



# Relationship Between Myocardial <sup>124</sup>I-evuzamitide Uptake and Cardiac Structure and Function: A Cardiac PET/MRI Study

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## BACKGROUND

- CMR allows for assessment of cardiac structure, function, and surrogates of amyloid load (i.e. ECV)
- <sup>124</sup>I-evuzamitide is a novel pan-amyloid PET radiotracer

## OBJECTIVE

We investigated the relationship between <sup>124</sup>I-evuzamitide myocardial uptake, ECV, and other measures of cardiac structure and function.

## METHODS

- The study was approved by the OHSU IRB and conducted under an FDA-approved IND.
- Cardiac amyloidosis was suspected or diagnosed in all patients prior to enrollment.
- Patients were diagnosed by standard clinical, laboratory, biopsy, and imaging criteria according to the guidelines.
- All patients underwent hybrid cardiac PET/MRI (GE Signa, 3T) with <sup>124</sup>I-evuzamitide (mean administered activity 1.04±0.02 mCi, 30 minute cardiac acquisition). All patients received potassium iodide 130 mg for 3 days, first dose at least 30 minutes prior to <sup>124</sup>I-evuzamitide administration.
- PET Images were analyzed qualitatively and quantitatively for cardiac involvement. Ratio of mean LV septum standardized uptake value (SUV) to mean LV blood pool SUV was calculated.
- On cardiac MRI, cardiac structure (LV wall thickness, mass, and volumes) were analyzed. T1 and T2 mapping were performed. Hematocrit was measured and gadolinium contrast agent was administered in all patients.
- T1 mapping was performed using identical modified Look-Locker inversion recovery (MOLLI) sequences pre-gadolinium and at 14-minutes post-gadolinium to quantify extracellular volume fraction (ECV).

## RESULTS

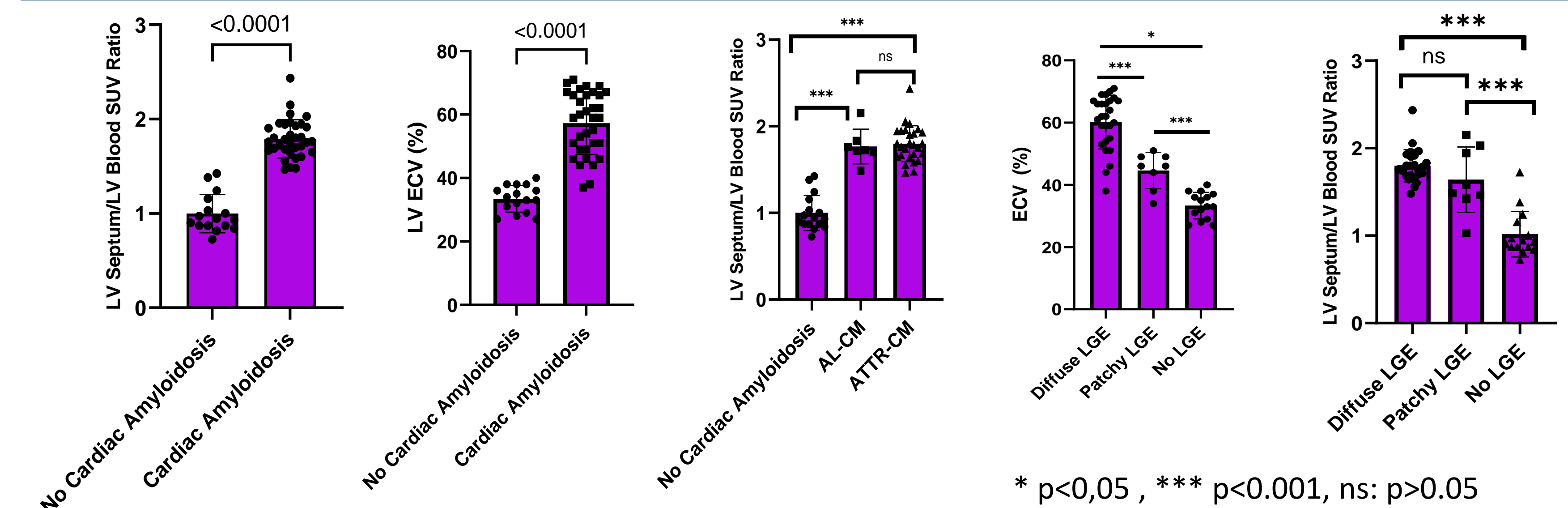
- 50 patients were enrolled from January through August 2023. All subjects completed the study protocol.
- <sup>124</sup>I-evuzamitide was safe without any serious adverse events and no tracer-related adverse events. There was a mild AE of redness at the site of peripheral line in one subject and the AE resolved in less than 24 hours.
- Time from <sup>124</sup>I-evuzamitide injection to start of cardiac PET was 4.0±0.6 hours.
- The baseline characteristics are shown in Table 1.

## RESULTS

**Table 1: Baseline characteristics of patients diagnosed with cardiac amyloidosis vs those without cardiac involvement/controls.**

Variable	Cardiac Amyloidosis (N=34)	Controls (N=16)	p-value
Age (years)	74.7±8	66.44±9	0.002
Male sex	31 (91%)	6 (37.5%)	<0.001
Cardiac Amyloidosis subtype			
Light chain	7 (20.6%)	-	
Transthyretin	27 (79.4%)	-	
Controls Underlying Phenotype:			
LVH/HCM		4 (25%)	
Extracardiac AL amyloidosis		5 (31%)	
Transthyretin variant carrier		5 (31%)	
Orthopedic amyloid deposit		2 (13%)	
Systemic amyloidosis without cardiac involvement	0%	7 (43.8%)	
Pathogenic transthyretin variant	4 (11.8%)	5 (31.3%)	0.250
Left ventricular hypertrophy (basal LV septum ≥12 mm)	33 (97%)	10 (62.5%)	0.366
<sup>124</sup> I-evuzamitide administered activity (mCi)	1.05 (0.02)	1.04 (0.01)	0.124
Mean time from <sup>124</sup> I-evuzamitide to start of cardiac PET (hours)	3.15	3.05	0.571
Mean myocardial SUV	7.58 (2.12)	3.43 (0.75)	<0.001
Mean LV blood pool SUV	4.28 (1.20)	3.39 (0.63)	0.001
SUVr (myocardium over LV blood)	1.76 (1.67, 1.93)	0.94 (0.87, 1.06)	<0.001
Mean LA blood pool SUV	3.67 (0.95)	3.52 (0.85)	0.602
Mean Myocardium SUV – LA SUV	3.40 (2.58, 3.36)	0 (0, 0.55)	<0.001
Basal septal LV wall thickness (mm)	16 (15.00, 20.00)	12 (10.00, 13.25)	<0.001
Basal inferolateral LV wall thickness (mm)	11 (9.00, 12.75)	8 (6.00, 9.00)	<0.001
LV mass (g)	184.0 (160.8, 209.8)	124.5 (86.0, 146.2)	<0.001
LV mass indexed to body surface area (g/m <sup>2</sup> )	91.77 (79.21, 108.42)	63.45 (49.47, 79.23)	<0.001
LV end-diastolic volume (ml)	170.4 (38.91)	141.5 (36.12)	0.016
LV end-systolic volume (ml)	78.38 (27.60)	51.38 (24.82)	0.002
LVEF (%)	54.53 (11.24)	64.38 (12.08)	0.007
Stroke volume (ml)	92.79 (28.71)	90.12 (26.19)	0.754
T2 relaxation time (basal, ms)	51.00 (49.00, 53.75)	47.00 (44.75, 48.50)	<0.001
Native T1 relaxation time (basal, ms, 3T)	1382 (1338, 1435)	1214 (1190, 1236)	<0.001
ECV (%)	57.20 (9.86)	33.51 (4.20)	<0.001
LGE pattern			<0.001
None	1 (2.9%)	14 (87.5%)	
Patchy	7 (20.6%)	2 (12.5%)	
Diffuse	26 (76.5%)	0 (0.0%)	

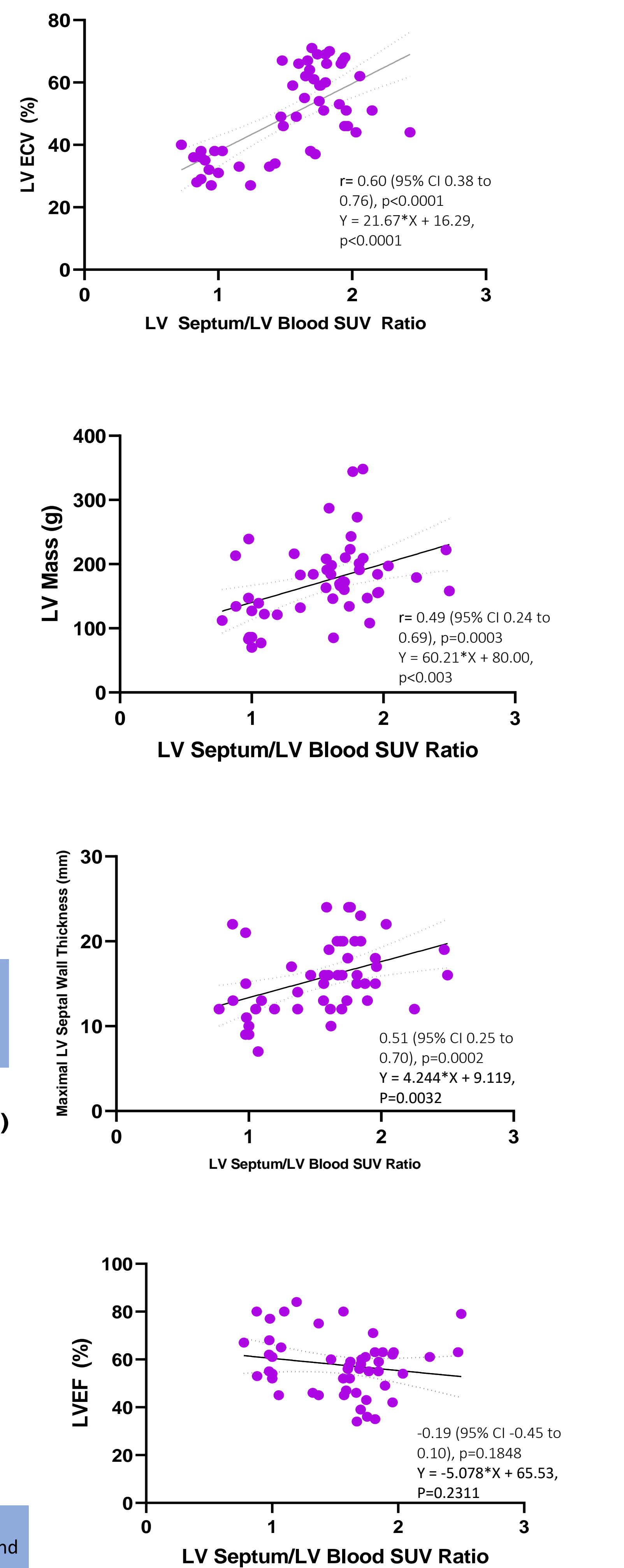
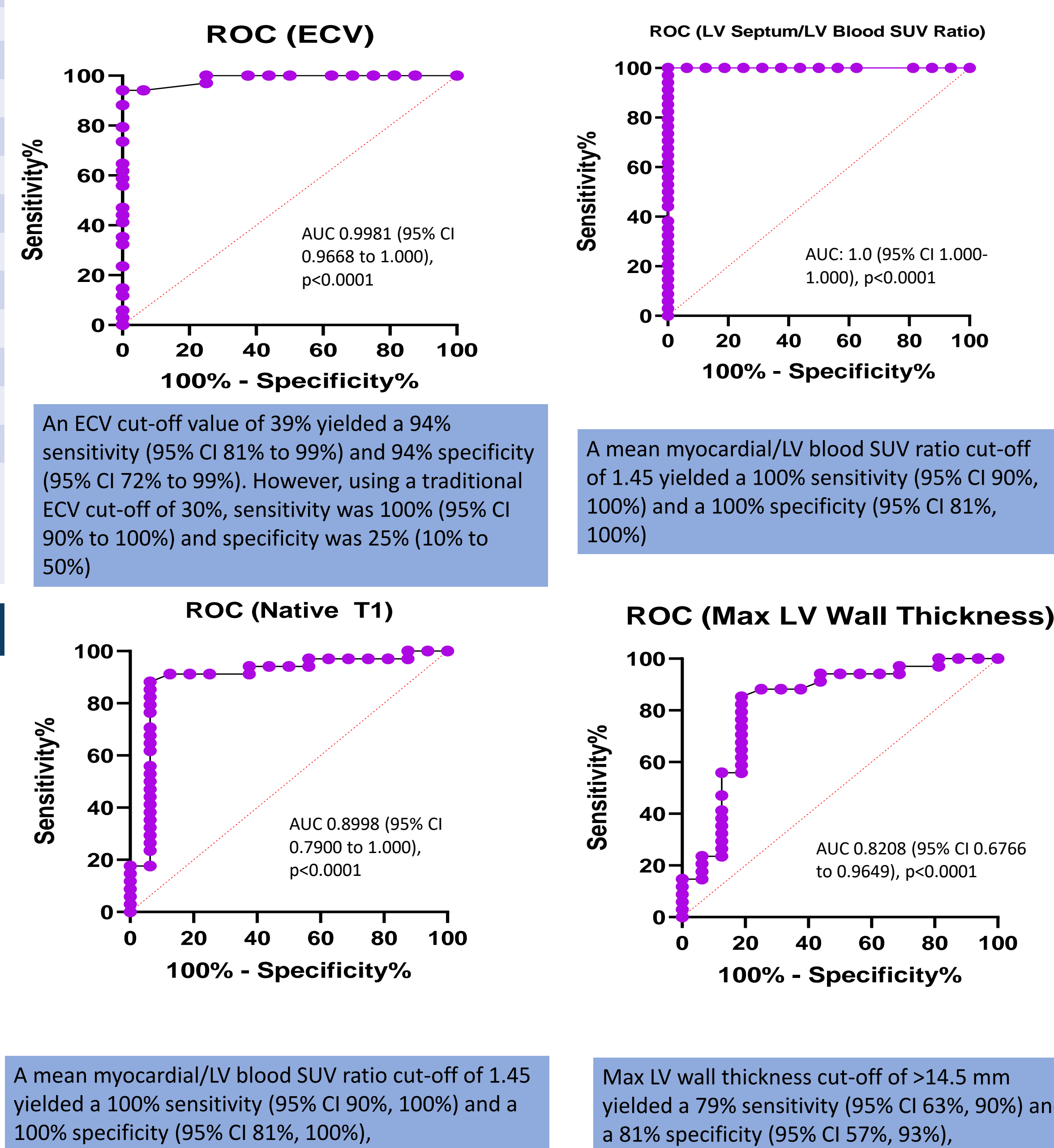
**Distribution of ECV and LV septum/LV blood SUV ratio among different groups**



**Correlation of <sup>124</sup>I-evuzamitide uptake and measures of cardiac structure and function on CMR**

CMR Variable	Correlation with myocardial <sup>124</sup> I-evuzamitide SUVr (Spearman r, 95% CI)	p-value
Basal septal LV wall thickness (mm)	0.51 (0.26 to 0.70)	0.0002
Basal inferolateral LV wall thickness (mm)	0.50 (0.25 to 0.69)	0.0002
LV mass (g)	0.49 (0.24 to 0.69)	0.0003
LV mass indexed to body surface area (g/m <sup>2</sup> )	0.41 (0.14 to 0.62)	0.0003
LV end-diastolic volume (ml)	0.43 (0.17 to 0.64)	0.0017
LV end-systolic volume (ml)	0.42 (0.15 to 0.63)	0.0025
LVEF (%)	-0.19 (-0.45 to 0.10)	0.1848
Stroke volume (ml)	0.25 (-0.04 to 0.50)	0.0846
T2 relaxation time (basal, ms)	0.34 (0.054 to 0.57)	0.0175
Native T1 relaxation time (basal, ms, 3T)	0.51 (0.27 to 0.70)	0.0001
ECV (%)	0.60 (0.38 to 0.76)	<0.0001

**ROC Curves for the Diagnosis of Cardiac Amyloidosis**



## CONCLUSIONS

- <sup>124</sup>I-evuzamitide cardiac PET/MRI provides comprehensive diagnostic evaluation of cardiac structure, function, and surrogates for amyloid load.
- In this high-risk group without healthy controls, an ECV cut-off of 39% yielded a higher diagnostic performance than a cut-off of 30%.
- While both ECV and <sup>124</sup>I-evuzamitide mean myocardial SUVr performed well for the diagnosis of cardiac amyloidosis, they had a correlation coefficient of 0.6, suggesting commonalities and differences in the composition of what they measure.
- Further studies are needed to elucidate the best surrogate measure for cardiac amyloid load, particularly for longitudinal monitoring of cardiac amyloid load in response to therapy.

## DISCLOSURES

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