

PREVALENCE AND CLINICAL CHARACTERISTICS OF TRANSTHYRETIN CARDIAC AMYLOIDOSIS AMONG HEART FAILURE WITH PRESERVED EJECTION FRACTION



Aims

Transthyretin cardiac amyloidosis (ATTR-CA) is an increasingly recognized cause of heart failure. In ATTR-CA, cardiomyopathy caused by amyloid deposition manifests as heart failure with restrictive physiology. Bone scintigraphy shows a sensitivity of about 92.2% and a specificity of 95.0% in diagnosing ATTR-CA. This study aimed to identify the prevalence and clinical characteristics of ATTR-CA using non-invasive ^{99m}Tc-DPD bone scintigraphy in heart failure with preserved ejection fraction (HFpEF) patients.

Methods

A prospective single-center study included patients aged > 65 years with a diagnosis of HFpEF (EF >50%) between November 2021 and December 2022. A total of 124 patients were included (median age 82.9 years, 78% male) was conducted. Clinical, analytical, and diagnostic imaging data were collected. Visual grading was evaluated with ^{99m}Tc-DPD bone scintigraphy, and the degree of myocardial uptake compared to bone uptake was visually analyzed by dividing it into grades 0 to 3 (Figure 1). ATTR-CA was diagnosed by positive scintigraphy (Visual grade 2 or 3) and exclusion of light-chain amyloidosis or positive biopsy typing.

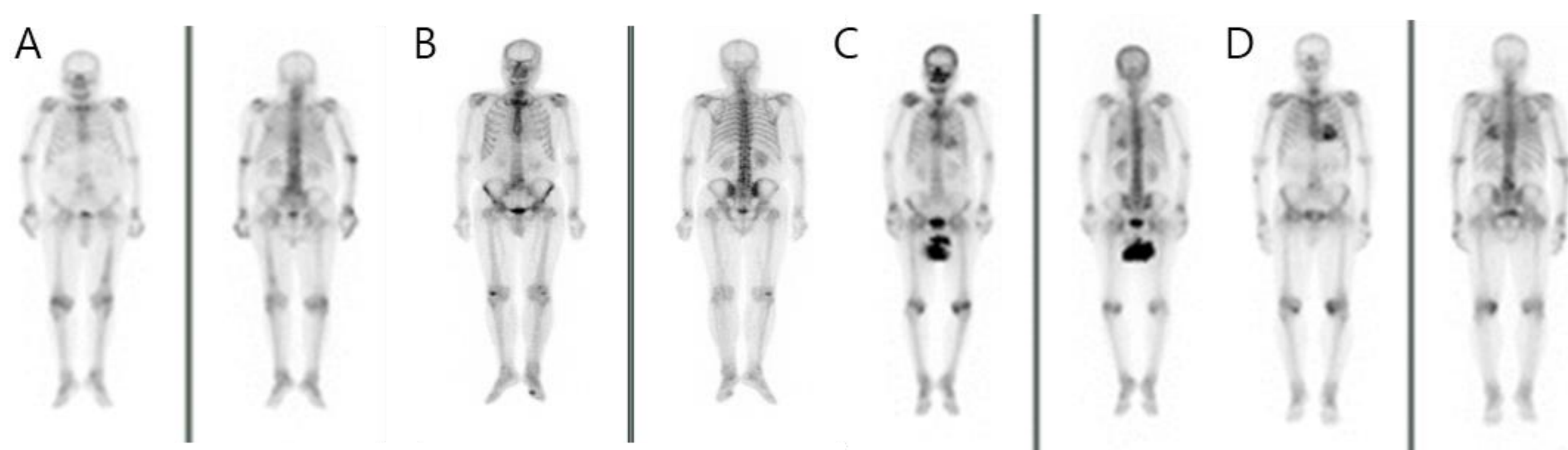


Figure 1. Examples of ^{99m}Tc-DPD scintigraphy images of grade 0-3 groups: (A) No cardiac uptake, (B) cardiac uptake less than bone, (C) Cardiac uptake equal to bone, (D) Cardiac uptake greater than bone

Results

ATTR-CA prevalence among HFpEF was 9.7% (12/124). ATTR-CA patients were older ($p = 0.0019$) and had higher values of septal wall thickness ($p = 0.001$), posterior wall thickness ($p < 0.001$), left ventricular mass index ($p = 0.021$), relative wall thickness ($p < 0.001$), and N-terminal pro-B-type natriuretic peptide (NT-proBNP, $p < 0.001$). On the other hand, there was no significant difference in Agent Orange exposure history, body mass index, presence of hypertension, diabetes, hyperlipidemia, atrial fibrillation, heart rate, left ventricular EF, stroke volume, left ventricular mass, ratio of peak velocity of early diastolic transmitral flow to peak velocity of early diastolic mitral annular motion, and estimated glomerular filtration rate values (Table 1). As a result of evaluating the level of myocardial uptake on ^{99m}Tc-DPD scintigraphy images using visual grade, most ATTR-CA groups showed uptake levels of grades 2 and 3 (grade 2; 6 patients, grade 3; 5 number of people). On the other hand, there were no cases of grade 2 or 3 increased intake in the non-ATTR-CA group, and all showed grade 0 (80.4%, 90/112) or 1 (19.6%, 22/112). Therefore, in qualitative analysis evaluated by visual grade, there was a significant difference between the ATTR-CA and non-ATTR-CA groups ($p < 0.001$).

Conclusion

This study identified a higher prevalence (9.7%) of ATTR-CA in HFpEF patients than in the general population. Additionally, these patients tended to have thicker ventricular walls, higher LV mass index, and higher levels of NT-proBNP. We should realize that cardiac amyloid profoundly alters the myocardium, and ATTR-CA may be one cause of the HFpEF.

Variables	Negative for ATTR-CA (n=112)	Positive for ATTR-CA (n=12)	P value
Age	79.16 ± 8.14	86.83 ± 6.01	0.0019
Sex (Female:Male)	23:89	4:8	0.3093
History of exposure to Agent of Orange (%)	55.4%	66.7%	0.4545
Body mass index (kg/m ²)	1.71 ± 0.20	1.62 ± 0.13	0.1249
Hypertension (%)	75.0%	75%	1.000
Diabetes (%)	22.3%	33/3%	0.3937
Dyslipidemia (%)	50%	66/7%	0.2732
Atrial fibrillation (%)	17.9%	25%	0.5468
Heart rate	76.28 ± 13.86	83.92 ± 22.98	0.094
LVEF (%)	57.86 ± 7.73	53.51 ± 13.36	0.0909
LV stroke volume (mL)	71.36 ± 17.23	61.21 ± 22.86	0.072
Septal wall thickness (mm)	12.21 ± 1.40	13.83 ± 2.92	0.001
Posterior wall thickness (mm)	10.18 ± 1.65	12.33 ± 3.26	< 0.001
Left ventricular mass (g)	213.25 ± 46.93	235.26 ± 69.77	0.160
LVMI (g/m ²)	125.17 ± 25.12	144.93 ± 46.56	0.021
Relative wall thickness	0.41 ± 0.08	0.58 ± 0.26	< 0.001
E/e'	69.86 ± 216.46	19.27 ± 5.51	0.512
eGFR	58.75 ± 20.79	48.40 ± 21.15	0.280
NT-proBNP (pg/mL)	1119.92 ± 1889.39	5604.41 ± 4564.52	< 0.001

Table 1. Clinical characteristics and echocardiographic parameters of patients with suspected transthyretin cardiac amyloidosis (ATTR-CA)

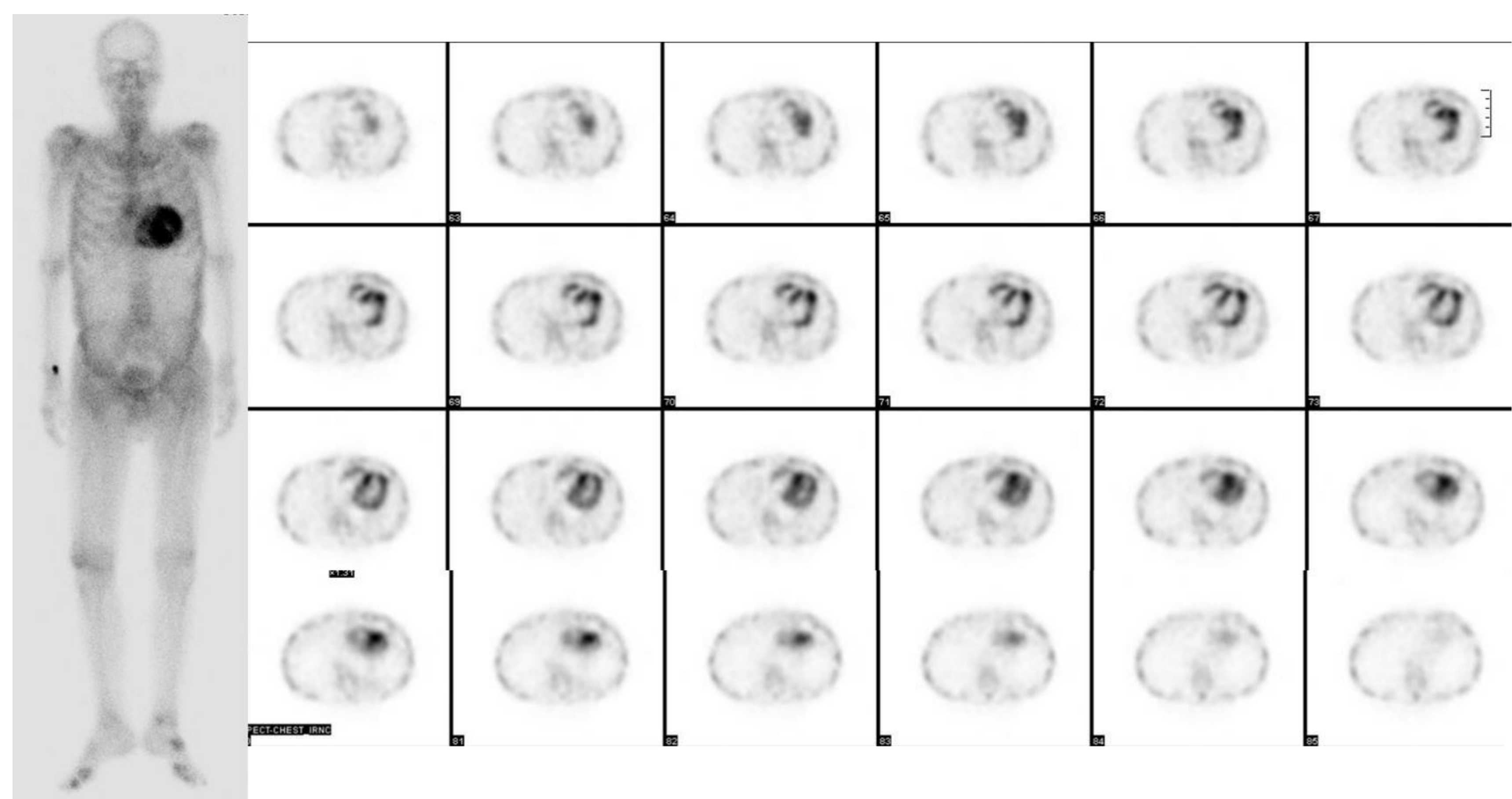


Figure 2. Representative images of bone scintigraphy and single photon emission computed tomography (SPECT) in a patient with transthyretin cardiac amyloidosis. A 77-year-old man with a new onset of symptoms of heart failure underwent ^{99m}Tc-DPD bone scintigraphy and SPECT imaging. The anterior image was reported as showing grade 3 myocardial uptake suggestive of ATTR-CA, and SPECT images demonstrated diffuse amyloid deposition along the left ventricular wall.

References

- McDonagh TA, et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J*. 2021 Sep 21;42(36):3599-3726
- Dorbala S, et al. ASNC/AHA/ASE/EANM/HFSA/ISA/SCMR/SNM Expert Consensus Recommendations for Multimodality Imaging in Cardiac Amyloidosis: Part 2 of 2- Diagnostic Criteria and Appropriate Utilization. *J Card Fail*. 2019 Nov;25(11):854-865
- Prasad M, et al. Evolving epidemiology of transthyretin amyloid cardiomyopathy due to increased recognition in women. *Int J Cardiol*. 2023 Mar 1;374:116-119
- Lyng CS, et al. Gude E, Hodt A, Knudsen EC. First Norwegian case of hereditary ATTR amyloidosis with a novel transthyretin variant. *Scand Cardiovasc J*. 2023 Dec;57(1):2174269
- Moore PT, et al. The Utility of ^{99m}Tc-DPD Scintigraphy in the Diagnosis of Cardiac Amyloidosis: An Australian Experience. *Heart Lung Circ*. 2017 Nov;26(11):1183-1190
- González-López E, et al. Wild-type transthyretin amyloidosis as a cause of heart failure with preserved ejection fraction. *Eur Heart J*. 2015 Oct 7;36(38):2585-94.
- Castañó A, et al. Unveiling transthyretin cardiac amyloidosis and its predictors among elderly patients with severe aortic stenosis undergoing transcatheter aortic valve replacement. *Eur Heart J*. 2017 Oct 7;38(38):2879-2887
- Bennani Smires Y, et al. Pilot study for left ventricular imaging phenotype of patients over 65 years old with heart failure and preserved ejection fraction: the high prevalence of amyloid cardiomyopathy. *Int J Cardiovasc Imaging*. 2016 Sep;32(9):1403-1413
- Jacobson DR, et al. Prevalence of the amyloidogenic transthyretin (TTR) V122I allele in 14 333 African-Americans. *Amyloid*. 2015;22(3):171-4