“Use of imaging in the diagnosis and differentiation of Amyloidosis”

Camilletti Jorge, MD, FACC
Past President Argentine Federation of Cardiology
Chief, Cardiology Area.
Staff, Nuclear Medicine Service.
Hospital Italiano La Plata
Buenos Aires, Argentina
Imaging Cardiac Amyloidosis

Cardiac amyloidosis was an underdiagnosed disease, untreated and lethal.

Amyloidosis can be diagnosed by imaging without biopsy.

Is treatable in 2021!
Imaging Targets in Cardiac Amyloidosis

Echocardiographic Features of Cardiac Amyloidosis

- Echogenic myocardium
- Concentric LVH
- Preserved LVEF
- Restrictive filling pattern
- Bi-atrial enlargement
- Atrial septal thickening

Echocardiographic Features of Cardiac Amyloidosis
Echocardiographic Features of Cardiac Amyloidosis
Echocardiography: Advanced structural changes

Insufficient to distinguish between Amyloidosis from LVH or AL from ATTR

Thickened ventricle with sparkly myocardium / Global Longitudinal Strain / Restrictive LV Filing

Dorbala S, Cuddy S and Falk R. JACC Imag 2020
MRI Features of Cardiac Amyloidosis

CMR provides high-definition structural imaging and tissue characterization that is often incremental to information obtained on Echo in amyloidosis.

Increased myocardial mass, bi-atrial enlargement, as well as atrial and ventricular function and other typical morphological features of restrictive cardiomyopathy.
MRI Features of Cardiac Amyloidosis

Classic LGE of the ventricles and atria
CRM: Structure and Tissue Characterization
Insufficient to distinguish AL from ATTR

Advanced Features

Early Features

Apical 4 Chamber View

LGE

Native T1 Imaging

ECV Imaging

Prolongation of T1 Time and expansión of the ECV

Molecular imaging of Amyloidosis

Targeted molecular imaging provides a “virtual histology” image of the entire heart

- **Bone-avid Compounds**
  - 99mTc-MDP
  - 99mTc-DPD
  - 99mTc-HMDP
  - 99mTc-PYP

- **Amyloid-directed molecules**
  - 123I-SAP
  - 99m Tc-Aprotinin

- **Positron emission tomography amyloid agents**
  - 11C-Pittsburgh B Compound (PiB)
  - 18F-florbetapir, Florbetaben, Flumetamol
DPD or PYP uptake in AL and TTR cardiac amyloidosis

Perugini E, et al. JACC 2005; 46: 1076-84
Planar imaging (qualitative and semiquantitative methods) visual análisis

A

B

Grado 0  Grado 1  Grado 2  Grado 3

Relación Corazón/pulmón: 2.04

ASNC
99mTc(PYP or DPD) Based Imaging of Cardiac Amyloidosis
Semi-quantitative visual analysis

Radionuclide Imaging of Amyloidosis
Imaging Considerations

99m Tc PYP/HMDP/DPD
Dose 10-20 mCi

Blood Pool
Myocardium
Bone

Planar
SPECT (blood pool vs myocardium)
H/CL ratio
99m Tc PYP

Planar
SPECT: pattern of uptake
Compare to bone for grading
99m Tc PYP/HMDP/DPD
Diagnosis of ATTR-CA: $^{99m}$TcPYP, DPD, HMDP

Nearly 100% specific in select patients

Nuclear Imaging

High probability:
1 Hs: H/CL > 1.5
3 Hs: H/CL > 1.3
Grading of 99m Tc PyP Uptake

Planar imaging (qualitative and semiquantitative methods) and single-photon emission (SPECT) imaging (without and with computed tomography)

Hanna et al. JACC Vol. 75, N° 22 June 9, 2020: 2851-62
Accurate Use of Cardiac Scintigraphy for the Diagnosis of Transthyretin Amyloid Cardiomyopathy Contrasted with Key Causes of Misdiagnosis

Hanna et al. JACC Vol. 75, N° 22 June 9, 2020: 2851-62
Quantitation of Cardiac 99mTc-PYP Using SPECT/CT: The Next Frontier in ATTR Cardiac Amyloidosis

Dorbala S, DiCarli MF. J Nucl Med. 2020

Scully et al. J Am Coll Cardiol Img. 2020; 1353-1363.
18F-florbetapir/Amyloid PET/CT
AL amyloidosis

Systemic AL organ involvement

Early cardiac AL amyloidosis

Ehman E, Dorbala S. J Nucl Med 2019
Cuddy S, Dorbala S. JACC Imaging 2020
Rosengren S, Et al. JACC Img. 2020
Genovese et al. JACC Img. 2020
Lee SP et al. JACC. 2020

ASNC
Radionuclide Imaging of Amyloidosis
Criteria for Clinical Diagnosis of ATTR-CM

Clinical diagnosis of ATTR cardiac amyloidosis: $^{99m}$Tc-PYP, $^{99m}$DPD, $^{99m}$HMDP

1. ATTR cardiac amyloidosis is diagnosed when the following criteria are met: ATTR
   a. $^{99m}$Tc-PYP, DPD, HMDP Grade 2 or 3 myocardial uptake of radiotracer AND
   b. Absence of a clonal plasma cell process as assessed by serum FLCs and serum and urine immunofixation AND
   c. Typical cardiac imaging features (as defined below)

Typical imaging features of cardiac amyloidosis

Typical cardiac echo or CMR: ANY of the following imaging features with all other causes for these cardiac manifestations, including hypertension, reasonably excluded.

1. Echo
   a. LV wall thickness >12 mm
   b. Relative apical sparing of global LS ratio (average of apical LS/average of combined mid+basal LS >1)
   c. ≥ Grade 2 diastolic dysfunction

2. CMR
   a. LV wall thickness >ULN for sex on SSFP cine CMR
   b. Global ECV >0.40
   c. Diffuse LGE
   d. Abnormal gadolinium kinetics typical for amyloidosis, myocardial nulling before blood pool nulling

Hanna et al. JACC Vol. 75, No 22 June 9, 2020: 2851-62
Consensus algorithm for noninvasive diagnosis of cardiac amyloidosis

Heart failure, syncope, or bradyarrhythmia, with echocardiogram and/or cardiac magnetic resonance imaging (CMR) suggesting/indicating cardiac amyloid

Bone scintigraphy with $^{99m}$Tc-DPD/HMDP/PYP

- Grade 0
- Grade 1
- Grade 2 to 3

Serum immunofixation + Urine immunofixation + serum free light chain assay (Freelite)

- Monoclonal protein present?
  - No
  - Yes
  - Yes
  - No

- Cardiac AL/ATTR amyloidosis unlikely
- Review/request CMR
- Need specialized assessment for Diagnosis: Histological confirmation and typing of amyloid
- Cardiac ATTR amyloidosis
- TTR genotyping

- Cardiac amyloidosis (AL/AAPoAl/ATTR/other)
- Variant ATTR amyloidosis
- Wild-Type ATTR amyloidosis

A Test in Contrast: Role of 99mTc Cardiac Scintigraphy in the Diagnosis of CA

Hanna et al. JACC Vol. 75, N° 22 June 9, 2020: 2851-62
Conclusion

Use of imaging in the diagnosis and differentiation of Amyloidosis

- Cardiac amyloidosis is a lethal cause of cardiomyopathy if left untreated
- It is underdiagnosed
- Echo and CMR provide excellent delineation of abnormality in cardiac structure and function, and tissue characterization
- Molecular imaging may help differentiate ATTR from AL and limits the need for additional biopsy
Gracias!
Thank you!