OBSERVATIONAL STUDY TO DETERMINE THE PREVALENCE OF TRANSTHYRETIN AMYLOIDOSIS IN AN UNDIFFERENTIATED HEART FAILURE WITH PRESERVED EJECTION FRACTION POPULATION

Introduction Heart failure with preserved ejection fraction (HFpEF) is a common but heterogeneous clinical syndrome. Transthyretin amyloidosis cardiomyopathy (ATTR-CM) can now be diagnosed non-invasively with high sensitivity incorporating Technitium-99m, 3,3-diphosphono-1,2-propanodicarboxylic acid (Tc-DPD) scintigraphy. ATTR-CM has been found as the underlying aetiology of heart failure in 13% in HFpEF syndrome with left ventricular hypertrophy (LVH). Timely diagnosis of ATTR-CM has become even more relevant given the recent availability of targeted treatments. However, the prevalence and spectrum of ATTR-CM has not previously been studied in all-comer HFpEF cohort.

Aims To determine the prevalence and spectrum of ATTR-CM in an undifferentiated multicentre HFpEF population using the non-invasive diagnostic pathway incorporating Tc-DPD scintigraphy.

Methods Consecutive patients ≥60 years attending the heart failure services with a diagnosis of HFpEF and New York Heart Association class II-V symptoms across 4 sites were prospectively enrolled. Severe valvular pathology or a prior history of symptomatic myeloma, AL amyloidosis or mononclonal gammopathy of unknown significance (MGUS) were excluded. Transthoracic 2D strain echocardiography, 12 lead electrocardiogram (ECG), biomarker analysis and Tc-DPD scintigraphy were performed. Tc-DPD findings were graded visually according to the Perugini classification (grades 0–3). Those patients with Perugini grade 2–3 on Tc-DPD (moderate-severe uptake; highly suggestive of ATTR-CM) underwent additional laboratory and haematological assessment and transthyretin (TTR) gene sequencing.

Results To date, 45 patients (49% female, mean age 77.6 ± 7.9 years) have been prospectively enrolled. A history of atrial fibrillation and hypertension were present in 60% and 80% respectively. In keeping with ATTR-CM, no participant had a low voltage pattern on ECG. Three patients (6.7%) had Perugini grade 3 uptake on Tc-DPD and 6 patients (13.3%) had grade 1 uptake (mild uptake, inferior to bone; diagnostic significance undetermined). No patients had grade 2 uptake. All those with grade 3 uptake had AL amyloid excluded on further haematological testing and no mutation was detected in the TTR gene confirming wild type ATTR-CM. Significant differences across Tc-DPD uptake grades were seen according to increasing age and LV wall thickness (figure 1).

Conclusion ATTR-CM, characterised by high grade uptake (Perugini 3) on Tc-DPD scintigraphy and negative haematological markers, was present in 6.7% of this undifferentiated HFpEF cohort and was associated with older age, and increased left ventricular wall thickness. Low grade uptake (Perugini grade 1) was present in a further 13.3%. While the diagnostic significance of this phenotype is undetermined, this may represent early ATTR-CM, suggesting that Tc-DPD scintigraphy may be able to identify a spectrum of disease according to uptake that correlates with wall thickness. Further follow up in this study will explore this potential.