Effects of Tafamidis on Quantification of Myocardial Amyloid Deposition in Patients with Transthyretin Amyloid Cardiomyopathy

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BACKGROUND. Tafamidis is a kinetic stabilizer of transthyretin (TTR) that prevents tetramer dissociation and amyloidogenesis in patients with TTR amyloid cardiomyopathy (ATTR-CM), resulting in delayed disease progression. However, the endomyocardial effects of tafamidis are still unknown.

OBJECTIVES. We aimed to investigate the effects of tafamidis on the quantification of myocardial amyloid deposition measured by myocardial standardized uptake value (SUV) peak and SUV retention index and to observe their association with clinical parameters.

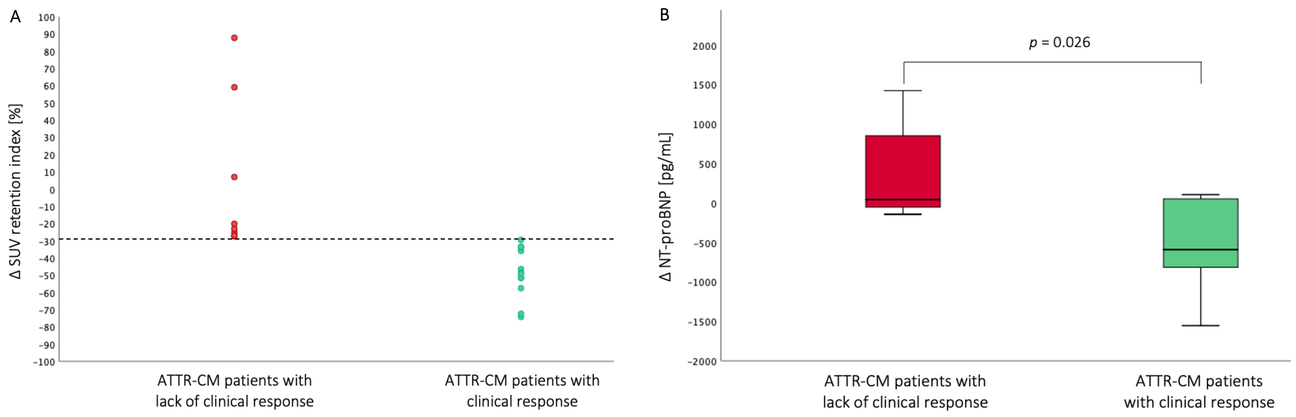
METHODS. Twenty ATTR-CM patients who received a daily dose of tafamidis 61 mg over a six-month period underwent serial quantitative single photon emission computed tomography (SPECT/CT) of the thorax.

Table 1. Baseline and follow-up characteristics of ATTR-CM patients after six months of tafamidis treatment.

	Overall (n=20)			Clinical response (n=12)			Lack of clinical response (n=8)		
Characteristic	**Baseline**	**Follow-up**	**p-Value**	**Baseline**	**Follow-up**	**p-Value**	**Baseline**	**Follow-up**	**p-Value**
Clinical parameters									
Age – years (SD)	79.7 (5.5)			80.6 (6.5)			78.3 (3.5)		
Male – n (%)	16 (80.0)			9 (75.0)			7 (87.5)		
NYHA functional class III – n (%)	14 (70.0)	8 (40.0)	**0.009**	10 (83.3)	5 (41.7)	**0.047**	4 (50.0)	3 (37.5)	0.082
6-min walk distance – m (SD)	379.2 (82.3)	385.6 (107.2)	0.678	349.5 (79.2)	356.7 (94.4)	0.736	428.7 (65.9)	433.7 (118.2)	0.836
Laboratory parameters									
Hemoglobin – g/dL (SD)	13.9 (1.6)	13.2 (1.8)	0.067	13.2 (1.7)	13.3 (1.8)	0.957	14.9 (0.9)	13.2 (1.8)	**0.025**
Creatinine – mg/dL (SD)	1.43 (1.00)	1.42 (0.96)	0.951	1.60 (1.26)	1.52 (1.22)	0.037	1.17 (0.31)	1.27 (0.35)	0.188
Troponin T – ng/L (SD)	56.7 (24.0)	61.3 (30.5)	0.091	57.8 (24.5)	60.6 (31.6)	0.452	54.9 (24.8)	62.4 (30.9)	0.094
NT-proBNP – pg/mL (IQR)	2341.0 (1395-3164)	1904.0 (1353-2865)	0.398	2765.0 (1510-3164)	1904.0 (1504-2865)	**0.041**	1825.0 (1364-4573)	1944.0 (1261-6898)	0.208
Myocardial SUV parameters									
SUV peak (SD)	15.50 (4.20)	11.61 (2.96)	**<0.001**	15.77 (3.80)	11.95 (3.37)	**<0.001**	15.09 (4.98)	11.11 (2.33)	**0.012**
SUV retention index (SD)	5.64 (2.60)	3.58 (1.54)	**0.001**	6.37 (2.68)	3.13 (1.27)	**<0.001**	4.56 (2.20)	4.26 (1.75)	0.654
Echocardiographic parameters									
LA length – mm (SD)	58.6 (9.2)	57.1 (6.2)	0.471	58.7 (12.0)	56.3 (7.0)	0.457	58.4 (4.6)	58.1 (5.2)	0.916
RA length – mm (SD)	58.3 (10.9)	56.3 (7.0)	0.294	55.5 (13.1)	54.1 (7.4)	0.668	61.9 (6.4)	59.1 (5.8)	0.120
Interventricular septum – mm (SD)	19.9 (6.0)	21.5 (5.6)	0.091	16.9 (3.3)	18.7 (3.7)	0.283	23.3 (6.7)	24.6 (6.0)	0.147
LV end-diastolic diameter – mm (SD)	42.9 (7.5)	41.2 (8.1)	0.379	44.1 (6.7)	42.6 (8.1)	0.576	41.5 (8.5)	39.6 (8.3)	0.531
RV end-diastolic diameter – mm (SD)	34.9 (5.5)	35.1 (4.2)	0.865	37.3 (5.2)	35.8 (5.3)	0.174	32.1 (4.5)	34.3 (2.8)	0.231
LV ejection fraction – % (SD)	50.6 (9.1)	50.4 (12.3)	0.929	48.5 (10.3)	52.7 (15.3)	0.287	53.2 (7.0)	47.5 (7.2)	**0.012**
LV strain – % (SD)	-12.9 (3.3)	-12.2 (4.4)	0.449	-12.0 (3.7)	-13.5 (4.2)	**0.049**	-13.9 (2.6)	-10.5 (4.3)	**0.035**
TAPSE – mm (SD)	17.5 (4.5)	14.9 (4.4)	**0.025**	16.6 (4.6)	16.0 (4.5)	0.168	19.2 (4.3)	12.6 (3.4)	**0.037**
CMR parameters	**n=11**			**n=6**			**n=5**		
LV ejection fraction – % (SD)	44.0 (10.4)	42.5 (11.4)	0.579	41.9 (11.2)	45.7 (8.1)	0.250	46.5 (10.1)	38.7 (14.5)	0.053
RV ejection fraction – % (SD)	40.5 (11.3)	38.4 (12.6)	0.626	36.2 (6.8)	40.1 (9.1)	0.159	45.7 (14.1)	36.4 (16.8)	0.296
MOLLI-ECV – % (SD)	47.4 (10.2)	52.4 (15.0)	0.101	47.3 (12.8)	53.4 (20.4)	0.181	47.5 (7.4)	51.2 (6.4)	0.437
T1 relaxation time – ms (SD)	1127.8 (48.8)	1106.4 (47.7)	0.323	1105.2 (37.4)	1122.1 (46.0)	0.456	1155.0 (50.1)	1087.6 (47.2)	0.064

NHYA indicates New York Heart association; NT-proBNP, N-terminal prohormone of brain natriuretic peptide; SUV, Standardized uptake value; LA, Left atrium; RA, Right atrium; LV Left ventricle; RV, Right ventricle; TAPSE, Tricuspid annular plane systolic excursion; CMR, Cardiac magnetic resonance imaging; MOLLI-ECV, Modified look–locker inversion recovery sequence derived extracellular volume. Values are given as mean ± standard deviation (SD), or median and interquartile range (IQR), or total numbers (n) and percent (%). Bold indicates p <0.05.

Figure 1. A) Classification based on clinical response: a threshold of -30% baseline in standardized uptake value (SUV) retention index distinguishes between ATTR-CM patients who respond clinically and those who do not respond. B) Change in serum NT-proBNP level from baseline for each cohort.



RESULTS. Main results are presented in Table 1. In brief, we observed a significant reduction in myocardial SUV peak (mean, baseline (BL): 15.50 vs. follow-up (FU): 11.61, p<0.001) and SUV retention index (mean, BL: 5.64 vs. FU: 3.58, p=0.001) after treatment with tafamidis (Figure 1A). In addition, a higher percentage decrease in the SUV retention index is more likely to be associated with clinical benefit, with a threshold of -30% distinguishing between patients who respond clinically (n=12) and those who do not (n=8, Figure 1B). Clinical response was reflected in improvements in exertional dyspnea (NYHA class III, BL: 83.3% vs. FU: 41.7%, p=0.047), functional capacity as measured by 6-minute walk distance (mean, BL: 349.5m vs. FU: 356.7m, p=0.736), and serum NT-proBNP levels (median, BL: 2765.0 pg/mL vs. FU: 1904.0 pg/mL, p=0.041; cohort comparison: p=0.026, Figure 1C). Echocardiographic findings showed improvements in left ventricular (LV) strain (mean, BL: -12.0% vs. FU: -13.5%, p=0.049) and LV ejection fraction (LVEF, mean, BL: 48.5% vs. FU: 52.7%, p=0.287) in the responder cohort, while significant worsening of LV function (LV strain, mean, BL: -13.9 vs. FU: -10.5, p=0. 035; LVEF, mean, BL: 53.2% vs. FU: 46. 5%, p=0. 012) and RV function measured by tricuspid systolic excursion (TAPSE, mean, BL: 19.2mm vs. FU: 12.6mm, p=0.037) was observed in the non-responder cohort. These results are consistent with changes in the LV and RV function in cardiac magnetic resonance imaging parameters in each of the two cohorts.

CONCLUSION. Treatment with tafamidis in ATTR-CM patients results in a significant reduction in myocardial amyloid deposition as measured by the SUV retention index, with a threshold of -30% distinguishing between patients who respond clinically and those who do not. However, a larger patient sample is needed to verify these results.

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