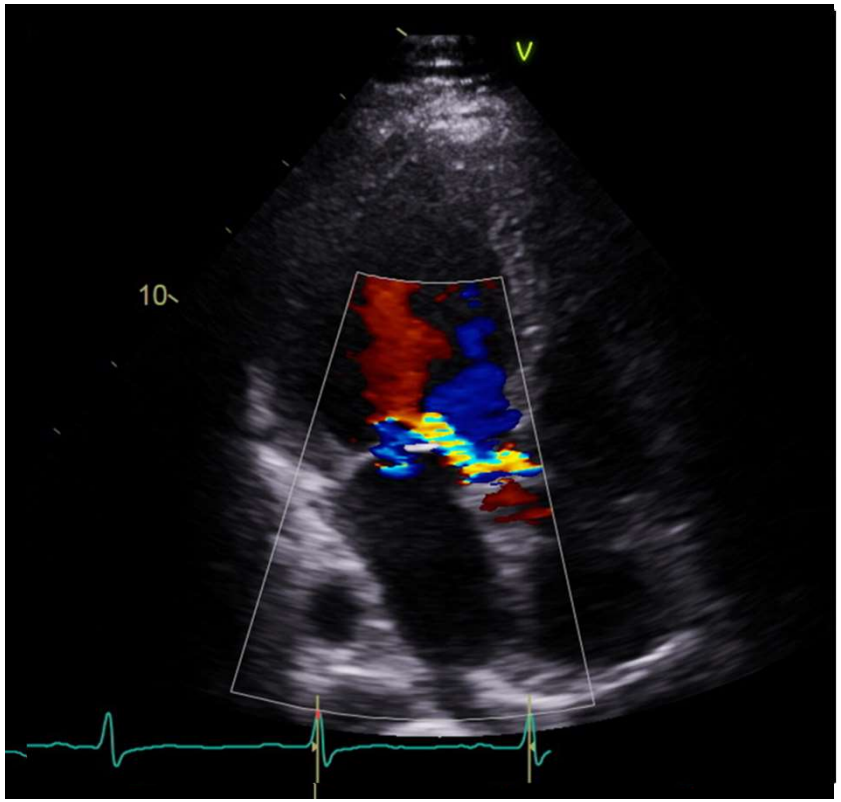
1. Tafamidis
2. Diflunisal
3. Patisiran
4. Heart transplant
5. **Something else**

- Serum free light chain assay
  - Kappa = 2.83 mg/dl (normal 0.33- 1.94)
  - **Lambda = 41.8 mg/dl (nl 0.57-2.63)**
  - Ratio = 0.07 (normal 0.25-1.65)
- Serum protein electrophoresis ***with immunofixation***: lambda monoclonal protein; same in urine
- Fat aspirate – negative for amyloid
- Bone marrow – 8% plasma cells, no definite amyloid
- EMB: + for AL

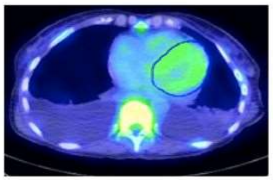
67 Year Old Male, progressive exertional dyspnea

- Bicuspid aortic valve with moderate aortic regurgitation, EF 49%, borderline increase wall thickness
- PYP positive (e/w): H/CL ratio = 1.8
- Diagnosis ATTRwt, Start tafamidis
- Mayo echo, mod-severe LV dilation (64 mm, normal < 55), moderate AR
- **Repeat PYP, Planar positive (due to LV dilation, AR); SPECT negative**
- TEE: Flail leaflet with severe AR

Diagnosis: Severe AR, no amyloid, stop tafamidis, proceed to AVR

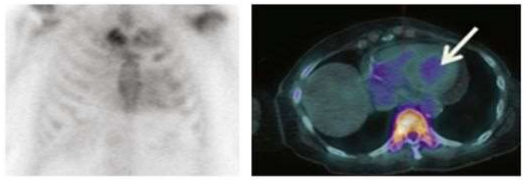


CENTRAL ILLUSTRATION: Accurate Use of Cardiac Scintigraphy for the Diagnosis of Transthyretin Amyloid Cardiomyopathy Contrasted With Key Causes of Misdiagnosis



Positive PYP ≠ ATTR; Diagnosis = AL

❖ Always screen for AL



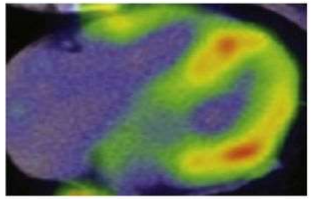
Positive PYP = blood pool uptake, no amyloid

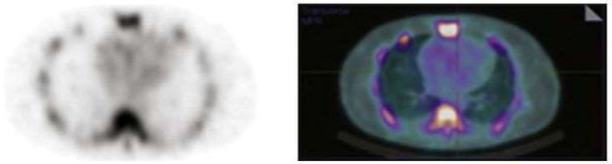
❖ Always perform SPECT

✓ Heart Failure with typical echo and/or CMR
✓ Negative sFLC, serum/urine IFE
✓ Positive PYP with SPECT

Accurate Diagnosis = ATTR-CM

Perform TTR DNA sequence





Negative PYP, Clinical suspicion persists

Cardiac biopsy: Diagnosis = ATTRv

❖ Perform biopsy if strong clinical suspicion

Hanna, M. et al. J Am Coll Cardiol. 2020;75(22):2851-62.

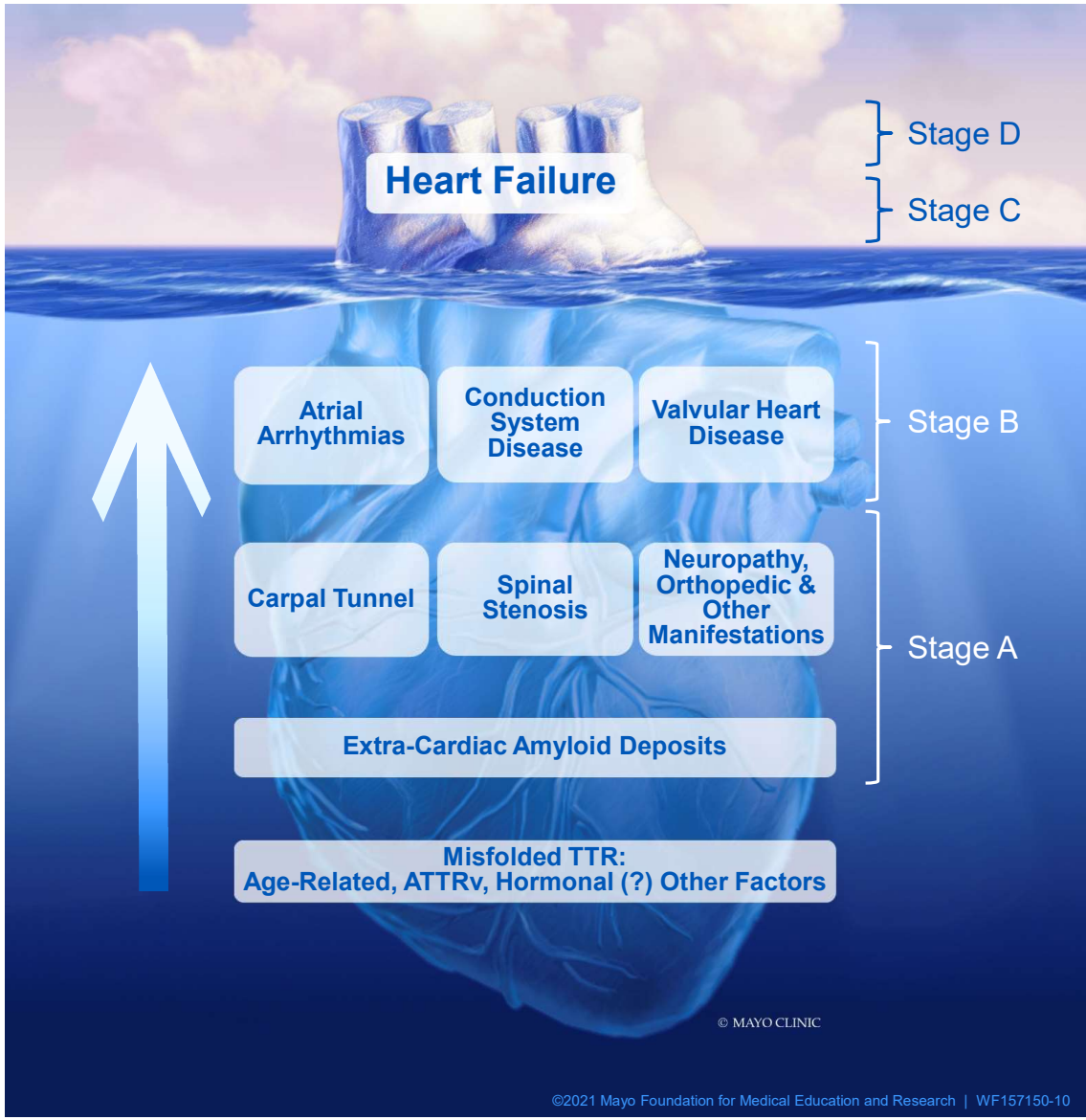
Mazen Hanna et al. J Am Coll Cardiol 2020;75:2851-2862

How to Avoid the Perils of PYP

1. Consensus guidelines *require* typical echo/CMR findings
   - *If echo/CMR not typical: need tissue biopsy*
   - Yes, PYP may detect early disease, but we don't know enough yet to use it in this situation
2. Always screen for monoclonal protein, need tissue if +
3. Always confirm myocardial uptake with SPECT
4. Recognize that there are other causes of PYP uptake
   - We will be learning these in next few years

ATTR: SCOPE OF THE PROBLEM

CURRENTLY DIAGNOSING MOSTLY AT THE TIP OF THE ICEBERG



Key Pitfalls in the Diagnosis of Cardiac Amyloidosis

1. Failure to understand screening tests for AL
2. Lack of understanding of criteria for non-biopsy diagnosis using PYP
3. *Amyloidosis is complex and we are all learning something new every day*

MAYO CLINIC

THANK YOU

