

*Program za napredovalo srčno popuščanje  
in transplantacije srca  
KO za kardiologijo  
UKC Ljubljana*



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# Transtiretinska amiloidoza srca ATTR-CM

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junij 2024

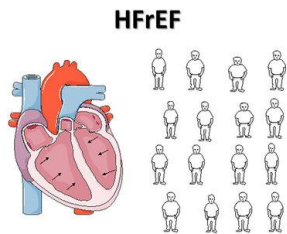
# HFpEF



## bazen bolnikov s starostno (wt)ATTR-CM

30 – 50 %

wtATTR

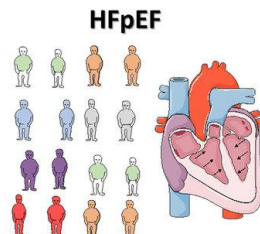


HFREF

Homogeneous response to treatment

Several pharmacological and non-pharmacological interventions with established benefit on CV mortality and HF hospitalizations

*«One size fits all approach»*

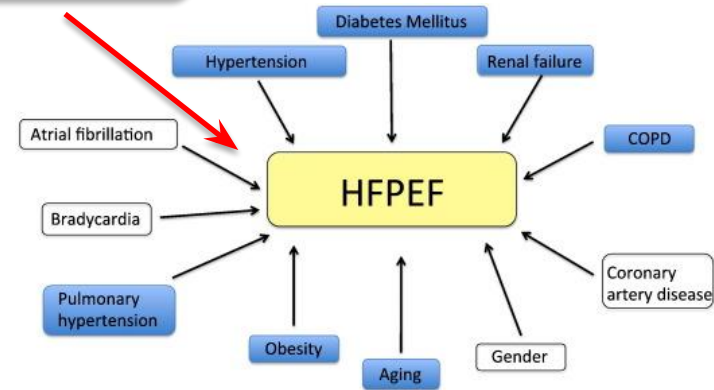


HFpEF

Heterogeneous population

No effective treatments on CV mortality  
Benefit of decongestion and MRA (trend with Candesartan and ARNI) on HF hospitalizations  
Benefit of lifestyle interventions on symptoms and QoL

*«Phenotype-specific treatment»*



  = involvement of inflammation

[1-s2.0-S0033062020300839-gr3\\_lrg.jpg \(3160x1953\) \(els-cdn.com\)](https://els-cdn.com/1-s2.0-S0033062020300839-gr3_lrg.jpg)

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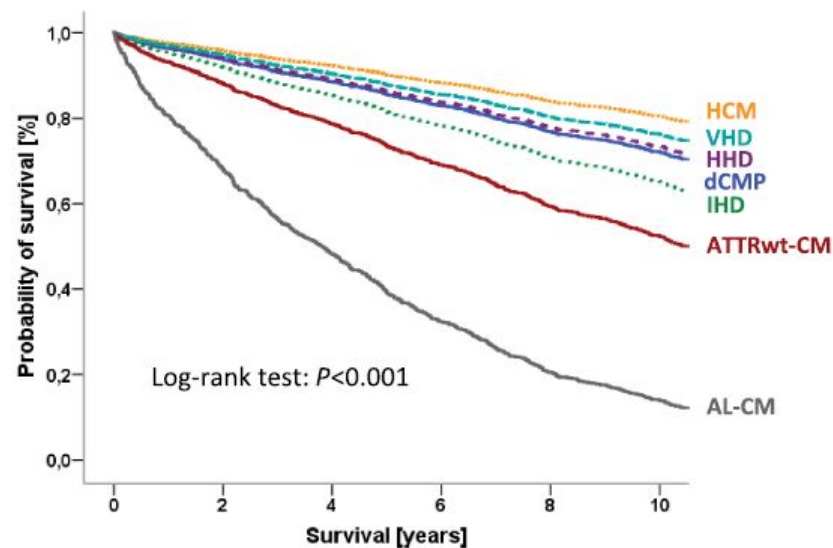
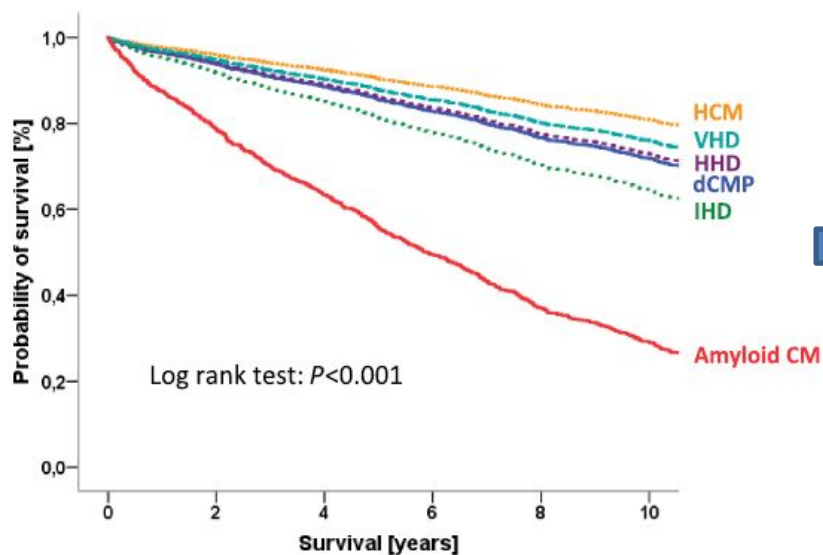
Study	Year	Sample size	Design	Age mean or median (males' percentage %)	Hypertension %	DM%	CAD	Diagnosis of amyloidosis	Prevalence of ATTR
Esther Gonzalez-Lopez/Spain	2015	120	Prospective analysis	82 (males 41%)	84%	37%	9%	99m Tc-DPD scan. Followed by TTR gene test if scan is positive	16 patients (13.3%)
Omar F. AbouEzzeddine/USA	2021	286	Prospective analysis	78 (males 52%)	96%	50%	65%	99m Tc-pyrophosphate scintigraphy	8 patients (6.3%)
Ana Devesa/Spain	2021	58	Prospective analysis	79 (males 54%)	83%	36%	14%	99m Tc-DPD scan then TTR gene testing if scan is positive	3 patients (5%)
Saberio Lo Presti/USA	2019	100	Retrospective analysis	76 (males 64%)	85%	32%	34%	99mTc-PYP	19 patients (19%)
Selma F. Mohammed/USA	2013	106	Retrospective analysis	74 (males 43%)	78%	42%	62%	Autopsy and histological analysis	18 patients (17%)

5 19 %



# Preživetje: HFpEF vs. **amyloidna CM** vs. starostna ATTR-CM

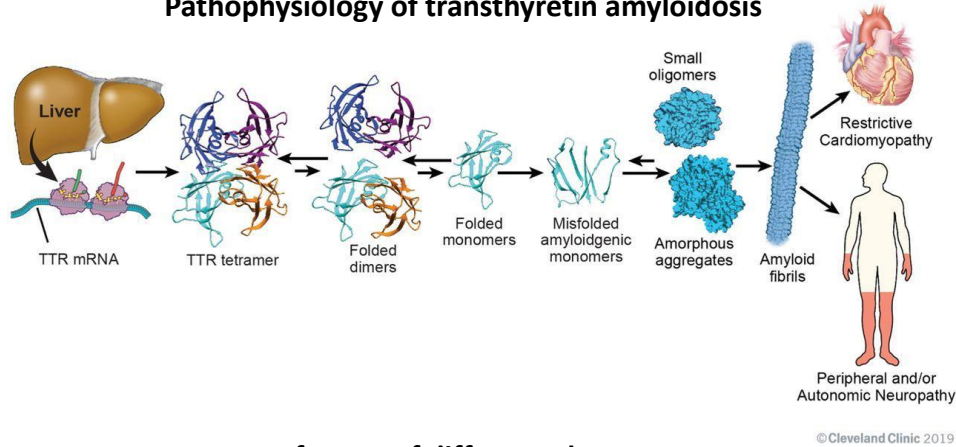
Pomembne razlike v prognozi!



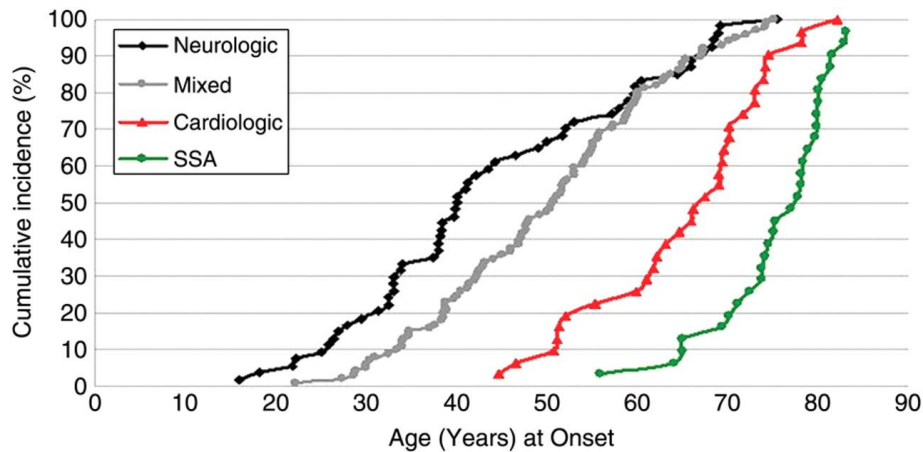


# Starostna ATTR (wild-type) vs. dedna ATTR (mutation)

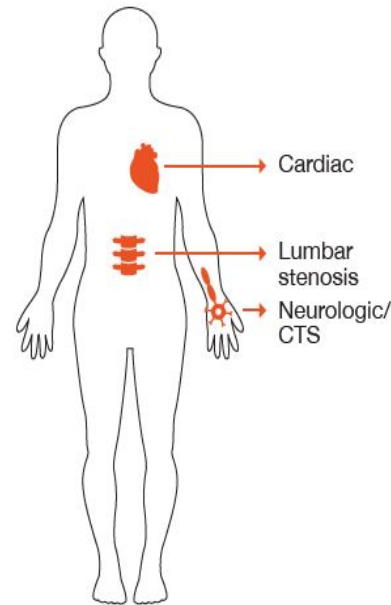
## Pathophysiology of transthyretin amyloidosis



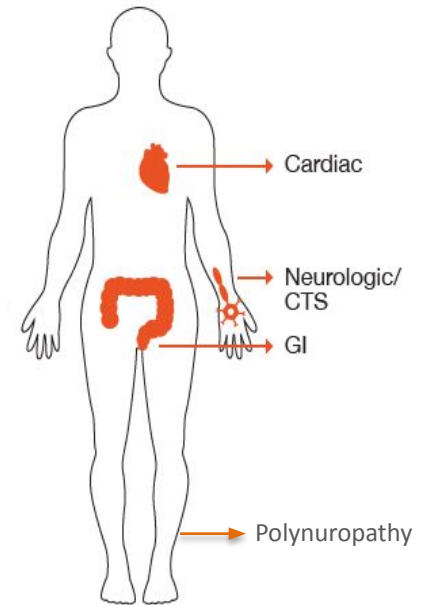
## Age of onset of different phenotypes



## Wild-type (wtATTR)



## Hereditary (hATTR)

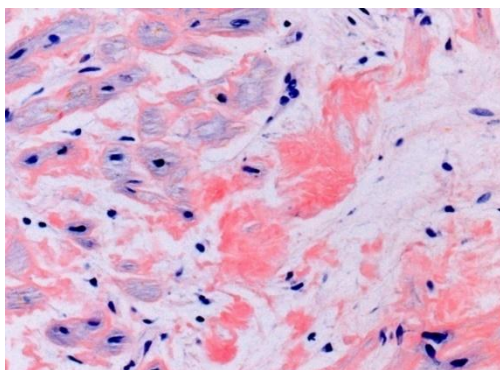




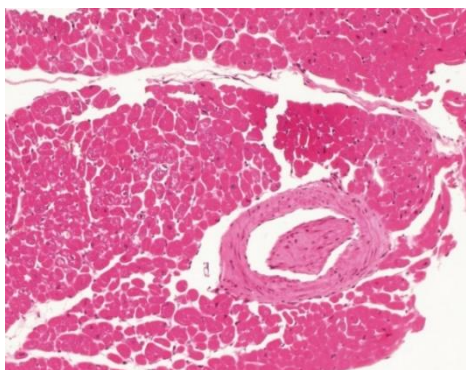
# Starostna (wt)ATTR-CM

## Mehanizmi srčne okvare in opozorilni znaki

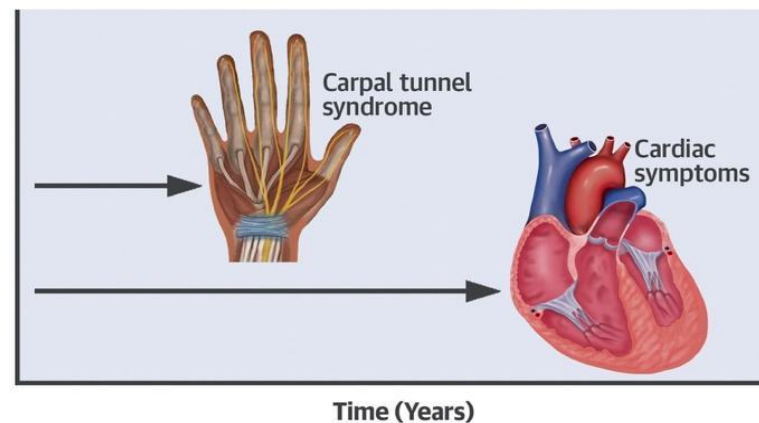
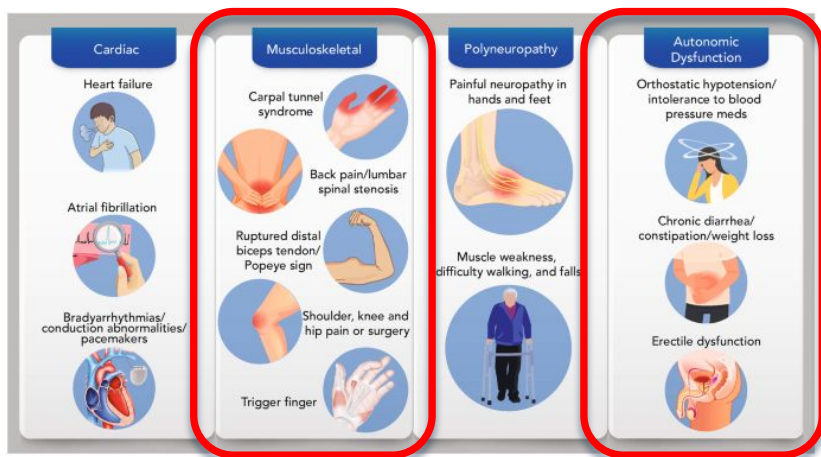
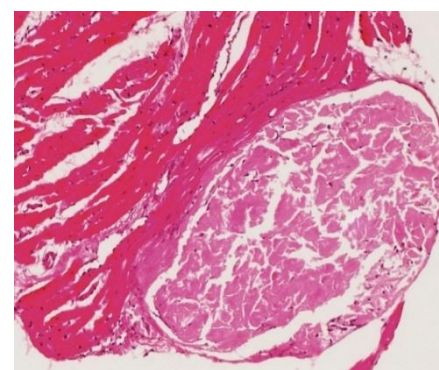
### Medcelično kopičenje



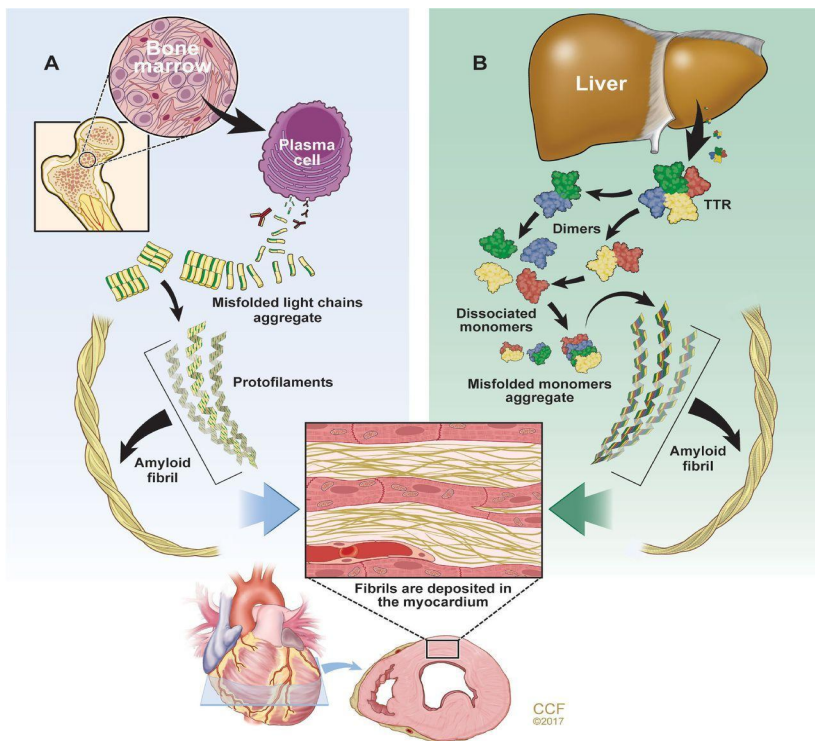
### Kopičenje v žilni steni



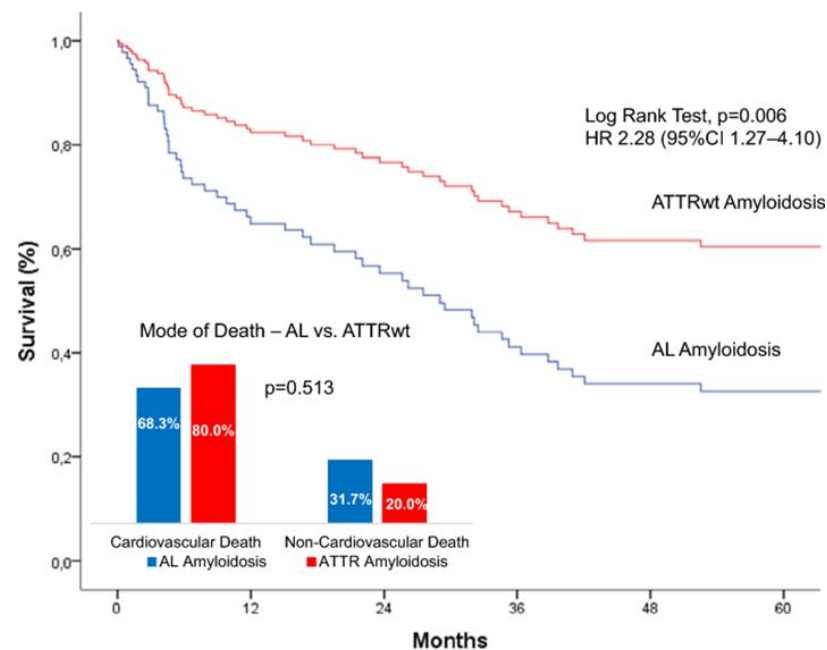
### Lokalno kopičenje



# Preživetje: Amyloidoza lahkih verig (AL) vs. starostna ATTR-CM



## Pomembna razlika v prognozi!



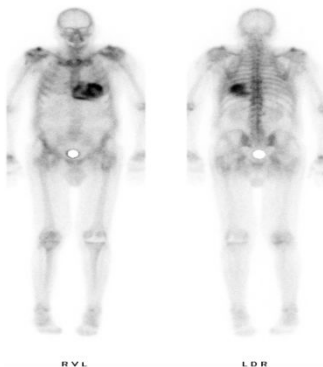


# Starostna (wt)ATTR-CM: kako postaviti diagnozo?

## Simptomi in znaki srčnega popuščanja



## Scintigrafija skeleta



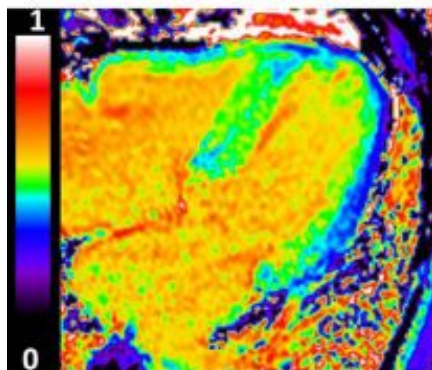
## UZ srca



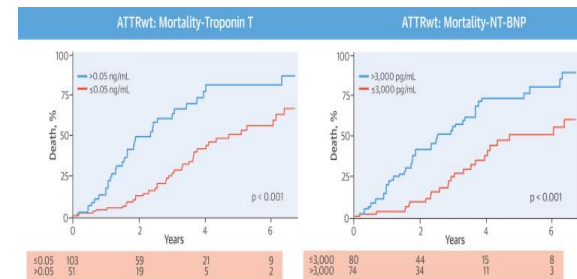
## Anamneza sindroma karpalnega kanala



## MR srca



## Biomarkerji



# wtATTR-CM: UZ najdbe



Koncentrična zadebelitev sten

Diastolična disfunkcija levega prekata

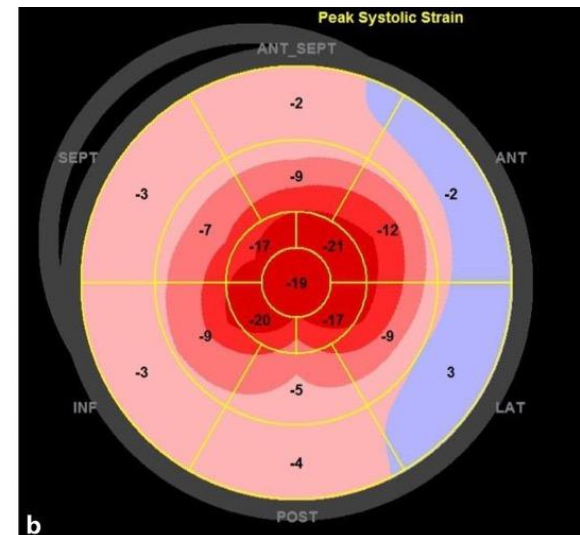
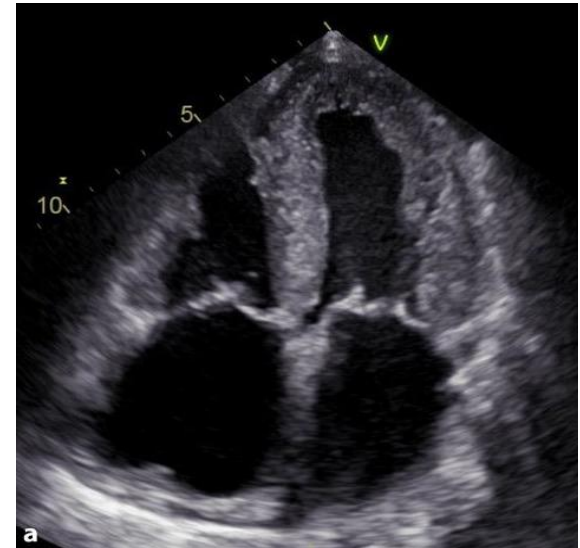
Perikardialni izliv

Povečana preddvora

Zadebeljen interatrijski septum

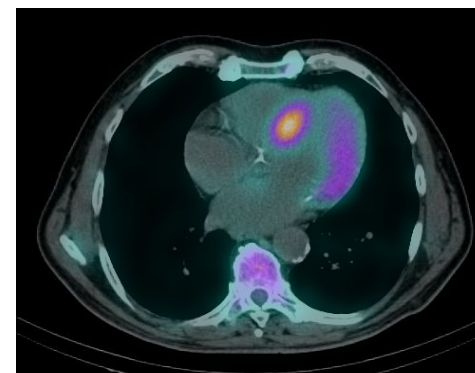
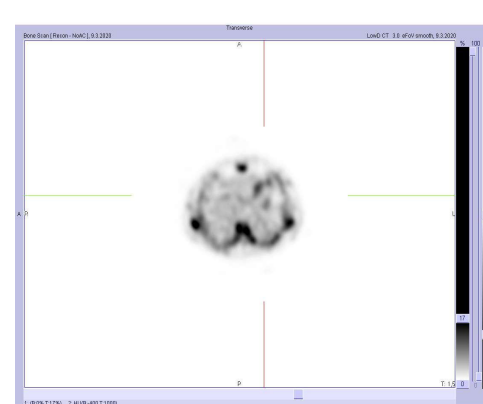
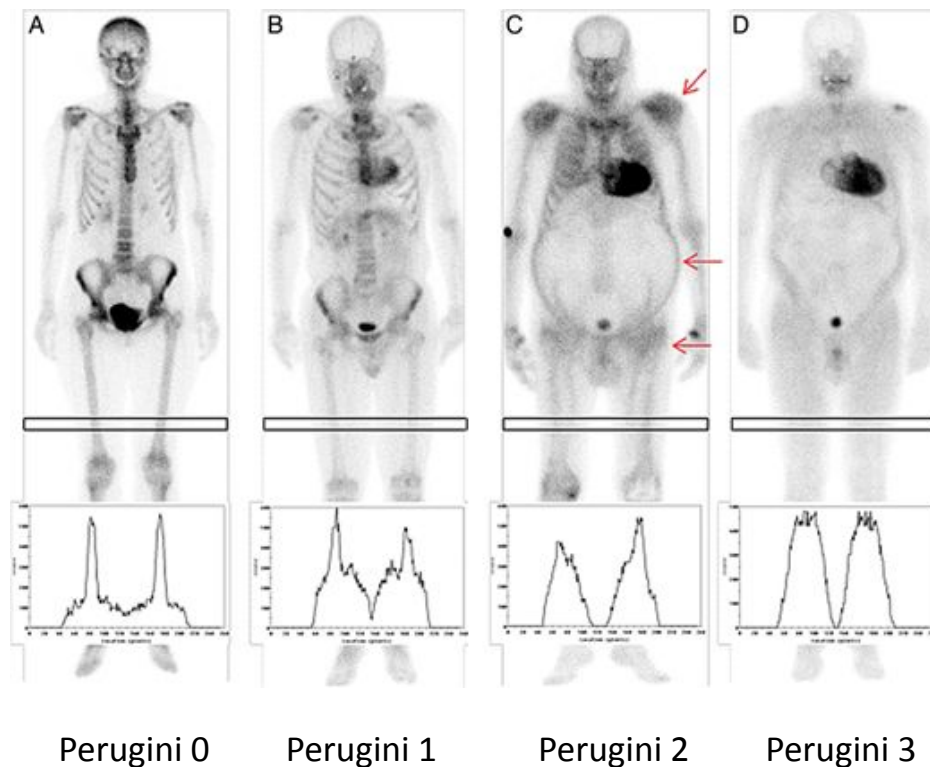
Znižane hitrosti tkivnega doplerja ( $S'$ ,  $E'$ ,  $A'$ )

**UZ točkovno sledenje:** „apical sparing“ - ohranjena vzdolžna deformacija apikalnih segmentov





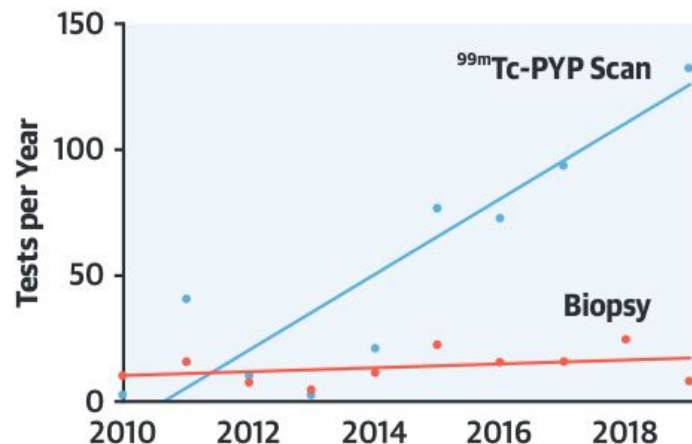
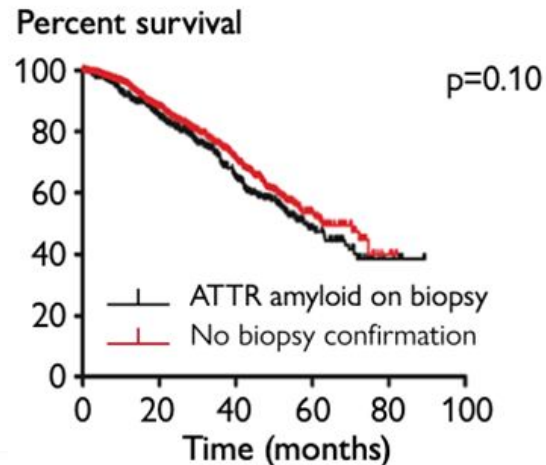
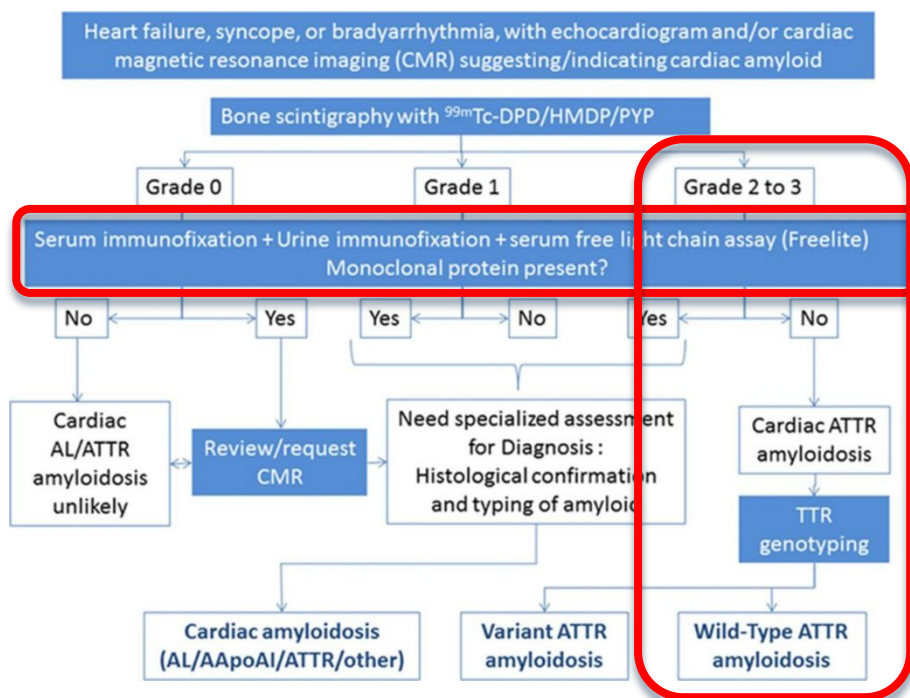
# wtATTR-CM: Scintigrafija skeleta - SPECT/CT



# Postavitev diagnoze wtATTR-CM Algoritem



V več kot >70% diagnoza postavljena brez potrebe po biopsiji



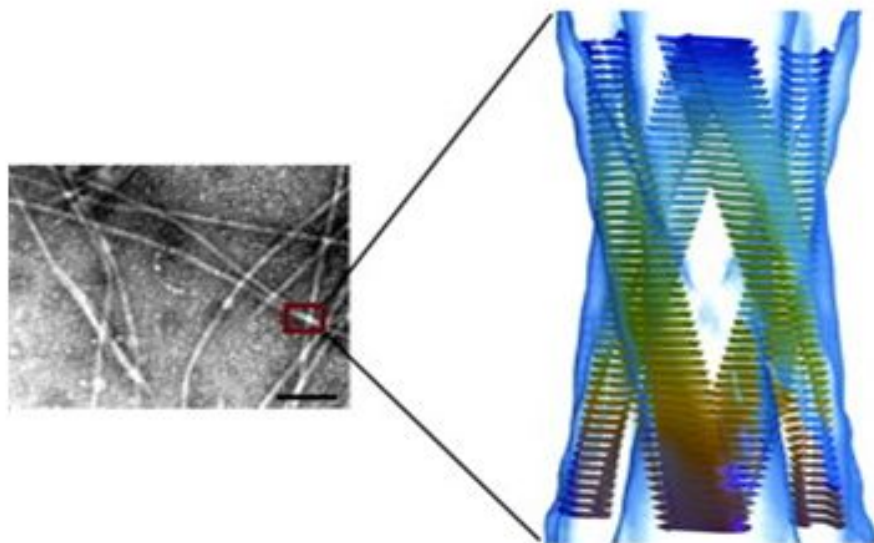


## Od prvega opisa amiloidoze do ...

Amiloid = starch

latin - *amylum*,

greek - ἄμυλον *amylon*

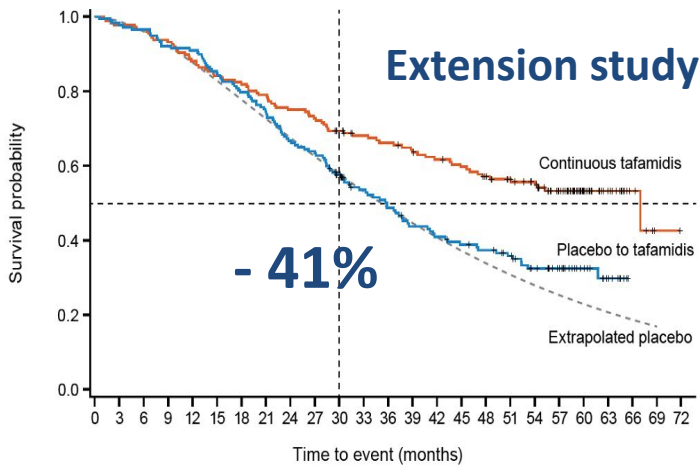
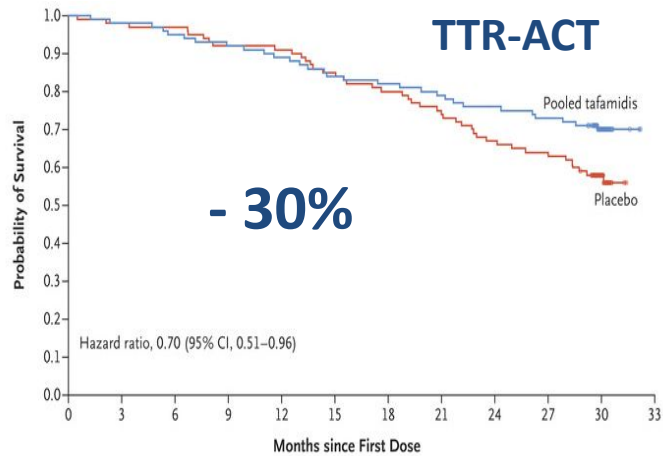


Rudolf Virchow

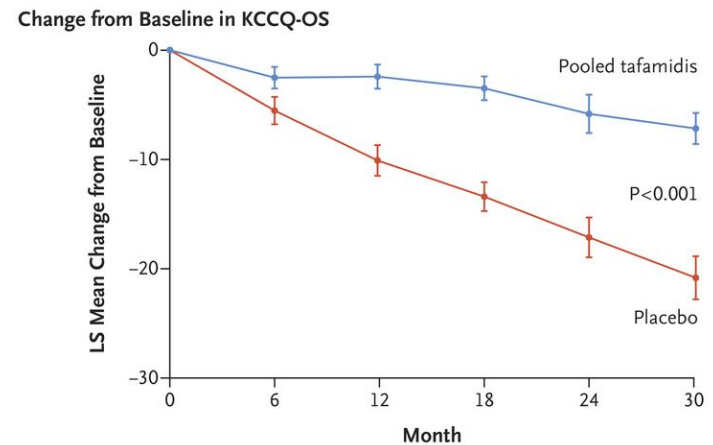
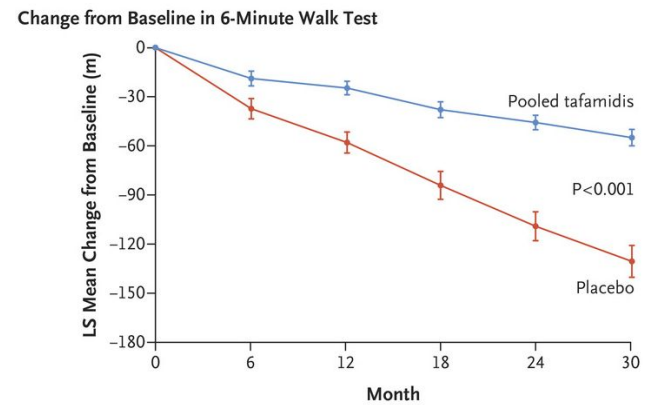
# ...zdravljenja ATTR-CM s tafamidisom



## Vpliv na preživetje



## Vpliv na kvaliteto življenja



# 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)

With the special contribution of the Heart Failure Association (HFA) of the ESC

## Recommendations for treatment of patients with HF and amyloidosis

Tafamidis is recommended in patients with genetic testing proven **hereditary hTTR-CMP and NYHA class I or II symptoms** to reduce symptoms, CV hospitalization and mortality.

**I**

**B**

Tafamidis is recommended in patients with **wtTTR-CA and NYHA class I or II symptoms** to reduce symptoms, CV hospitalization and mortality.

**I**

**B**

# Ambulanta za infiltrativne bolezni in amiloidozo srca

## Značilnosti bolnikov



	<b>wtATTR- CM</b>	<b>vATTR- PN/CM</b>	<b>AL- CM</b>
All patients (n)	148	5	42
Deceased (n, %)	22 (15%)	1 (20%)	12 (28%)
Heart Tx (n, %)	0 (0%)	1 (20%)	3 (7%)
In diagnostic process (n)	4	1	3
Male (n, %)	115 (78%)	2 (40%)	27 (65%)
Age (years)	79±6	46±11	68±10
Carpal tunnel syndrome (n, %)	93 (63%)	1 (20%)	4 (9%)
Latency between CTS and ATTR-CM (years)	9.3±3.6	NA	NA

# Ambulanta za infiltrativne bolezni in amiloidozo srca







## Bolniki na tafamidisu



	wtATTR- CM	mATTR- CM
Patients currently monitored (n)	126	3
NYHA I (n, %)	8 (6%)	3 (100%)
NYHA II (n, %)	79 (63%)	0 (0%)
NYHA III (n, %)	25 (20%)	0 (0%)
NYHA IV (n, %)	14 (11%)	0 (0%)
On Tafamidis (n, %)	84 (67%)	3 (100%)
Awaiting Tafamidis initiation (n, %)	3 (2%)	0

# „Standardna“ terapija srčnega popuščanja pri bolnikih s **starostno ATTR–CM**



	<i>Yes</i>	<i>Sometimes</i>	<i>No</i>
Diuretics ± aldosterone antagonists			
Renin-angiotensin system inhibitors			
Beta-adrenoreceptor blockers			
Alpha-1-adrenoreceptor agonists			
Calcium channel blockers			
Digoxin *			

- HFpEF - **SGLT2 inhibitorji**





# Starostna (wt)ATTR-CM: kdaj torej pomisliti?

Screen for ATTR!



+ ≥1 of the following Red-flags

Category	Red-flags
Demographic	Elderly men over the age of 60 years
Family history	Progressive neuropathy HF at early age
Clinical history	HFpEF in the absence of hypertension Bilateral carpal tunnel syndrome Lumbar spinal stenosis Newly diagnosed hypertrophic cardiomyopathy over the age of 60 years Low flow aortic valve stenosis Angina despite normal coronary angiogram Repeated episodes of embolic stroke Pacemaker implantation for an advanced atrioventricular block or symptomatic bradycardia
Clinical examination	Signs of right-sided HF Intractable pleural effusions Signs of peripheral neuropathy Orthostatic hypotension
Imaging	Low QRS voltage or pseudo-infarction pattern on ECG Any heart block on ECG Atrial fibrillation on ECG Right ventricular hypertrophy on Echo Biatrial enlargement with normal ventricular chamber size on Echo Atrial septal or cardiac valve thickening on Echo Pericardial effusion on Echo Restrictive filling pattern on Echo Apical sparing pattern on Echo CMR with LGE
Alert signs	Intolerance to standard HF medications: ACE-I, ARB, beta-blockade, CCB, digitalis Symptomatic hypotension or resolution of hypertension in previously hypertensive patients



European Heart Journal (2021) 42, 1554–1568  
doi:10.1093/eurheartj/ehab072

**SPECIAL ARTICLE**  
*Heart failure and cardiomyopathies*

## Diagnosis and treatment of cardiac amyloidosis: a position statement of the ESC Working Group on Myocardial and Pericardial Diseases

Pablo Garcia-Pavia<sup>1,2,3\*</sup>, Claudio Rapezzi<sup>4,5</sup>, Yehuda Adler<sup>6</sup>, Michael Arad<sup>7</sup>,

- HFpEF
- Zadebeljene stene LP(≥ 1,2 cm)
- 1 „red –flag“ sign: cardiac or extracardiac



## ...in kam poslati?

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- **Ambulanta za infiltrativne bolezni in amiloidozo srca**
  - del Programa za napredovalo srčno popuščanje in transplantacije srca, KO za kardiologijo, UKC Ljubljana
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  - izr. prof. dr. Gregor Poglajen, dr.med. (sarkoidoza srca)

# Hvala za pozornost!



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