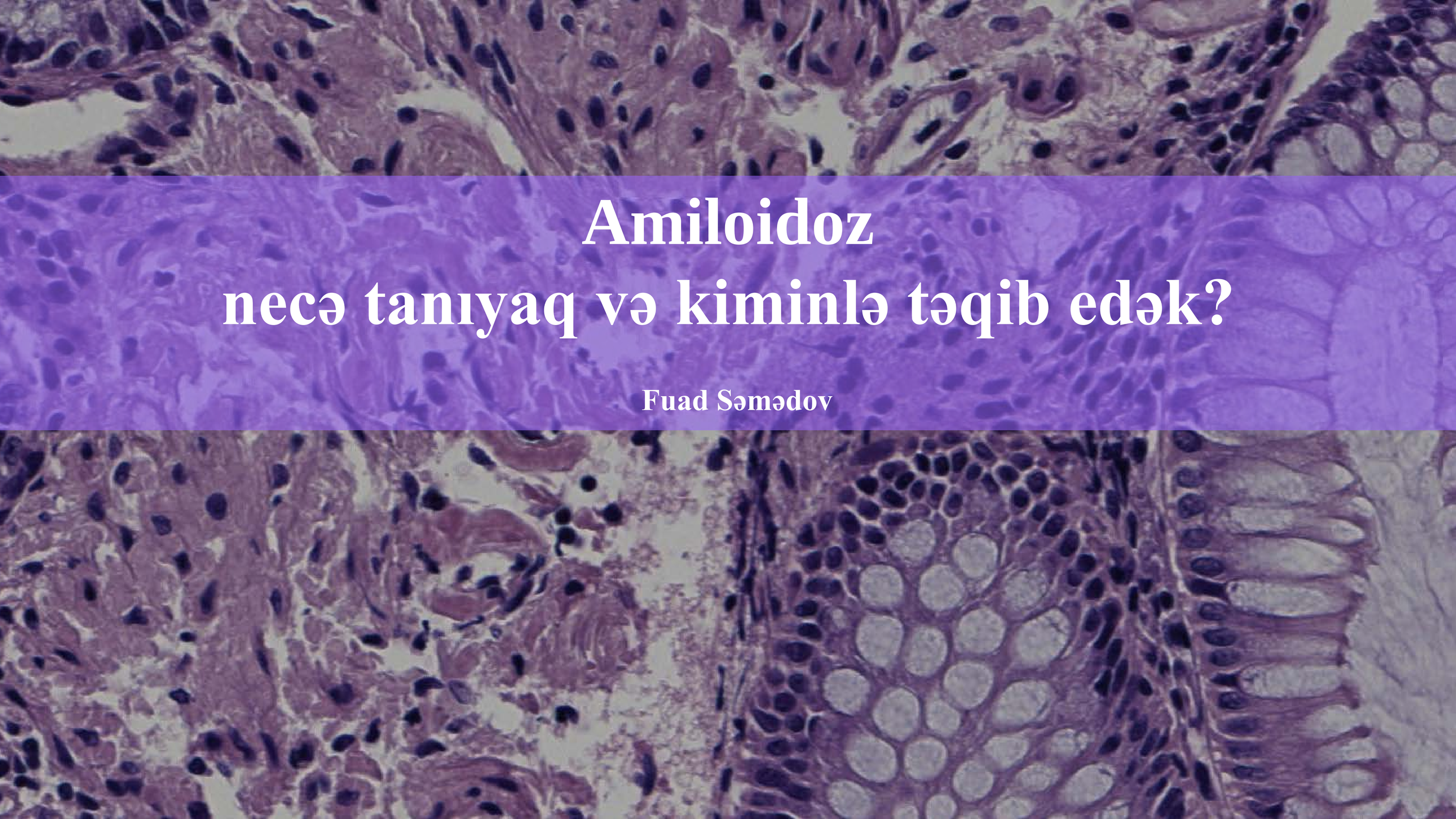


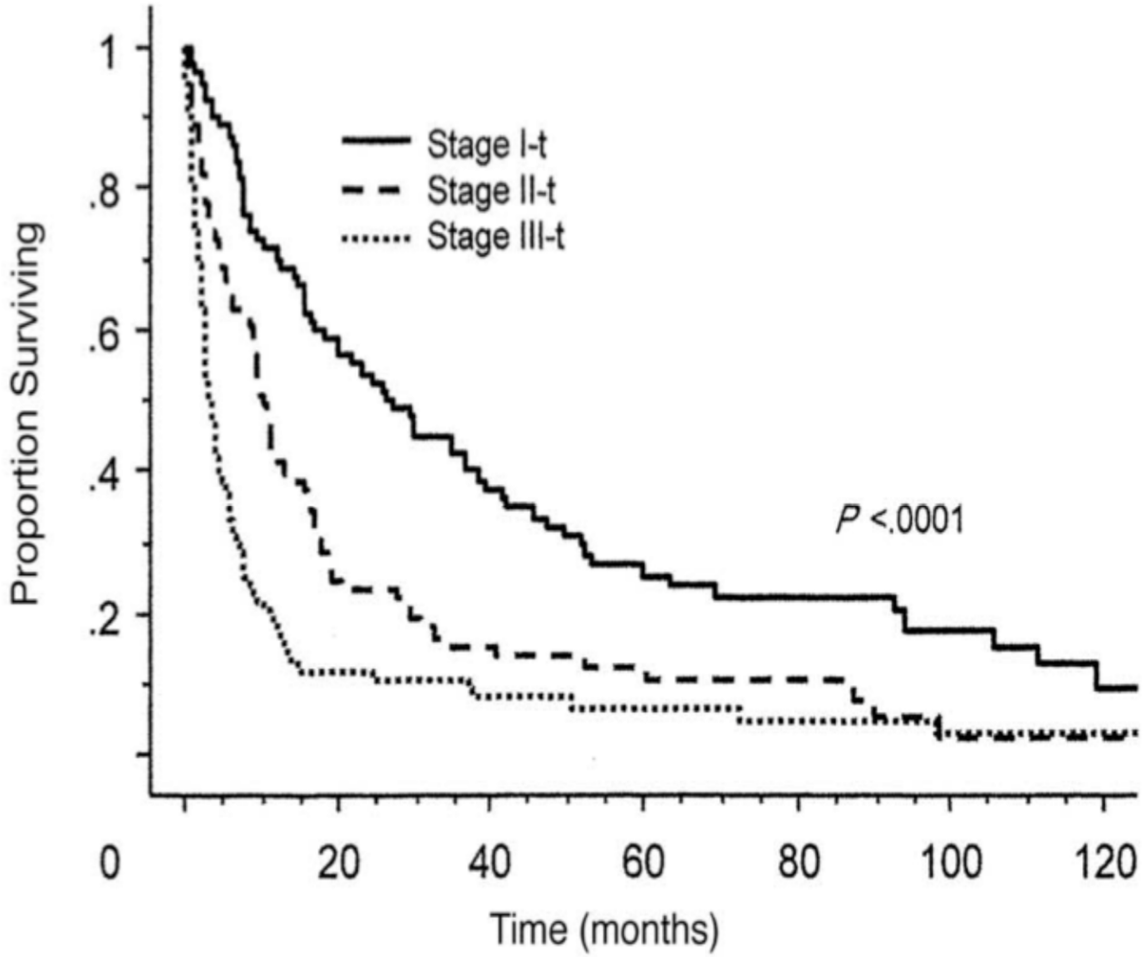
Amiloidoz
necə tanıyaq və kiminlə təqib edək?

Fuad Səmədov

AMİLOİDOZ

AL Amiloidoz prognozu – Mayo 2004 mərhələləndirmə

- Ürəyin vəziyyəti proqnozu təyin edir.
- Mayo klinikası, 1979-2000-ci illər, 261 AL pasienti
- Faktorlar
  - cTnT<0.035ug/L
  - NT-pro-BNP<332ng/L



Dispenzieri J Clin Oncol 2004

The PHYSICAL AND SOCIAL IMPACT on cardiac amyloidosis patients is SIGNIFICANT

76% of patients agreed that due to their cardiac amyloidosis they often had to **PUT THEIR LIFE ON PAUSE** (eg, by avoiding things like):

- **TRAVELING**
- **SWITCHING JOBS**
- **SOCIALIZING**
- **PHYSICAL FITNESS**

Nearly **70%** of patients living with cardiac amyloidosis said they generally **NEVER FEEL WELL**

More than **70%** of patients said cardiac amyloidosis negatively impacts their **ROMANTIC RELATIONSHIPS/INTIMACY** a lot or a great deal

The EMOTIONAL TOLL of cardiac amyloidosis on patients CANNOT BE OVERLOOKED

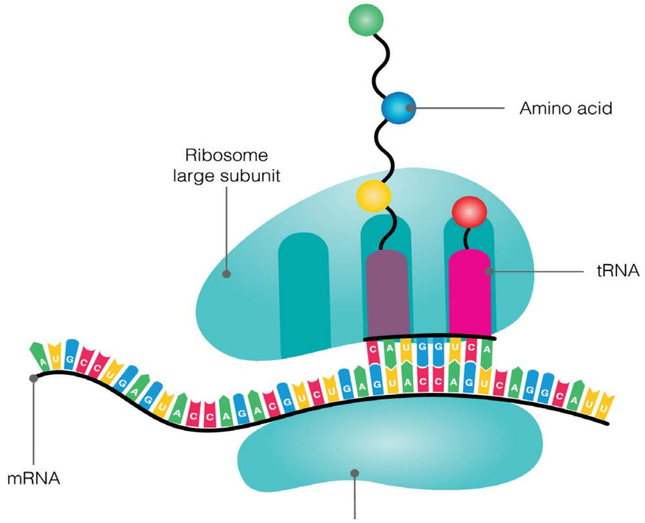
FRUSTRATED
STRESSED
OVERWHELMED

Common words patients used to **DESCRIBE THEIR FEELINGS** toward living with cardiac amyloidosis

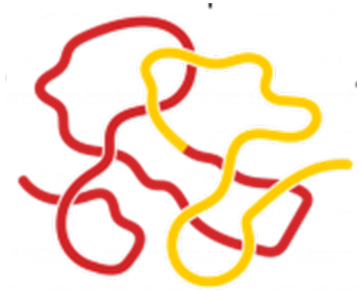
81% of patients reported that **NO ONE UNDERSTANDS** the **NEGATIVE IMPACT** cardiac amyloidosis has on their everyday life

2/3 of patients were either **VERY** or **EXTREMELY CONCERNED** about their current health

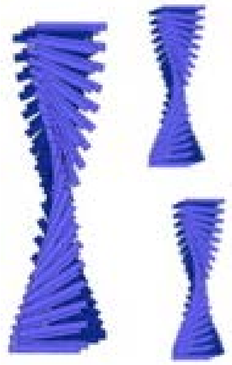
Survey Conducted by Harris Poll, 2018.



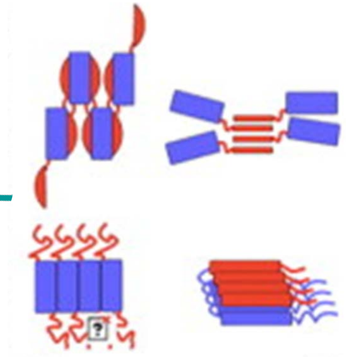
Düzgün qatlanmış, funksional zülal



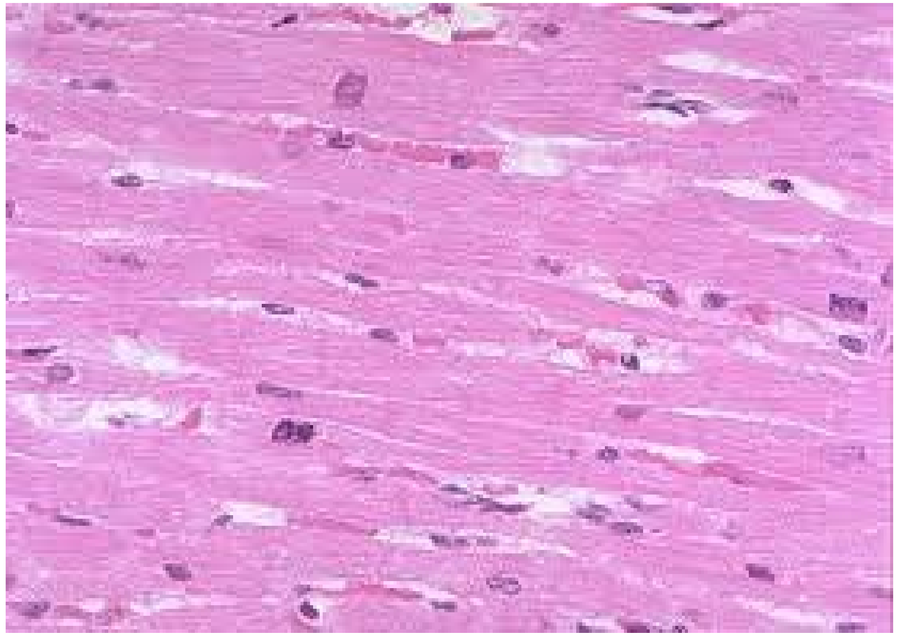
Düzgün qatlanmamış, toksik zülal



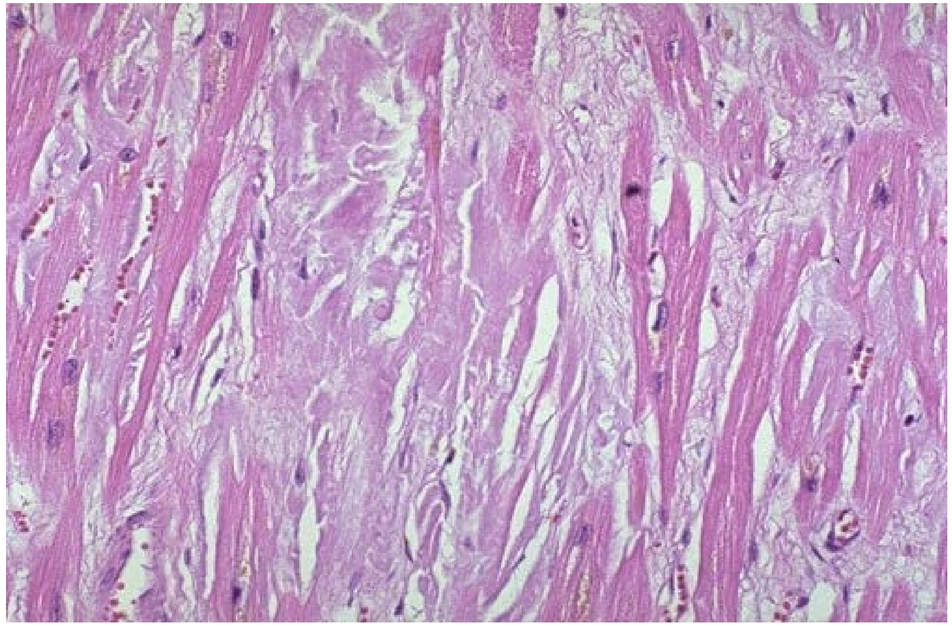
Amiloid fibril

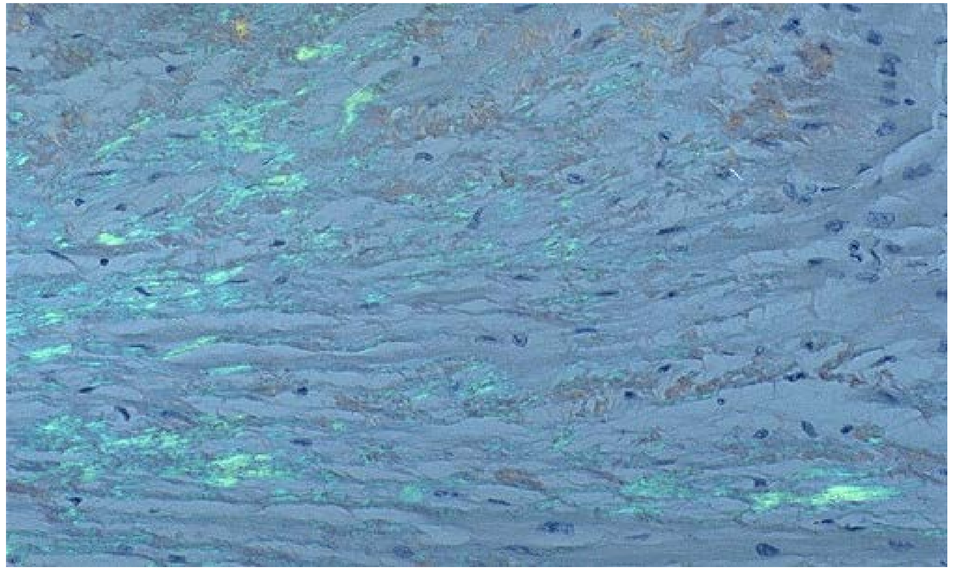


Agregat düzümü β-struktur

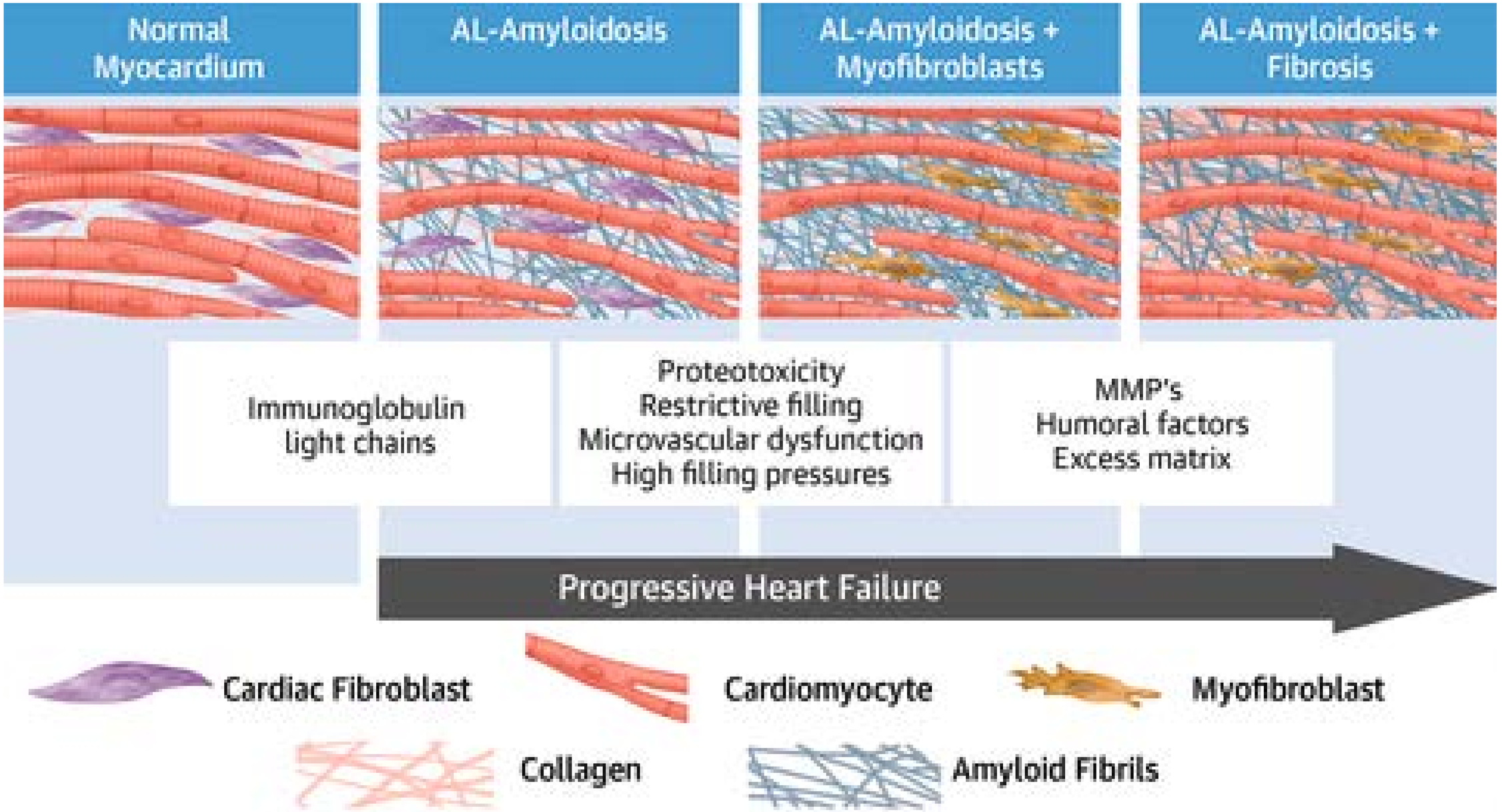


VS





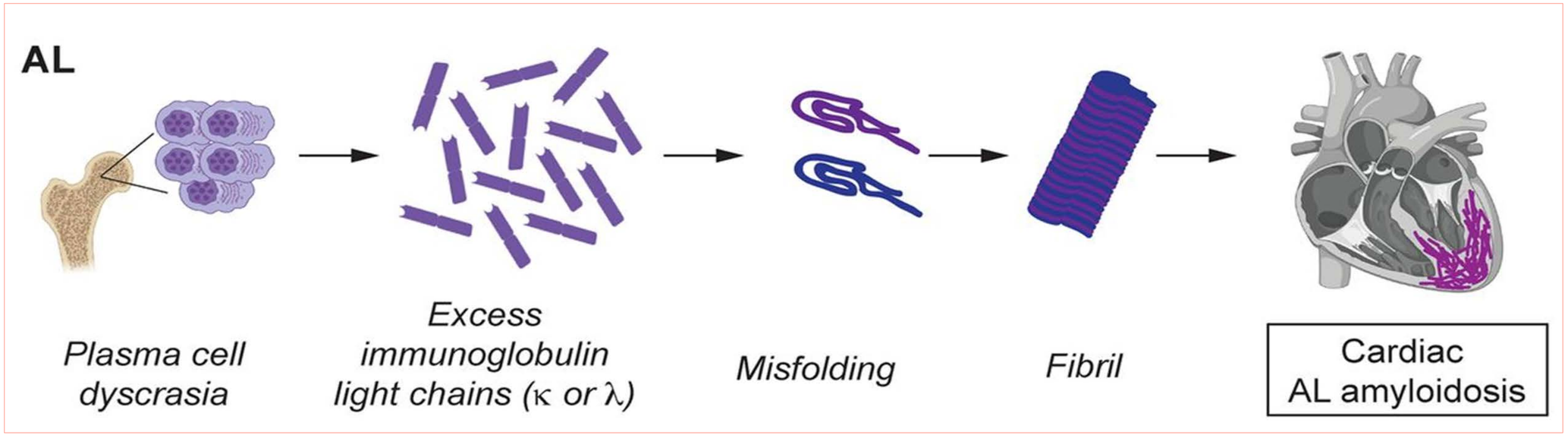
https://webpath.med.utah.edu/CVHTML/CV073.html

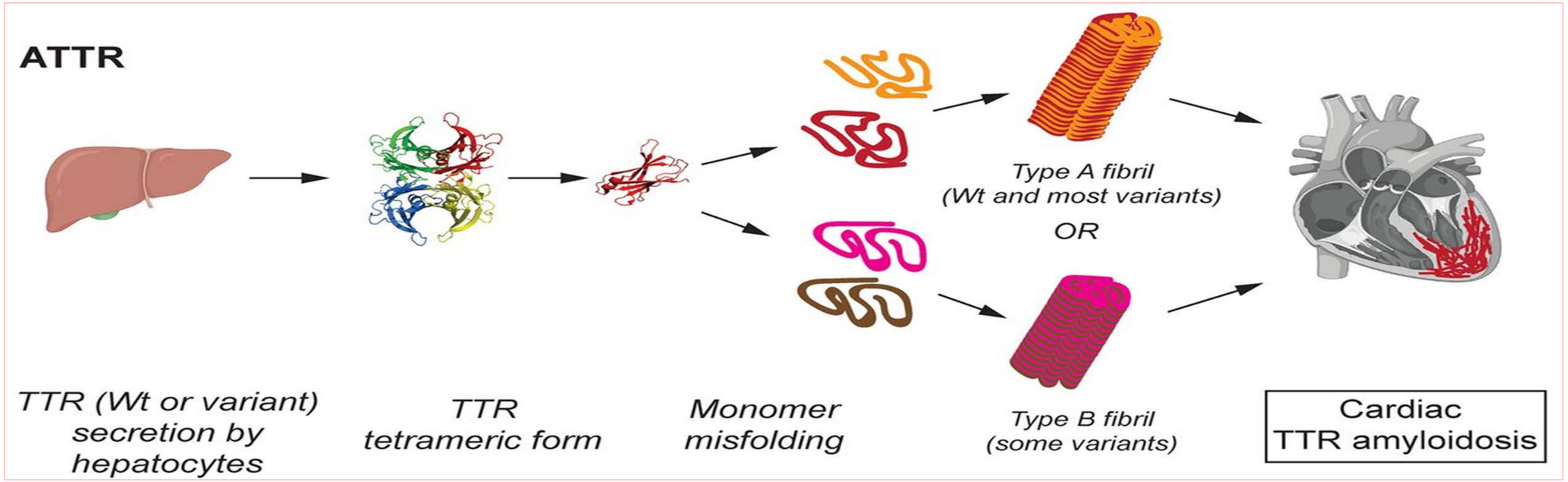


J Am Coll Cardiol Img. 2022 Nov, 15 (11) 1971–1973

Amyloid protein	Precursor	Systemic (S) or localized, organ restricted (L)	Syndrome or involved tissues
AL	Immunoglobulin light chain	S, L	Primary
			Myeloma-associated
AH	Immunoglobulin heavy chain	S, L	Primary
			Myeloma-associated
Aβ_2M	β_2-microglobulin	S	Hemodialysis-associated
		L?	Joints
ATTR	Transthyretin	S	Familial
			Senile systemic
		L?	Tenosynovium
AA	(Apo)serum AA	S	Secondary, reactive
AApoAI	Apolipoprotein AI	S	Familial
		L	Aorta, meniscus
AApoAII	Apolipoprotein AII	S	Familial
AApoAIV	Apolipoprotein AIV	S	Sporadic, associated with aging
AGel	Gelsolin	S	Familial (Finnish)
ALys	Lysozyme	S	Familial
AFib	Fibrinogen α-chain	S	Familial
ACys	Cystatin C	S	Familial
ABri	ABriPP	S	Familial dementia, British
ALect2	Leukocyte chemotactic factor 2	S	Mainly kidney
ADan*	ADanPP	L	Familial dementia, Danish
Aβ	Aβ protein precursor (AβPP)	L	Alzheimer's disease, aging
APrP	Prion protein	L	Spongioform encephalopathies
ACal	(Pro)calcitonin	L	C-cell thyroid tumors
AIAPP	Islet amyloid polypeptide**	L	Islets of Langerhans
			Insulinomas
AANF	Atrial natriuretic factor	L	Cardiac atria
APro	Prolactin	L	Aging pituitary
			Prolactinomas
AIns	Insulin	L	Iatrogenic
AMed	Lactadherin	L	Senile aortic, media
AKer	Kerato-epithelin	L	Cornea, familial
ALac	Lactoferrin	L	Cornea
AOaap	Odontogenic ameloblast-associated protein	L	Odontogenic tumors
ASemI	Semenogelin I	L	Vesicula seminalis

*Proteins are listed, when possible, according to relationship. Thus, apolipoproteins are grouped together, as are polypeptide hormones.
†ADan comes from the same gene as ABri.
‡Also called 'amylin'.


AL
Plasma cell dyscrasia
Excess immunoglobulin light chains (κ or λ)
Misfolding
Fibril
Cardiac AL amyloidosis


ATTR
TTR (Wt or variant) secretion by hepatocytes
TTR tetrameric form
Monomer misfolding
Type A fibril (Wt and most variants)
OR
Type B fibril (some variants)
Cardiac TTR amyloidosis

Diaqnoza qədər keçən yol

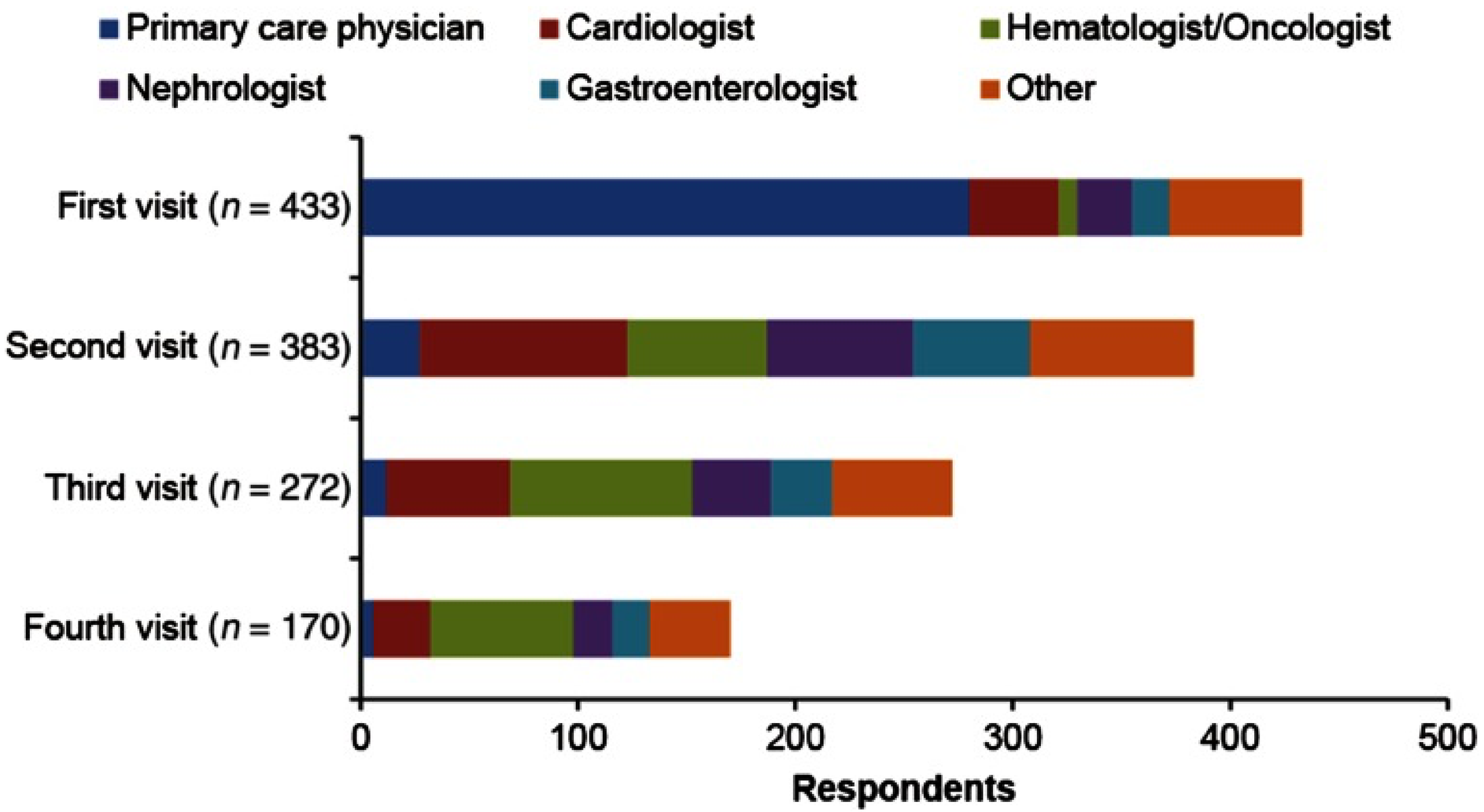
Time from initial symptoms to diagnosis of amyloidosis, *n* (%), *n* = 459	
<6 months	171 (37.3)
6–12 months	118 (25.7)
12–18 months	44 (9.6)
18–24 months	34 (7.4)
2–3 years	44 (9.6)
>3 years	48 (10.5)

Different physicians visited before establishment of a diagnosis, *n* (%), *n* = 459	
1	35 (7.6)
2	108 (23.5)
3	93 (20.3)
4	77 (16.8)
≥5	146 (31.8)

Specialty of diagnosing physician, *n* (%), *n* = 402	
Hematologist/oncologist	137 (34.1)
Nephrologist	91 (22.6)
Cardiologist	75 (18.7)
Gastroenterologist	32 (8.0)
Neurologist	19 (4.7)
Primary care physician	16 (4.0)
Other[a]	32 (8.0)

Lousada, Adv Ther. 2015; 32(10): 920–928.

Diaqnoza qədər keçən yol

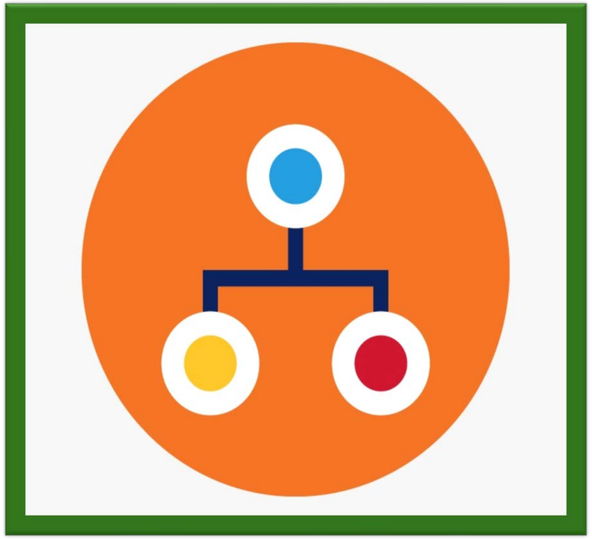


Lousada, Adv Ther. 2015; 32(10): 920–928.

Diaqnoz üçün 3 əsas mərhələ

Amiloidozu ağla gətir!
Şübhələn!

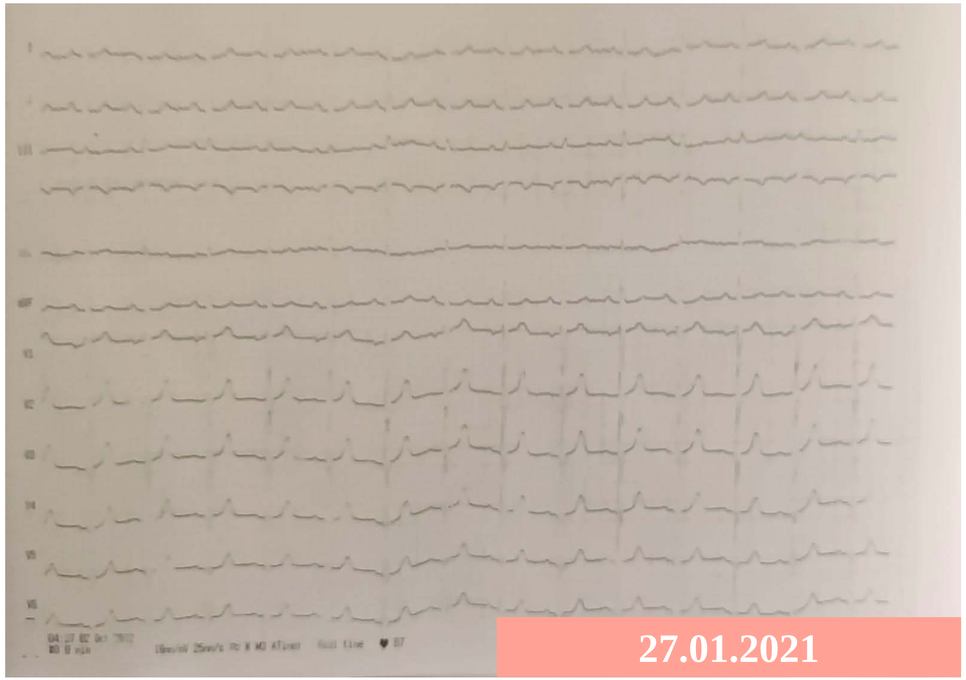
Vaxt itirmədən
təsdiq/inkar et!



Tipi müəyyənləşdir və
müalicəyə başla!

Kardiak amiloidoz şübhəsi oyadan əlamətlər (RED FLAGS)	
Sol mədəcik divar qalınlığı >12mm + EKQ-də aşağı voltajlı QRS kompleksləri	
ExoKQ – sağ mədəcik sərbəst divarının, qapaqların qalınlaşması	
KAQ - adekvat izahı olmadan troponinin davamlı yüksək olması və ya troponin yüksəkliyi ilə təkrari müraciət	
İzah oluna bilməyən AV blokada, AF	
B-blokator və ya AÇF inhibitorlarına dözümsüzlük	
HT anamnezi olan pasientdə AT dəyərinin aşağı/normal olması	
İkitərəfli karpal tunnel sindromu, adətən əməliyyat tələb edən	
AL amiloidoz	**ATTR amiloidoz**
HFpEF + nefrotik sindrom	>60yaş kişidə HFpEF + karpal tunnel sind/spinal stenoz anamnezi
Makroglossiya +/- periorbital purpura	Yaşlı insanlarda yeni diaqnoz qoyulmuş HKMP
Ortostatik hipotenziya	Yaşlı insanlarda yeni diaqnoz qoyulmuş LFLG AS
Periferik neyropatiya	Ailədə ATTRm anamnezi
MGUS	

- 1963 təvəllüdlü kişi xəstə
- 2019 fevral – MI – LAD müdaxilə
- Sentyabr 2022 – boğulma, təngnəfəslik, ayaqlarda şişkinlik
- ARNI qəbul etdiyi halda son aylarda dayandırmağa məcbur olub.



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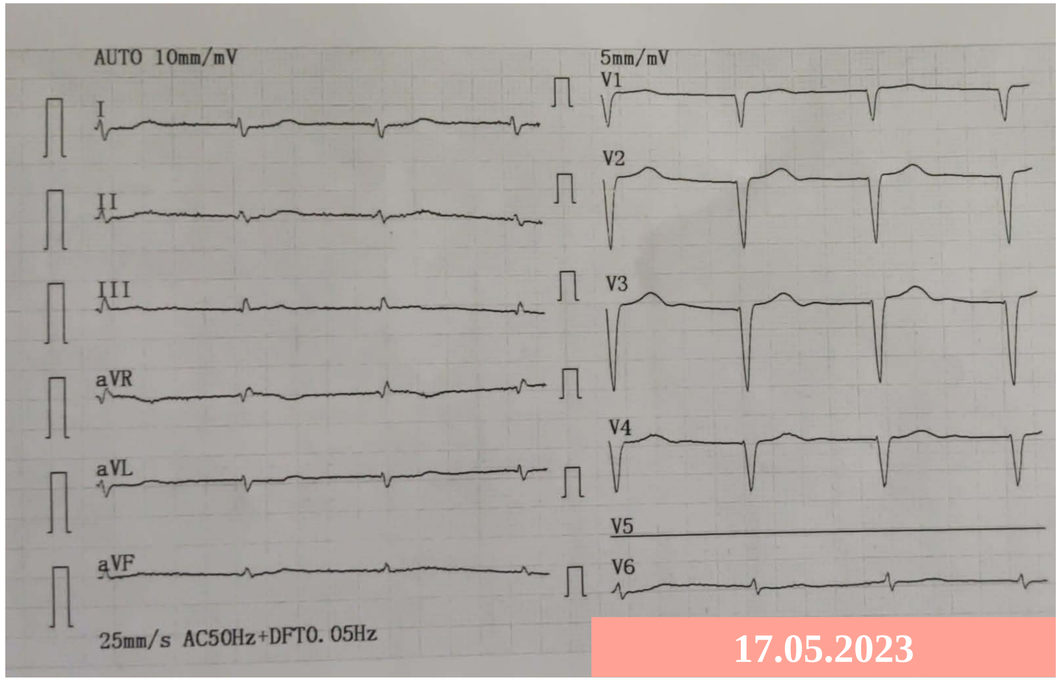
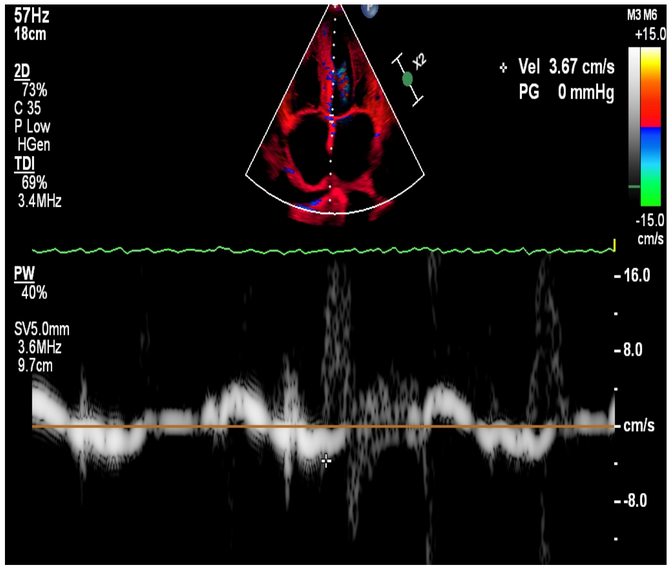
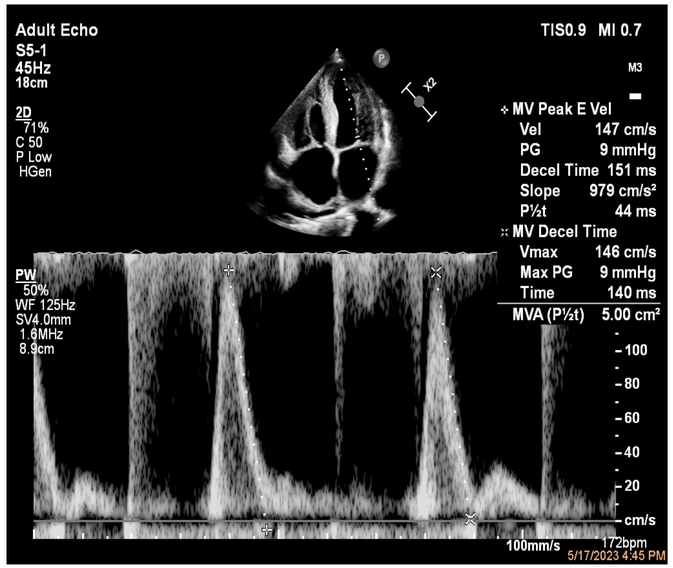
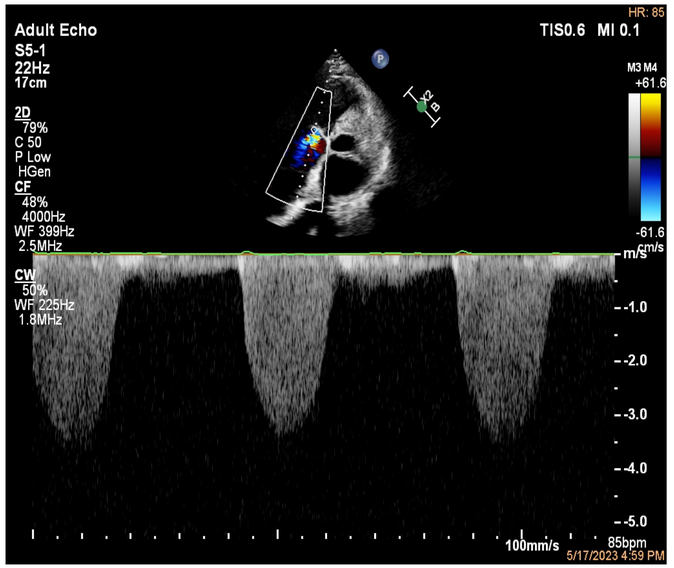


17.05.2023

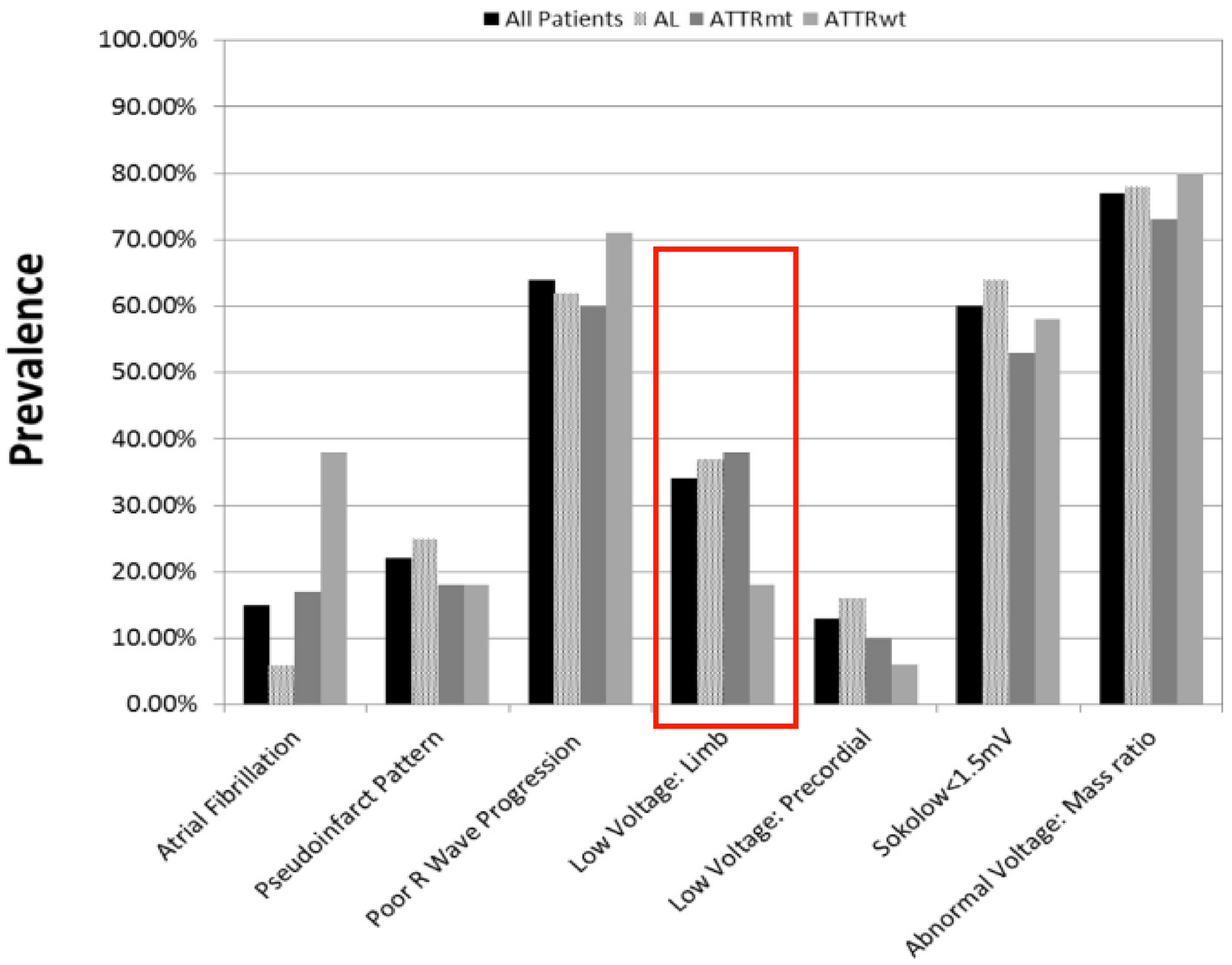

57Hz
18cm
2D
73%
C 35
P Low
HGen
TDI
69%
3.4MHz
M3 M6
+15.0
-15.0
cm/s
Vel 3.67 cm/s
PG 0 mmHg
PW
40%
SV5.0mm
3.6MHz
9.7cm
16.0
8.0
cm/s
-8.0


Adult Echo
S5-1
45Hz
18cm
2D
71%
C 50
P Low
HGen
TIS0.9 MI 0.7
M3
MV Peak E Vel
Vel 147 cm/s
PG 9 mmHg
Decel Time 151 ms
Slope 979 cm/s²
P½t 44 ms
MV Decel Time
Vmax 146 cm/s
Max PG 9 mmHg
Time 140 ms
MVA (P½t) 5.00 cm²
PW
50%
WF 125Hz
SV4.0mm
1.6MHz
8.9cm
100
80
60
40
20
cm/s
100mm/s
172bpm
5/17/2023 4:45 PM

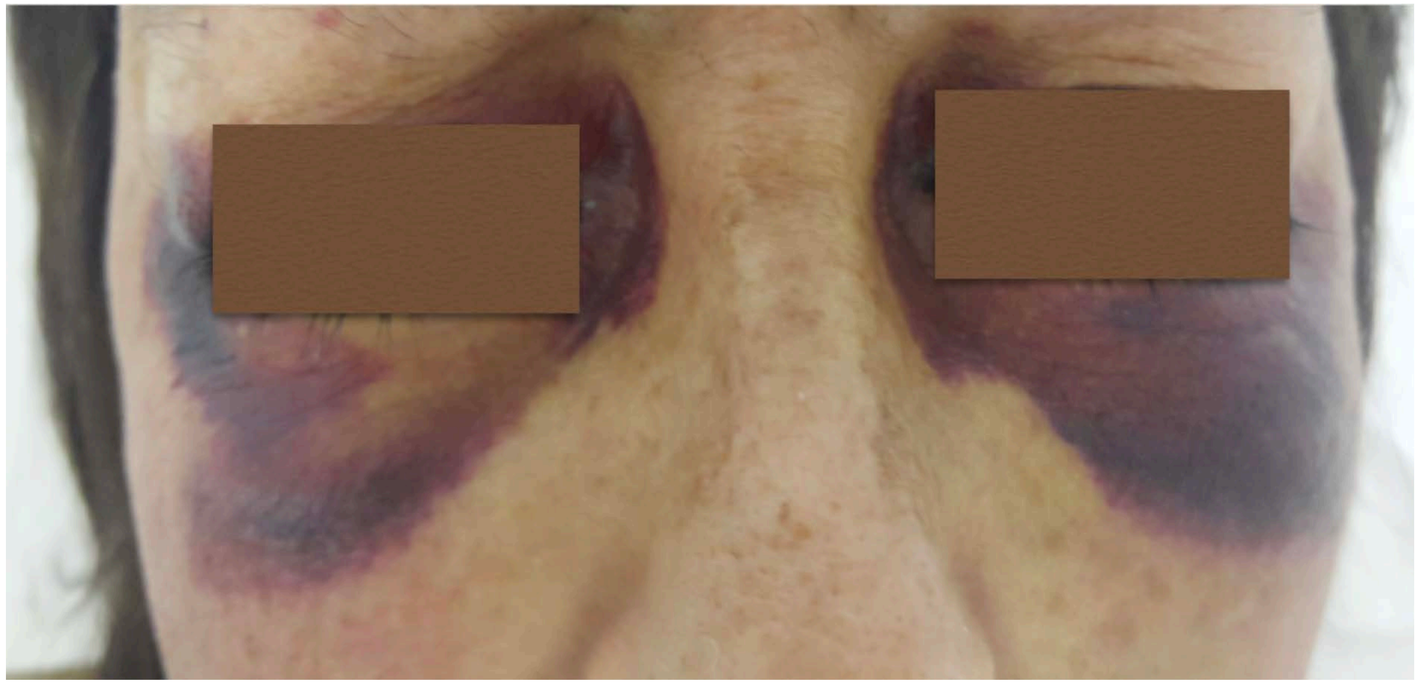

Adult Echo
S5-1
22Hz
17cm
2D
79%
C 50
P Low
HGen
CF
48%
4000Hz
WF 399Hz
2.5MHz
TIS0.6 MI 0.1
HR: 85
M3 M4
+61.6
-61.6
cm/s
m/s
CW
50%
WF 225Hz
1.8MHz
1.0
2.0
3.0
4.0
5.0
100mm/s
85bpm
5/17/2023 4:59 PM

Prevalence and Prognostic Significance of Low QRS Voltage Among the Three Main Types of Cardiac Amyloidosis

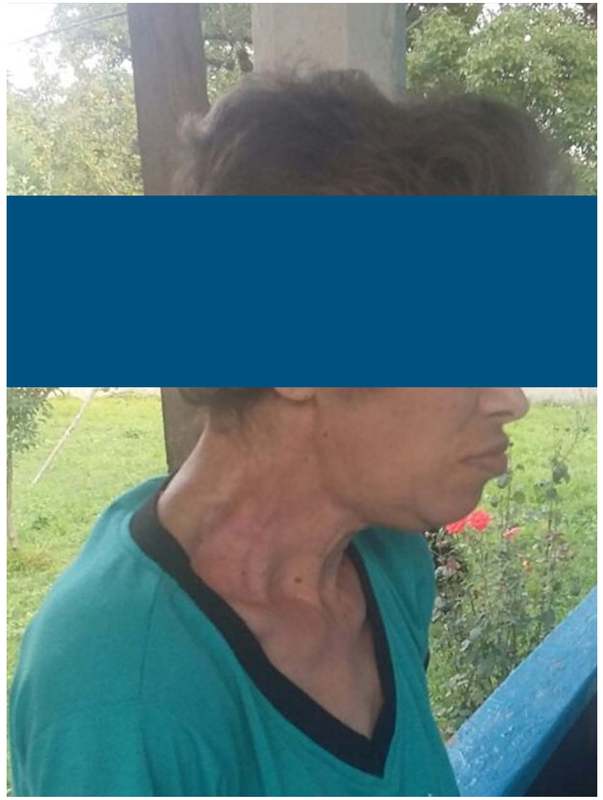
Nicole B. Cyrille, MD[a], Jeff Goldsmith, PhD[b], Julissa Alvarez, MD[c], and Mathew S. Maurer, MD[c,*]

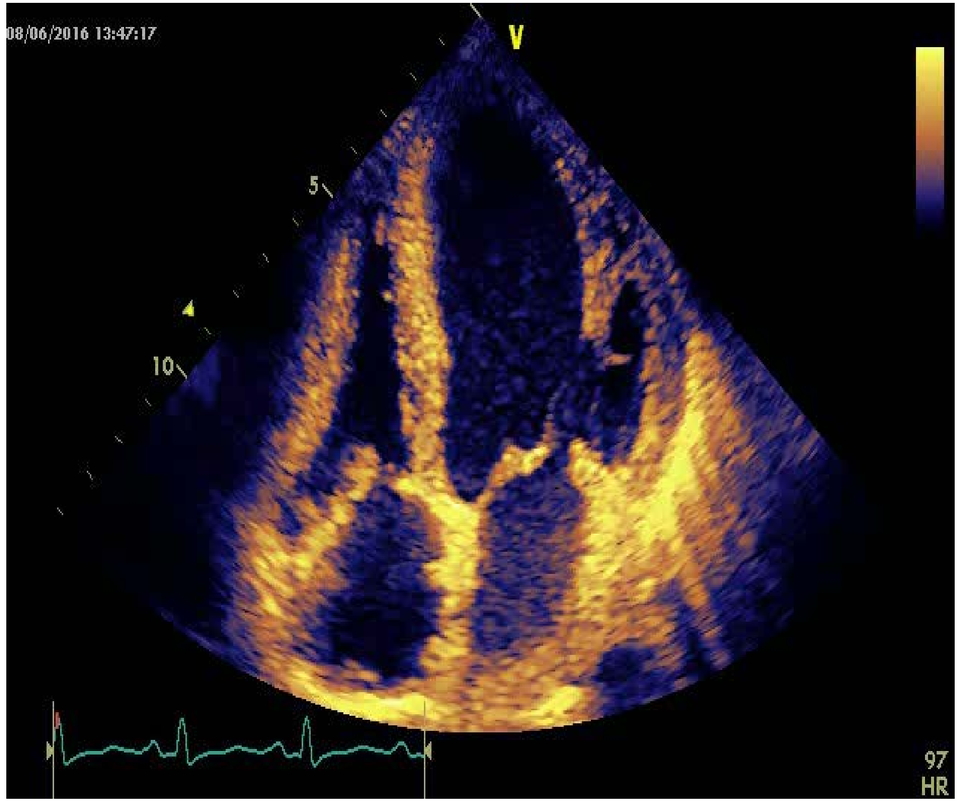


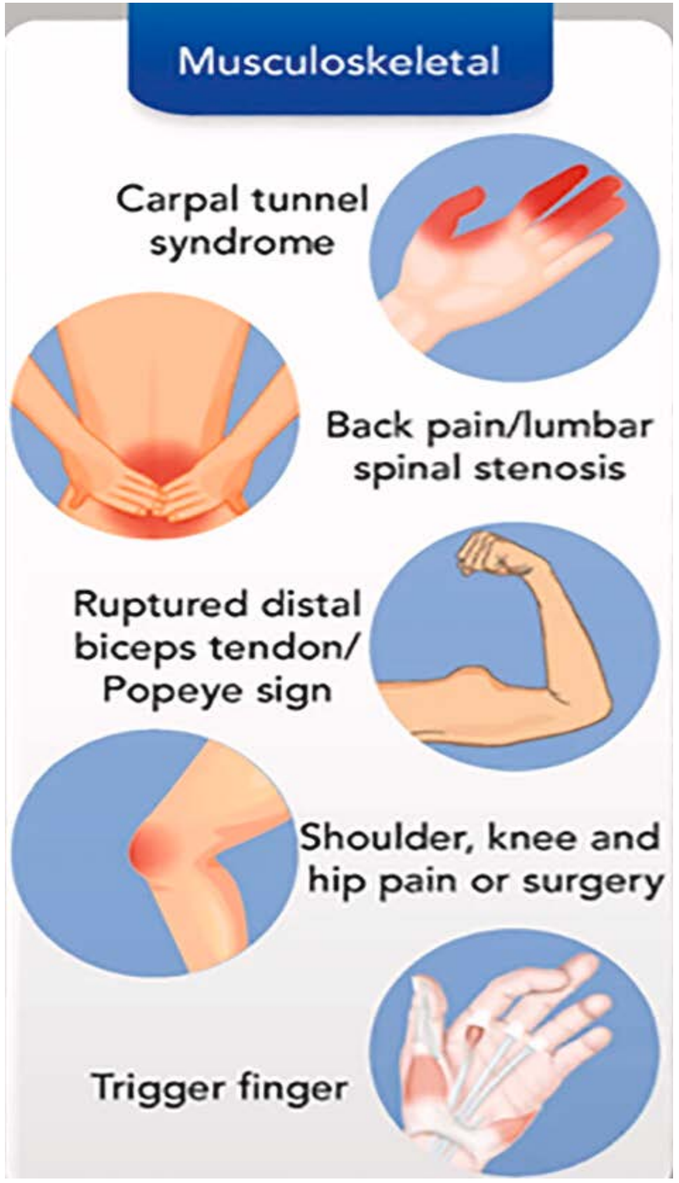
Am J Cardiol 2014 Oct 1;114(7):1089-93



- **AL amiloidoz – damar divarında AL depo, FX qazanılmış defisiti**
- Kəllə əsası sınıqları
- Neyroblastoma




08/06/2016 13:47:17
V
5
10
97
HR



J Am Coll Cardiol. 2022 Sep 6;80(10):967-977. doi: 10.1016/j.jacc.2022.06.026.

Screening for Cardiac Amyloidosis 5 to 15 Years After Surgery for Bilateral Carpal Tunnel Syndrome

Oscar Westin [1], Emil L Fosbøl [2], Mathew S Maurer [3], Birgitte P Leicht [4], Philip Hasbak [5], Anne Kærsgaard Mylin [6], Sara Rørvig [7], Thomas Hartvig Lindkær [7], Helle Hjorth Johannesen [5], Finn Gustafsson [2]

Affiliations + expand

PMID: 36049804 DOI: 10.1016/j.jacc.2022.06.026

Abstract

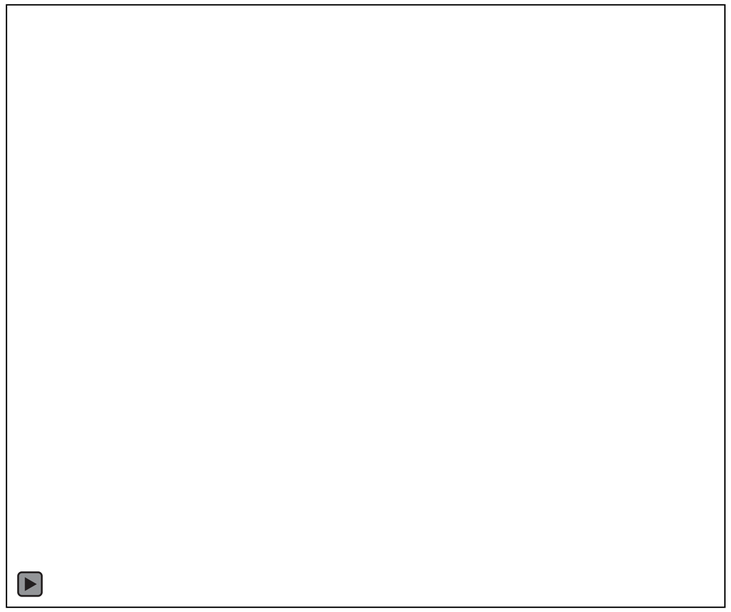
Background: Bilateral carpal tunnel syndrome (CTS) is a common extracardiac manifestation of amyloidosis and usually predates overt cardiac amyloidosis (CA) by several years. Screening studies on patients undergoing CTS surgery have shown a low yield of CA (2.0%), but high prevalence of amyloid in the carpal ligament. The proportion of patients with amyloid in the carpal ligament who later develop CA is unknown.

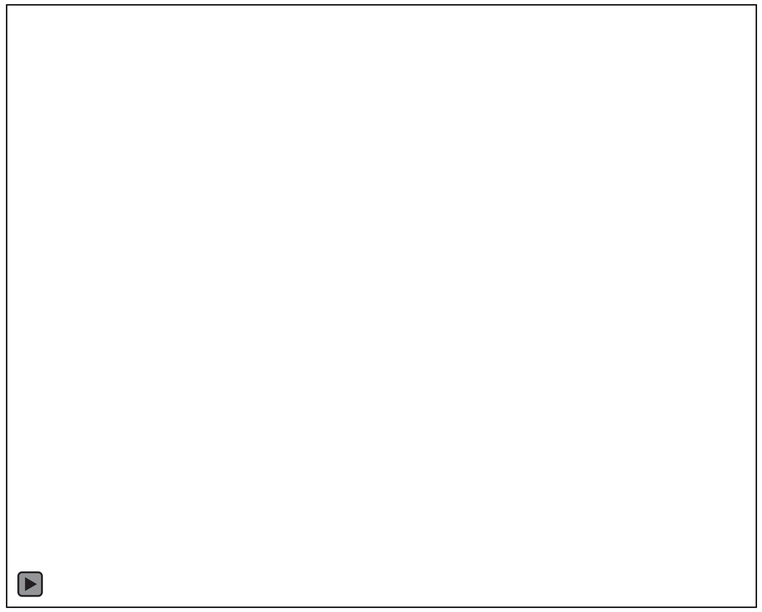
Objectives: The authors sought to investigate the prevalence of undiagnosed CA 5 to 15 years after surgery for bilateral CTS.

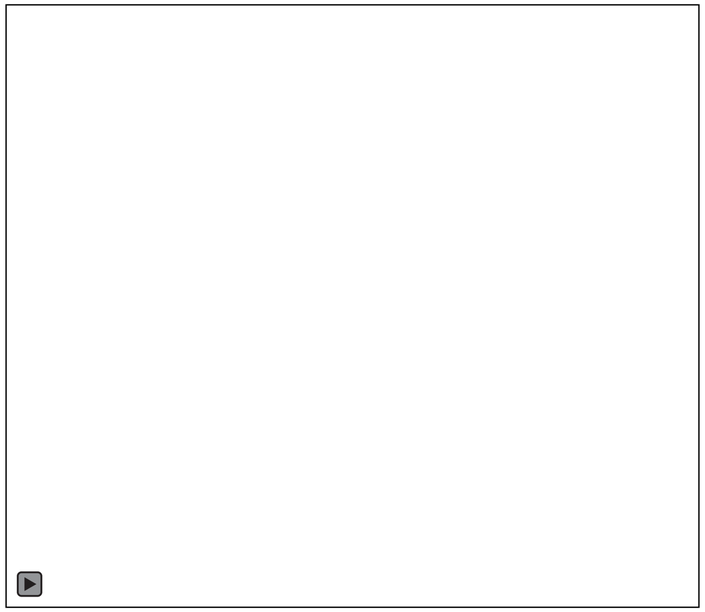
Methods: Using national registries, the authors identified subjects aged 60 to 85 years with prior CTS surgery, where the first procedure on the second wrist was performed 5 to 15 years earlier. Invitations to participate in the study were sent by mail. Per international recommendations, the initial cardiac evaluation included echocardiography, ^{99m}technetium-pyrophosphate scintigraphy, and assessment of monoclonal proteins in serum and urine.

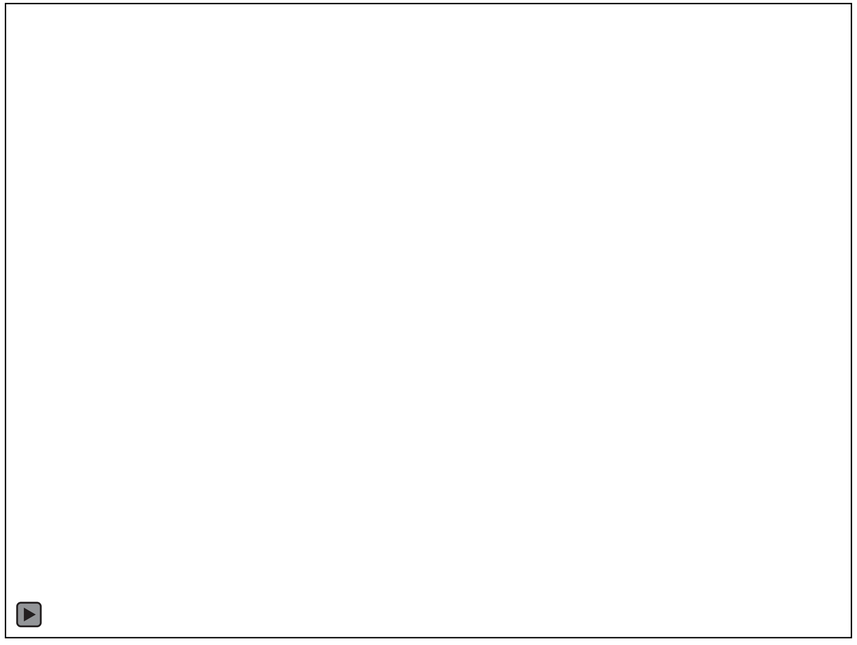
Results: A total of 250 subjects (35.7% of those invited) participated in the study. The median age was 70.4 years, and 50% were female. CA was diagnosed in 12 patients (4.8%; 95% CI: 2.5%-8.2%), and all cases were wild-type transthyretin amyloidosis (ATTRwt). The prevalence of ATTRwt in men was 8.8% (95% CI: 4.5%-15.2%; n = 11), and 21.2% (95% CI: 11.1%-34.7%) in male subjects ≥70 years with a BMI <30 kg/m^2. All but 2 patients diagnosed with ATTRwt were in the lowest disease severity score (Mayo score).

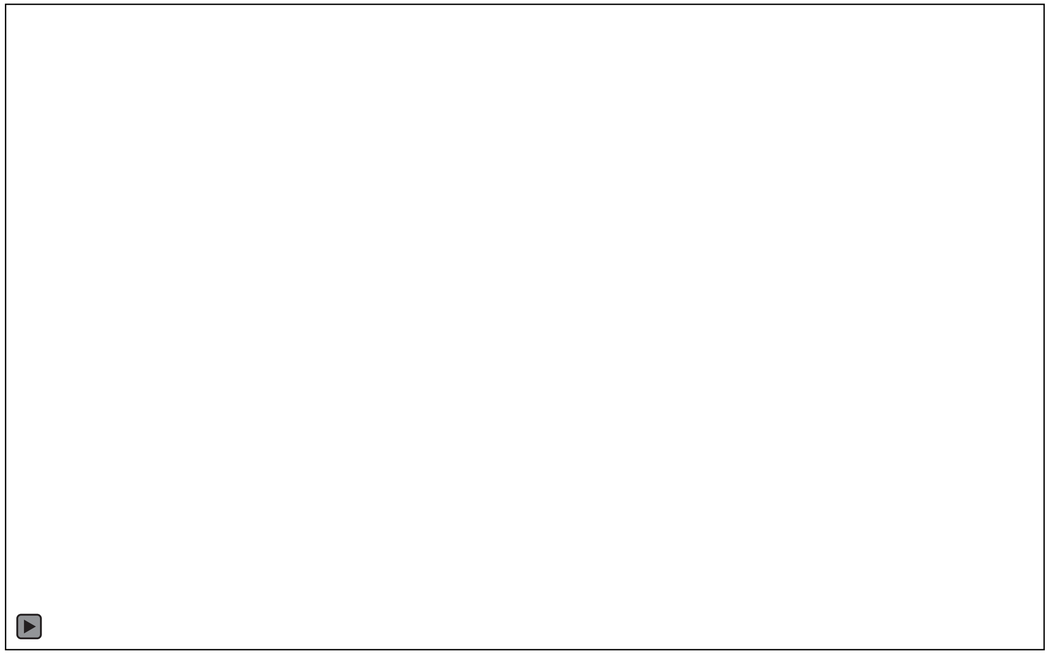
Conclusions: Screening for CA in patients with prior surgery for bilateral CTS finds approximately 5% with early-stage transthyretin CA. The clinical yield was higher (>1 in 5) when focusing on nonobese men ≥70 years, showing potential for systematic screening.







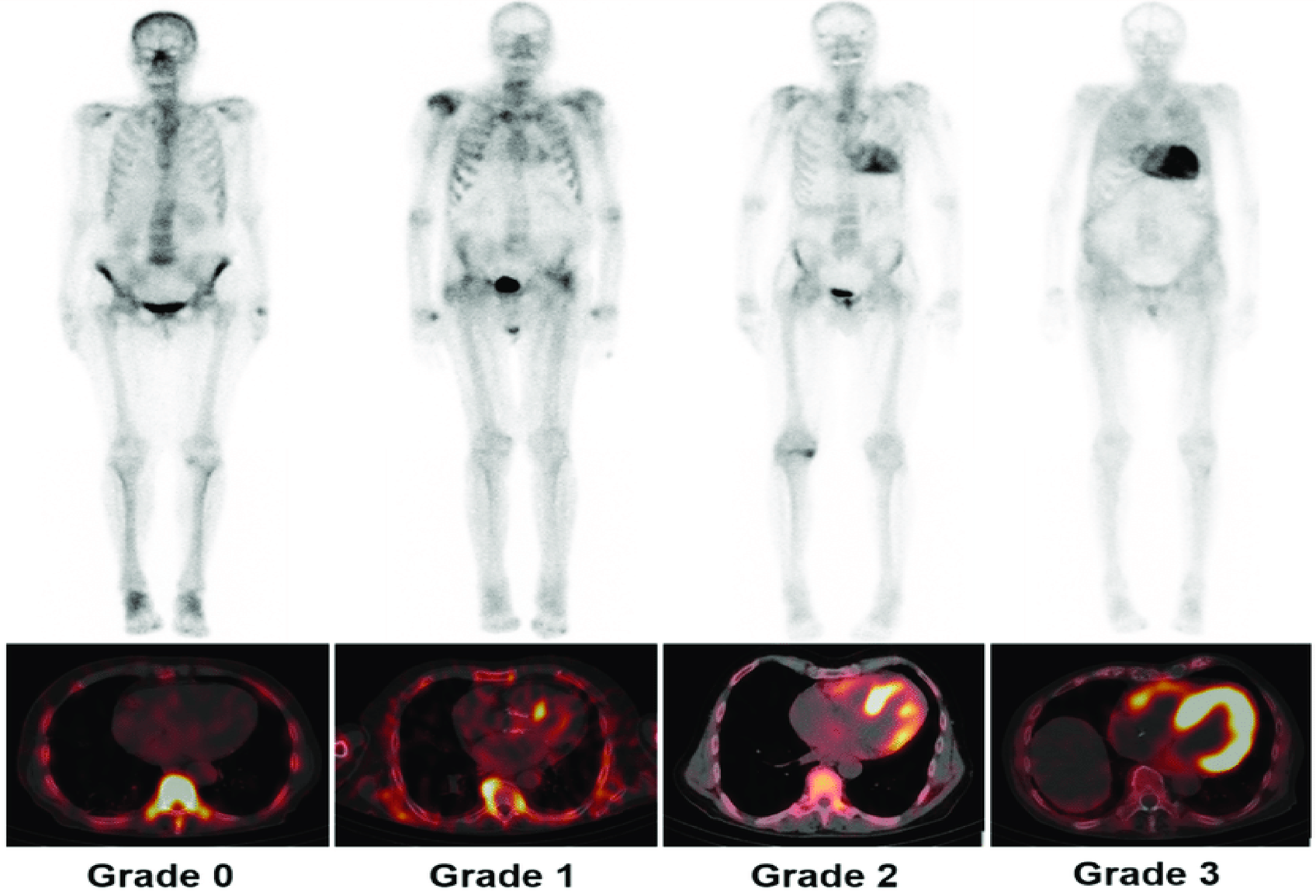




ATTR amiloidoz

- ATTRwt - yaşlı kişilərdə - gec başlayan hipertrofik restriktiv Kmp,
- ATTRwt - KMP-dən 5-15 il əvvəl başlayan bilateral KTS və spinal steno (50%)
- ATTRm - TTR genində nöqtə mutasiyalar - polineyropatiya, kardiomiopatiya
- ATTRwt - median sağqalma 4 il. ATTRm - mutasiyadan asılıdır.
- > 85 yaş autopsiya olunmuş şəxslərin 25%-də ATTRwt
- >60 yaş + HFPF diaqnozu ilə hospitalize xəstələrin 13%-də ATTRwt (^{99m}TcPYP)

Sümük ssintiqrafiyası (Perugini)

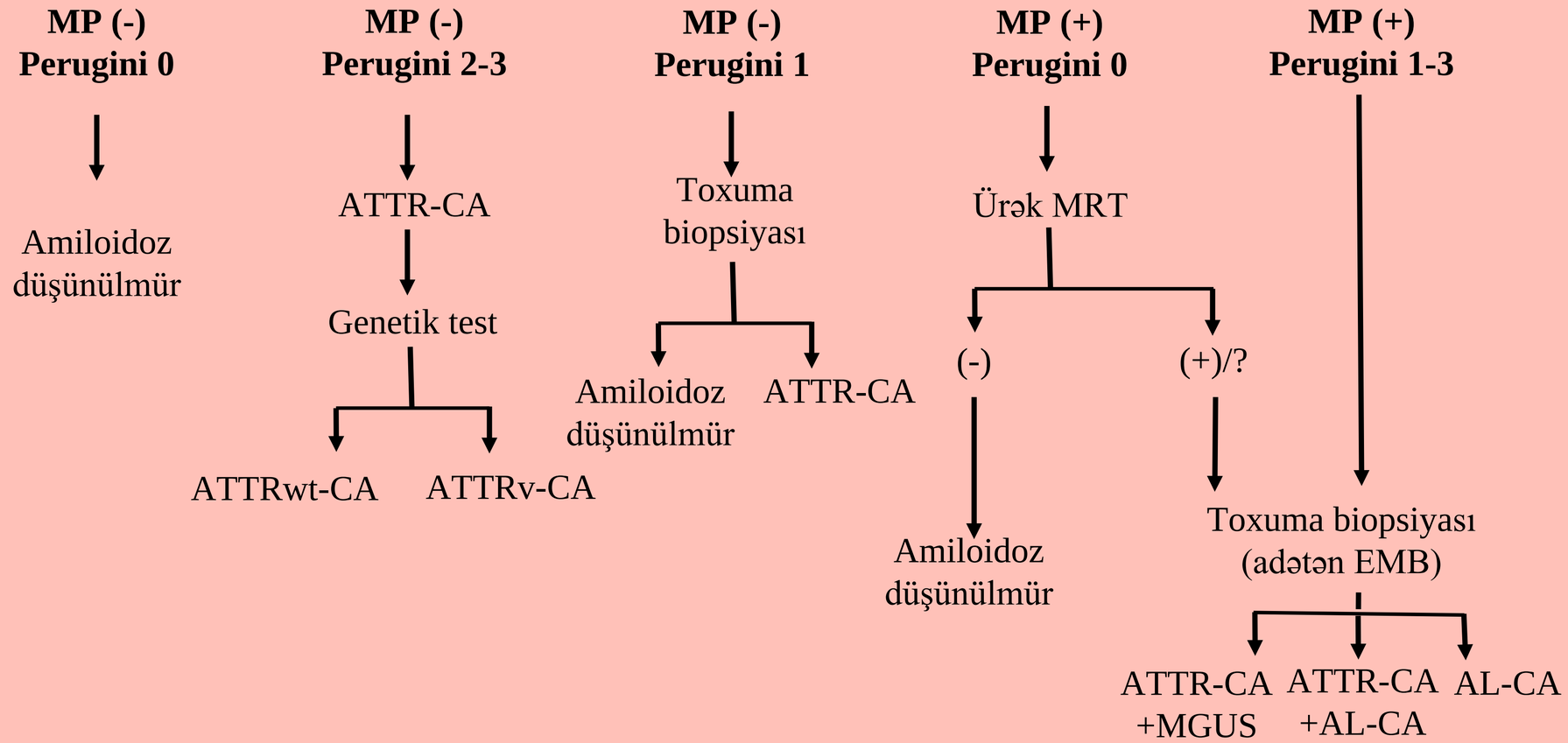


Zhao Min et al. (2022). Biology. 11. 1395. 10.3390/biology11101395.

Amiloidoz şübhəsi

Klinik əlamətlər
EKQ
Exokardioqrafiya

Monoklonal protein + Ssintiqrafiya yolu

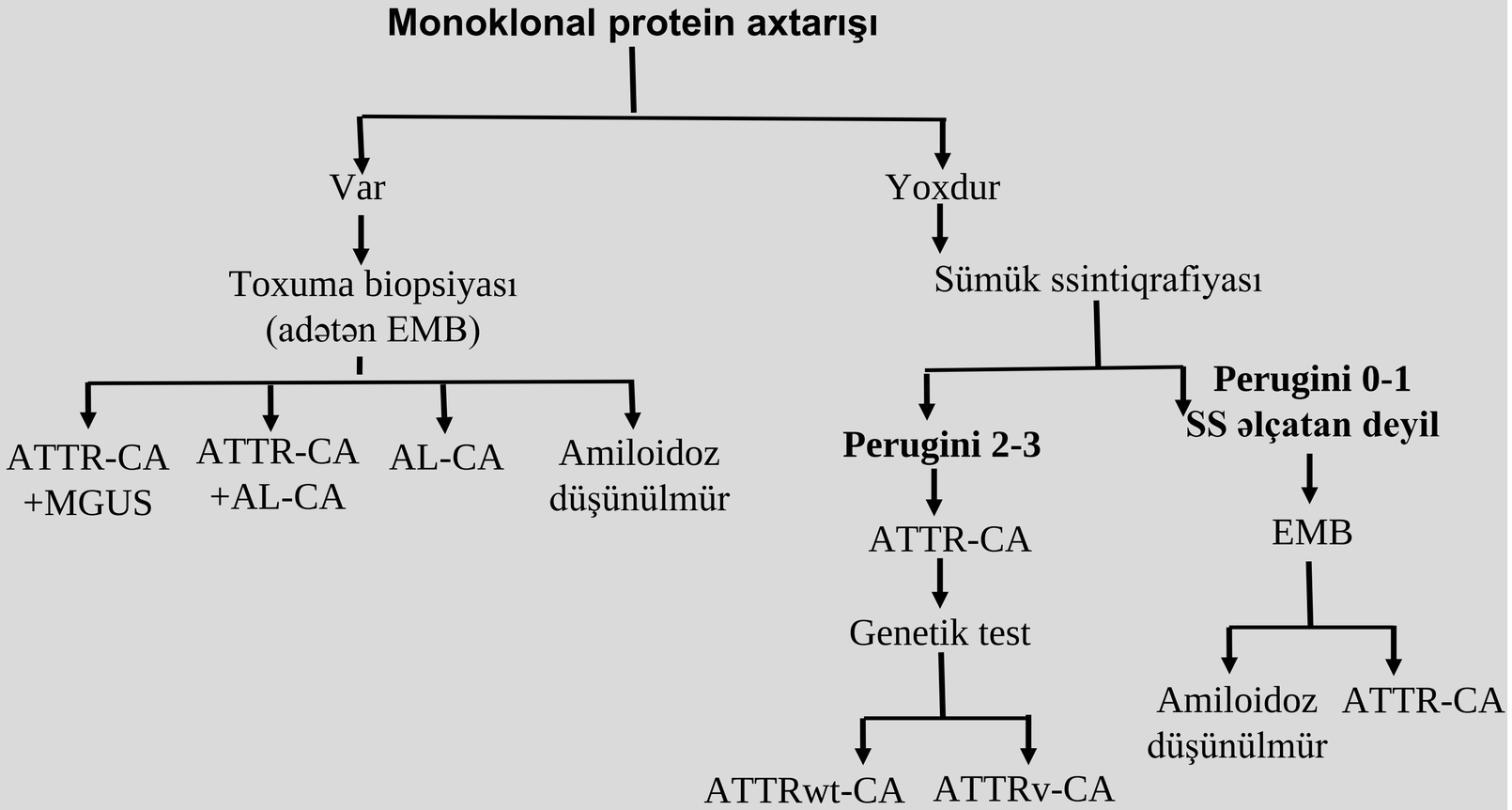


Rapezzi et al. J Am Coll Cardiol 2022;79:1288–1303

Amiloidoz şübhəsi

Klinik əlamətlər
EKQ
Exokardioqrafiya

Monoklonal protein yolu

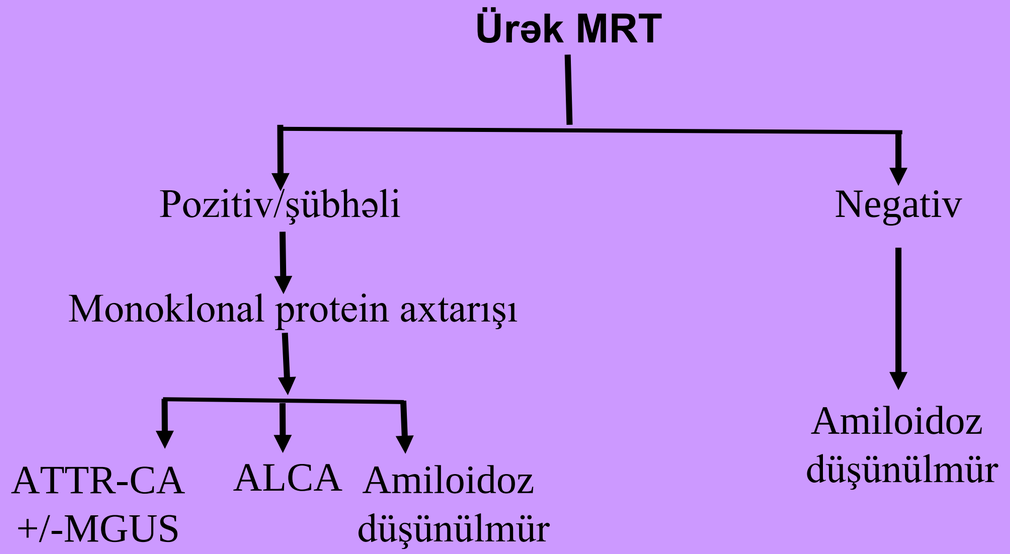


Rapezzi et al. J Am Coll Cardiol 2022;79:1288–1303

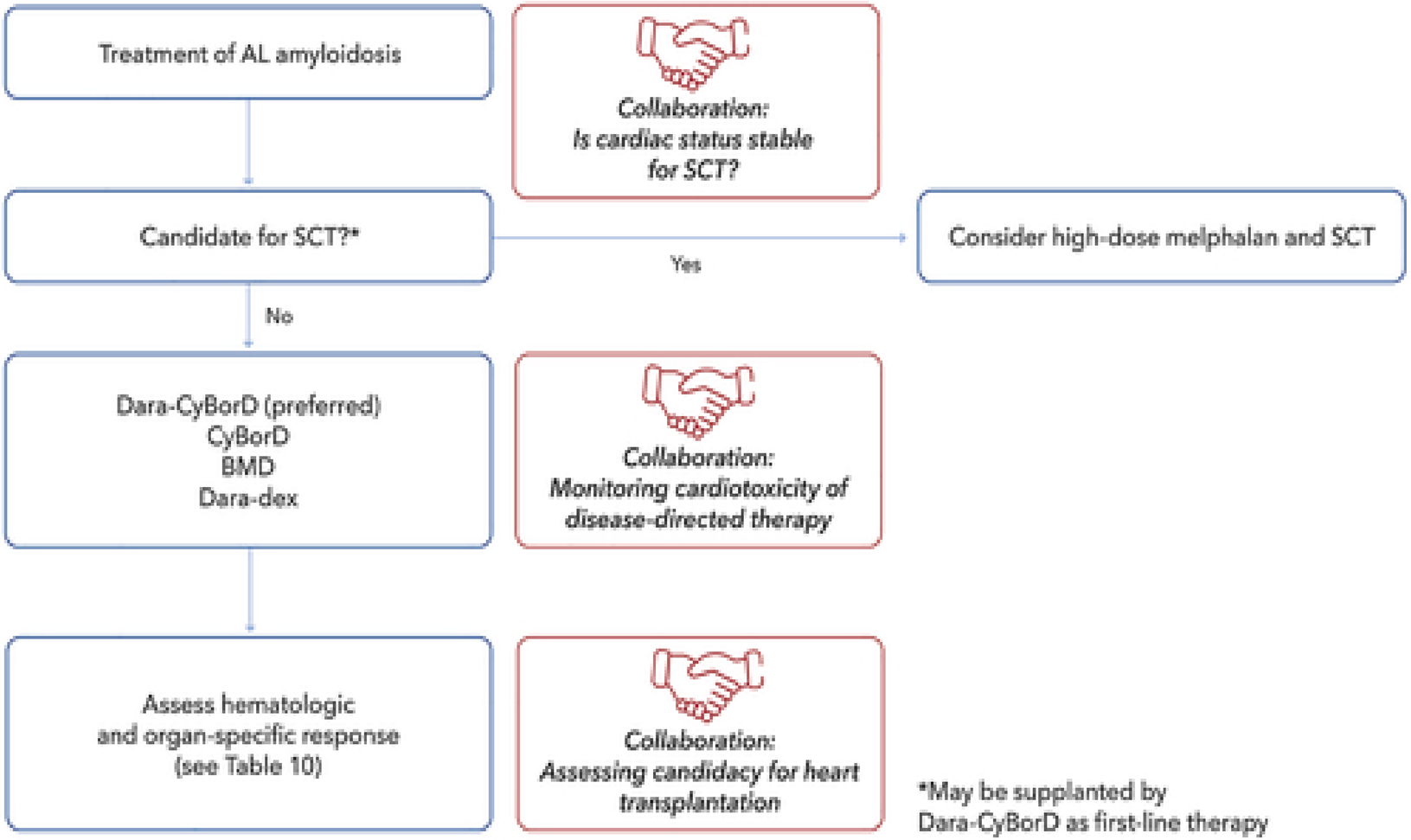
Amiloidoz şübhəsi

Klinik əlamətlər
EKQ
Exokardioqrafiya

Ürək MRT yolu



Rapezzi et al. J Am Coll Cardiol 2022;79:1288–1303



Kittleson M, et al. 2023 ACC Expert Consensus Decision Pathway on Comprehensive Multidisciplinary Care for the Patient With Cardiac Amyloidosis. J Am Coll Cardiol. 2023 Mar, 81 (11) 1076–1126.

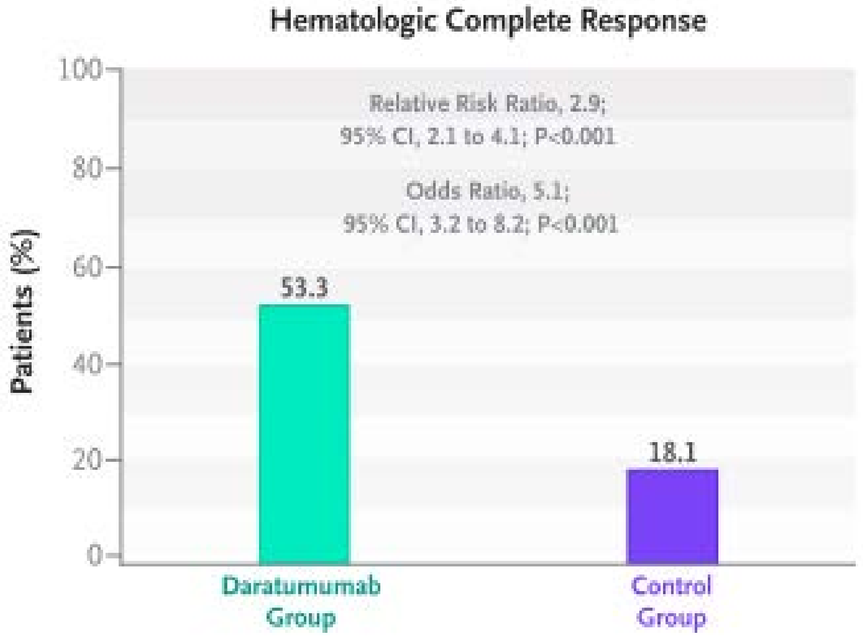
Daratumumab-Based Treatment for Immunoglobulin Light-Chain Amyloidosis

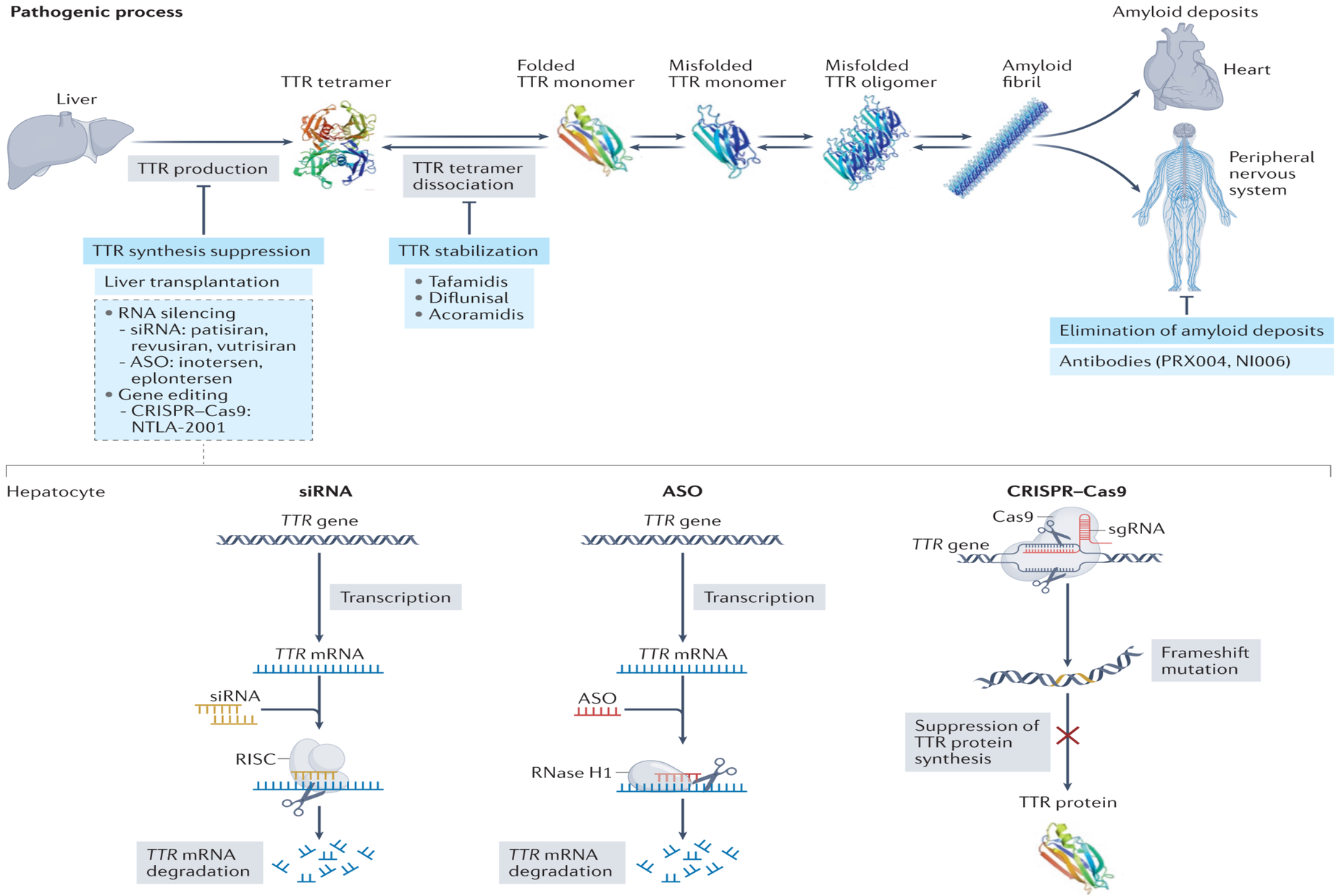
Kastritis E et al. DOI: 10.1056/NEJMoa2028631

Faz 3 tədqiqat

388 AL amiloidoz

- **CyBorD**
- **CyBorD + Daratutumab**



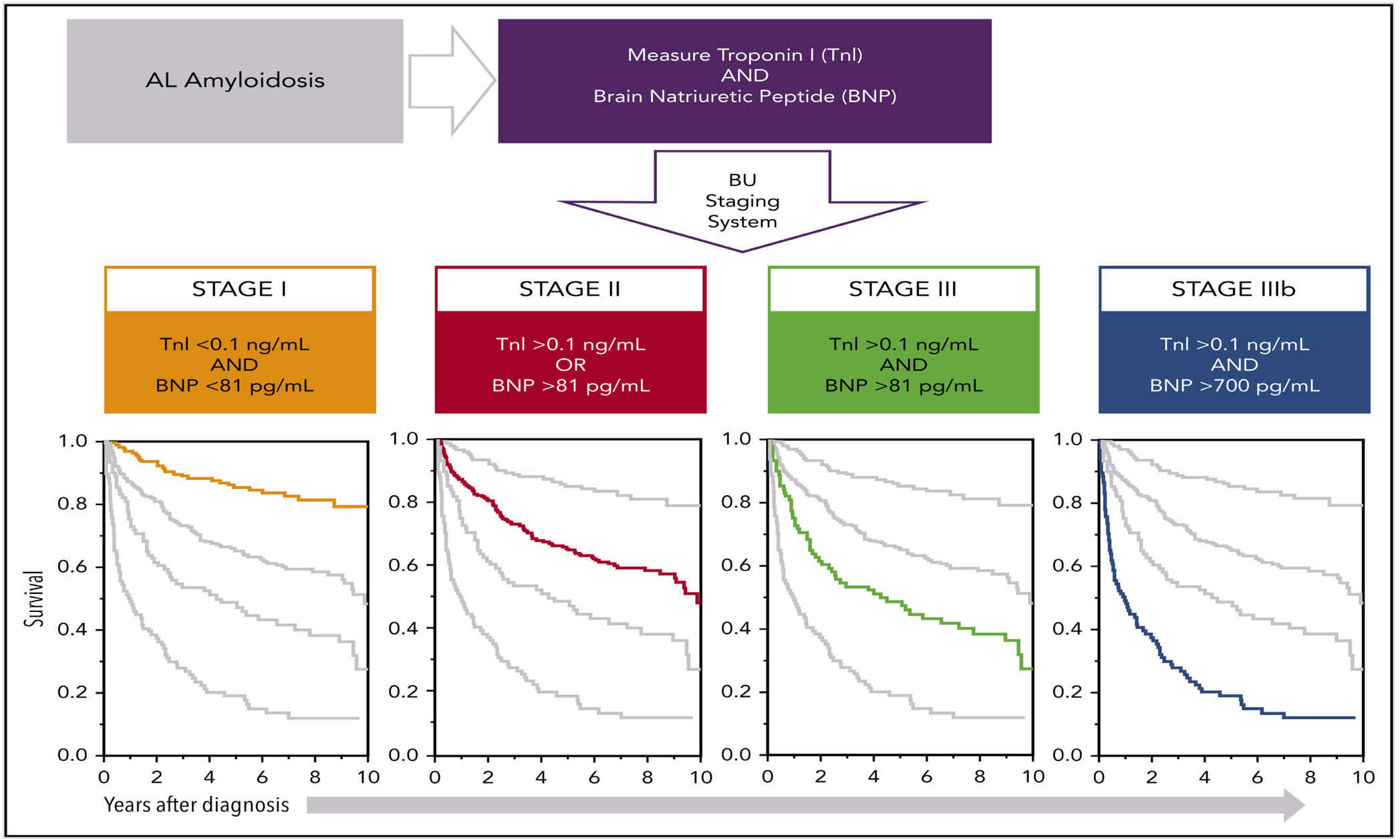


Aimo et al. Nature Reviews Cardiology volume 19, pages655–667 (2022)

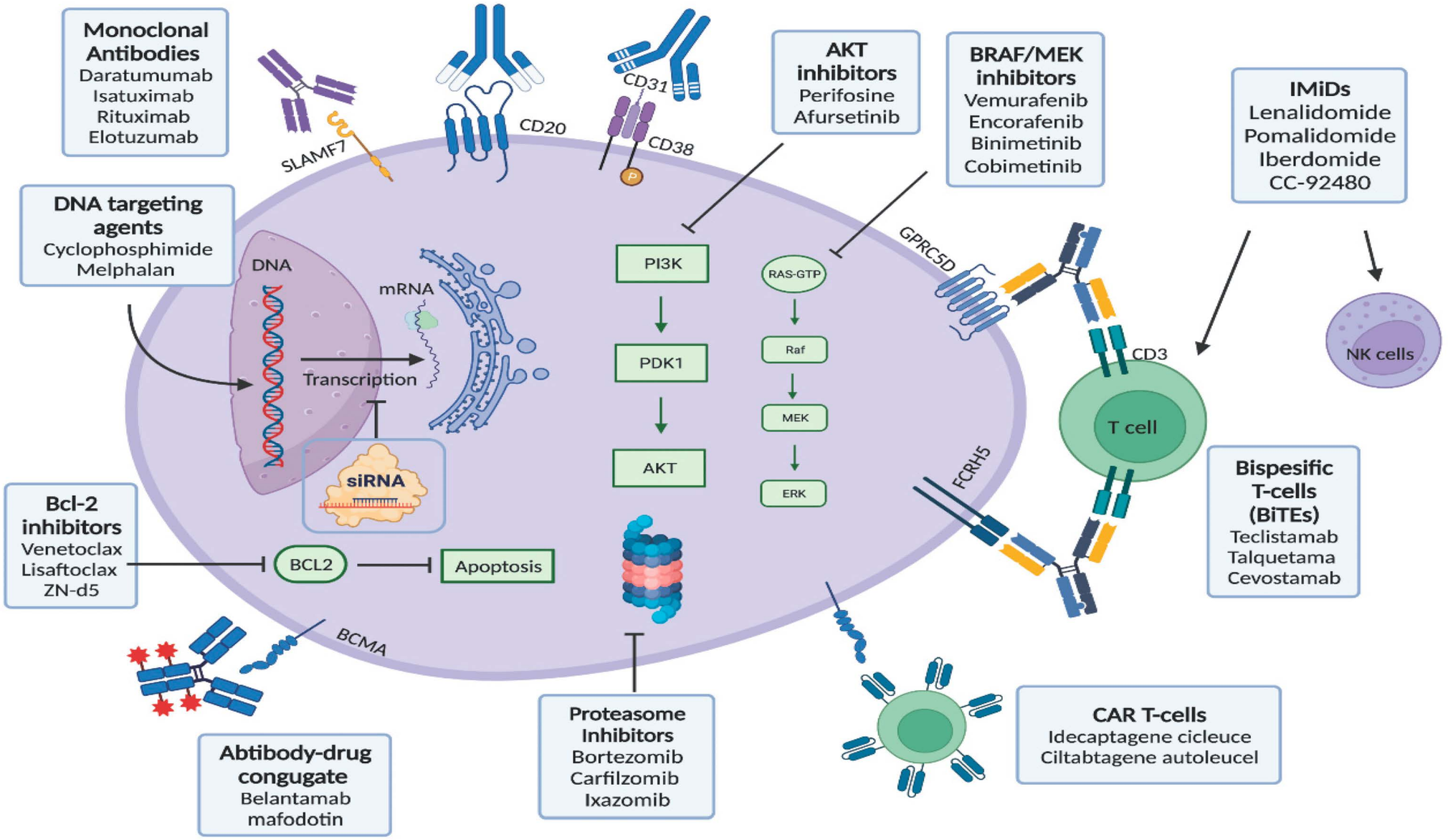
Drug	ESC[1]	DGK[2]	CCS/CHFS[3]	AHA[5]	JCS[6]
HF setting					
Loop or thiazide diuretics	Recommended[a]	Recommended[a]	Recommended[a]	Recommended, but avoid underfilling and worsening renal function from restrictive physiology[a]	Recommended[a]
Nitrates or carperitide (AHF)	No recommendation	No recommendation	No recommendation	No recommendation	Might be considered[a]
Catecholamines, PDE inhibitor (AHF)	No recommendation	No recommendation	No recommendation	No recommendation	Might be considered[a]
Beta-blockers	Not recommended, deprescribe (should be avoided)[a]	Avoid or very cautious use[a]	Avoid or very cautious use[a]	No data for benefit; may not be tolerated given fixed stroke volume (should be avoided)[a]	Tolerated dosing might be considered[a]
ACE inhibitor/ARB	Not recommended (should be avoided)[a]	Avoid or very cautious use[a]	Avoid or very cautious use[a]	No data for benefit; may exacerbate amyloid-related hypotension from autonomic dysfunction (should be avoided)[a]	Tolerated dosing might be considered[a]
Sacubitril/valsartan	No recommendation	No recommendation	No recommendation	No data for benefit; may exacerbate amyloid-related hypotension from autonomic dysfunction (should be avoided)[a]	No recommendation
MRA	No recommendation	No recommendation	Recommended[a]	Might be considered in conjunction with loop diuretics if adequate blood pressure and renal function[a]	Tolerated dosing might be considered[a]

Drug	ESC[1]	DGK[2]	CCS/CHFS[3]	AHA[5]	JCS[6]
AF/flutter/tachycardia setting					
Digoxin	Might be considered[b]	Avoid or very cautious use[b]	Avoid or very cautious use[b]	Might be considered; use cautiously[b]	Not recommended (should be avoided)[a]
Amiodarone	Might be considered (first choice)[a]	No recommendation	Might be considered (first choice)[a]	Might be considered (first choice)[a]	No recommendation
Beta-blockers	Not recommended (should be avoided)[a]	Avoid or very cautious use[a]	Avoid or very cautious use[a]	Might be considered[a]	Case-by-case decision (may be considered)[a]
Non-DHP CCB: ATTR-CA, preserved LV function	No recommendation	Avoid or very cautious use[a]	Avoid or very cautious use[a]	Avoid whenever possible[a]	Case-by-case decision (may be considered)[a]
Non-DHP CCB: ATTR-CA, reduced LV function					Not recommended (should be avoided)[a]
Non-DHP CCB: AL-CA				Not recommended (should be avoided)[a]	Not recommended (should be avoided)[a]
Anticoagulation regardless of CHA_2DS_2-VASc score?	Yes (recommended)[a]	No recommendation	Yes (recommended)[a]	Yes (recommended)[a]	No recommendation
Anticoagulation in SR?	Might be considered[a]	No recommendation	No recommendation	Might be considered[a]	No recommendation

Rapezzi et al. J Am Coll Cardiol 2022;79:1288–1303



Lilleness B., Blood 2019 - 133:215–223



https://www.mdpi.com/2673-6357/3/1/12