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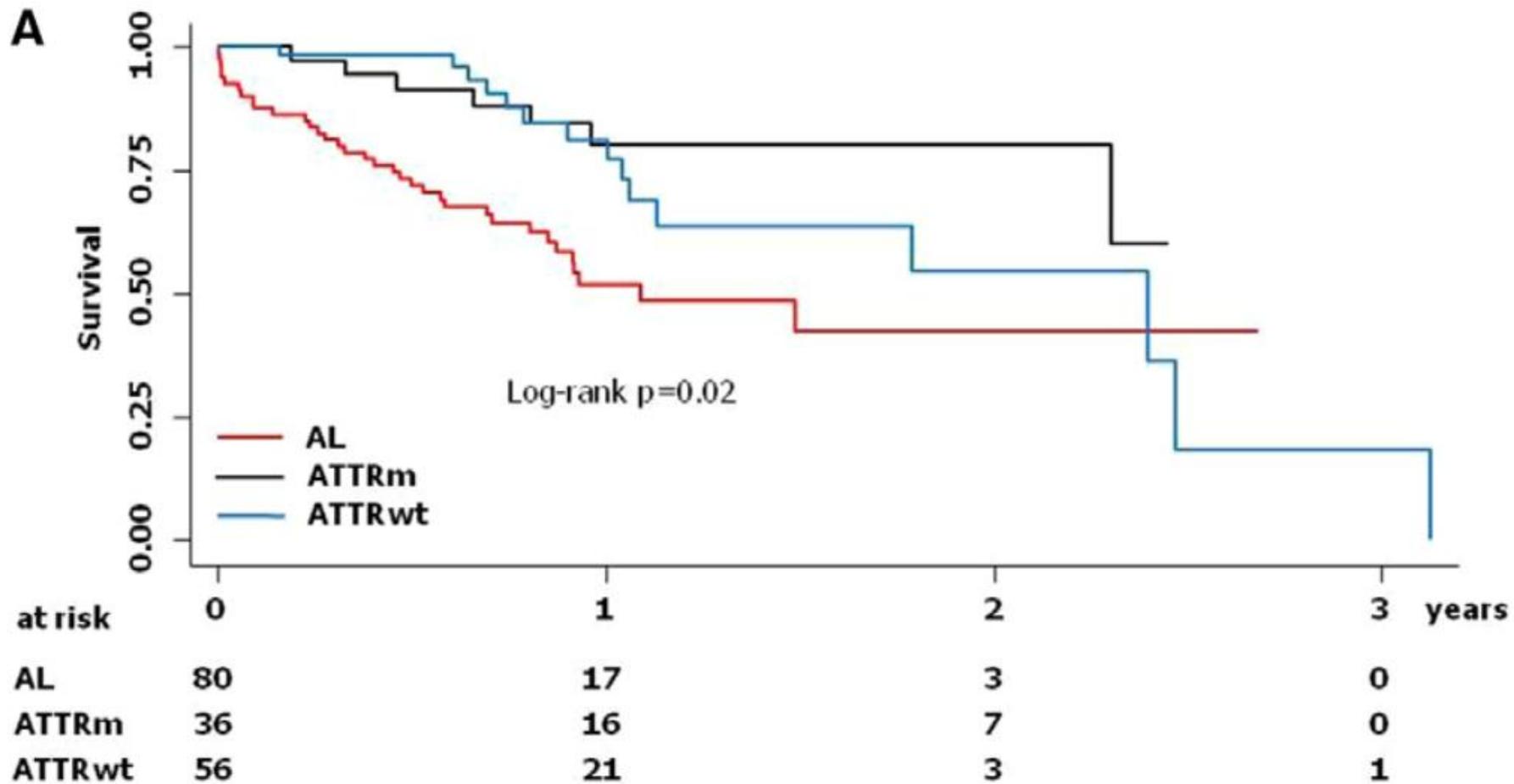
KOMPLEXNÍ
KARDIOVASKULÁRNÍ CENTRUM
FAKULTNÍ NEMOCNICE OLOMOUC

Riziková stratifikace u ATTR, prognóza nemocných s ATTR

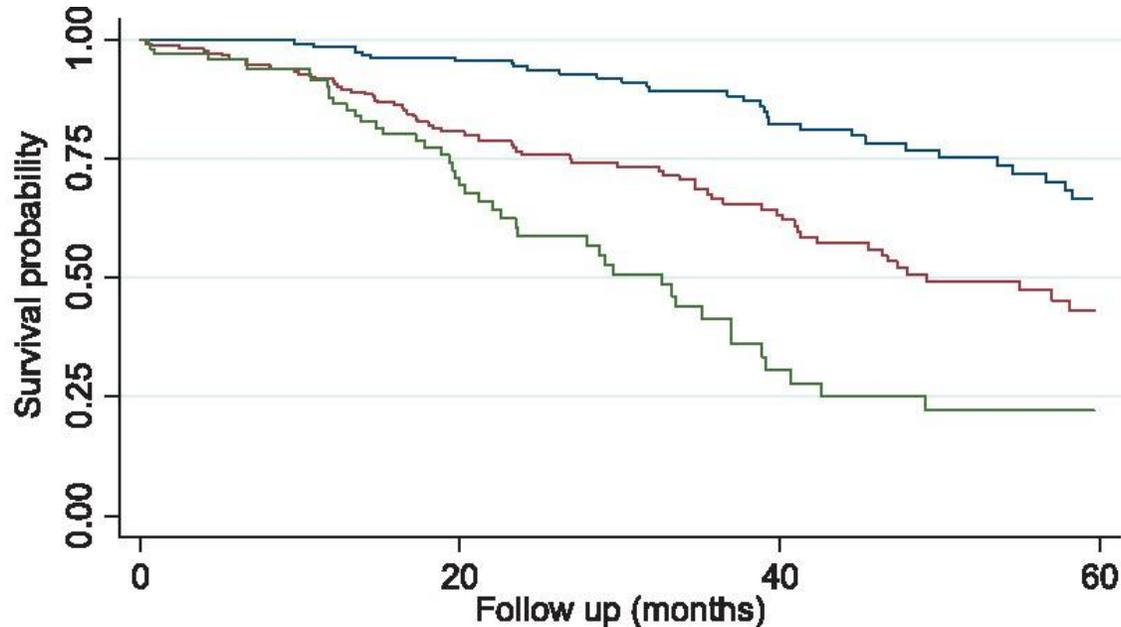
MUDr. Renáta Aiglová, Ph.D.
I. interní klinika – kardiologická
Fakultní nemocnice Olomouc

Přednáška je podpořená společností Pfizer

Prognóza srdeční amyloidózy



Prognóza ATTR-kardiomyopatie



Number at risk	
Stage I	234
Stage II	219
Stage III	100

155	66	34
120	55	20
43	11	5



Medián přežití v jednotlivých stadiích ATTR-CM:

Stadium I méně než 6 let

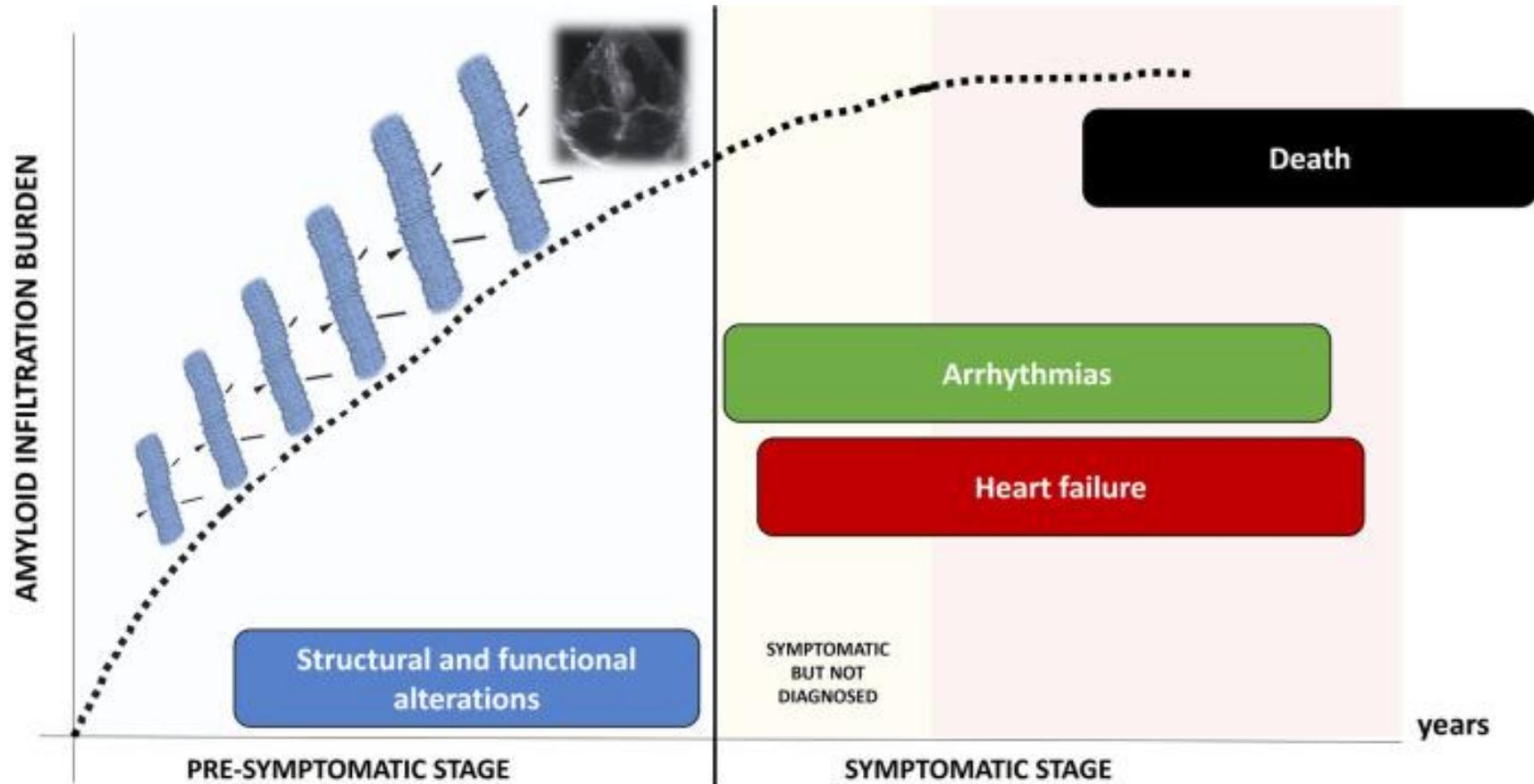
Stadium II méně než 4 roky

Stadium III 2 roky

Včasné stanovení diagnózy významně ovlivňuje prognózu pacientů

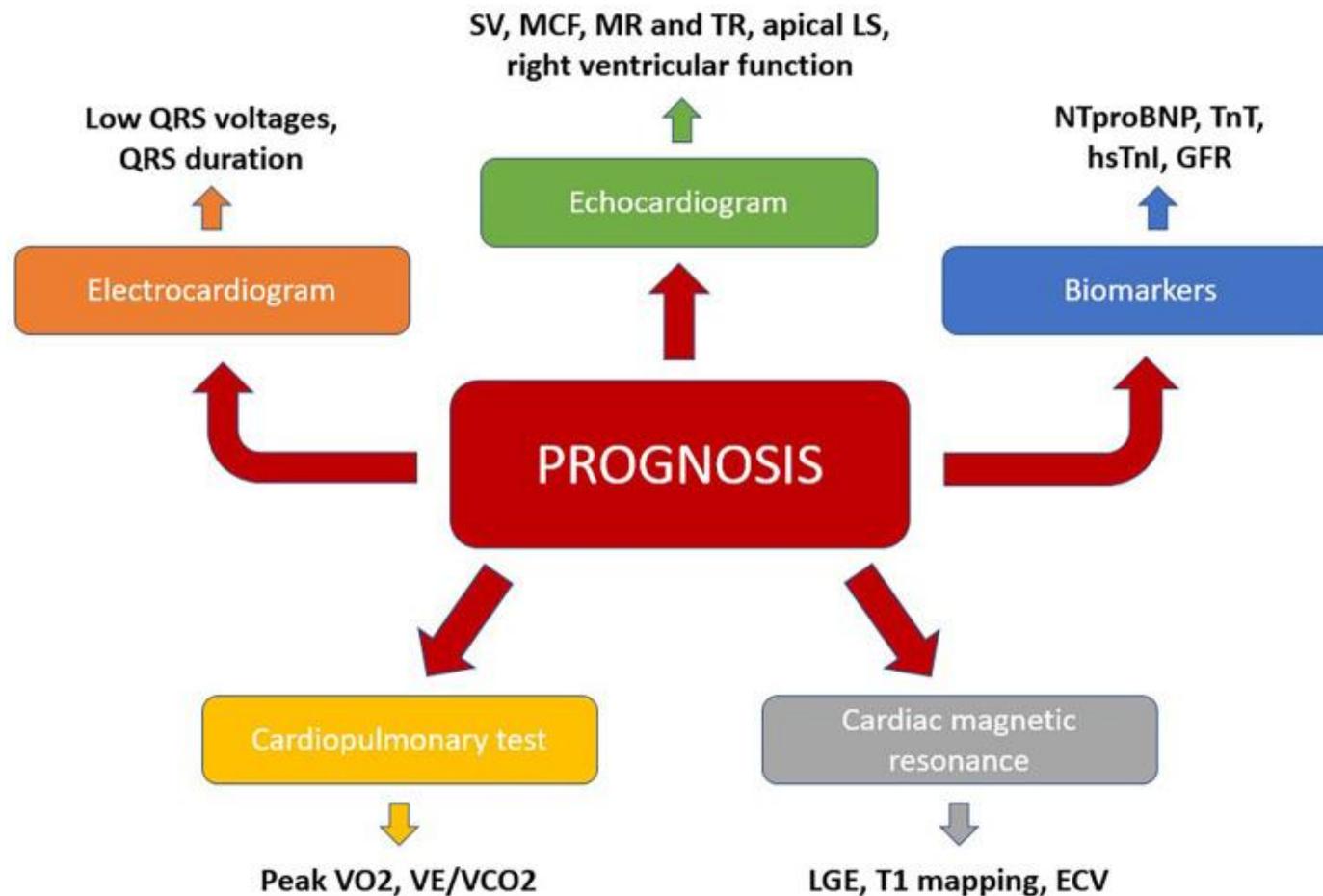
Gonzalez-Lopez E, et al. Eur Heart J 2017;38:1895–1904

Vývoj ATTR-CM



- doi: [10.3389/fcvm.2023.1151803](https://doi.org/10.3389/fcvm.2023.1151803)

Komplexní přístup v hodnocení prognózy u ATTR-CM



- doi: [10.3389/fcvm.2023.1151803](https://doi.org/10.3389/fcvm.2023.1151803)

Stagingové systémy u srdeční amyloidózy

ATTR Amyloidosis

Mayo: Stage 1-3

Cutoffs:

NTproBNP: 3000 ng/L

cTnT: 0.05 ng/mL

pubmed.ncbi.nlm.nih.gov/27585505/

Stage 1	Stage 2	Stage 3
NTproBNP < 3000 ng/L AND cTnT < 0.05	NTproBNP > 3000 ng/L OR cTnT > 0.05	NTproBNP > 3000 ng/L AND cTnT > 0.05

NAC/UK: Stage 1-3

Cutoffs:

NTproBNP: 3000 ng/L

eGFR: 45 mL/min

pubmed.ncbi.nlm.nih.gov/29048471/

Stage 1	Stage 2	Stage 3
NTpBNP < 3000 AND eGFR > 45	NTpBNP > 3000 OR eGFR < 45	NTpBNP > 3000 AND eGFR < 45

Columbia Staging

Stage I	1-3 points
Stage II	4-6 points
Stage III	7-9 points

Mayo score + diuretic dose + NYHA functional class

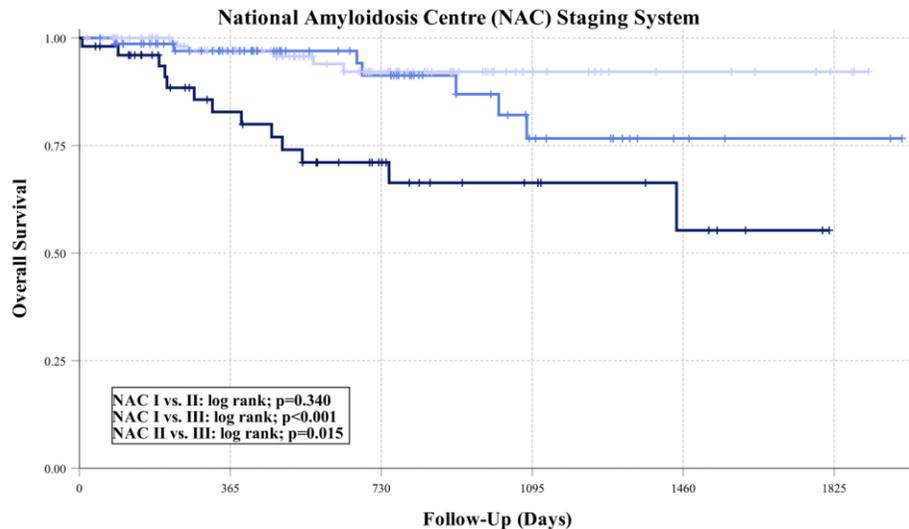
- Smiley DA et al., *Cardiol Clinics* 2022;40

Accuracy of Established Prognostic Staging Systems for Cardiac Transthyretin Amyloidosis in the Tafamidis Era



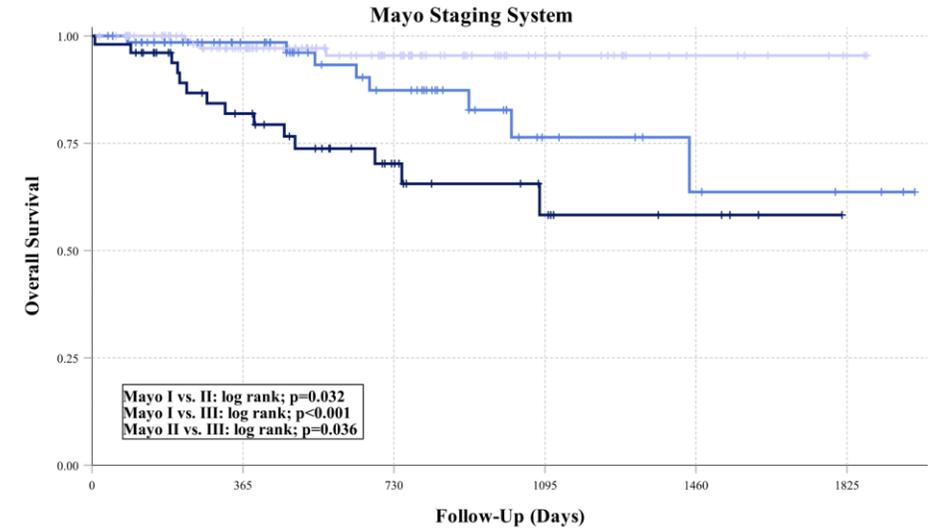
Maximilian Leo Müller, MD,^{a,b,c} Sebastian Spethmann, MD,^{a,b,c,d} Daniel Messroghli, MD,^{a,b,c,d,e} Anna Brand, MD,^{a,b,c,d}
 Isabel Mattig, MD,^{a,b,c,d,f} Katrin Hahn, MD,^{b,c,f,g} Ulf Landmesser, MD,^{a,b,d} Bettina Heidecker, MD^{a,b,c,f}

FIGURE 1 Overall Survival Across Disease Stages of the National Amyloidosis Centre Staging System



Number at Risk:						
NAC I	126	86	42	14	7	3
NAC II	74	51	32	13	4	2
NAC III	51	29	17	9	5	0

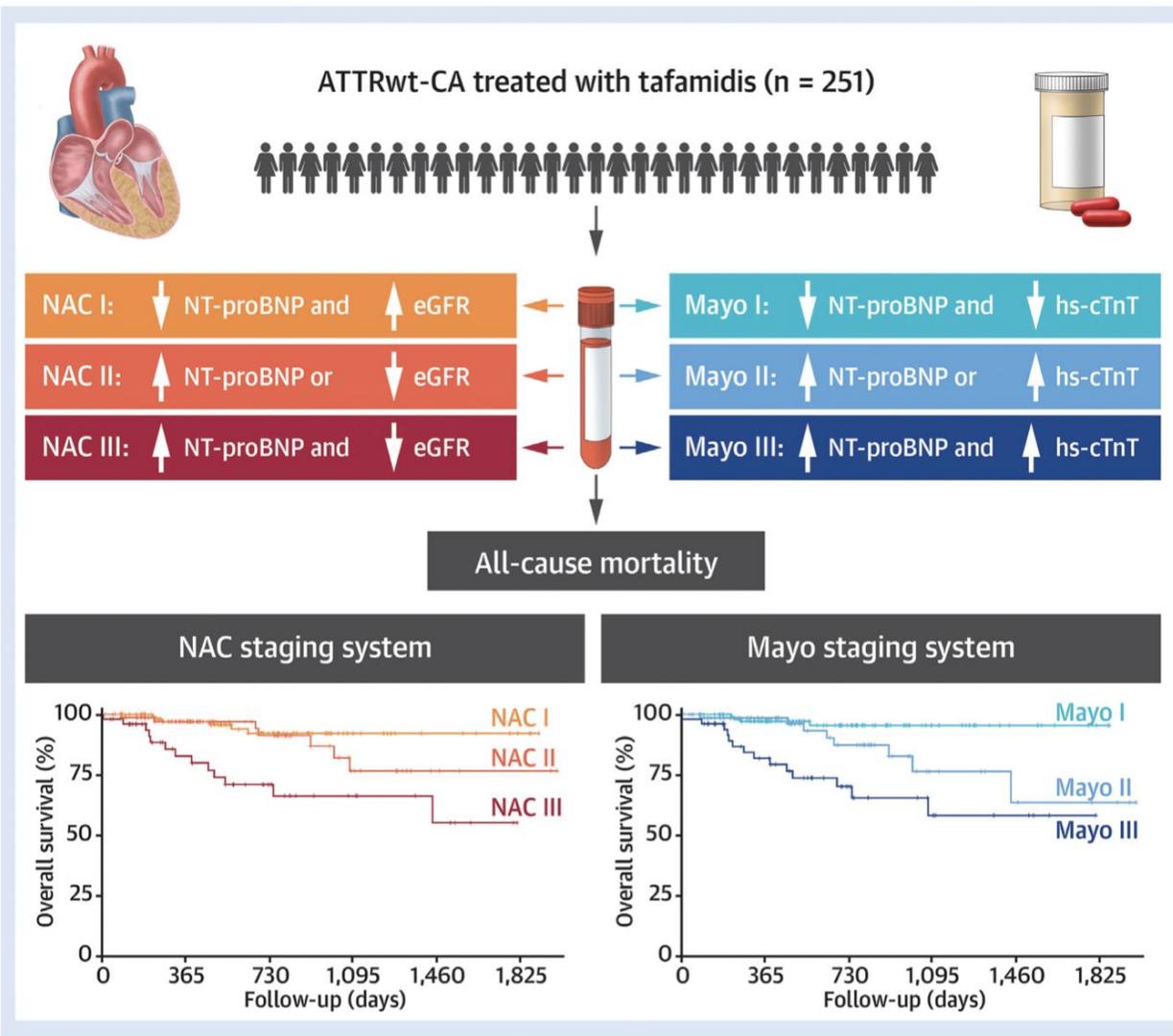
FIGURE 2 Overall Survival Across Disease Stages of the Mayo Staging System



Number at Risk:						
Mayo I	132	87	46	19	7	2
Mayo II	68	46	28	9	5	3
Mayo III	51	33	17	8	4	0

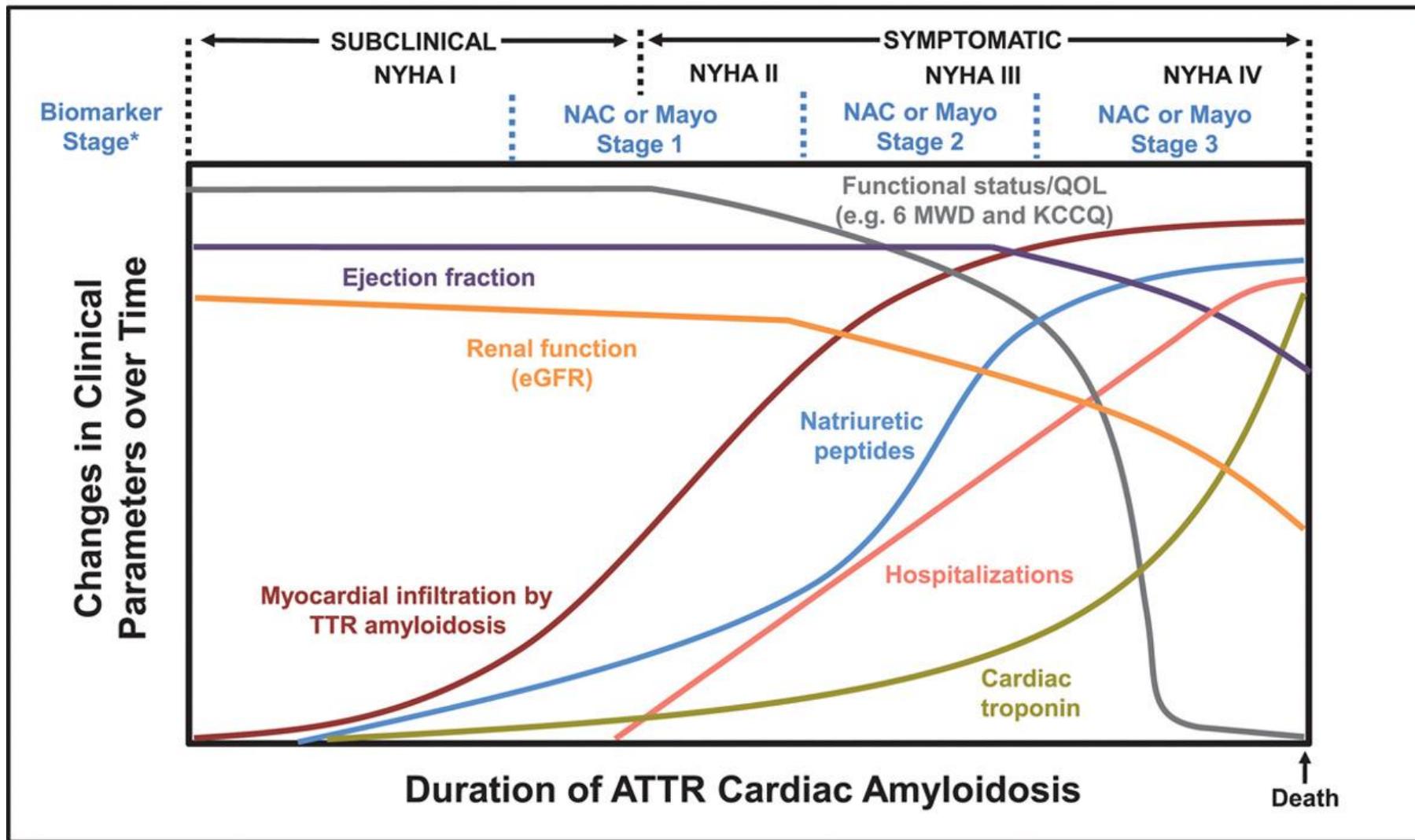
• <https://doi.org/10.1016/j.jacadv.2024.101568>

CENTRAL ILLUSTRATION Accuracy of Established Prognostic Staging Systems for Cardiac Transthyretin Amyloidosis in the Tafamidis Era



Müller ML, et al. JACC Adv. 2025;4(2):101568.

Ideal Emerging Therapeutic Window



Expert consensus on the monitoring of transthyretin amyloid cardiomyopathy

Pablo Garcia-Pavia^{1,2,3*}, Frank Bengel⁴, Dulce Brito⁵, Thibaud Damy^{3,6}, Franz Duca⁷, Sharmila Dorbala⁸, Jose Nativi-Nicolau⁹, Laura Obici¹⁰, Claudio Rapezzi^{11,12}, Yoshiki Sekijima¹³, and Perry M. Elliott¹⁴

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Received 23 December 2020; revised 21 April 2021; accepted 23 April 2021; online publish-ahead-of-print 24 May 2021

Criteria for disease progression in patients with ATTR-CM

Clinical and functional

Increase in HF-related hospitalization
OR
Increase in NYHA class
OR
Decline in QoL: KCCQ (5–10 pts)/ EQ-5D (10%)
OR
30–40 m decline in 6MWT every 6 months

+

Laboratory biomarker

30% increase in NT-proBNP (300 pg/mL cut-off)
OR
30% increase in troponin
OR
Advance in NAC staging scale

+

Imaging and ECG

Increased LV wall thickness (2 mm)
OR
Increase in diastolic dysfunction grade
OR
Change in systolic measurement (≥5% decrease in LVEF; ≥5 mL decrease in stroke volume; ≥1% increase in GLS)
OR
New onset conduction disturbance

One marker from each domain provides the minimum requirement for assessing ATTR-CM progression

Long-term tafamidis efficacy in patients with transthyretin amyloid cardiomyopathy by baseline left ventricular ejection fraction

Brian Drachman¹, Thibaud Damy², Mazen Hanna³, Ronnie Wang⁴, Franca S. Angeli⁵, and Pablo Garcia-Pavia^{6,7,8*}

¹University of Pennsylvania Health System, Philadelphia, PA, USA; ²Referral Center for Cardiac Amyloidosis, CHU Henri Mondor, Créteil, France; ³Department of Cardiovascular Medicine, Cleveland Clinic, Cleveland, OH, USA; ⁴Pfizer Inc., Groton, CT, USA; ⁵Pfizer Inc., New York, NY, USA; ⁶Hospital Universitario Puerta de Hierro Majadahonda, IDIPHISA, CIBERCV, Madrid, Spain; ⁷Centro Nacional de Investigaciones Cardiovasculares (CNIC), Madrid, Spain; and ⁸Universidad Francisco de Vitoria (UFV), Pozuelo de Alarcon, Spain

Received 26 January 2024; revised 1 May 2024; accepted 27 May 2024; online publish-ahead-of-print 26 June 2024

Table 2 Observed all-cause mortality by left ventricular ejection fraction at baseline

	LVEF <50%		LVEF ≥50%	
	Tafamidis 80/61 mg	Placebo/tafamidis	Tafamidis 80/61 mg	Placebo/tafamidis
<i>n</i>	88	89	85	86
All-cause mortality, <i>n</i> (%)	52 (59.1)	73 (82.0)	35 (41.2)	52 (60.5)
First event, <i>n</i> (%)				
All-cause death	45 (51.1)	69 (77.5)	33 (38.8)	50 (58.1)
Heart transplant	5 (5.7)	4 (4.5)	2 (2.4)	2 (2.3)
Implantation of a cardiac mechanical assist device	2 (2.3)	0	0	0

LVEF, left ventricular ejection fraction.

Heart transplant and implantation of a cardiac mechanical assist device were treated as death. Statistical analyses were conducted using the Kaplan–Meier method and are shown in Figures 2 and 3.

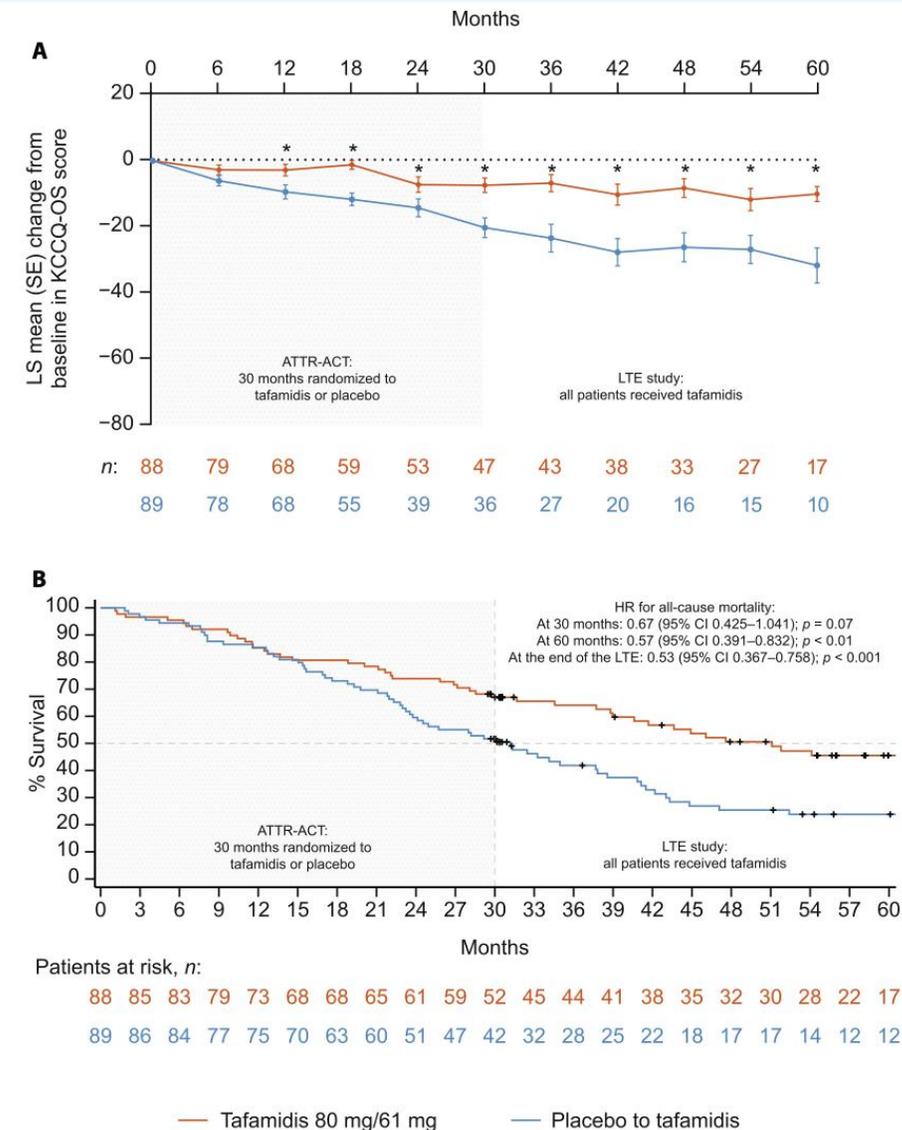


Figure 2 Health-related quality of life (A) and Kaplan–Meier plot of all-cause mortality (B) in patients with baseline left ventricular ejection fraction <50%. End of survival defined as death, heart transplant, or implantation of a cardiac mechanical assist device. ATTR-ACT, Tafamidis in Transthyretin Cardiomyopathy Clinical Trial; CI, confidence interval; HR, hazard ratio; KCCQ-OS, Kansas City Cardiomyopathy Questionnaire overall summary; LS, least squares; LTE, long-term extension; SE, standard error. **p* < 0.05; + = censored.

Long-term tafamidis efficacy in patients with transthyretin amyloid cardiomyopathy by baseline left ventricular ejection fraction

Brian Drachman¹, Thibaud Damy², Mazen Hanna³, Ronnie Wang⁴, Franca S. Angeli⁵, and Pablo Garcia-Pavia^{6,7,8*}

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This study assessed the long-term efficacy of tafamidis in subgroups of patients with ATTR-CM and baseline LVEF <50% or ≥50%



After 30 months in the phase 3 ATTR-ACT, patients treated with tafamidis versus placebo in both LVEF subgroups had:

- Numerically lower all-cause mortality
- Significantly smaller decline in KCCQ-OS



After an additional 30 months in the open-label LTE study (month 60 of treatment), patients treated continuously with tafamidis versus those who initially received placebo in ATTR-ACT in both LVEF subgroups had:

- Significantly lower all-cause mortality
- Significantly smaller decline in KCCQ-OS

At month 60, continuous tafamidis (80/61mg) treatment was associated with a 47% reduction in all-cause mortality risk versus delayed tafamidis treatment in both subgroups ($p < 0.01$)

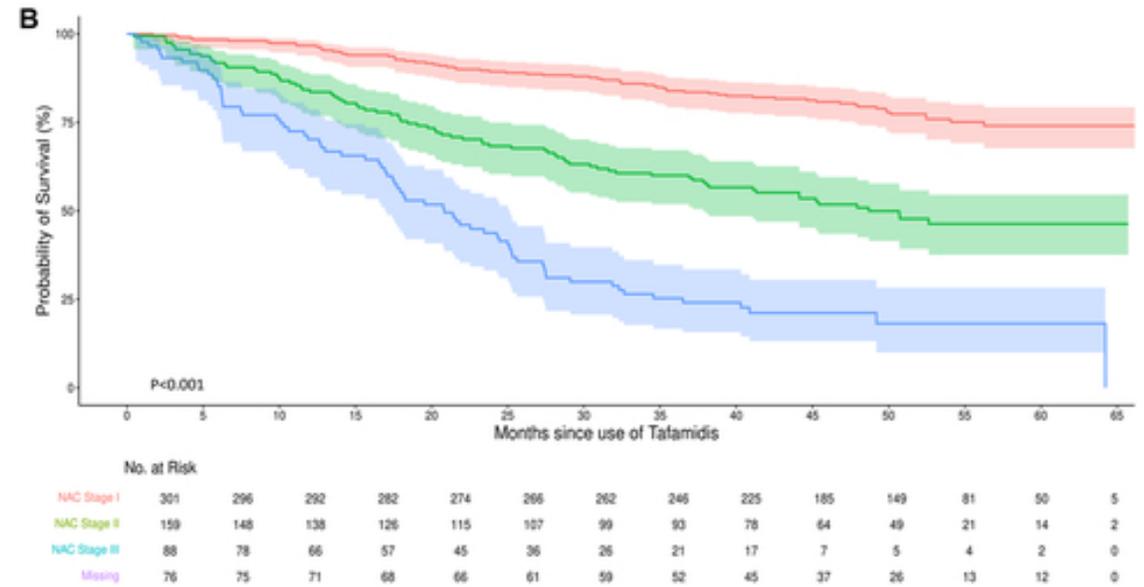
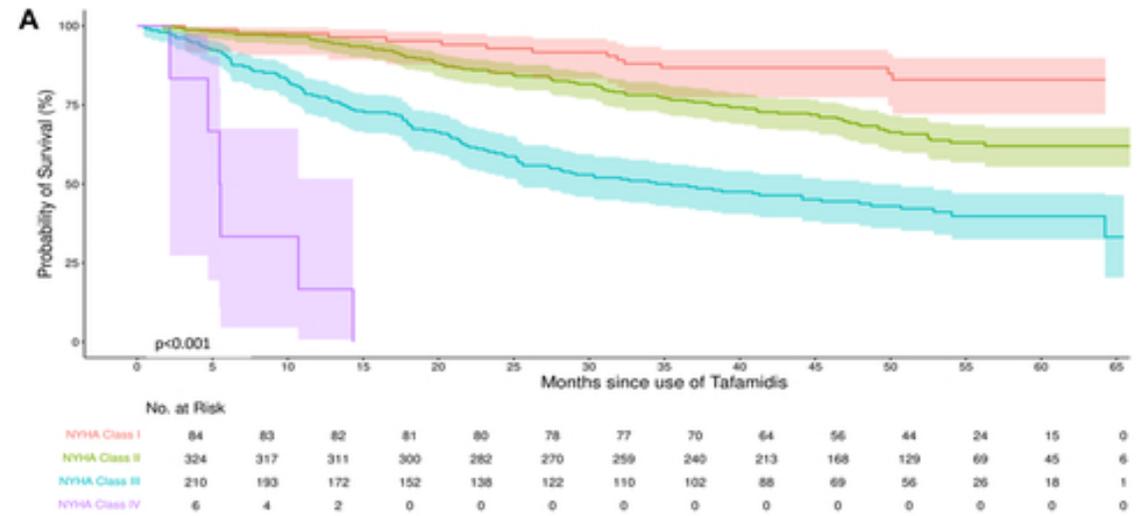
Baseline LVEF <50%
HR 0.53 (95% CI 0.367-0.758)

Baseline LVEF ≥50%
HR 0.53 (95% CI 0.344-0.818)

A Multicenter Study of Contemporary Long-Term Tafamidis Outcomes in Transthyretin Amyloid Cardiomyopathy



Ahmad Masri, MD, MS,^a Priyanka Bhattacharya, MD,^b Brent Medoff, MD,^c Ain U. Ejaz, MD,^d
 Miriam R. Elman, MS, MPH,^a Pranav Chandrashekar, MD,^a Lauren Ives, MPH,^a Alfonsina Mirabal Santos, MD,^b
 Sergio L. Teruya, MD,^b Yuanzi Zhao, MD, PhD,^a Shuaiqi Huang, PhD,^f Xiaofeng Wang, PhD,^f Brett W. Sperry, MD,^d
 Mathew S. Maurer, MD,^b Prem Soman, MD, PhD,^c Mazen Hanna, MD^g

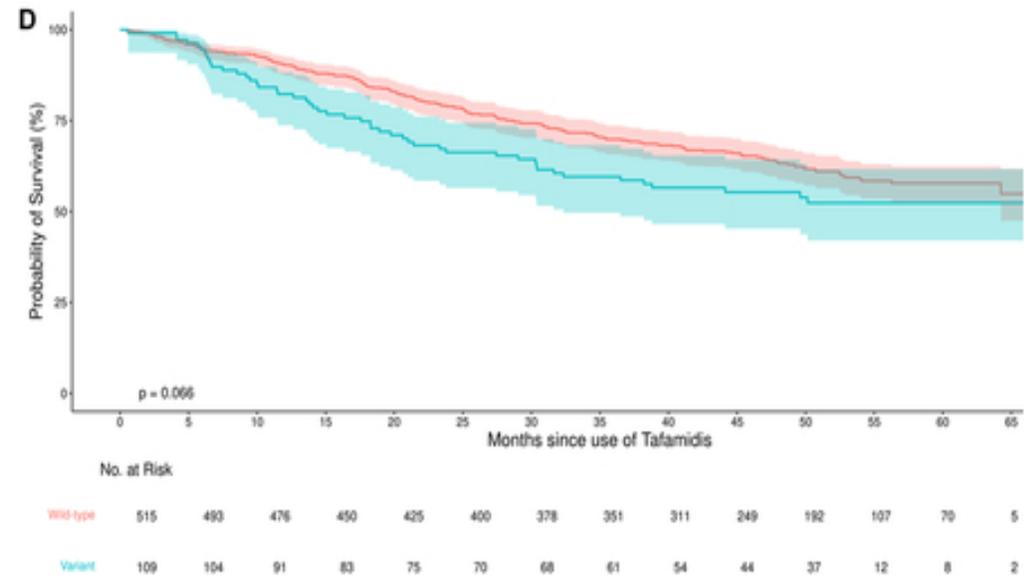
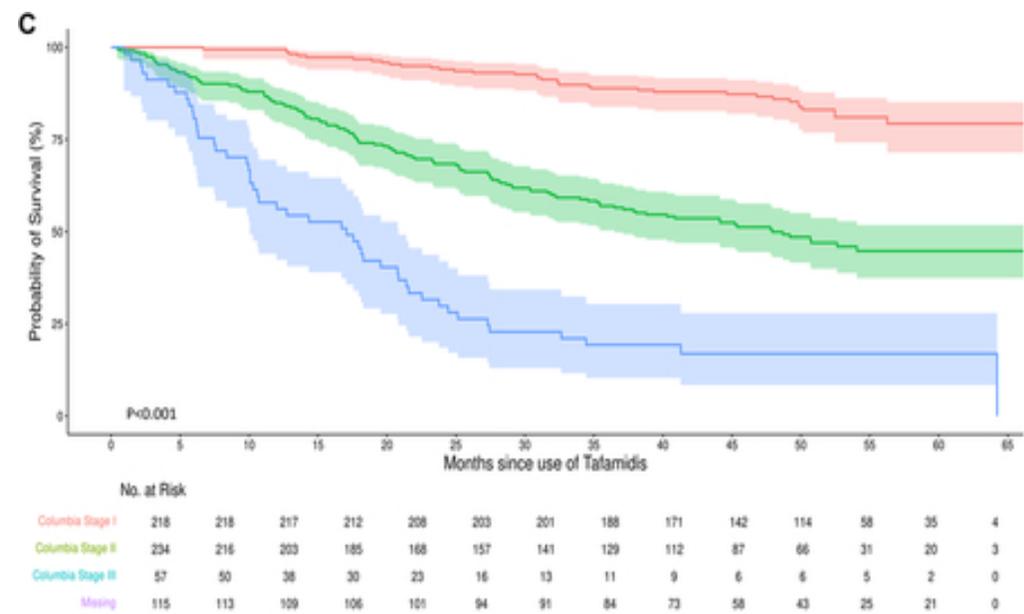


- Ahmad Masri et al. *J Am Coll Cardiol CardioOnc* 2025; 7:282-293.

A Multicenter Study of Contemporary Long-Term Tafamidis Outcomes in Transthyretin Amyloid Cardiomyopathy



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- Ahmad Masri et al. *J Am Coll Cardiol CardioOnc* 2025; 7:282-293.

Survival in a Real-World Cohort of Patients With Transthyretin Amyloid Cardiomyopathy Treated With Tafamidis: An Analysis From the Transthyretin Amyloidosis Outcomes Survey (THAOS)

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 MARTIN CARLSSON, MS⁶ LESLIE AMASS, PhD⁶ FRANCA STEDILE ANGELI, MD, PhD⁶ and
 MATHEW S. MAURER, MD⁷, on behalf of the THAOS investigators^a

Madrid, and Pozuelo de Alarcon, Spain; Heidelberg, Germany; and Philadelphia, and New York, USA

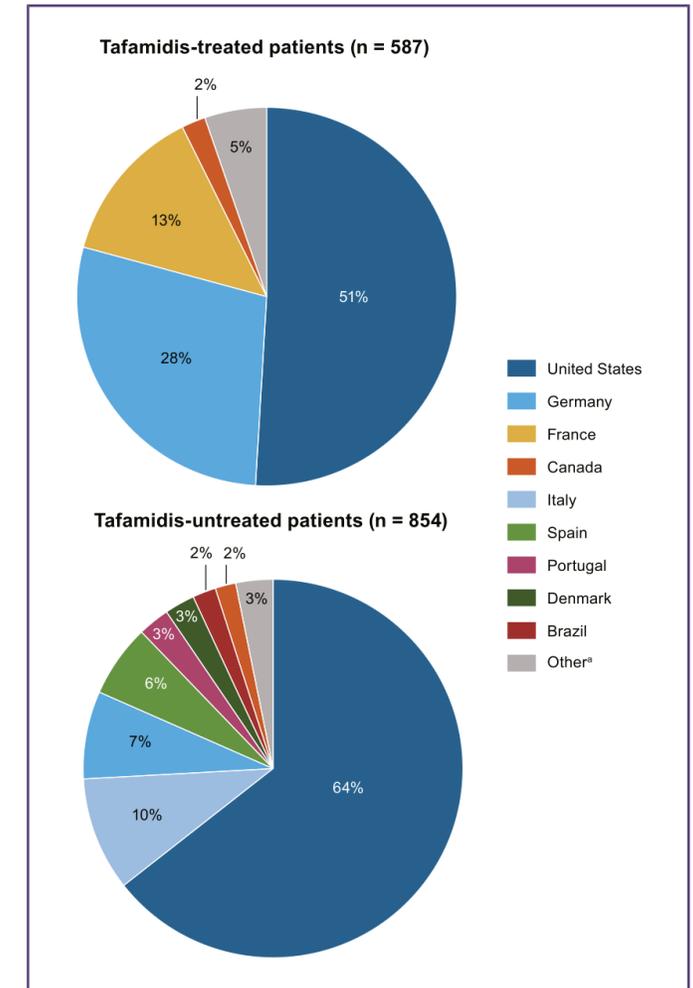
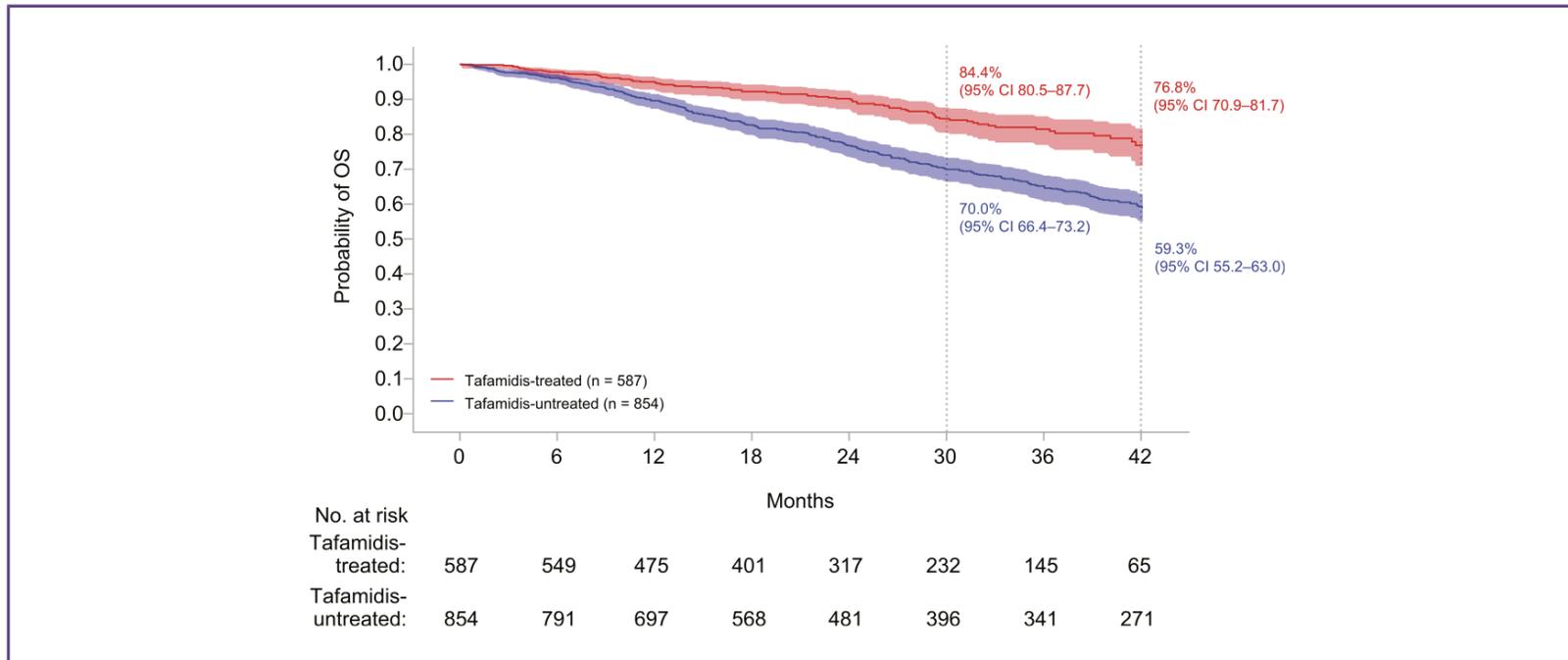


Fig. 1. Country of enrollment for tafamidis-treated and tafamidis-untreated patients. ^aIncludes countries with fewer than 10 enrolled patients.

	Tafamidis-treated (n = 587)	Tafamidis-untreated (n = 854)	P Value
Sex, n (%)			0.25
Male	539 (91.8)	769 (90.0)	
Female	48 (8.2)	85 (10.0)	
Race/ethnicity,*n (%)	502	767	<0.001
Afro-Caribbean	1 (0.2)	8 (1.0)	
American Hispanic	1 (0.2)	0	
Asian	9 (1.8)	8 (1.0)	
Black or African American	28 (5.6)	72 (9.4)	
Latino American	0	12 (1.6)	
White	463 (92.2)	659 (85.9)	
Other	0	8 (1.0)	
Age at symptom onset (y), n	500	783	0.86
Median (10th, 90th percentile)	72.5 (59.5, 82.5)	72.5 (57.5, 82.5)	
Time from symptom onset to diagnosis (y), n	495	726	0.45
Median (10th, 90th percentile)	1.6 (0.0, 13.0)	1.4 (0.0, 10.7)	
Year of enrollment, n (%)			<0.001
2007–2012	13 (2.2)	147 (17.2)	
2013–2018	143 (24.4)	468 (54.8)	
2019–2023	431 (73.4)	239 (28.0)	
Age at enrollment (y), median (10th, 90th percentile)	77.7 (68.0, 85.9)	76.4 (65.2, 85.7)	0.02
Symptom duration at enrollment (y), n	500	783	0.30
Median (10th, 90th percentile)	3.0 (0.4, 13.7)	2.7 (0.3, 11.9)	
Follow-up time, [†] (y), median (10th, 90th percentile)	2.2 (0.5, 5.3)	2.3 (0.6, 5.7)	0.07

• <https://doi.org/10.1016/j.cardfail.2024.06.003>.

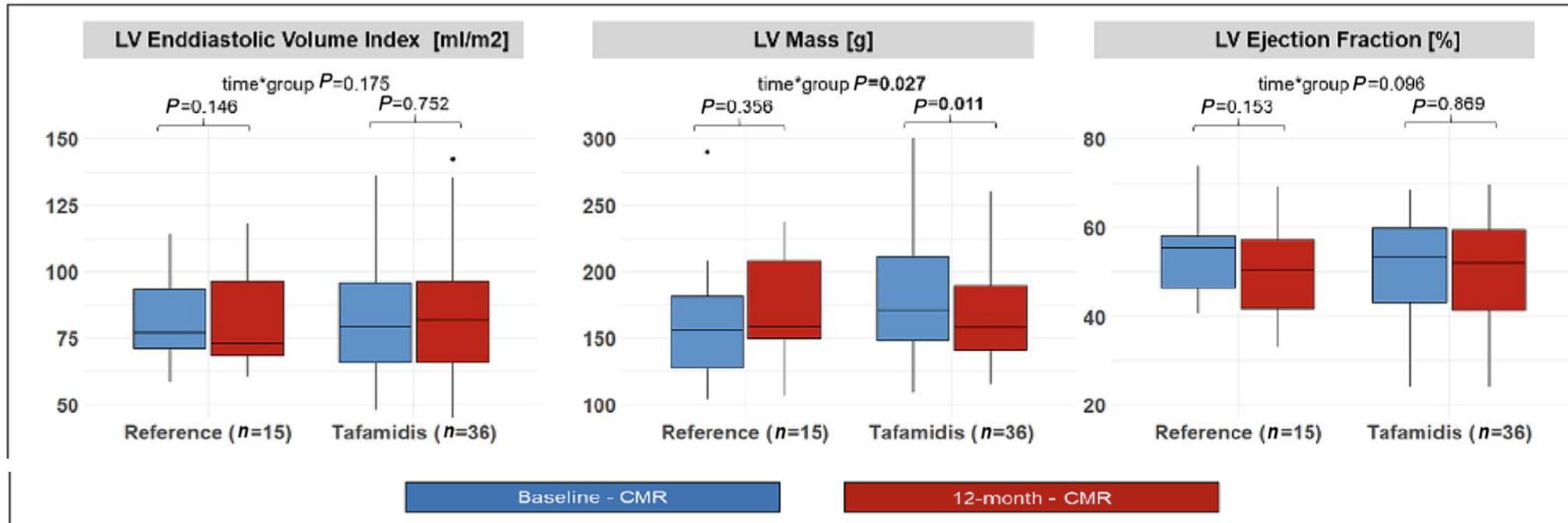
TTR genotype, n (%)			<0.001
Variant	48 (8.2)	138 (16.2)	
Wild-type	539 (91.8)	716 (83.8)	
Most Common TTR Variants, [‡] n (%)			0.01
V122I (p. V142I)	21 (3.6)	69 (8.1)	
V30M (p.V50M) [§]	3 (0.5)	18 (2.1)	
I68L (p.I88L)	5 (0.9)	10 (1.2)	
Heart failure, n (%)	509 (86.7)	787 (92.2)	<0.001
NYHA functional class, n (%)	484	769	<0.001
I	76 (15.7)	80 (10.4)	
II	305 (63.0)	456 (59.3)	
III	102 (21.1)	207 (26.9)	
IV	1 (0.2)	26 (3.4)	
NT-proBNP (pg/mL), n	157	487	0.04
Median (10th, 90th percentile)	1883.0 (459.0, 6837.0)	2498.0 (466.0, 8256.0)	
LV septum thickness (mm), n	464	611	0.13
Median (10th, 90th percentile)	17.0 (13.0, 22.0)	17.0 (13.0, 22.0)	
LV ejection fraction (%), n	472	609	0.02
Median (10th, 90th percentile)	50.0 (33.0, 63.0)	49.0 (29.0, 62.0)	
mBMI, n	403	473	0.23
Median (10th, 90th percentile)	1077.6 (851.8, 1346.5)	1060.2 (806.4, 1344.1)	
Past or current clinical trial participation, n (%)	581	752	0.70
Yes	120 (20.7)	149 (19.8)	
Tafamidis trial	7 (1.2)	0	
Non-tafamidis trial	113 (19.4)	149 (19.8)	
No	461 (79.3)	603 (80.2)	
Diagnostic method, [¶] n (%)			-
Clinical symptoms	546 (93.0)	734 (85.9)	
Amyloid confirmed on tissue biopsy	244 (41.6)	460 (53.9)	
TTR confirmed as precursor protein on tissue biopsy	218 (37.1)	401 (47.0)	
Scintigraphy	352 (60.0)	228 (26.7)	
Other	66 (11.2)	34 (4.0)	

- <https://doi.org/10.1016/j.cardfail.2024.06.003>.

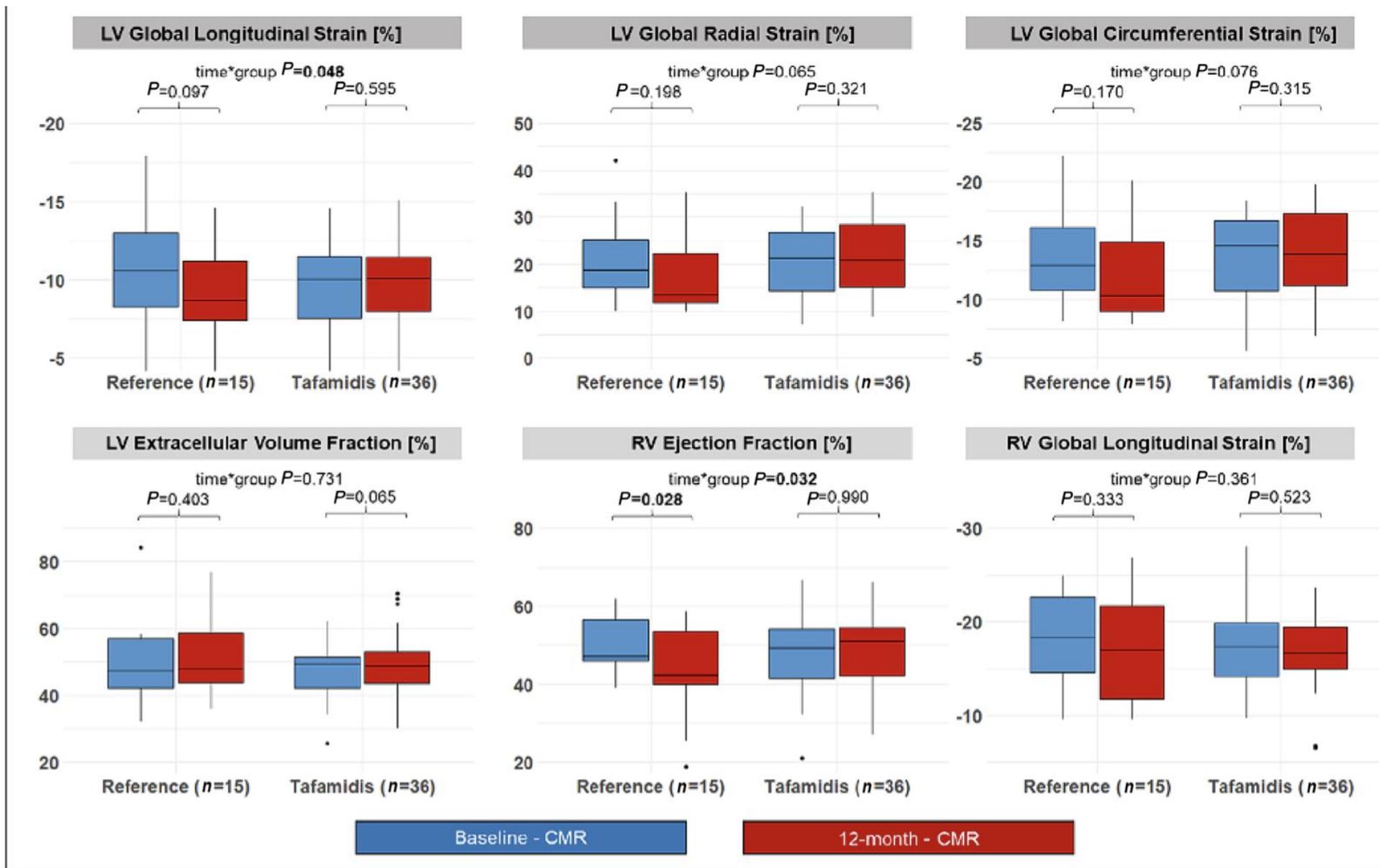
Impact of tafamidis on myocardial function and CMR tissue characteristics in transthyretin amyloid cardiomyopathy

Stephan Dobner , Benedikt Bernhard, Lorenz Ninck, Monika Wieser, Adam Bakula, Andreas Wahl, Valentin Köchli, Giancarlo Spano, Martina Boscolo Berto, Elena Elchinova, Yasaman Safarkhanlo, Stefan Stortecky, Jonathan Schütze, Isaac Shiri, Lukas Hunziker and Christoph Gräni*

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• DOI: [10.1002/ehf2.14815](https://doi.org/10.1002/ehf2.14815)



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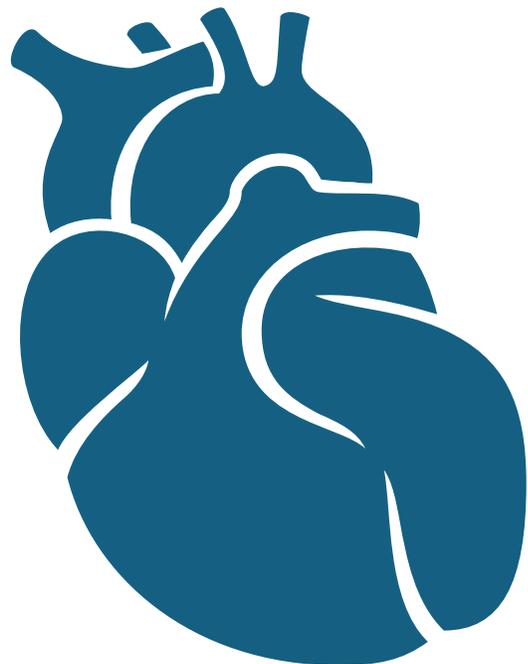
Závěr

- Srdeční transthyretinová amyloidóza se stále pojí s nepříznivou prognózou
- Včasná diagnostika a včasné zahájení léčby
- Dostupné různé stagingové systémy a metodika pro sledování progresu onemocnění
- Stabilizace tetramerů transthyretinu – první zkušenosti a dostupná data z klinické praxe

Výdej léčivého přípravku Vyndaqel je vázán na lékařský předpis a je hrazen z prostředků veřejného zdravotního pojištění.

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Děkuji za pozornost.