FLAT-ATTR: A fully automated machine learning algorithm to track disease progression in ATTR-CM

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Disclosures

- I have nothing to declare

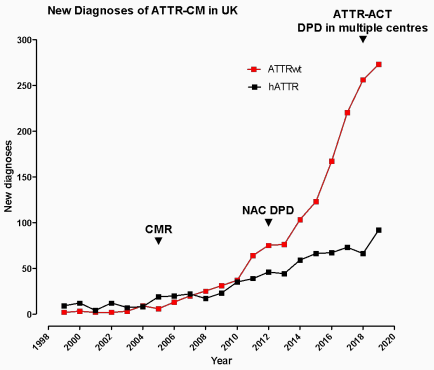
Background

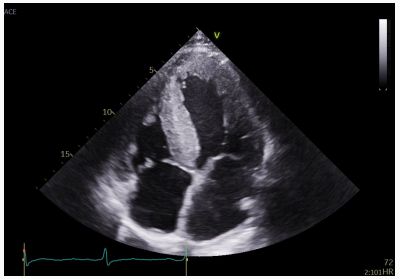
- Transthyretin cardiac amyloidosis (ATTR-CM) is a progressive and fatal cardiomyopathy with a steadily increasing diagnosis over the past two decades[1] and with a highly variable clinical course among individuals

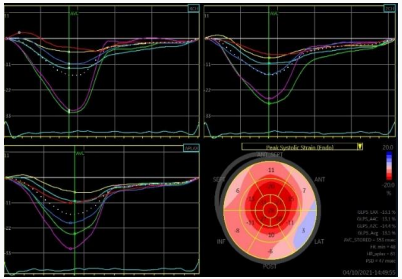
- Echocardiography has the potential to be a useful tool for tracking disease progression. In a large echocardiographic study, changes in SV and minor changes in MR and TR were associated with mortality[2]

- However, variability in manual measurements by clinicians, currently limits the suitability of echocardiography for longitudinal monitoring and therefore there are no established echocardiographic parameters to assess disease progression in cardiac amyloidosis practice

- Artificial intelligence (AI)-based deep learning algorithms have demonstrated significant promise in cardiovascular imaging for the increased reproducibility and precision over manual measurements







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[1]Lane T *et al*, Circulation 2019 [2]Chacko L *et al*, 2022

Objectives

- This study aimed to evaluate the association between changes in fully automated AI-measured echocardiographic parameters and prognosis in a large cohort of ATTR-CM patients

Methods

- Echocardiographic DICOM images were processed using a fully automated machine learning algorithm, without human interaction (**Us2.ai – FDA approved)**

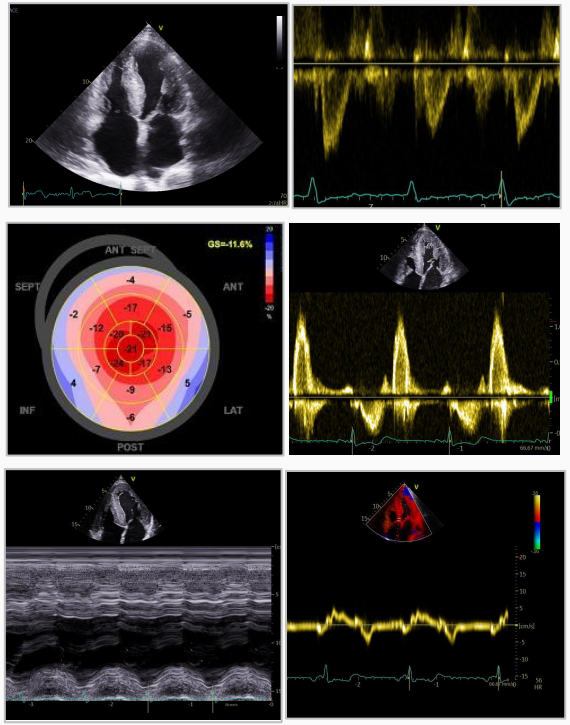
- Twelve-month landmark survival analysis to assess the association between changes in echocardiographic parameters and mortality in patients with ATTR-CM followed at the National Amyloidosis Centre (NAC) 2007-2021.

Results

- 752 patients were recruited in the study, 661 patients (87.9%) were male, 495 (65.8%) with ATTRwt-CM and 257 (34.2%) with ATTRv-CM (145 with V122I; 67 with T60A; 45 non-V122I, non-T60A)

- During a median (IQR) follow-up of 40 months (25.5-60), 334 (44.4%) died

Univariable Cox regression analysis of risk of mortality using change in echocardiographic parameters



Parameter	Univariable from baseline		Baseline to 12- months change	Univariable for 12-months change	
	HR (95% CI)	P value		HR (95% CI)	P value
LVOT-VTI cm	0.95 (0.93-0.97)	**<0.001**	Absolute change	0.97 (0.94-0.99)	**0.004**
-	-	-	Percentage change	0.99 (0.98-0.99)	**0.005**
-	-	-	>5% reduction	1.44 (1.17-1.76)	**0.001**
LVETms	0.99 (0.99-0.99)	**<0.001**	Absolute change	1.00 (0.99-1.002)	0.77
LA ESV ml(biplane)	1.01 (1.007-1.021)	**<0.001**	Absolute change	0.99 (0.98-1.006)	0.24
LAA 4-ch cm_2	1.06 (1.03-1.08)	**<0.001**	Absolute change	0.99 (0.98-1.005)	0.38
RAA 4-ch cm_2	1.03 (0.99-1.06)	0.095	Absolute change	1.001 (0.96-1.045)	0.96
TAPSE mm	0.99 (0.97-1.01)	0.25	Absolute change	0.98 (0.96-0.99)	**0.012**
RV S' m/s	0.91 (0.88-0.95)	**<0.001**	Absolute change	0.93 (0.89-0.97)	**0.001**
IVSd mm	1.08 (1.04-1.12)	**<0.001**	Absolute change	0.98 (0.93-1.04)	0.55
PWd mm	1.07 (1.04-1.10)	**<0.001**	Absolute change	1.02 (0.99-1.05)	0.25
LVM g/m_2	1.003 (1.001-1.005)	**<0.001**	Absolute change	1.00 (0.99-1.001)	0.26
RWT	3.33 (1.98-5.63)	**<0.001**	Absolute change	0.86 (0.48-1.53)	0.61
LVEF%	0.98 (0.96-0.99)	**<0.001**	Absolute change	1.00 (0.99-1.002)	0.48
lateral S' m/s	0.80 (0.74-0.86)	**<0.001**	Absolute change	1.00 (0.95-1.06)	0.99
LV GLS %	1..10 (1.06-1.15)	**<0.001**	Absolute change	1.04 (0.96-1.12)	0.35
LV LS 4-ch%	1.06 (1.04-1.09)	**<0.001**	Absolute change	0.99 (0.97-1.02)	0.47
LV SV ml(biplane)	0.98 (0.97-0.99)	**<0.001**	Absolute change	0.99 (0.98-1.01)	0.76
E/A	1.70 (1.27-2.67)	**<0.001**	Absolute change	1.05 (0.69-1.62)	0.80
average E/e'	1.05 (1.03-1.07)	**<0.001**	Absolute change	0.99 (0.96-1.02)	0.60
lateral E/e'	0.86 (0.81-0.91)	**<0.001**	Absolute change	0.98 (0.97-0.99)	**0.008**

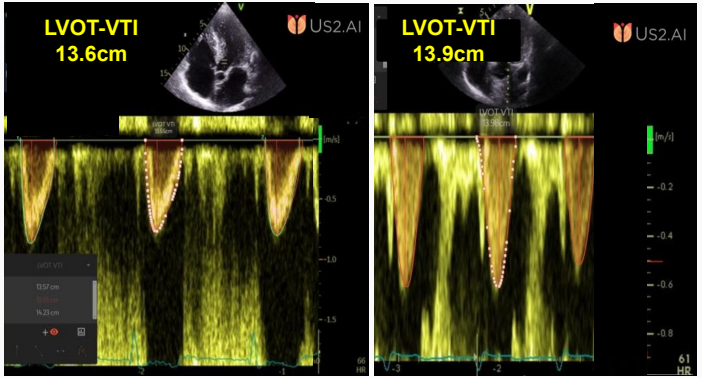
Multivariable analysis of risk of mortality using change in echocardiographic parameters

Parameter	HR (95% CI)	P value
Age	1.04 (1.02-1.06)	**<0.001**
Hereditary TTR genotype	0.46 (0.33-0.63)	**<0.001**
log NTproBNP baseline	3.24 (2.02-5.21)	**<0.001**
eGFR baseline	0.99 (0.98-1.00)	0.19
LVOT-VTI decrease ≥5% at 12-months	1.48 (1.09-2.02)	**0.012**
TAPSE absolute change at 12-months	1.00 (0.97-1.02)	0.98
Lateral E/e' absolute change at 12-months	1.00 (0.98-1.02)	0.56

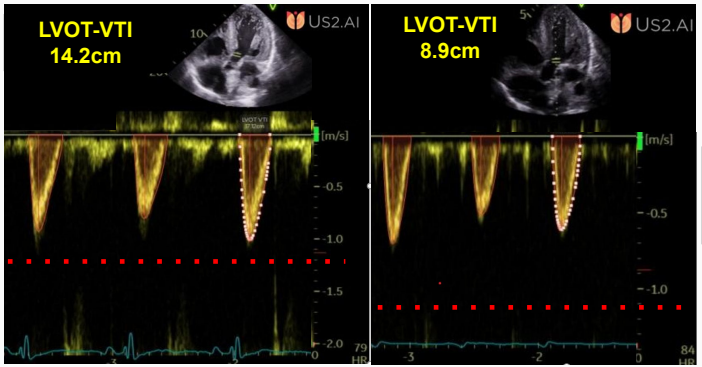
12-Month LVOT-VTI changes: a clinically significant marker of SV changes

baseline

1-year FU



Stable LVOT-VTI (<5% decrease, n=380)

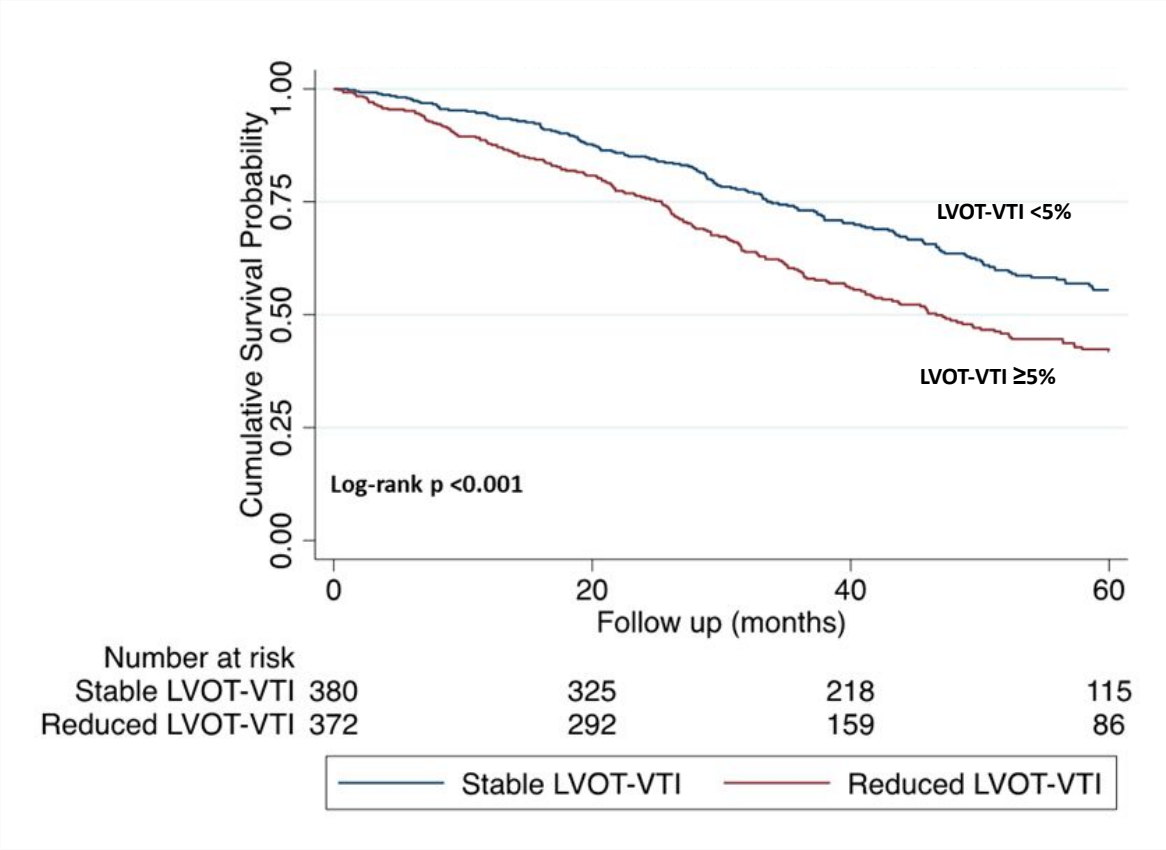


Reduced LVOT-VTI (≥5% decrease n=372)

- Nearly half of the patients experienced significant SV decline at 1-year follow-up

	All (n=752)	Stable LVOT-VTI (<5% decrease, n=380)	Reduced LVOT-VTI (≥5% decrease, n=372)	P value
Age, y	74.1±8.8	73.4±9.1	74.8±8.3	**0.044**
Male	661 (87.9%)	329 (86.6%)	332 (89.2%)	0.26
Genotype				0.74
Wild-type	495 (65.8%)	248 (65.3%)	247 (66.4%)	
Hereditary	257 (34.2%)	132 (34.7%)	125 (33.6%)	
AF/AFlutter	373 (49.6%)	192 (50.5%)	181 (48.7%)	0.60
IHD	139 (18.5%)	65 (17.1%)	74 (19.9%)	0.32
Diabetes mellitus	119 (15.8%)	58 (15.3%)	61 (16.4%)	0.67
HTN	222 (29.5%)	101 (26.6%)	121 (32.5%)	0.07
NYHA				0.44
I	127 (17.6%)	71 (19.4%)	56 (15.7%)	
II	468 (64.8%)	234(63.9%)	234(65.7%)	
III	118 (16.3%)	58 (15.8%)	60 (16.9%)	
IV	9 (1.2%)	3 (0.8%)	6 (1.7%)	
NAC ATTR stage				**0.020**
I	424 (56.8%)	226 (60.1%)	198 (53.5%)	
II	242 (32.4%)	121 (32.2%)	121 (32.7%)	
III	80 (10.7%)	29 (7.7%)	51 (13.8%)	
MWT	15.5±2.9	15.5±3.0	15.5±2.7	0.73
Lateral E/e'	14.3±5.5	13.8±5.4	14.8±5.6	**0.014**
RWT	0.68±0.20	0.67±0.21	0.70±0.19	0.09
LVEF	49.1±12.3	48.7±12.3	49.5±12.4	0.33
LV-LS	-14.6±5.3	-14.5±5.3	-14.7±5.3	0.54
LVOT-VTI	16.8±5.3	15.5±5.0	18.1±5.2	**<0.001**
TAPSE	16.7±5.2	16.3±5.1	17.0±5.3	0.10

Survival in ATTR-CM patients according to 12-months LVOT-VTI change



Conclusion

- Reduction in stroke volume assessed by LVOT-VTI is frequent, occurring in almost half of the patients at 1-year, and is associated with increased risk of mortality

- A fully automated machine learning algorithm for LVOT-VTI can be used to track disease progression in patients with ATTR-CM

- This has the potential to become the first simple and widely applicable tool to track disease progression and treatment response using echocardiography in patients with ATTR-CM

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