Impact of cardiac 99mTc-HMDP uptake on myocardial function and left ventricular filling pressure in patients with transthyretin amyloidosis

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Transthyretin amyloidosis?

- Amyloidosis is an infiltrative disease characterized by extracellular deposition of fibrillary protein into one (localized) or multiple organs (diffuse or systemic).
- Important cause of restrictive cardiomyopathy and congestive heart failure.
- Two major types of cardiac amyloidosis:
  - Cardiac amyloid light-chain (AL),
  - Transthyretin-related cardiac amyloidosis (ATTR)
• Differentiating the type of cardiac amyloidosis (AL vs ATTR) is crucial in guiding patient care.

• Endomyocardial biopsy with immunohistochemistry staining is the gold standard for the diagnosis.

• Electrocardiogram, echocardiography, and cardiac magnetic resonance imaging (CMR)

• Nuclear imaging:
  
  > 99m Tc-DPD (technetium-3,3-diphosphono-1,2-propanodicarboxylic acid) and 99m Tc-PYP (technetium pyrophosphate)

  > PET…
Bone scintigraphy with transthyretin amyloidosis

- Multicenter study 1200 patients

- >99% sensitive and 86% specific for TTR CA,

- With false positives almost exclusively from uptake in patients with AL CA.

- The combined findings of visual score 2 or 3 myocardial radiotracer uptake on bone scintigraphy and the absence of a monoclonal protein in serum or urine has a specificity and positive predictive value for TTR CA of 100%.

Methods

• Fifty patients with TTR cardiac amyloidosis

• $^{99m}$Tc- hydroxymethylene-diphosphonate ($^{99m}$Tc-HMDP) scintigraphy:
Cardiac retention by scintigraphy was assessed by visual scoring and the heart/whole body (H/B) ratio was calculated by dividing counts in the heart by counts in late whole body images.

• Echocardiography:
Measure of LV morphology, longitudinal strain (LS), systolic and diastolic functions.
0 = absent cardiac uptake and intense bone uptake;

1 = mild cardiac uptake < bone uptake

2 = moderate cardiac uptake = bone uptake

3 = high cardiac uptake > bone uptake.

Quantitative assessment using heart retention, and heart to whole body retention, is assessed using counts in the region of interest.
Increased LV wall thickness (ATTR/AL); overlap with other infiltrative disease such as hypertrophic CM, severe LVH, Fabry’s disease

Increased interatrial septal thickness, pleural and pericardial effusion, valve thickening (non-specific)

Apical sparring on Bull’s eye plot of Global Longitudinal strain: SN 96%, SP 88% (in patients without CAD). Does not differentiate AL vs ATTR

Strain longitudinal
Ea
mean left ventricular wall thickness
E/Ea ratio
LVEF
Results

• Mean population age: 79±10 years.

• Visual score:
  – 2 for 6 patients (12%)
  – 3 for 44 patients (88%)

• Mean H/WB ratio: 12±7.

• Mean LV ejection fraction and global LS were 51±10% and -10±3%, respectively.
Results (2)

- H/WB ratio was correlated with:
  - global LS (R=0.408, P=0.003),
  - Ea (R=-0.566, P<0.001)
  - mean left ventricular wall thickness (R=0.476, P<0.001)

- ….but not with LV ejection fraction (R=-0.109, P=0.453).

- Segmental myocardial uptake normalized by H/WB ratio was correlated with segmental LS (n = 850 segments, R = 0.162, P<0.001).

- H/WB ratio was not correlated with NT-proBNP levels (R=0.219, P=0.148) neither E/Ea ratio (R=0.204, P=0.184).
Global longitudinal strain (%) vs Heart/Whole Body Ratio:
- \( R = 0.408, P = 0.003 \)

Left ventricular ejection fraction (%)
- \( R = -0.109, P = 0.453 \)

Mitrval Annulus Lateral Ea Velocity (cm/s)
- \( R = -0.566, P < 0.001 \)

Left ventricular mean wall thickness (mm)
- \( R = 0.476, P < 0.001 \)
Conclusion

In patients with TTR cardiac amyloidosis, myocardial uptake by $^{99m}$Tc-HMDP scintigraphy is correlated with decrease of myocardial LS.