Abstract 2 Figure 2 Bar chart comparing LVA burden in both SR and AF

Figure 2: Bar chart representing the absolute values of low voltage areas (mm²) mapped in each anatomical segment indicating a remarkable difference in Posterior LA wall compared to other anatomical segments. The left graph demonstrates Dense Scar and the right graph Diseased LA Tissue as per predefined voltage criteria. *Denotes significance. LVA=Low voltage area; LA= Left Atrium; SR=Sinus Rhythm; AF=Atrial Fibrillation.

was observed on the posterior wall, once again with the highest correlation of all segments ($R=0.314$, $p=0.015$).

Conclusions The automated VHA tool demonstrated the posterior wall as the only anatomical segment to be significantly higher in LVAs consistent with dense scar burden (i.e. ≤ 0.2 mV), when mapped in AF. Mapping rhythm has a substantial impact on surrogate readings of both 'Diseased Tissue' 0.21-0.5mV and 'Dense Scar' ≤ 0.2 mV on the posterior wall. These findings mandate careful interrogation of posterior wall voltages and may partially explain the debated outcome for posterior wall ablation. It is best interrogated in both rhythms to confirm the presence of arrhythmogenic substrates over artifactual rhythm effect.

3

ATRIAL UPTAKE ON TECHNETIUM PYROPHOSPHATE SCINTIGRAPHY: CLINICAL IMPLICATIONS OF THIS NEW PHENOMENON

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Transthyretin cardiac amyloidosis (ATTR-CA) is an increasingly recognized disease in which atrial fibrillation (AF) has been shown to be highly prevalent. 99m-Technetium pyrophosphate (99mTc-PyP) scanning is used to non-invasively make the diagnosis of ATTR-CA. Assessment of atrial wall uptake (AU) on 99mTc-PyP is currently not utilized in the clinical setting. We hypothesize that AU by 99mTc-PyP is associated with higher rates of AF, and AU corresponds to atrial wall infiltration by TTR fibril deposition. All patients that underwent consecutive 99mTc-PyP at our institution for suspected ATTR-CA from January 2012 to September 2019 were included. Presence or absence of AU was assessed visually using Corridor 4DM software (v2015) using fused/composition computed tomography-single photon emission computed tomography (SPECT) imaging in all cases (figure 1). ATTR-CA diagnosis was defined using institutional guidelines. Patient characteristics were obtained through electronic medical records. Retrospective review of the patient population identified those who had left atrial tissue available from heart transplantation, left atrial resection or autopsy to allow for direct tissue-imaging correlation (figure 1). A total cohort of 580 patients were identified (table 1). 164 (28%) patients had scans consistent with ATTR-CA. 296 (51%) had a diagnosis of AF. 117 (20%) patients had AU. Table 2 shows the relative interaction of AU, ATTR-

Abstract 3 Figure 1 99m-Technetium pyrophosphate scan (99mTc-PyP) illustrating atrial uptake (AU) in patients with/without a clinical diagnosis of transthyretin cardiac amyloidosis (ATTR-CA) with histopathological correlation.

Caption:

A: Left atrial appendage resection specimen in a patient AU+, ATTR-CA- with Congo red stain (40x) showing apple-green and orange birefringence (arrow), confirming the material is amyloid.

B: 99mTc-PyP scan showing AU+ in a patient ATTR-CA-.

C: 99mTc-PyP scan showing AU- in a patient ATTR-CA-.

D: Left atrial appendage resection specimen in a patient AU+, ATTR-CA+ with immunohistochemistry positive for TTR (20x). Brown staining visible in the amyloid nodules (arrow).

E: 99mTc-PyP scan showing AU+ in a patient ATTR-CA+.

F: 99mTc-PyP scan showing AU- in a patient ATTR-CA+.

Abstract 3 Table 1 Baseline patient characteristics at the time of 99mTc-PvP scan

Caption: Data is provided for the total cohort; for those with and without a clinical diagnosis of transthyretin cardiac amyloidosis; for those with and without a clinical diagnosis of atrial fibrillation (AF): and for those with and without atrial uptake on 99mTc-PvP scan respectively.

Characteristic	Total Cohort N= 580	Amyloid		p value	AF		p value	Atrial Uptake		p value
		+	-		+	-		+	-	
		n=164	n=416		n=296	n=284		n=117	n=463	
Median age, years (IQR)	74 (17)	79 (11)	72 (18)	p<0.001	76 (14)	70 (19)	p<0.001	77 (12)	72 (18)	p<0.001
Gender										
Male	398 (69%)	135 (23%)	263 (45%)	p<0.001	203 (35%)	195 (34%)	p=1.00	81 (14%)	317 (55%)	p=0.84
Female	182 (31%)	29 (5%)	153 (26%)	p<0.001	93 (16%)	89 (15%)	p=1.00	36 (6%)	146 (25%)	p=0.85
Race										
White	377 (65%)	109 (19%)	268 (46%)	p=0.50	220 (38%)	157 (27%)	p<0.001	84 (14%)	293 (50%)	p=0.11
Black	188 (32%)	54 (9%)	134 (23%)	p=1.00	72 (12%)	116 (20%)	p<0.001	33 (6%)	155 (27%)	p=0.41
Other	15 (3%)	1 (<1%)	14 (2%)	p=0.08	4 (<1%)	11 (2%)	p=0.020	0 (0%)	15 (3%)	p=0.06
Body mass index (kg/m²)										
>30	215 (37%)	46 (8%)	169 (29%)	p=0.004	103 (18%)	112 (19%)	p=0.32	35 (6%)	180 (31%)	p=0.07
25-30	220 (38%)	73 (13%)	147 (25%)	p=0.015	125 (22%)	95 (16%)	p=0.025	57 (10%)	163 (28%)	p=0.005
<25	145 (25%)	45 (8%)	100 (17%)	p=0.32	68 (12%)	77 (13%)	p=0.27	25 (4%)	120 (21%)	p=0.26
CV risk factors										
Hypertension	481 (83%)	124 (21%)	357 (62%)	p=0.004	242 (42%)	239 (41%)	p=0.52	90 (16%)	391 (67%)	p=0.07
Hyperlipidemia	409 (71%)	120 (21%)	289 (50%)	p=0.34	221 (38%)	188 (32%)	p=0.018	90 (16%)	319 (55%)	p=0.09
Current/ previous smoker	328 (57%)	88 (15%)	240 (41%)	p=0.38	169 (29%)	159 (27%)	p=0.81	64 (11%)	264 (45%)	p=0.70
Diabetes mellitus	230 (40%)	40 (7%)	190 (33%)	p<0.001	116 (20%)	114 (20%)	p=0.81	41 (7%)	189 (33%)	p=0.23
Labs median, (IQR)										
Creatinine	1.33 (0.81)	1.34 (0.62)	1.31 (0.92)	p=0.84	1.40 (0.95)	1.27 (0.73)	p=0.07	1.42 (0.74)	1.30 (0.81)	p=0.84
eGFR	40 (21)	44 (20)	38 (24)	p=0.15	40 (21)	40 (23)	p=1.00	42 (17)	40 (23)	p=0.89
Hemoglobin	12.3 (3.3)	12.8 (2.7)	12.2 (3.6)	p<0.001	12.1 (3.2)	12.6 (3.4)	p=0.07	12.3 (2.8)	12.4 (3.5)	p=0.78
NT-pro BNP	2494 (5700)	3412 (5363)	2040 (5936)	p<0.001	3141 (5502)	1854 (5986)	p=0.008	2799 (4971)	2443 (6040)	p=0.15
Troponin T	0.059 (0.11)	0.055 (0.09)	0.065 (0.16)	p=0.004	0.058 (0.12)	0.059 (0.11)	p=0.92	0.053 (0.09)	0.062 (0.13)	p=0.49
Gilmore stage										
Gilmore stage1	222 (38%)	61 (11%)	161 (28%)	p=1.00	101 (17%)	121 (21%)	p=0.026	48 (8%)	174 (30%)	p=0.55
Gilmore stage2	178 (31%)	49 (8%)	129 (22%)	p=1.00	90 (16%)	88 (15%)	p=0.80	34 (6%)	144 (25%)	p=0.67
Gilmore stage3	138 (24%)	44 (8%)	94 (16%)	p=0.13	85 (15%)	53 (9%)	p=0.005	32 (6%)	106 (18%)	p=0.36
Gilmore stage unknown	42 (7%)	5 (<1%)	37 (6%)		21 (4%)	22 (4%)		4 (<1%)	38 (7%)	
Echo										
LVEF, % Median (IQR)	54 (18)	51 (17)	55 (20)	p=0.025	52 (18)	56 (20)	p=0.012	50 (20)	55 (18)	p=0.009
Severe mitral valve disease	8 (1%)	4 (<1%)	7 (<1%)	p=0.47	4 (<1%)	3 (<1%)	p=1.00	2 (2%)	5 (1%)	p=0.37

Abstract 3 Table 2 Relative interaction of atrial uptake, transthyretin cardiac amyloidosis (ATTR-CA) and atrial fibrillation (AF).
Caption: Total includes total number of patients between the 2 groups

Total Cohort N=580	Atrial Uptake(+)				Atrial Uptake(-)			
	Total	%	AF(+)	%	Total	%	AF(+)	%
ATTR-CA(-)	58	10%	51	9%	358	62%	146	25%
ATTR-CA(+)	59	10%	56	10%	105	18%	43	7%

Abstract 3 Figure 2 Freedom from atrial fibrillation in patients with and without atrial uptake

CA and AF. Of 117 patients with AU, 107 (91%) had AF. In contrast, of 463 patients without AU 189 (41%) had AF. AU was associated with a significantly higher incidence of AF in those with and without ATTR-CA ($p<0.001$). On Cox proportional hazards analyses, freedom from AF at 1-year in patients with ATTR-CA was significantly lower in patients with AU (HR: 2.27; 95% CI: 1.37-3.78; $p<0.0001$) (figure 2). Similarly, freedom from AF at 1-year in patients without ATTR-CA was significantly lower in patients with AU (HR: 2.21; 95% CI: 1.46-3.34; $p<0.0001$). On Kaplan-Meier survival analysis, there were no significant differences in mortality rates in patients with AF and ATTR-CA; with AU vs. without AU (all-cause mortality, $p=0.79$; 1-year mortality, $p=0.76$). There were no significant differences in mortality rates in patients with AF and without ATTR-CA; with AU vs. without AU (all-cause mortality, $p=0.20$; 1-year mortality, $p=0.57$). For the first time, we described that the presence of AU was independent of ATTR-CA diagnosis and was associated with higher rates of AF. AU was not associated with increased mortality in those with AF. This leads to the question of the role of AU in AF diagnosis/management and the interaction of AU with ATTR-CA diagnosis.

4 PREDICTIVE GENETIC TESTING IN INHERITED CARDIAC CONDITIONS: FINDINGS FROM A LARGE IRISH COHORT

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Introduction Inherited cardiac conditions comprising cardiomyopathies (hypertrophic, dilated, arrhythmogenic) and cardiac ion channelopathies (long QT/Brugada syndromes, CPVT) predispose to sudden cardiac death. Predictive genetic testing of at-risk family members informs patient management and is cost-effective as those who test negative can be discharged from lifelong cardiac follow-up. Aim: Through predictive testing uptake, investigate the demographics and genetic contribution of inherited cardiac conditions in the Republic of Ireland. **Methods** Predictive testing data from 2003 to 2020 was collated through interrogation of departmental databases and molecular genetic reports at a national genetics centre and two tertiary cardiac referral clinics.

Results Collectively, 1,535 predictive tests for pathogenic/likely pathogenic variants were undertaken in 1,508 individuals from 241 families, including 27 individuals tested for two familial variants. The median age at testing was 36 years (range 0.07–90 years). From 1,152 adults, more females (58%) presented for testing than males (42%). Amongst 365 children, marginally more boys (53%) were tested than girls (47%). On average, six individuals per family were tested (range 1 – 84). Seven hundred and nineteen individuals (48%) were found to be genotype-positive for their familial variant(s). Overall, predictive testing was performed for 26 genes. Testing for long QT syndrome (LQTS) and hypertrophic cardiomyopathy (HCM) genes represented 48% and 29% of the cohort, respectively. Other cardiomyopathies and arrhythmia syndromes accounted for 10% and 8% respectively, with 5% tested for syndromic disease genes. The most frequently tested gene was KCNQ1 (LQTS; 24% of tests), followed by MYBPC3 (HCM/DCM; 20%), KCNH2 (LQTS; 17%), MYH7 (HCM/DCM; 8%) and SCN5A (LQT/Brugada syndromes; 8%). There was an absence of testing for several sarcomeric