Temporal Changes in Myocardial Amyloid Burden Using ^{124}I-Evuzamitide (AT-01) PET/MRI Imaging

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BACKGROUND

- Cardiac magnetic resonance imaging (CMR) is currently considered the gold standard imaging modality to assess cardiac structure, function, and surrogates of amyloid load.
- ^{124}I-evuzamitide (AT-01) is a novel pan-amyloid PET radiotracer which binds directly to the amyloid fibrils.
- There are currently no clinically-available direct measures of amyloid burden, hence the use of surrogate imaging or circulating biomarkers.
- We characterized the temporal changes in ^{124}I-evuzamitide uptake and traditional measures on CMR over 1 year.

METHODS

- The study was approved by the OHSU IRB and conducted under an FDA-approved IND.
- Patients were diagnosed by standard clinical, laboratory, biopsy, and imaging criteria. ^{124}I-evuzamitide diagnostic performance was judged against comprehensive clinical evaluation (gold standard)
- All patients underwent hybrid cardiac PET/MRI followed by whole-body (WB) PET/MRI with ^{124}I-evuzamitide at baseline and then once again at 1 year. All patients received potassium iodide 130 mg for 3 days, first dose at least 30 minutes prior to ^{124}I-evuzamitide administration.
- Ratios of mean (and max) LV septum standardized uptake value (SUV) to mean (and max) LV blood pool SUV was calculated.
- Patients were receiving or started to receive standard of care amyloid-targeted therapies.

RESULTS

- We enrolled 70 patients with suspected or known systemic amyloidosis, and 21 patients (mean age 73.3 ±8.4, 74% male) underwent repeat ^{124}I-evuzamitide PET/MRI at 1 year.
- At baseline, the mean SUVR, mean ECV and median NT-proBNP were 1.8 ±0.2, 57 ±11%, and 864.0 (628, 4,488), respectively.

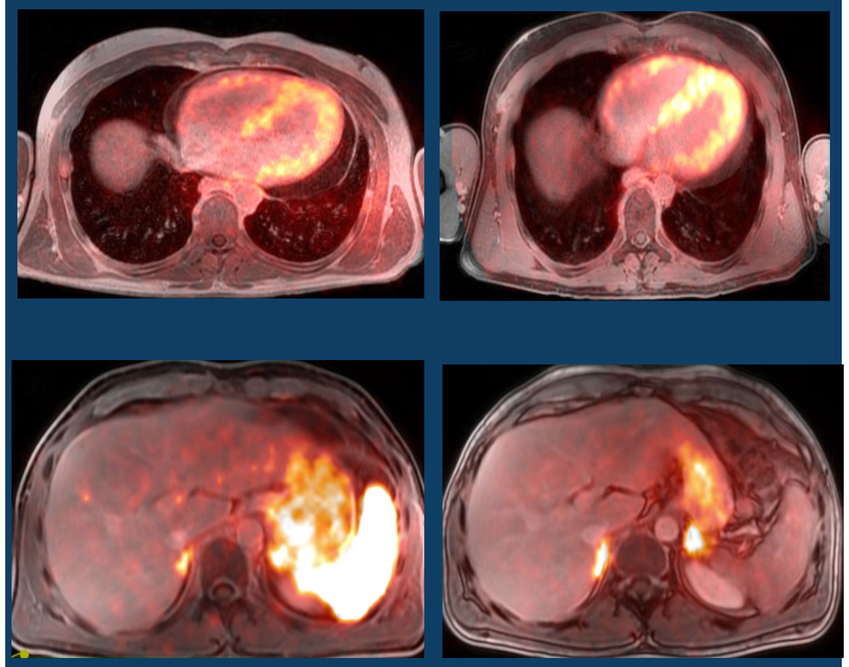
Table 1: Selected baseline characteristics

Characteristic	Overall (n = 21)	AL (n = 5)	ATTR (n = 16)
Mean SUVR, mean (SD)	1.8 (0.2)	1.7 (0.1)	1.8 (0.2)
Max SUVR, median (IQR)	1.7 (1.6, 1.8)	1.6 (1.6, 1.8)	1.7 (1.7, 1.9)
ECV (%), mean (SD)	57.0 (11.0)	57.2 (15.2)	56.9 (10.0)
LVEF (%), median (IQR)	56.0 (46.0, 61.0)	57.0 (45.0, 61.0)	56.0 (46.0, 60.3)
LVM (g), mean (SD)	192.6 (56.7)	181.6 (29.7)	196.0 (63.3)
NT-ProBNP (pg/ml), median (IQR)	864.0 (628.0, 4,488.0)	4,488.0 (2,480.0, 5,578.0)	841.0 (560.8, 1,384.0)
Troponin (ng/L), median (IQR)	28.0 (17.0, 60.0)	25.0 (19.0, 28.0)	35.0 (16.3, 70.5)

Conclusion

- In a pilot study of temporal changes in myocardial uptake of ^{124}I-evuzamitide and myocardial structure on PET/MRI, cardiac amyloidosis patients on treatment showed minimal change on average, which was well captured by stable ^{124}I-evuzamitide uptake.
- The study is ongoing with more than 50 patients undergoing serial follow-up ^{124}I-evuzamitide PET/MRI for up to 4 timepoints over 3 years.

Figure 4: Illustrative example of a patient with AL post ASCT with massive resorption of spleen amyloid (SUVR from 7.5 to 0.9) but persistent cardiac uptake (mild decline in SUVR from 2.0 to 1.7).



- At 1 year, mean LV SUVR was stable (Δ 0.0 (-0.3, 0.2), p=0.78), max LV SUVR was stable (Δ 0.0 (-0.3, 0.2), p=0.52, ECV slightly decreased (Δ -3.2 (-1.1, -8.7), p=0.04), LVM was stable (Δ 0.0 (-15.0, 5.0), p=0.28), and NT-proBNP increased (Δ 161 (13, 736), p=0.01).
- The change in mean LV SUVR trended with the change in ECV and NT-proBNP but not LVM.
- The change in max LV SUVR trended with the change in ECV, NT-proBNP and LVM.

Figure 1. Mean LV SUVR Change

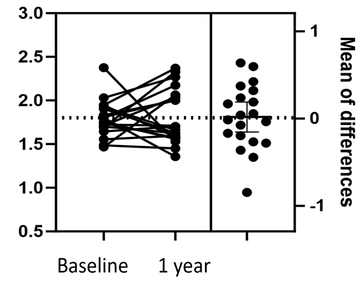


Figure 2: Scatterplots and correlations between change in mean LV SUVR and ECV, NT-proBNP, and LVM.

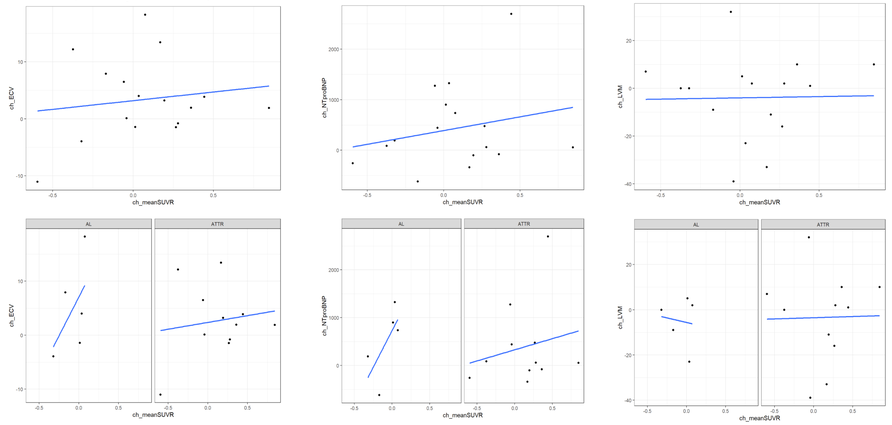
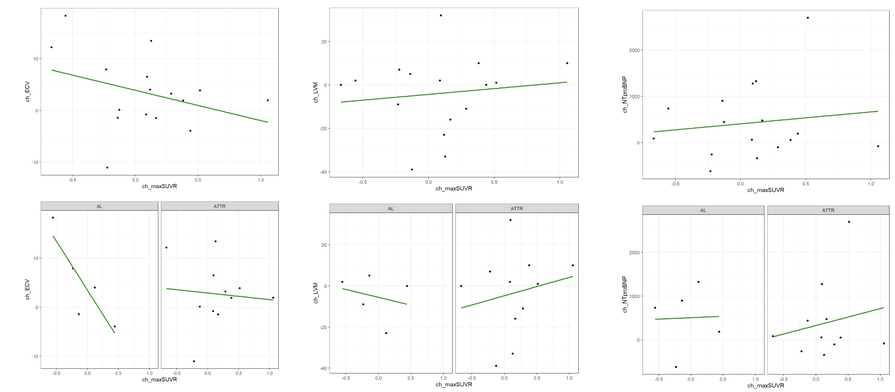


Figure 3: Scatterplots and correlations between change in max LV SUVR and ECV, NT-proBNP, and LVM.



DISCLOSURES and FUNDING

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