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Trajectories of laboratory and imaging biomarkers in patients with treated amyloid transthyretin cardiomyopathy - real world data from the CroATTR registry

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Introduction: Imaging and laboratory biomarkers are used in patients with transthyretin amyloid cardiomyopathy (ATTR-CM) to monitor disease progression.[1]

Patients and Methods: The CroATTR Registry has been initiated in September 2022 to collect data on patients with ATTR-CM as well as phenotype negative carriers of pathogenic TTR mutation in Croatia. The aim of this analysis was to analyze trajectories of imaging and laboratory biomarkers at 1- and 2-year follow-up (1yFUP, 2yFUP). This analysis includes only treated ATTR-CM patients that reached at least 1yFUP. Imaging biomarkers comprised left ventricular ejection fraction (LVEF), interventricular septum thickness in diastole (IVSd), and left atrial volume index (LAVI). Laboratory biomarkers used were NT-proBNP, troponin I (TnI), estimated glomerular filtration rate (eGFR), and NAC staging. Data are presented as mean (±SD) or median (with IQR) for continuous variables, and as counts (with %) for categorical variables. Changes from baseline to 1yFUP and 2yFUP were assessed in patients with paired measurements using linear regression. For NT-proBNP and hs-TnI, changes were expressed as geometric mean ratios derived from log-transformed values. For eGFR, IVSd, LVEF and LAVI, they were expressed as mean absolute changes with 95% CI.

Results: Out of 98 patients in the Cro-ATTR registry, 43 treated patients reached at least 1yFUP, and 25 patients reached 2yFUP. Baseline characteristics are shown in **Table 1**. At both 1yFUP and 2yFUP there was no significant change in LVEF, LAVI or IVSd compared to baseline (**Table 2**). NT-proBNP was on average 8% lower at 1yFUP (ratio of 0.92, 95% CI 0.81-1.05; p=0.22), and 11% lower at 2yFUP (ratio of 0.89, 95% CI 0.75-1.07; p=0.20). TnI was on average 11% lower at 1yFUP (ratio 0.89, 95% CI 0.73-1.08, p=0.23), and significantly lower, by 19% at 2yFUP (ratio 0.81, 95% CI 0.69-0.94, p=0.008). eGFR remained stable with mean change of -0.3ml/min/1.73m^2 at 1yFUP (95% CI -3.3 to 2.7, p= 0.86), and -1.4 ml/min/1.73m^2 at 2yFUP (-6.0 to 3.3, p= 0.55) (**Table 2**).

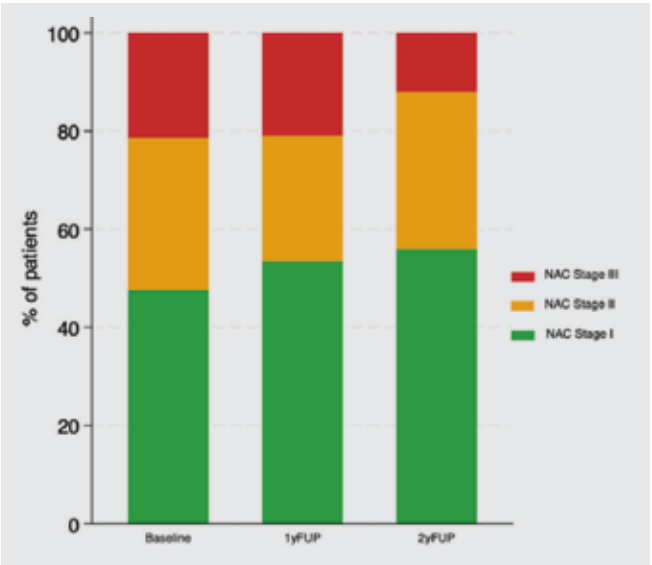


FIGURE 1. Distribution of National Amyloidosis Centre stages at baseline and follow-up.

1yFUP- 1-year follow-up, 2yFUP- 2-year follow-up, NAC- National Amyloidosis Centre

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TABLE 1. Baseline patient characteristics.

	hereditary ATTR cardiomyopathy	wild-type ATTR cardiomyopathy	p-value
	N=7	N=36	
Age at the disease onset (y)	55 (45-60)	76 (71-81)	<0.001
Time from clinical diagnosis to therapy (mo)	7.1 (3.1-11.1)	4.5 (2.2-7.1)	0.36
NYHA class			0.40
I	1 (14%)	2 (6%)	
II	6 (86%)	28 (78%)	
IIIa	0 (0%)	6 (17%)	
Atrial fibrillation/flutter	2 (29%)	23 (64%)	0.08
QRS (mm)	104 (92-115)	117 (99-142)	0.10
IVSd (mm)	20 (±3)	19 (±4)	0.50
LVEF (%)	43 (40-55)	50 (36.5-60)	0.47
LAVI (ml/m^2)	46 (42-54)	52 (43-61)	0.29
eGFR (ml/min/1.73m^2)	78 (±20)	56 (±21)	0.02
NTproBNP (pg/ml)	3041 (1531-3300)	1987 (989-3741)	0.51
Troponin I (ng/L)	68 (49-78)	56 (24-97)	0.63
NAC stage at baseline			0.31
Stage I	3 (50%)	17 (47%)	
Stage II	3 (50%)	10 (28%)	
Stage III	0 (0%)	9 (25%)	
ATTR cardiomyopathy specific therapy			0.66
acoramidis	0 (0%)	1 (3%)	
tafamidis	7 (100%)	35 (97%)	

ATTR- transthyretin amyloidosis, NYHA- New York Heart Association, IVSd- interventricular septum thickness in diastole, LVEF- left ventricular ejection fraction, LAVI- left atrial volume index, eGFR- estimated glomerular filtration rate, NTproBNP- N-terminal pro-brain natriuretic peptide, NAC- National Amyloidosis Centre

TABLE 2. Change in imaging and laboratory biomarkers from baseline to 1-year and 2-year follow-up.

	Change at 1-year FUP (95% CI)	P value	Change at 2-year FUP (95% CI)	P value
LVEF (%)*	2.1 (-0.3 to 4.6), n=42	0.08	3.8 (-0.4 to 8.0), n=24	0.07
IVSd (mm)*	0.4 (-0.5 to 1.3), n=41	0.37	0.1 (-1.0 to 1.2), n=24	0.82
LAVI (ml/m^2)*	-1.8 (-8.3 to 4.6), n=39	0.57	0.9 (-6.4 to 8.2), n=19	0.80
NTproBNP change (%)**	-8 (-19 to 5), n=43	0.22	-11 (-25 to 7), n=25	0.20
Troponin I change (%)**	-11 (-27 to 8), n=25	0.23	-19 (-31 to -6), n=15	**<0.01**
eGFR (ml/min/1.73m^2)*	-0.3 (-3.3 to 2.7), n=42	0.86	-1.4 (-6.0 to 3.3), n=25	0.55

* mean absolute change from baseline.

** geometric mean ratio of the FUP value to baseline, estimated by linear regression of log-transformed values (ratio<1.0 indicates decrease)

LVEF- left ventricular ejection fraction, IVSd- interventricular septum thickness in diastole, LAVI- left atrial volume index, NTproBNP- N-terminal pro-brain natriuretic peptide, eGFR- estimated glomerular filtration rate, FUP- follow-up, CI- confidence interval

Conclusion: In this real-world cohort of patients treated with specific ATTR-CM therapy no significant change of imaging parameters was observed, NT-proBNP showed a trend of decrease, eGFR remained stable, and significantly lower TnI was observed at 2yFUP, while more than 50% of patients remained in the NAC stage I (**Figure 1**).

LITERATURE

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