Utilizing ^{124}I-evuzamitide PET/MRI to Elucidate the Relationship between Renal Dysfunction and Amyloid Deposition in Transthyretin Amyloid Cardiomyopathy

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BACKGROUND

- In light chain (AL) amyloidosis, renal amyloid fibril deposition can precipitate kidney disease in >50% of patients.
- In transthyretin amyloid cardiomyopathy (ATTR-CM), it is unclear if kidney dysfunction is due to renal amyloid fibril deposition or progressive cardiomyopathy (i.e. cardio-renal syndrome).
- ^{124}I-evuzamitide (AT-01) is a novel pan-amyloid PET radiotracer that allows for assessment of amyloid deposition in target organs.
- This study assessed if the estimated glomerular filtration rate (eGFR) is associated with renal amyloid deposition (measured via renal radiotracer uptake) or cardiac structure and function on cardiac magnetic resonance imaging (MRI).

METHODS

- The study was approved by the OHSU IRB and conducted under an FDA-approved IND.
- Cardiac (AL and ATTR) amyloidosis was diagnosed in accordance with the national guidelines. Patients with renal AL amyloidosis were diagnosed through clinical presentation, laboratory findings, biopsy, and assessment of other alternative explanations for renal disease.
- All patients underwent cardiac and whole-body PET/MRI with ^{124}I-evuzamitide (mean administered activity 1.05±0.02 mCi). eGFR was measured immediately prior to tracer injection. Images were analyzed for tracer distribution and organ involvement. Proteinuria was not systematically assessed.
- Uptake was quantified using standardized uptake value ratio (SUVR) defined as the ratio of mean organ (e.g,. left ventricular septal myocardium and renal) SUV / left ventricular blood pool SUV.
- Myocardial and renal SUVR were compared for select strata. eGFR levels for patients with ATTR-CM were then compared to renal radiotracer uptake and select MRI measures.

RESULTS

- 50 patients were enrolled from January through August, 2023. All subjects completed the study protocol.
- The baseline characteristics are shown in Table 1.
- Median myocardial SUVR was 1.8 (1.7, 1.9) in cardiac amyloidosis vs 1.0 (0.9, 1.2) in controls without cardiac amyloid (p<0.001).
- Median myocardial SUVR was 1.8 (1.7, 1.9) in ATTR-CM compared to 1.7 (1.7, 1.8) in AL-CM (p=0.582).
- In 27 patients with ATTR-CM, median renal SUVR was 0.9 (0.8, 1.1), significantly lower than the median renal SUVR of 1.9 (1.4, 4.8) in 9 patients with renal AL amyloidosis (p<0.001).
- In patients with ATTR-CM, 14 (52%) had an eGFR < 45 mL/min (mean: 47.5±12.3 mL/min).
- In patients with ATTR-CM, eGFR did not correlate with renal SUVR (r=-0.014, p=0.946). However, eGFR did correlate with LV wall thickness (r=-0.535, p=0.004) and LV mass (r=-0.511, p=0.006).

Table 1: Baseline Characteristics Stratifying by Cardiac Amyloidosis and ATTR vs. AL Amyloidosis

Variable	Total (n=50)	With Cardiac Amyloid (n=34)	Without Cardiac Amyloid (n=16)	p-value	ATTR Amyloid (n= 28)	AL Amyloid (n=12)	p-value
Age (years)	72.0 ± 9.1	74.7 ± 8.0	66.4 ± 9.1	**0.002**	75.9 ± 7.1	67.8 ± 9.4	**0.017**
Male Sex (%)	37 (74%)	31 (91%)	6 (38%)	**<0.001**	26 (93%)	8 (67%)	**0.034**
Cardiac Amyloidosis (%)	34 (68%)	–	–	–	27 (96%)	7 (58%)	**0.002**
Underlying Phenotype for Select Controls:							
LVH/HCM	–	–	4 (25%)	–	–	–	–
Extracardiac AL Amyloidosis			5 (31%)				
Hereditary Transthyretin Carrier			5 (31%)				
Orthopedic Amyloid Deposits			2 (13%)				
^{124}I-evuzamitide administered activity (mCi)	1.05 ± 0.02	1.05 ± 0.02	1.04 ± 0.01	0.124	1.05 ± 0.02	1.04 ± 0.02	0.255
LVH (Basal LV Septum ≥ 12 mm)	43 (86%)	33 (97%)	10 (63%)	0.366	27 (96%)	11 (92%)	0.874
Myocardial SUV	6.3 ± 2.6	7.6 ± 2.1	3.4 ± 0.8	**<0.001**	7.7 ± 2.3	5.2 ± 1.8	**0.001**
Renal SUV	5.8 ± 5.6	5.8 ± 6.7	5.9 ± 2.2	0.894	3.8 ± 0.8	10.2 ± 10.2	0.054
LV Blood Pool SUV	4.0 ± 1.1	4.3 ± 1.2	3.4 ± 0.7	**0.001**	4.4 ± 1.3	3.6 ± 0.7	**0.021**
Myocardial SUVR (Myocardium / LV Blood Pool)	1.7 (1.1, 1.8)	1.8 (1.7, 1.9)	0.9 (0.9, 1.1)	**<0.001**	1.8 (1.7, 1.9)	1.6 (1.0, 1.7)	**0.026**
Renal SUVR (Kidney / LV Blood Pool)	1.2 (0.8, 1.6)	1.0 (0.8, 1.2)	1.6 (1.5, 1.9)	**<0.001**	0.9 (0.8, 1.1)	1.5 (1.1, 3.4)	**<0.001**
LVEF (%)	57.7 ± 12.3	54.5 ± 11.2	64.4 ± 12.1	**0.007**	55.4 ± 10.3	57.3 ± 15.2	0.709
LV Mass (g)	171 (134, 208)	184 (160, 210)	125 (86, 147)	**<0.001**	184 (157, 221)	171 (135, 196)	0.211
Basal Septal LV Wall Thickness (mm)	16 (12, 19)	16 (15, 20)	12 (10, 14)	**<0.001**	17 (15, 20)	13 (12, 15)	**0.001**
Basal Inferolateral LV Wall Thickness (mm)	10 (8, 12)	11 (9, 13)	8 (6, 9)	**<0.001**	11 (9, 13)	9 (7, 11)	0.063
eGFR (mL/min)	48.7 ± 14.9	46.9 ± 14.5	52.5 ± 15.4	0.232	48.1 ± 12.4	41.7 ± 17.9	0.278
NT-proBNP (pg/mL)	1931 ± 2332	2411 ± 2472	874 ± 1597	**0.014**	1905 ± 2408	2600 ± 2387	0.411

Figure 1: Mean Myocardial SUVR Stratifying by Cardiac Amyloidosis and ATTR-CM vs. AL-CM

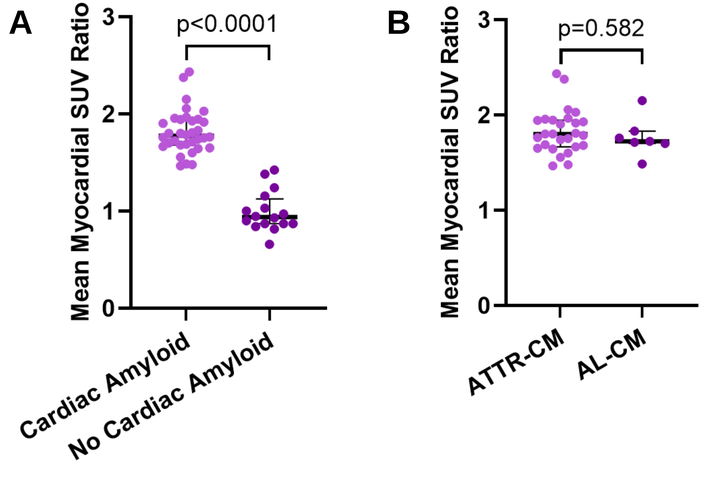


Figure 2: Mean Renal SUVR in ATTR-CM vs. Renal AL Amyloidosis

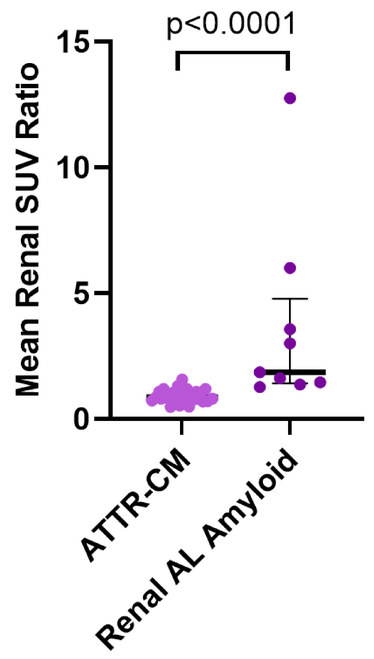
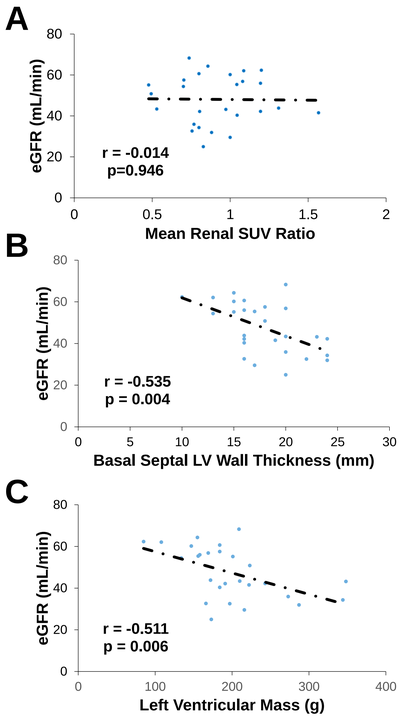


Figure 3: Comparison of eGFR and Select Variables in Patients with ATTR-CM



CONCLUSIONS

- ^{124}I-evuzamitide PET/MRI is feasible and can aid in the diagnosis of cardiac amyloidosis (previously shown to have 100% sensitivity and specificity using a mean LV myocardial SUVR of ≥1.45).
- In AL amyloidosis, a disease where renal amyloid fibril deposition is known to cause disease, PET/MRI demonstrated significant renal uptake of ^{124}I-evuzamitide. However, that was not seen in patients with ATTR-CM.
- Additionally, in patients with ATTR-CM, eGFR levels did not correlate with renal ^{124}I-evuzamitide uptake and instead correlated with cardiac MRI variables.
- As such, renal dysfunction in ATTR-CM is unlikely to be related to significant renal amyloid fibril deposition but rather worsening cardiomyopathy.
- Further studies correlating ^{124}I-evuzamitide imaging with histopathological findings are necessary.

DISLOSURES & FUNDING

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