National AL Amyloidosis Patient-to-Provider Connection Forum

March 12, 2025

The forum will begin promptly at 1:00pm ET.

While you wait, scan the QR code to complete the *Pre-Forum Survey* if you have not already!

National AL Amyloidosis Patient-to-Provider Connection Forum

March 12, 2025

Welcome & Introductions

Devin Marie Keating
Director of Operations, Clinical Studies
American Heart Association

Cayla Hadley
Program Implementation Manager
American Heart Association

Meeting Reminders

Please Note:

- This Forum is being recorded.
- All participants will be muted upon entry.
- Recordings of today's sessions will be enduring resources in a few weeks on www.heart.org

Questions?

- We encourage an open, conversational discussion, so please engage and share your thoughts!
- Q&A sessions are scheduled at the end of each forum session.
- Submit your questions in the chat anytime—they will be addressed during the designated Q&A.

If you are having issue with audio, please call in using the appropriate number below.

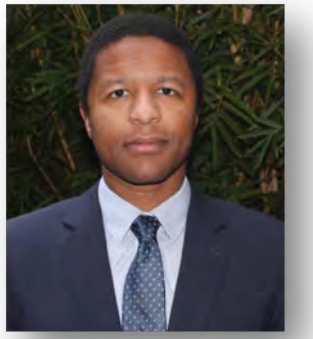
Dial by your location:

+1 (301) 715-8592	(Washington DC)
+1 (312) 626-6799	(Chicago)
+1 (646) 876-9923	(New York)
+1 (253) 215-8782	(Tacoma)
+1 (346) 248-7799	(Houston)
+1 (669) 900-6833	(San Jose)

Meeting ID: 882 0718 1979
Passcode: 832932

Thank you to
Alexion, Astra Zeneca Rare Disease
for being a proud supporter of the AHA's
National AL-Amyloidosis
Patient-to-Provider Connection Forum

AL Amyloidosis Expert Collaborative Leadership



Kevin M. Alexander, MD
Assistant Professor of Medicine,
Advanced Heart Failure and Transplant Cardiology,
Stanford Medicine

Melissa A. Lyle, MD, FACC, FHFSA
Assistant Professor of Medicine,
Division of Advanced Heart Failure and Transplant,
Mayo Clinic Florida

Mathew Maurer, MD
Professor of Medicine,
Arnold and Arlene Goldstein Professor of Cardiology,
New York-Presbyterian Hospital-Columbia University Medical Center

American Heart Association®

The Patient Journey

Linda Perez
Patient Advocate

American Heart Association®

The Power of Patient Advocacy: Advancing AL Amyloidosis Awareness, Education, Research & Outcomes

Amyloidosis Speakers Bureau & Mackenzie's Mission

Amyloidosis Support Groups

Amyloidosis Research Consortium

Mackenzie's Mission & Amyloidosis Speakers Bureau

Deborah D. Boedicker, CFA
Board Member

MACKENZIE'S MISSION

ASB AMYLOIDOSIS SPEAKERS BUREAU

BRIDGING KNOWLEDGE GAPS:

MEDICAL EDUCATION IS LACKING AMYLOIDOSIS COVERAGE IN CURRICULUM!

- **170+ US Medical Schools** that collectively graduate approximately over **17,000 new providers** annually.
- **600+ US Internal Medicine Residency Programs** where trainees are honing their diagnostic skills.

THIS EDUCATIONAL INITIATIVE REACHES BOTH CURRENT AND FUTURE PROVIDERS WHILE EMPOWERING THE PATIENT VOICE!

Our Beliefs:

Raising Disease Awareness → Earlier Diagnoses → Improved Patient Outcomes

The Patient Community is eager to help!

The Amyloidosis Speakers Bureau

A well-known business structure transformed into a nonprofit educational platform.

Education Through Patient Narratives

- Patients share their diagnosis and treatment journey—the highs and lows—delivering powerful, emotional, and lasting education.

Includes Clinical Information

- Designed with audience-specific clinical insights to ensure both emotional impact and medical relevance.

Monthly Amyloidosis Updates

- Amyloidosis Lecture Series
- Educational videos

ASB
AMYLOIDOSIS
SPEAKERS BUREAU

Our Journey of Impact

Now in our 6th Academic Year, we have:

- ✓ Delivered **400+** presentations
- ✓ Reached **20,000+** future and current medical professionals
- ✓ Engaged specialists across multiple fields, including, but not limited to:
  - Internal Medicine
  - Cardiology
  - Neurology
  - Nephrology
  - Gastroenterology
  - Orthopedics
- ✓ Provided monthly Amyloidosis updates to **1,100+** subscribers

The authenticity of the patient's own voice cannot be matched, providing a transformative impact that far exceeds what we can provide in the curriculum.

Gordon Huggins, MD
Tufts University School of Medicine

Amyloidosis Support Groups

Muriel Finkel

President, Co-Founder

Amyloidosis Support Groups

We are a phone call or email away!
TOLL FREE HELP/HOT LINE: 866-404-7539
EMAIL: Info@amyloidosissupport.org

SITE MENU

- Home Page
- Treatment Centers
- Webinars
- ASG Meetings
- Awareness Info
- Patient Resources
- ATTRwt & ATTRv
- Clinical Trials
- Patient Registry
- About ASG
- Contact ASG
- Donations
- Awareness Items
- Patient's Day
- Amy Blogs
- In Memoriam

HOW FAR ARE YOU FROM TREATMENT AND SUPPORT?

To find nearest treatment, select your state from the drop down list and click the Find Treatment button.

Select State | Find Treatment

Therapies for Amyloidosis 2025

AL Amyloidosis Treatment Chart (PDF)
ATTR Amyloidosis Treatment Chart (PDF)

AMYLOIDOSIS AWARENESS

SUPPORT GROUPS

- Arizona (Phoenix)
- California (L.A.)
- California (San Diego)
- Chicago
- Colorado
- Detroit
- Florida (Jacksonville)
- Florida (Miami)
- Florida (Tampa)
- Georgia
- Indianapolis
- Kansas City
- Louisiana
- Maryland (Baltimore)
- Maryland (Hagerstown)
- Massachusetts
- Minnesota

https://www.amyloidosissupport.org/

Amyloidosis Support Groups

@AmyloidosisSupportGroups · 2K subscribers · 87 videos

Welcome to the Amyloidosis Support Groups YouTube channel. Here you will find inform ...more

amyloidosissupport.org and 3 more links

Subscribed

Home Videos Playlists

For You

Cerebral Amyloid Angiopathy (CAA) Webinar, November 23, 2024

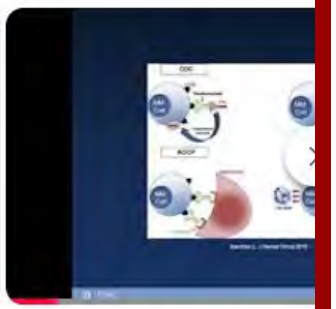
1.1K views • 2 months ago

Treatments for Transthyretin Amyloidosis (ATTR)

784 views • 13 days ago

ATTR Webinar 03-09-2024

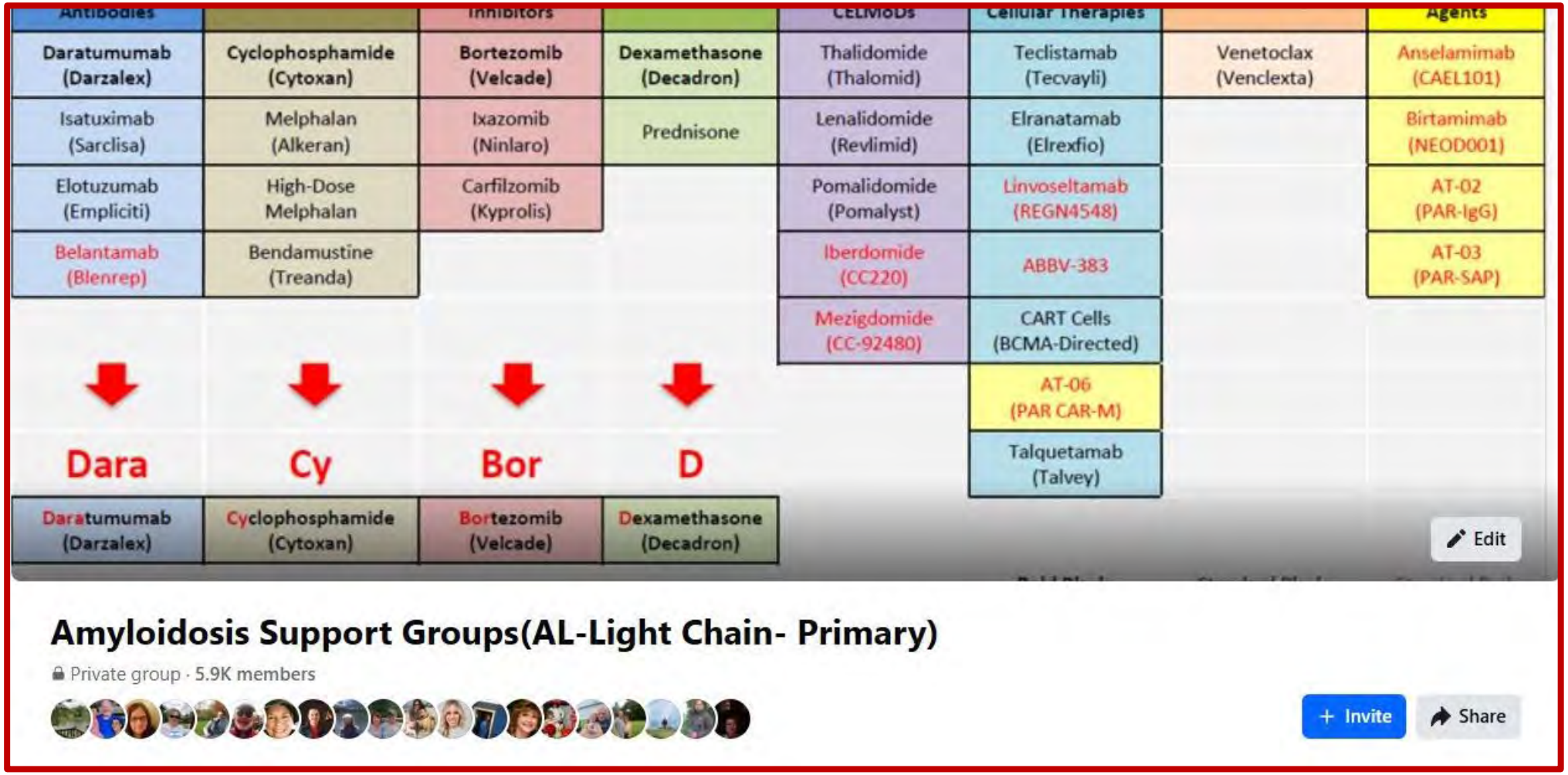
1.2K views • 10 months ago



AL Amyloidosis Webinar May 21,

1.9K views • 2 years ago

Connecting Patients: Amyloidosis Support Groups by Type



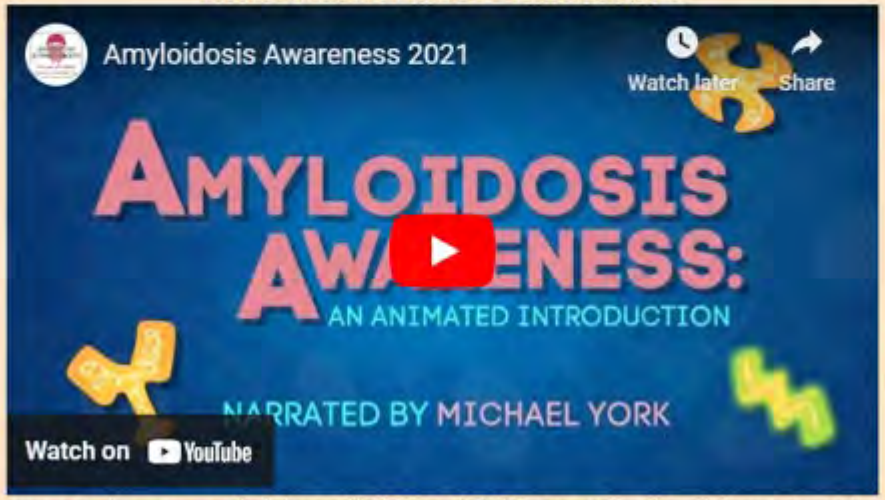
Amyloidosis Awareness Booklet

TRANSLATIONS

[GERMAN] [ITALIAN] [DUTCH] [SPANISH] [FRENCH] [PORTUGUESE] [CHINESE] [JAPANESE]

AMYLOIDOSIS VIDEO

WITH SUBTITLES IN 14 LANGUAGES



To turn on captions or subtitles, click the "CC" button in the video player's toolbar.

(Click here to watch video on Vimeo)

Got the diagnosis...shock...fear...sadness....Help!

What is my next step?

Email Info@AmyloidosisSupport.org or Call 866-404-7539.

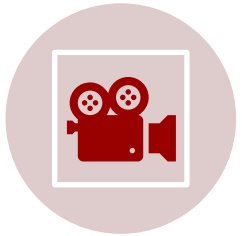
What will I learn from the call?

Where to go for a second opinion should I need one.

Where the nearest support group is located.

Which Facebook group I should join.

Which webinars should I watch.



If I don't know which type I have, it will be explained to me, and I will be referred to the video.

AMYLOIDOSIS SUPPORT GROUPS

You Are Not Alone

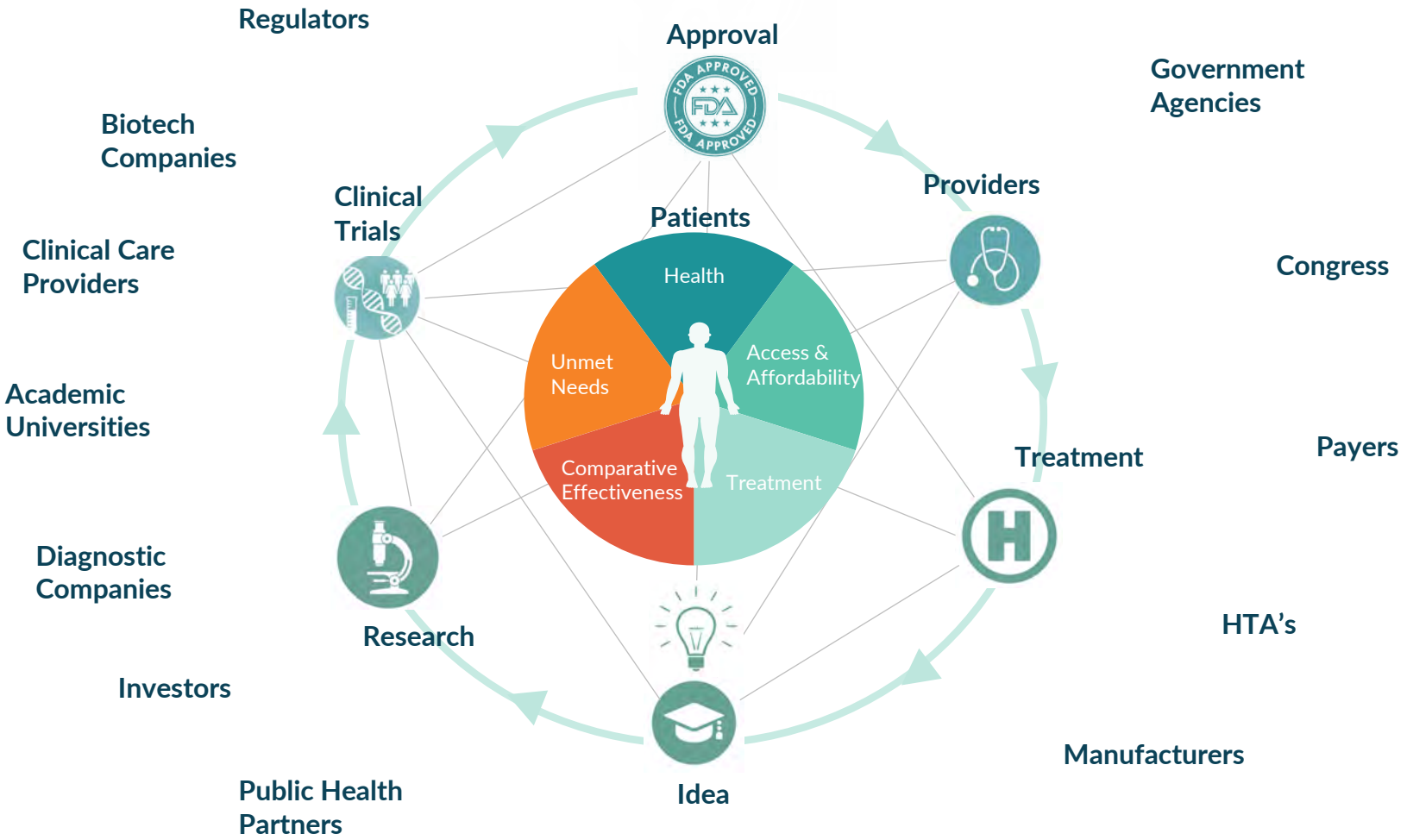
www.amyloidosissupport.org

Amyloidosis Research Consortium

Isabelle Lousada

Founder and CEO

Rare disease ecosystem- care to cures continuum



IT TAKES 15 YEARS & COSTS $1 BILLION

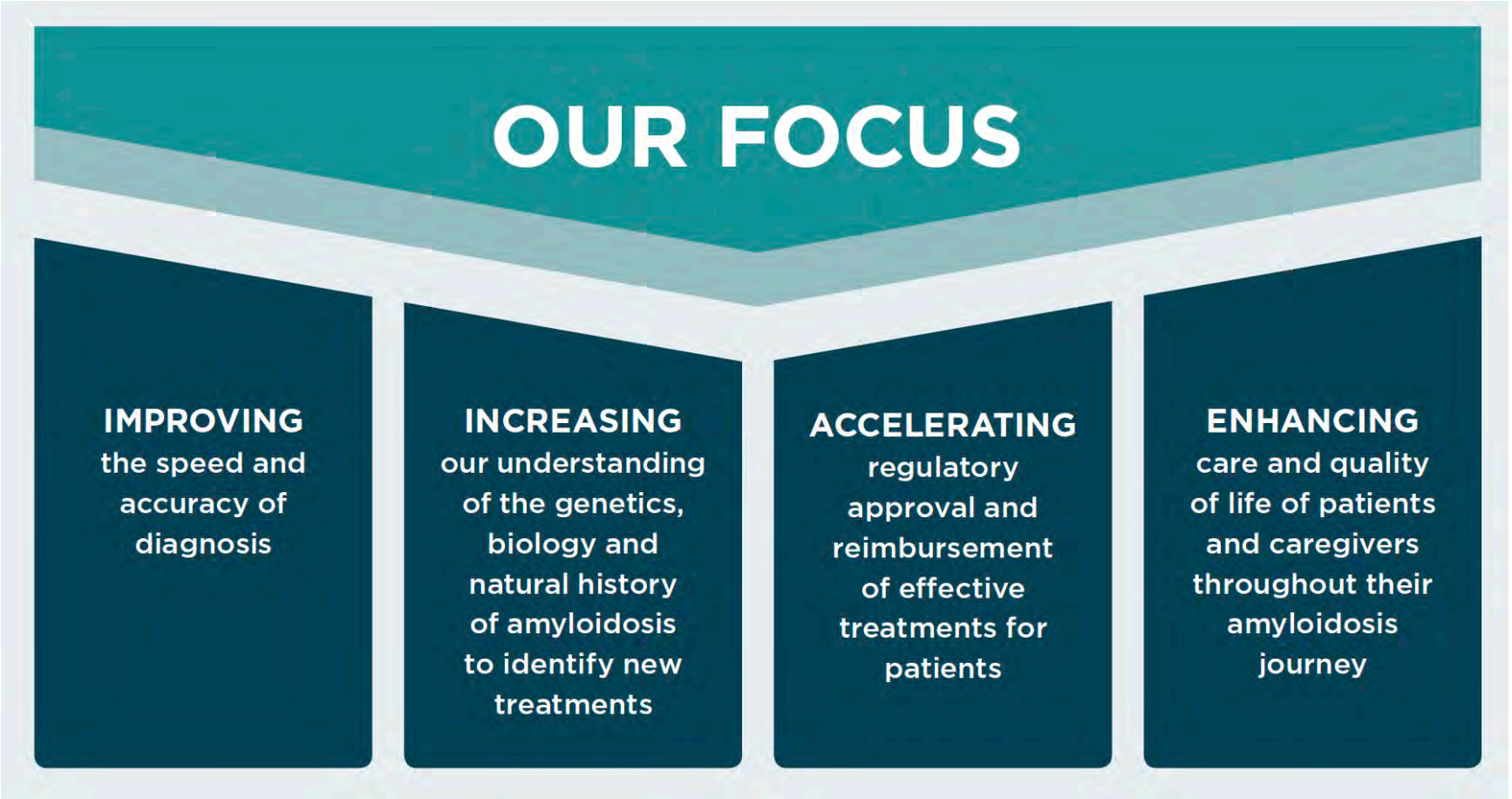
OVER $1 TRILLION IS SPENT ON RARE DISEASE HEALTHCARE DELIVERY ANNUALLY

About ARC

Our vision is to make a significant impact on the curability of amyloidosis

The Amyloidosis Research Consortium (ARC) harnesses the power of collaboration and innovation to advance science, and both improve and extend the lives of those with amyloidosis.

As a **patient-founded, patient-focused non-profit organization**, ARC is determined to shift this paradigm.

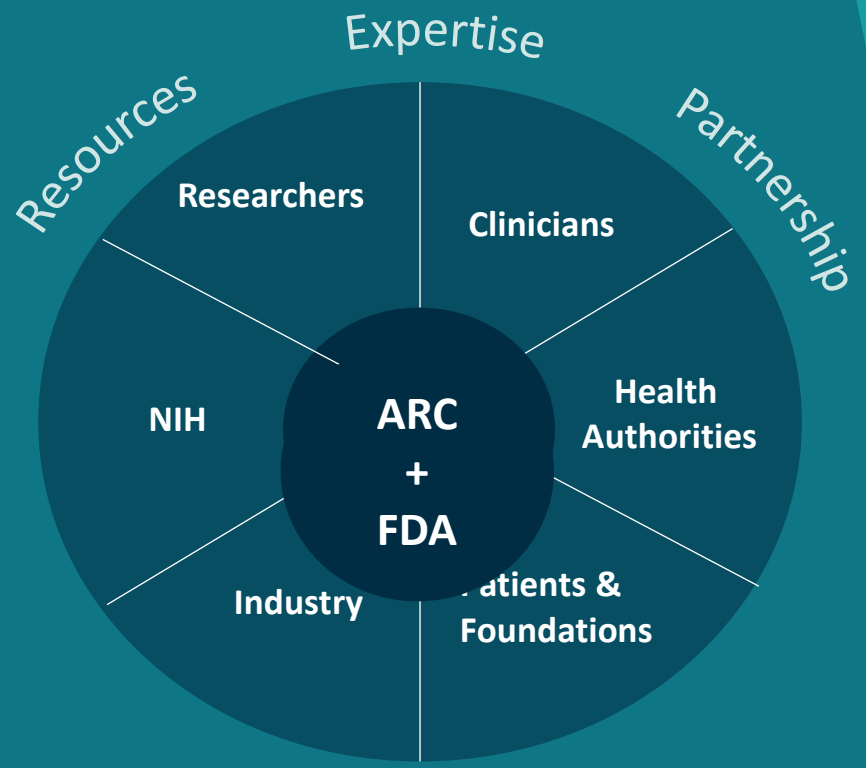


Amyloidosis Forum: A Public Private Partnership

Amyloidosis Research Consortium

The Amyloidosis FORUM

Amyloidosis Research Consortium | FDA U.S. FOOD & DRUG ADMINISTRATION



Mutually beneficial collaboration

Facilitate innovation through exchange of scientific knowledge

Bridge gaps in regulatory science

Bring new, safe, and efficacious treatments to patients with amyloidosis

Amyloidosis Forum areas of focus

Amyloidosis Research Consortium

1

Federated Analytics

Accelerate access to data-driven insights from completed clinical trials in amyloidosis to improve the design of future trials

2

Standardization of Imaging

Standardization of imaging modalities in ATTR and AL amyloidosis to improve use in care management and drug development

3

Prognostic Factors

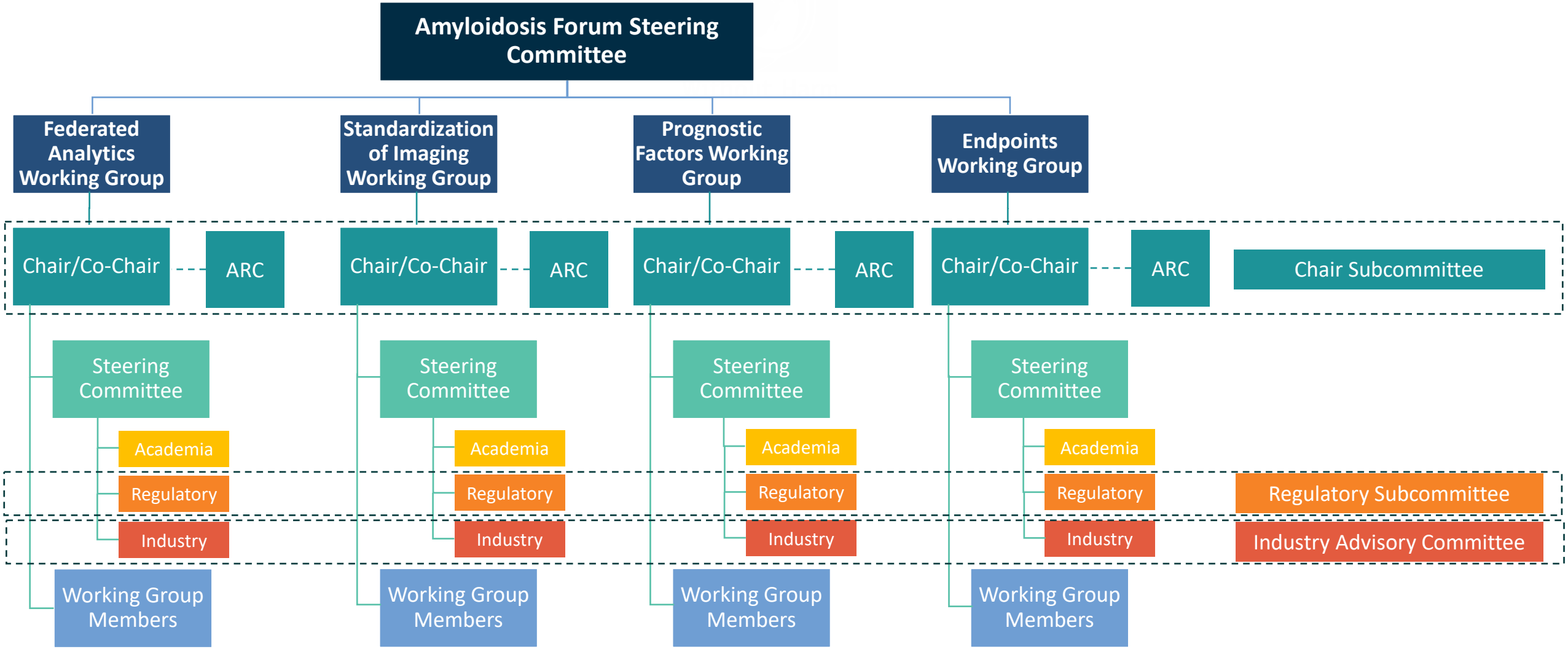
Develop prognostic factors for clinical trial endpoints, with quantitative assessments and validation that reflects current standards of care

4

Endpoints: Foundational Evidence

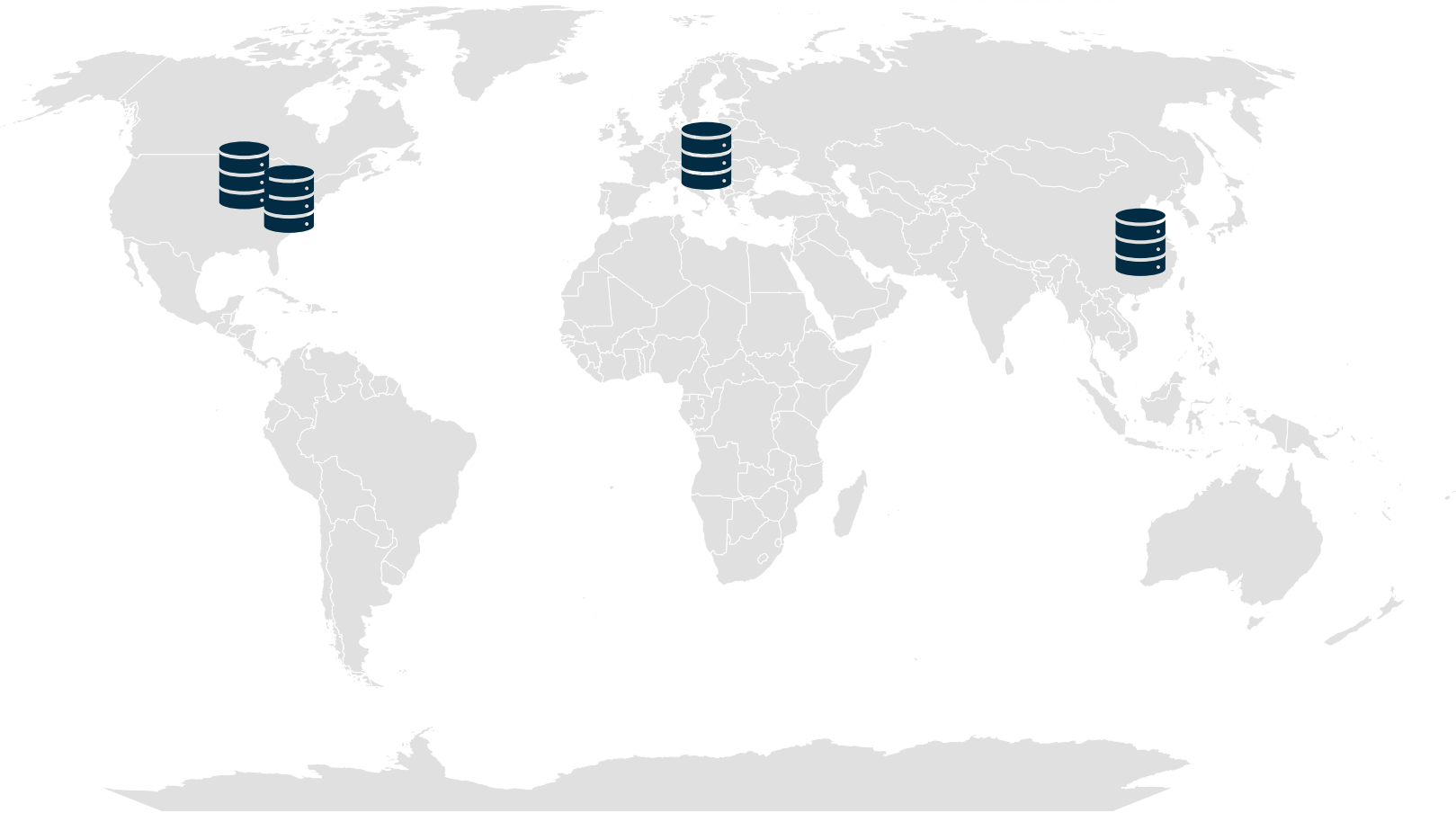
Accelerate the development of evidence and knowledge needed to optimize the selection, use and evaluation of endpoints in clinical trials from the drug developer and drug evaluator perspectives

Working Group Org Chart



Federated analytics:
Shared learning without waiting for shared data

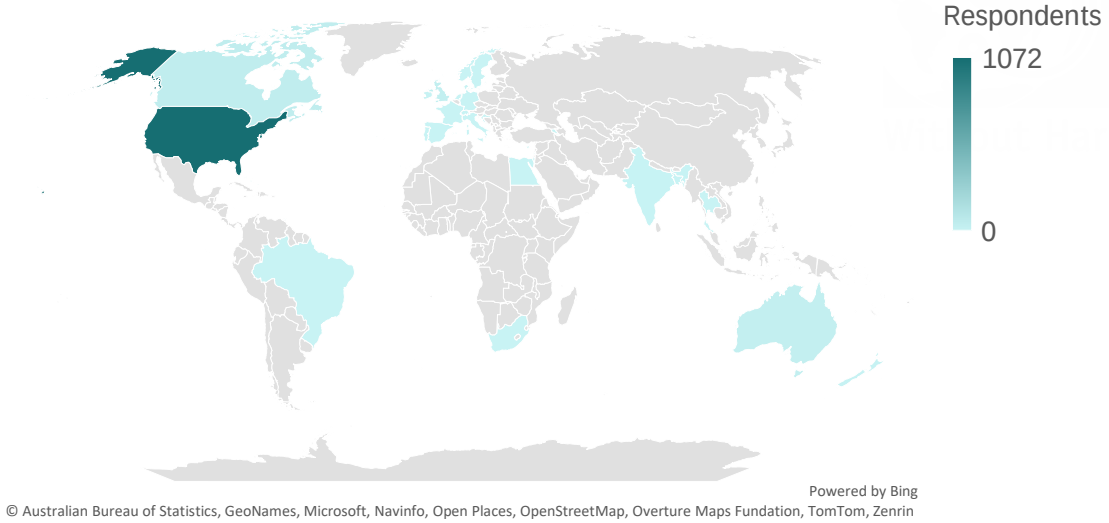
Data silos spread across the globe…

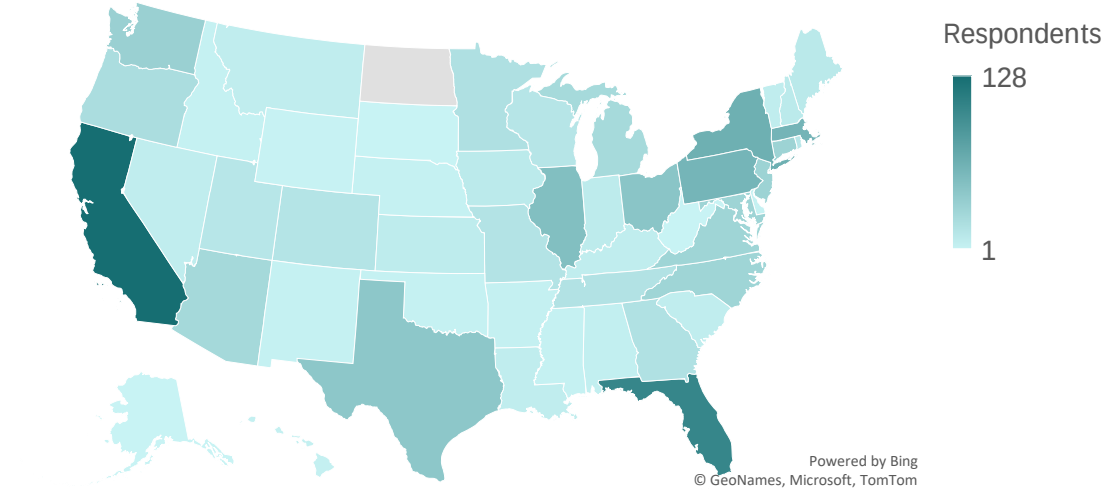


- **Challenge**: not possible to pool these patient data all in one place for analytics
- **Solution**: federated analytics runs standardized analytics locally and then pools results, not data, for collaborative learning
- **Why it matters**: avoid years of waiting for data. We can learn from valuable clinical data sources – and advance drug development – without waiting for patient-level data to be sharable across institutions and international boundaries

Annual Community Survey

Community Survey Participants

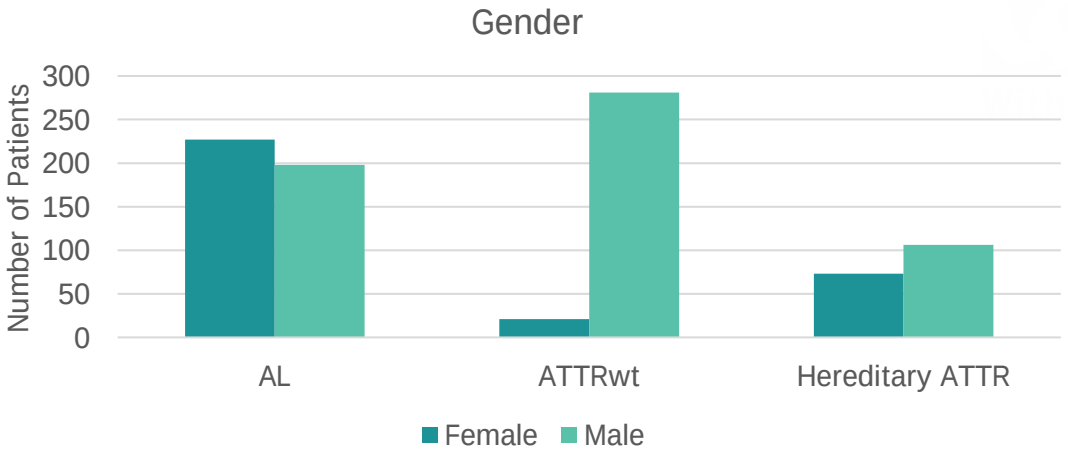


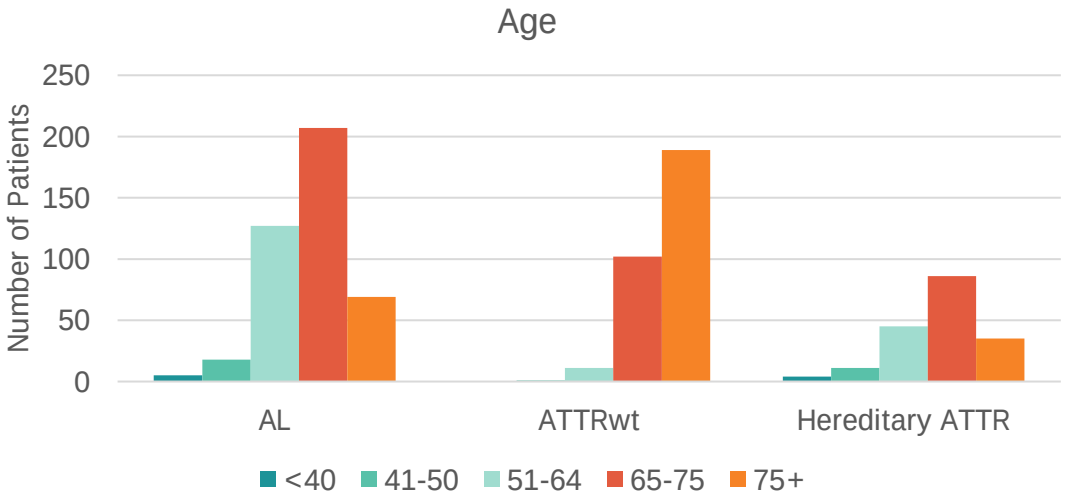


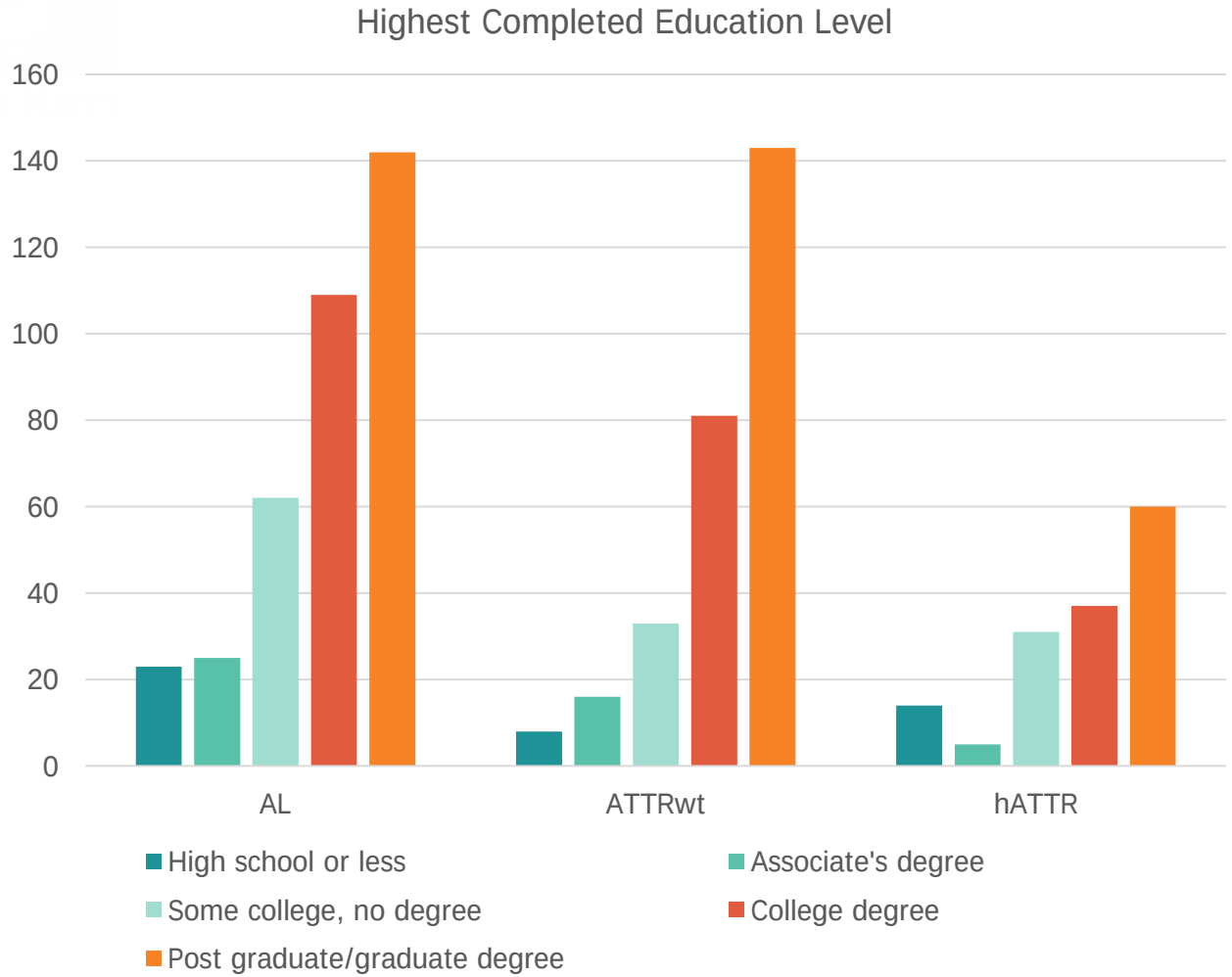
	Overall
	N = 1,238
Region	
Africa	2 (0.2)
Asia-Pacific	49 (4.0)
Europe	65 (5.3)
North America	1,120 (90)
South America	2 (0.2)

	Overall
California	128 (10)
Florida	105 (8.5)
New York	65 (5.3)
Massachusetts	61 (4.9)
Pennsylvania	60 (4.8)
Illinois	51 (4.1)
Ohio	45 (3.6)
Texas	43 (3.5)

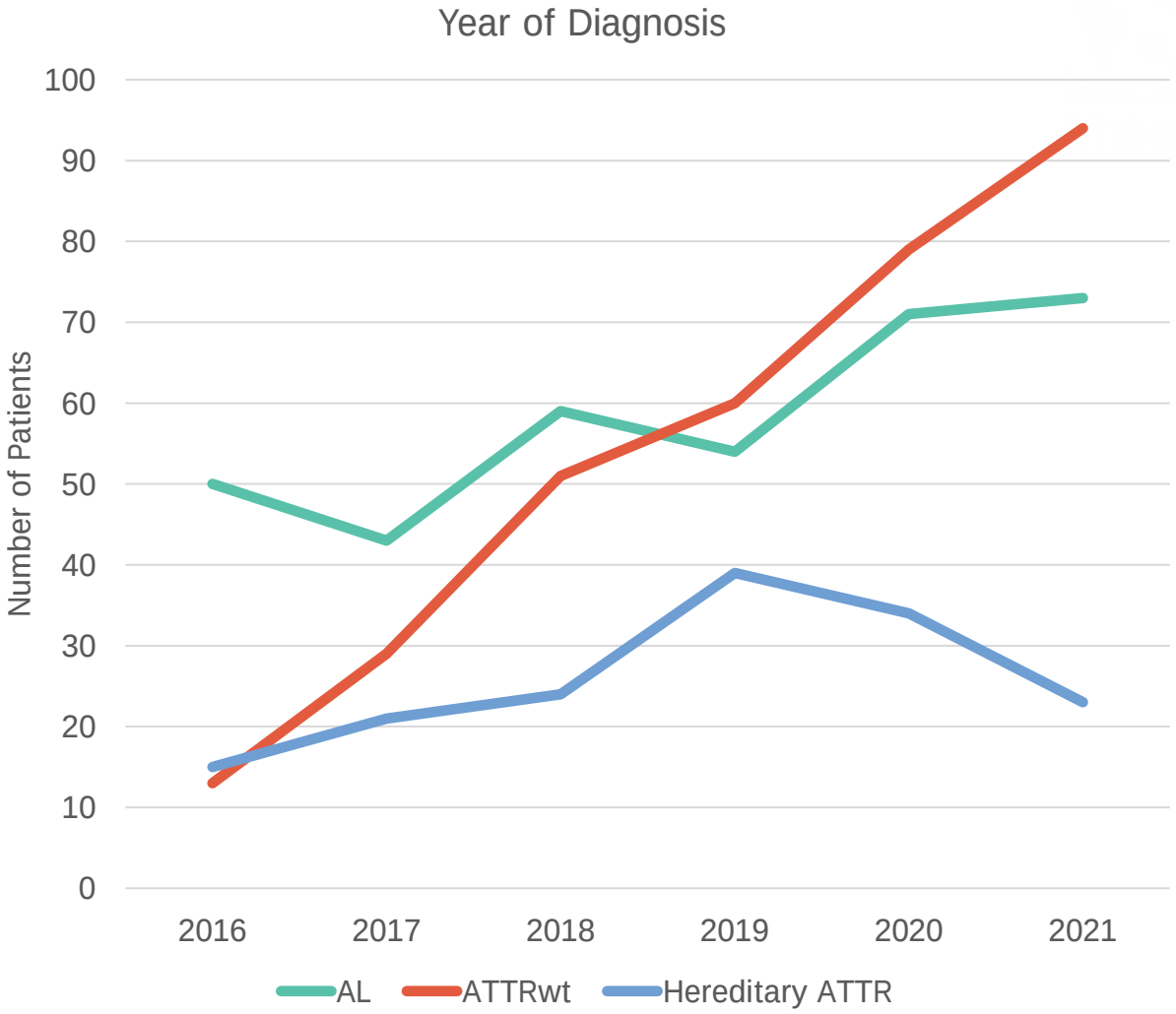
Demographic Characteristics by Type

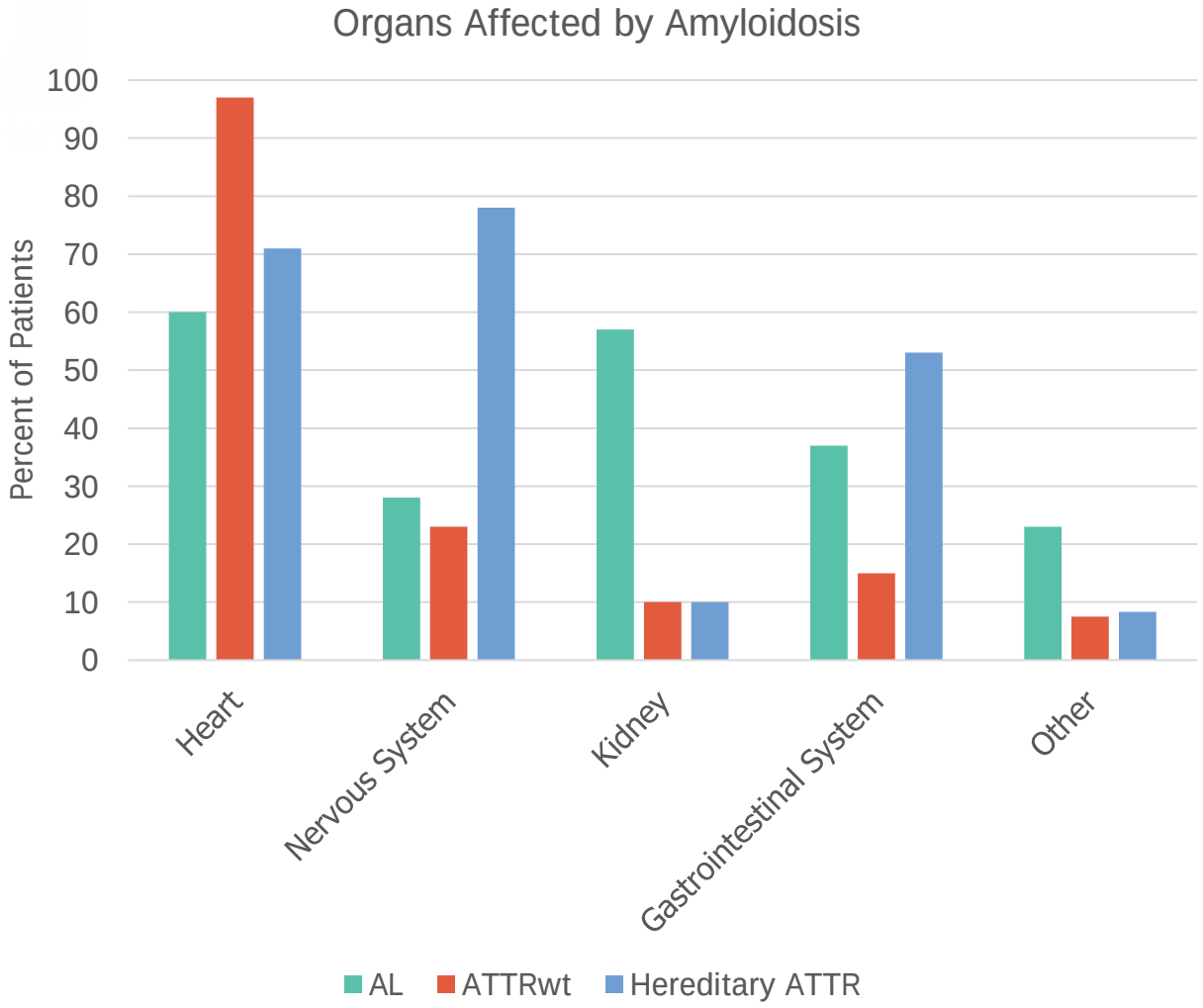




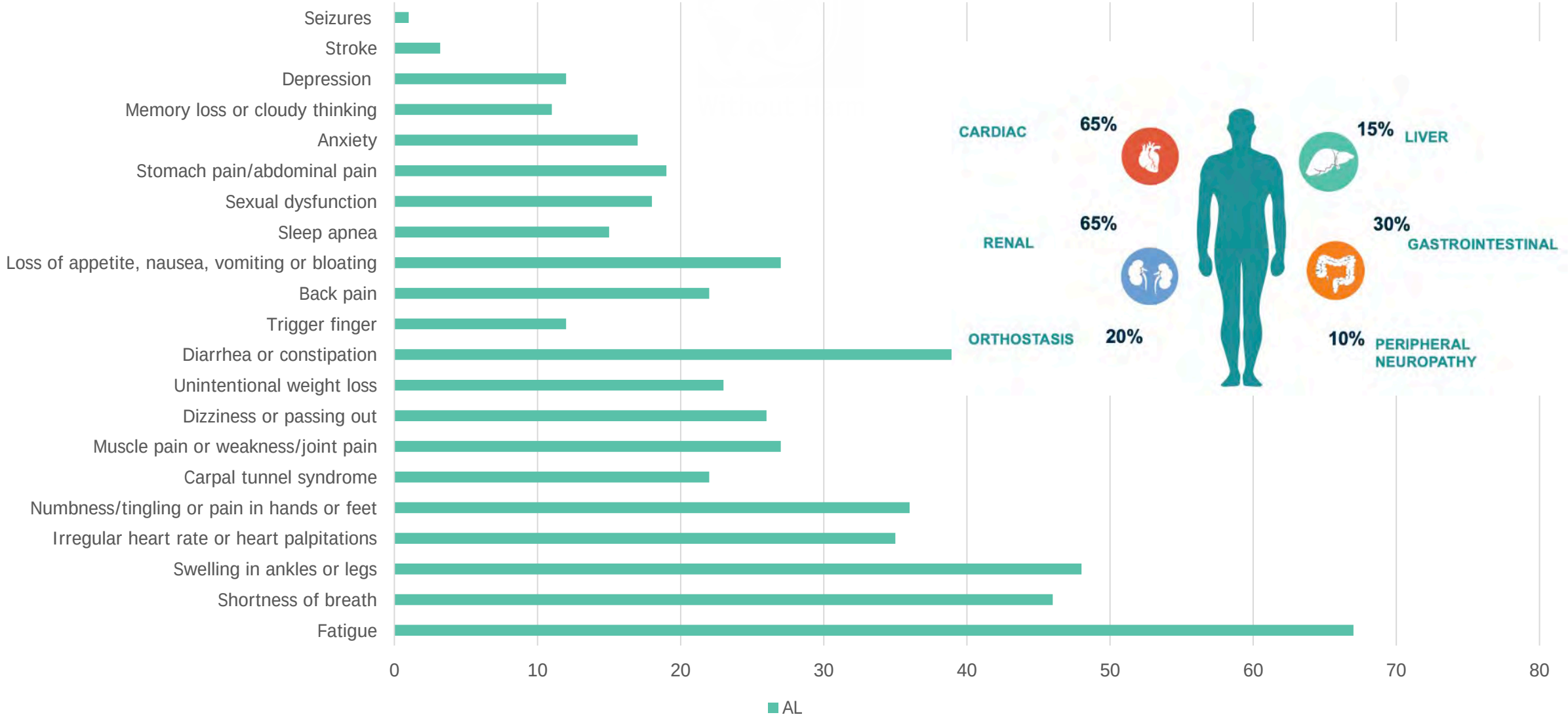


Disease Characteristics



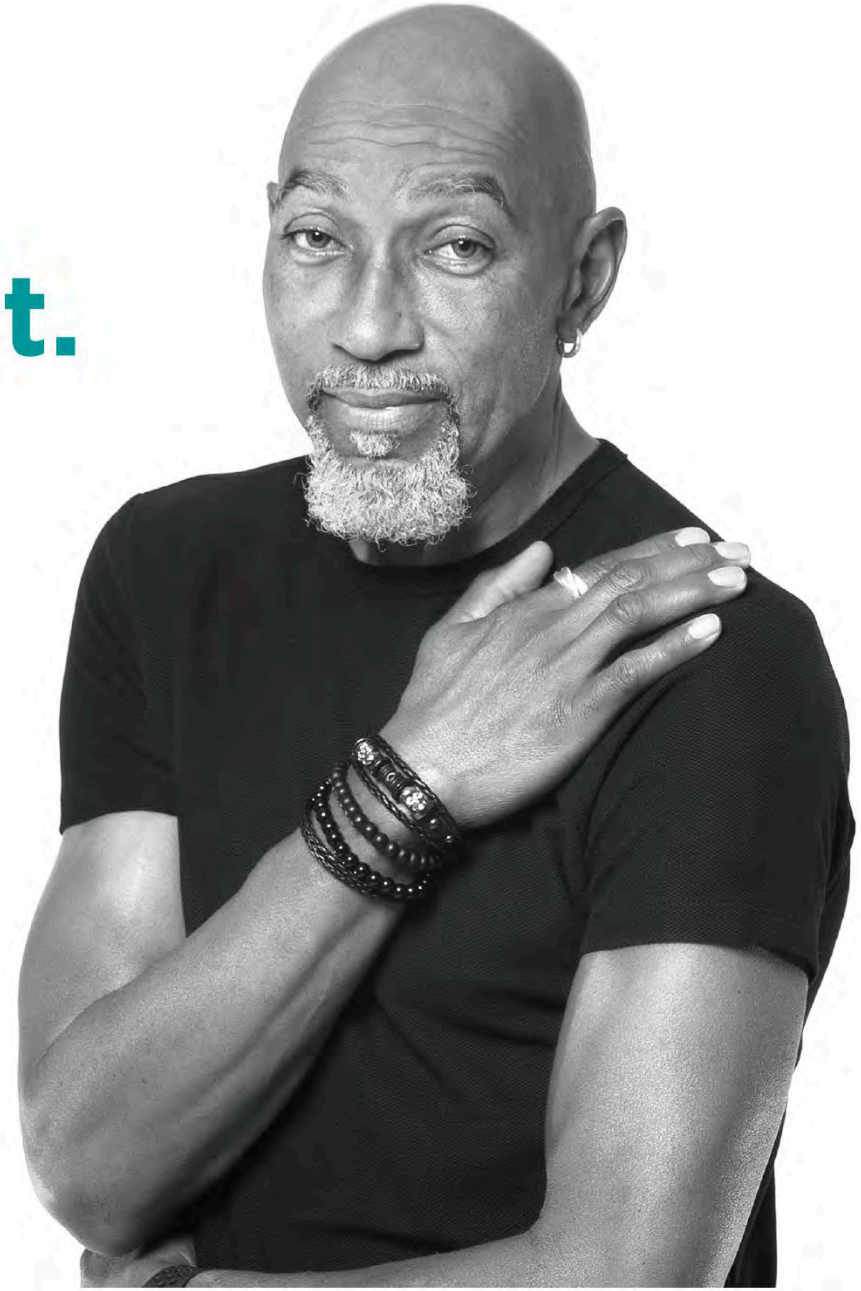


Journey to Diagnosis: Symptoms Prior to Start of Treatment

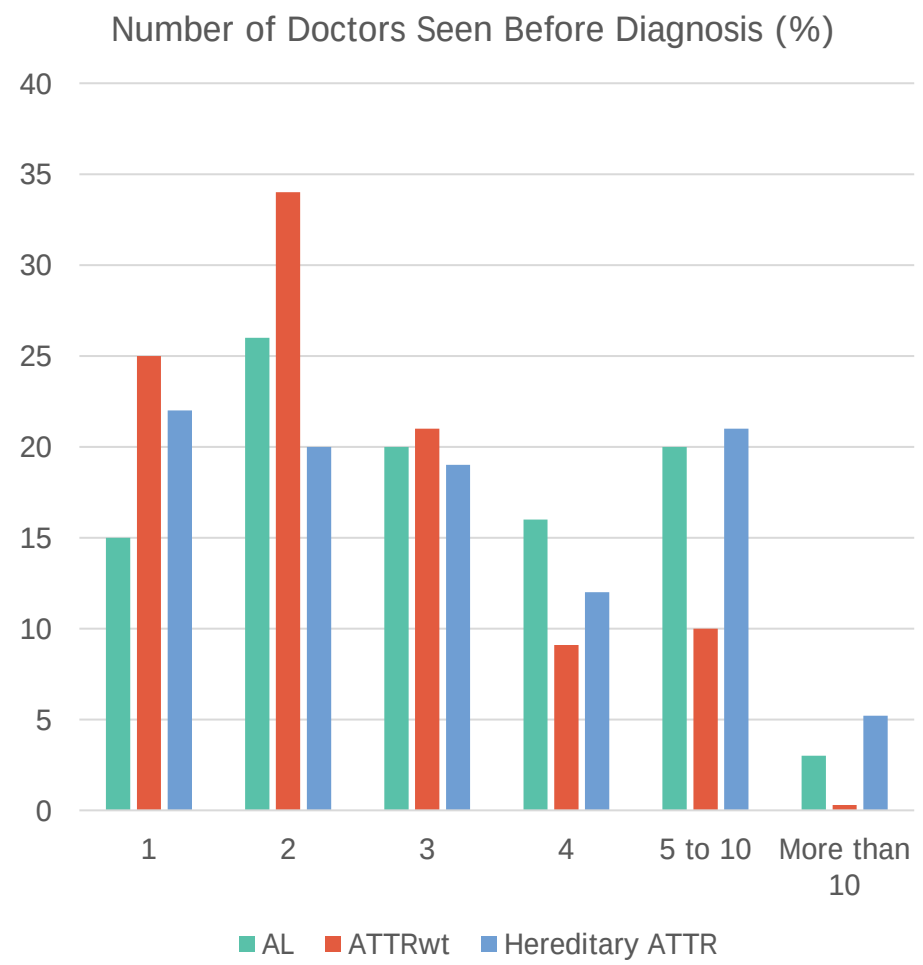


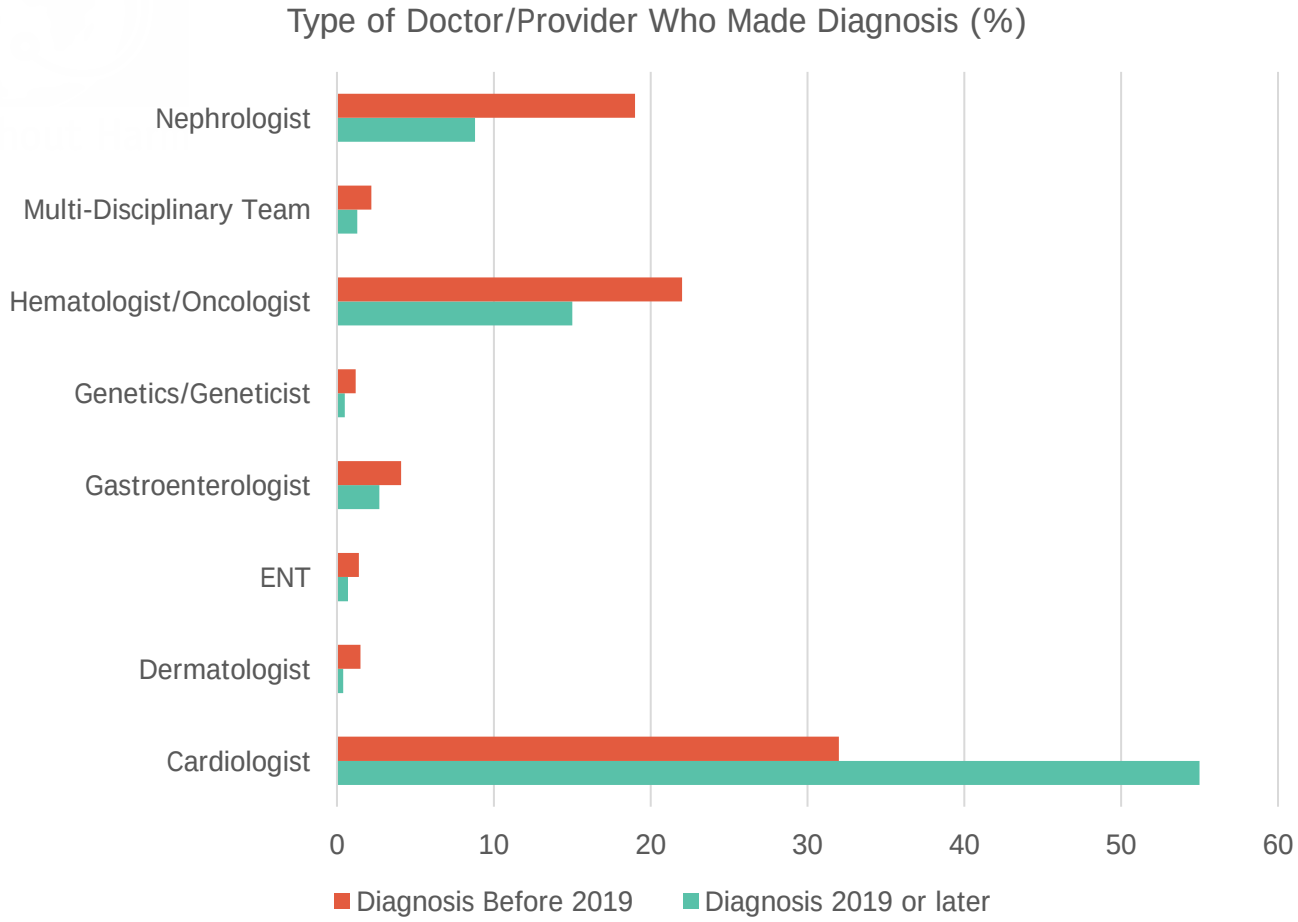
“4 doctors thought I had Athlete’s heart. I didn’t.”

GREG FOSTER
Olympian
AL amyloidosis

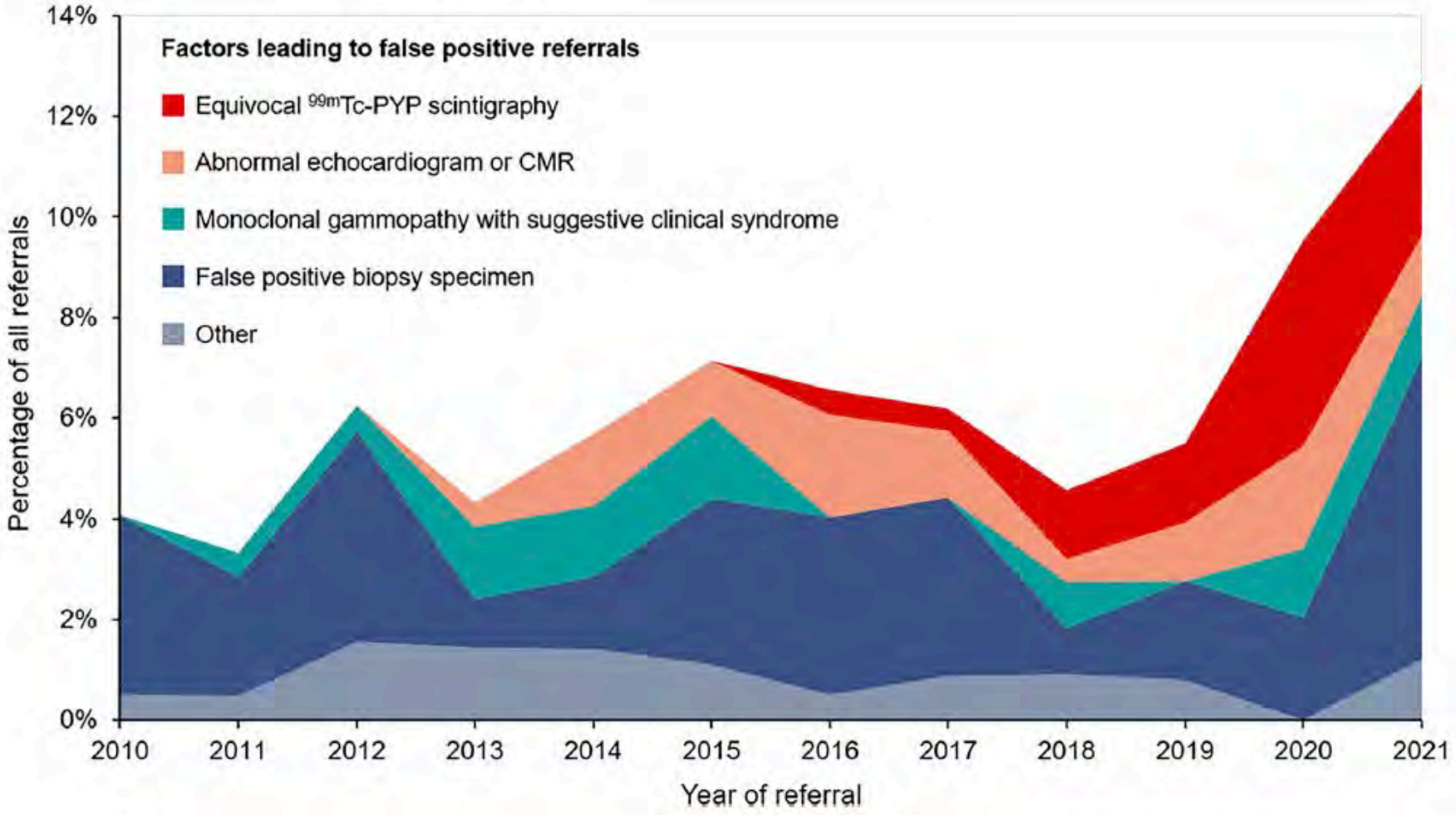


Journey to Diagnosis – Changes over time





Emergence of cardiac imaging as a major source of false positive referrals



Reference: A. Staron et al. *Factors affecting the accuracy of amyloidosis identification and referral to a specialty center*, Amyloid, DOI: 10.1080/13506129.2023.2171787

From one doctor to another

Advice from amyloidosis patient physicians

- Look me in the eye
- Be empathetic, it is kind to show concern
- Don’t underestimate the impact of fatigue
- Have humility; refer and confer

To learn more visit:
www.arci.org

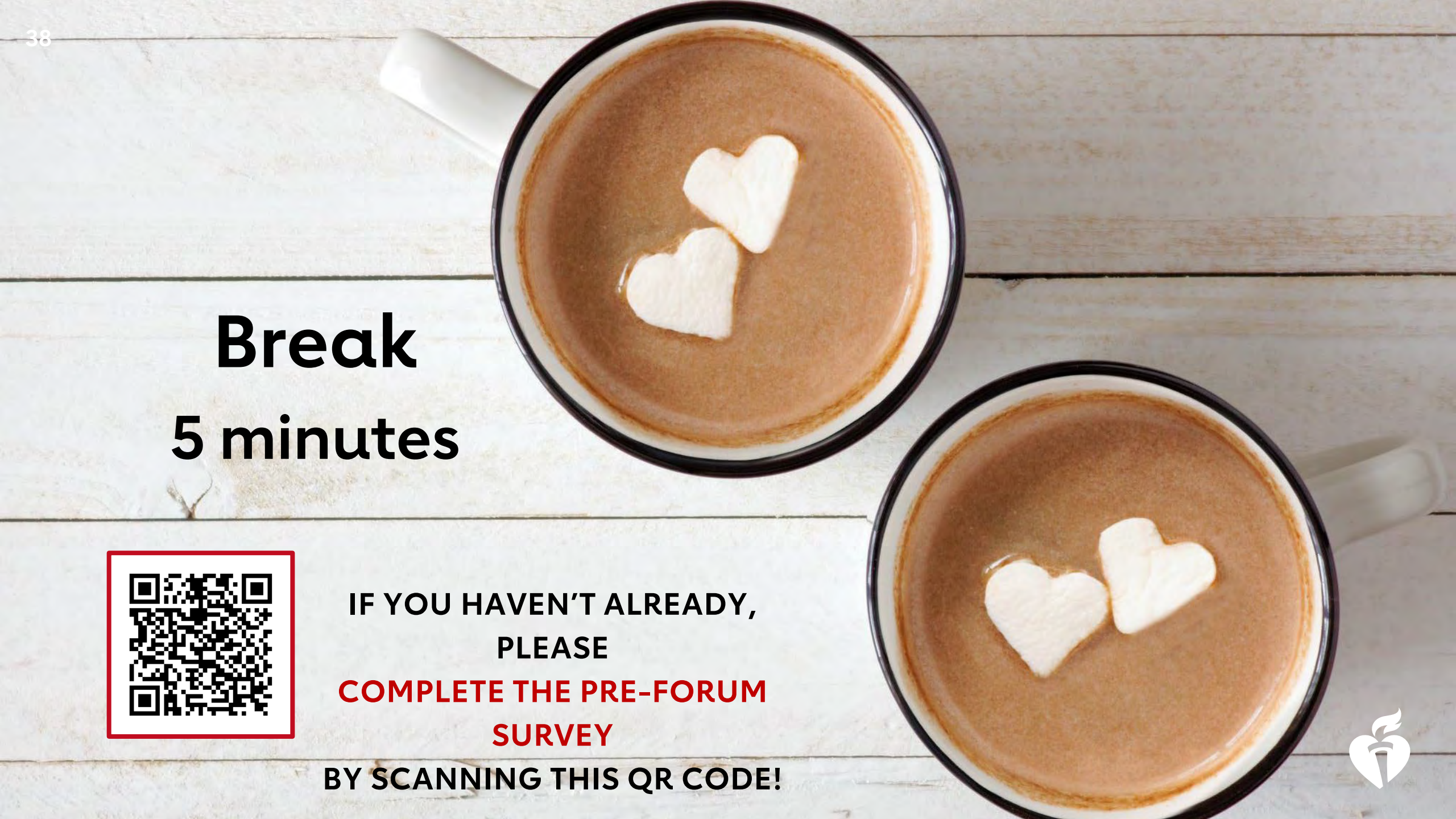
Q & A

Moderated by: **Devin Marie Keating,** Director of Operations, Clinical Studies, American Heart Association

Deborah D. Boedicker, CFA
Board Member,
Mackenzie's Mission
& Amyloidosis Speakers Bureau
https://mm713.org

Muriel Finkel
President & Co-Founder,
Amyloidosis Support Groups
https://www.amyloidosissupport.org

Isabelle Lousada
Founder and CEO,
Amyloidosis Research Consortium
https://arci.org



Break

5 minutes

IF YOU HAVEN'T ALREADY, PLEASE

COMPLETE THE PRE-FORUM SURVEY

BY SCANNING THIS QR CODE!

Welcome Back!
& Upcoming Sessions:

AL Amyloidosis Identification & Diagnosis
Melissa Lyle, MD, FACC, FHFSA

Modern Management of AL Amyloid by Hematology
Heather Landau, MD

Disease Identification & Diagnosis:
Case-Based Panel Discussion and Q&A
Moderated by Mathew Maurer, MD,
Panel: Mazen Hanna, MD, Jai Radhakrishnan, MD, MS,
John Clarke, MD, and Heather Landau, MD

Break (10min)

American Heart Association®

AL Amyloidosis Identification and Diagnosis

Melissa Lyle, MD, FACC, FHFSA

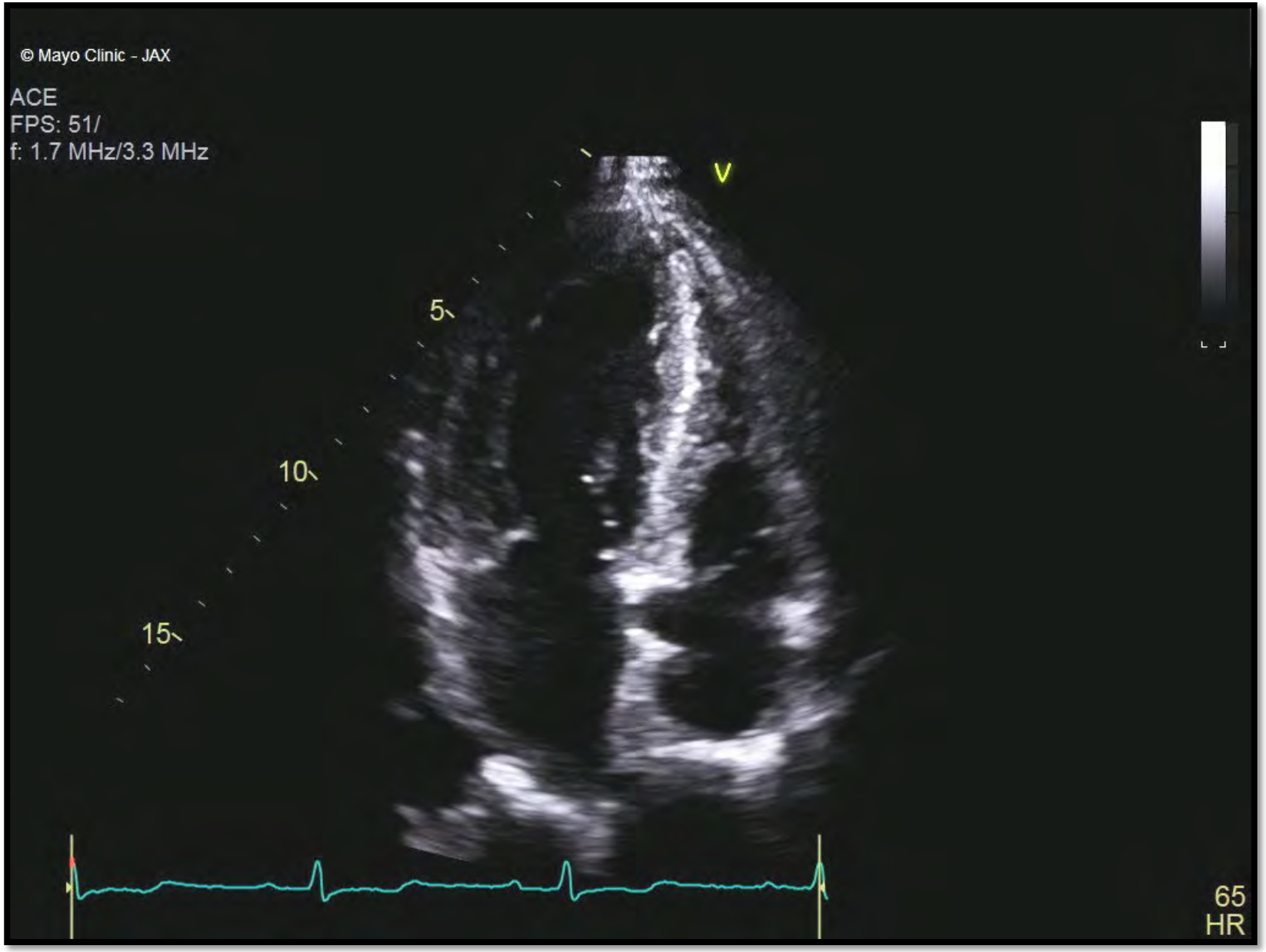
Assistant Professor of Medicine
Division of Advanced Heart Failure and Transplantation

Mayo Clinic Florida

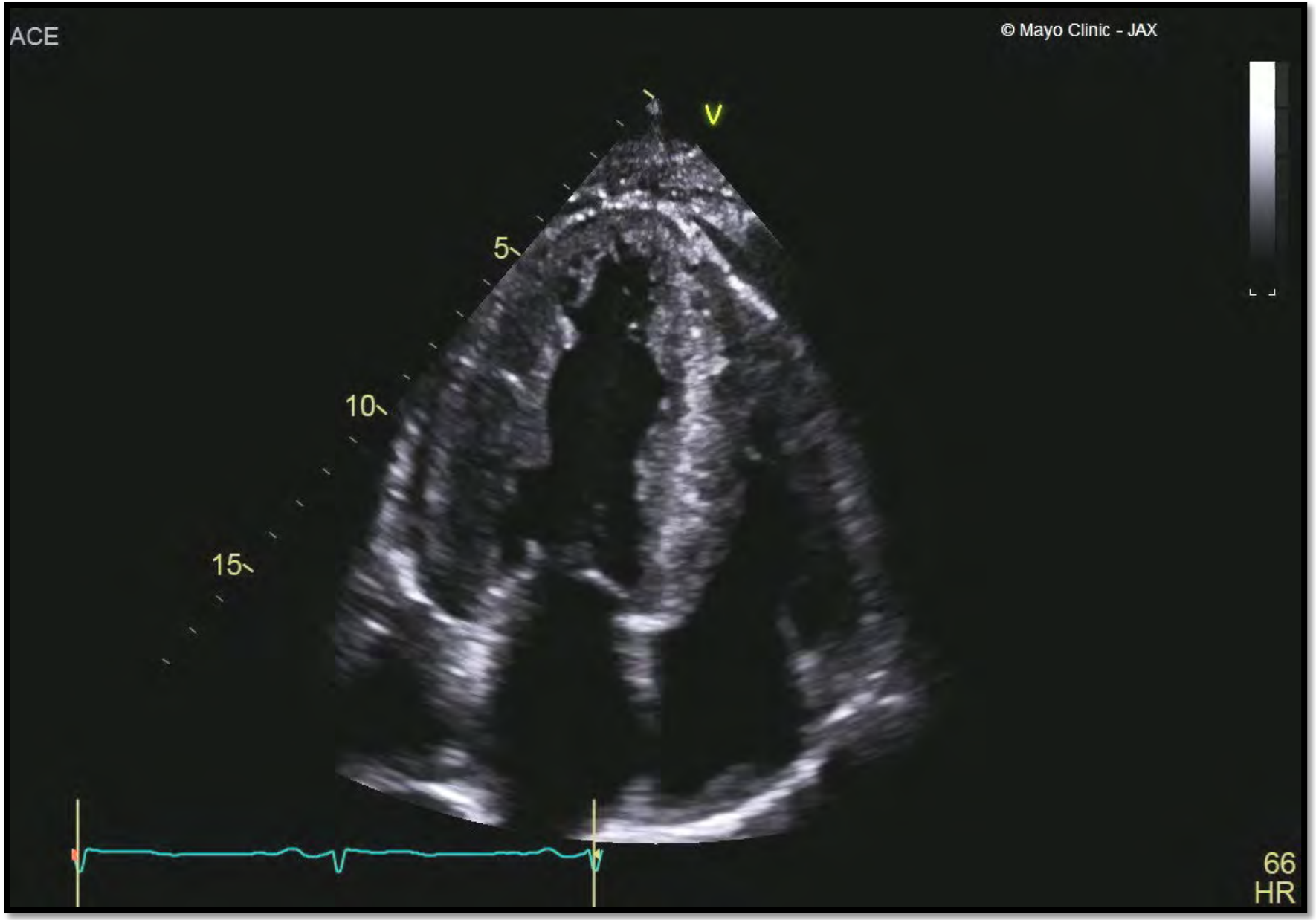
LEARNING OBJECTIVES

- Identify clinical clues to raise suspicion for AL amyloidosis
- Review amyloidosis diagnostic algorithm
- Discuss the role of advanced technologies to improve early detection
- Determine practical strategies for timely diagnosis

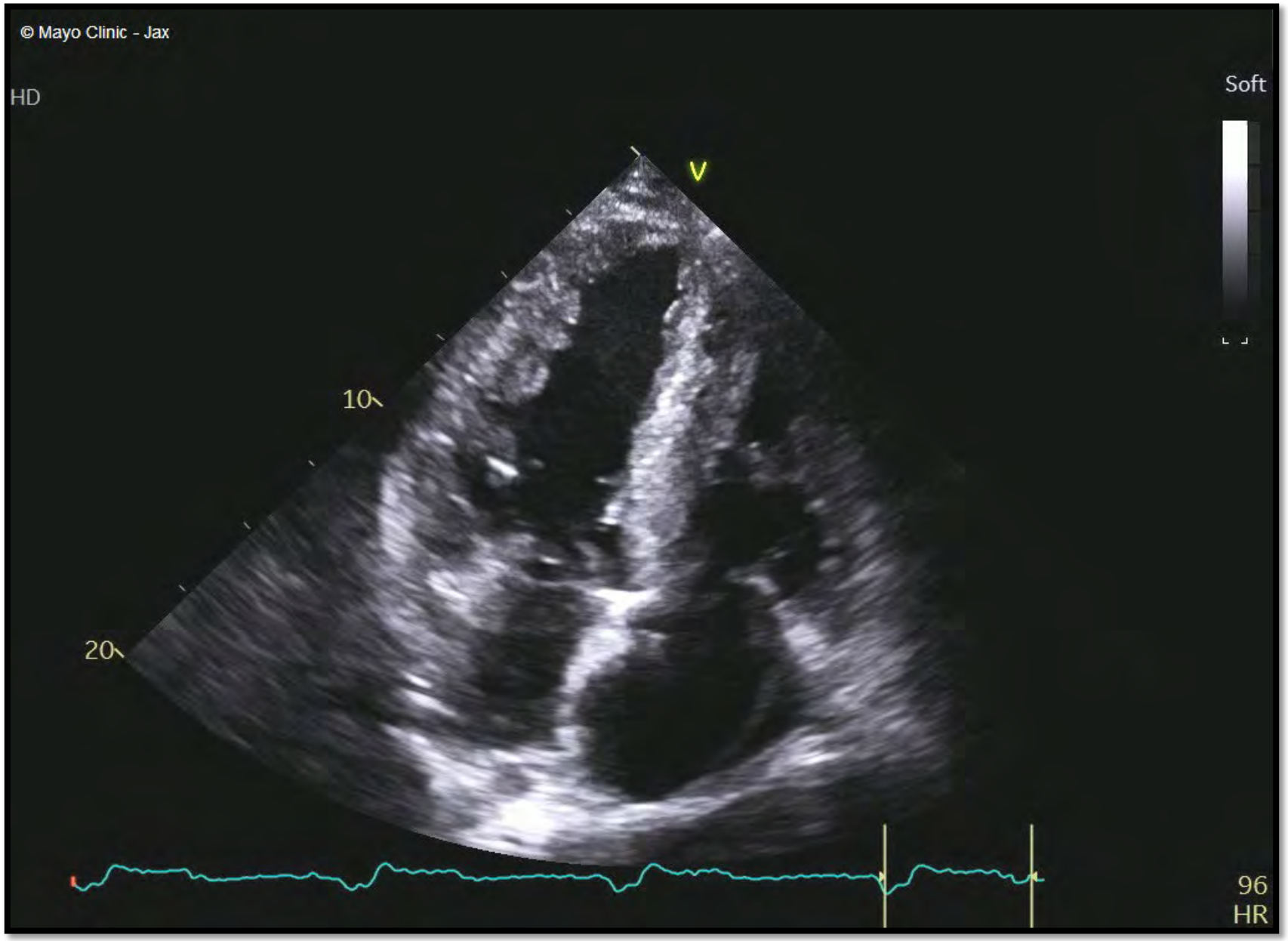
57-year-old female with bilateral carpal tunnel syndrome

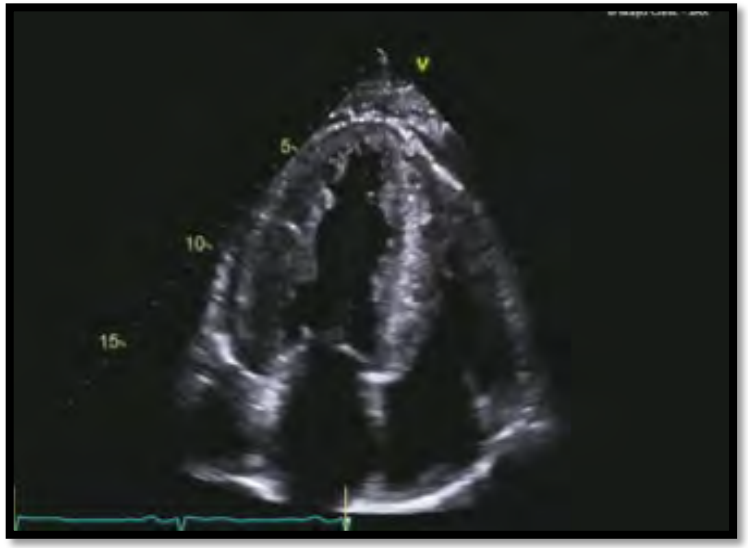
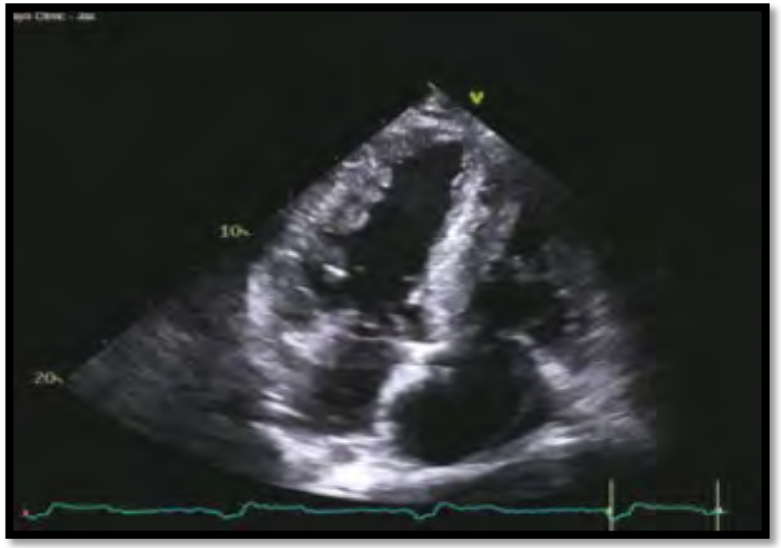
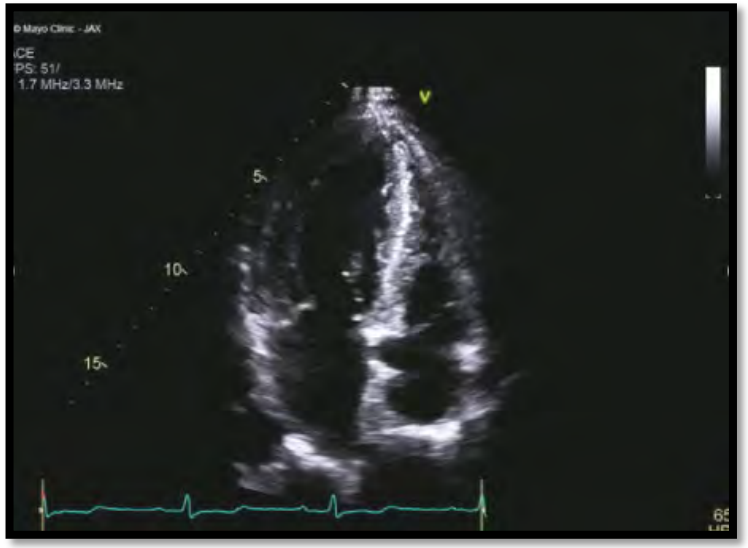


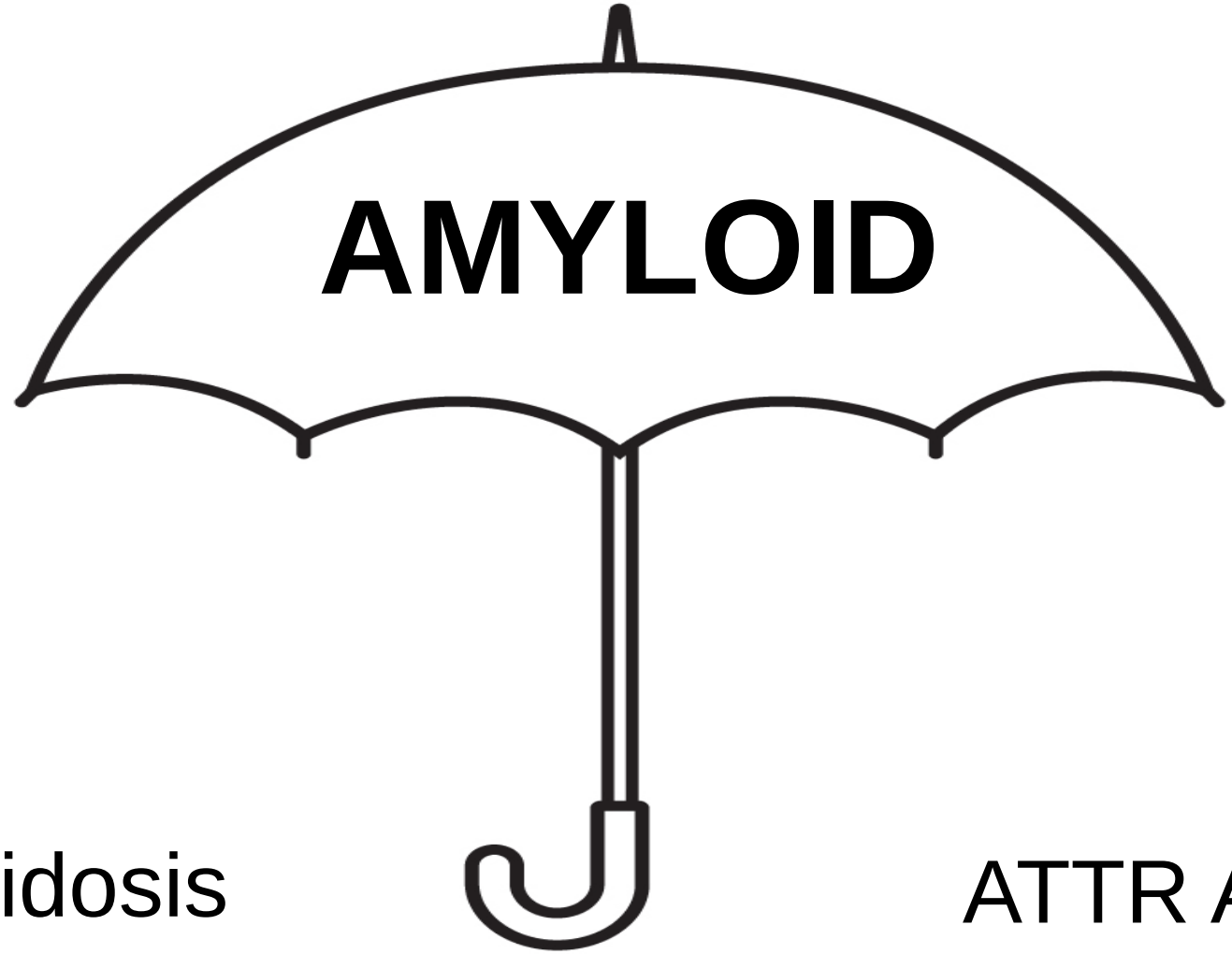
46-year-old male with lower extremity edema and proteinuria



62-year-old female with atrial fibrillation and periorbital purpura



57-year-old female	46-year-old male	62-year-old female
		
AL Amyloidosis	AL Amyloidosis	AL Amyloidosis

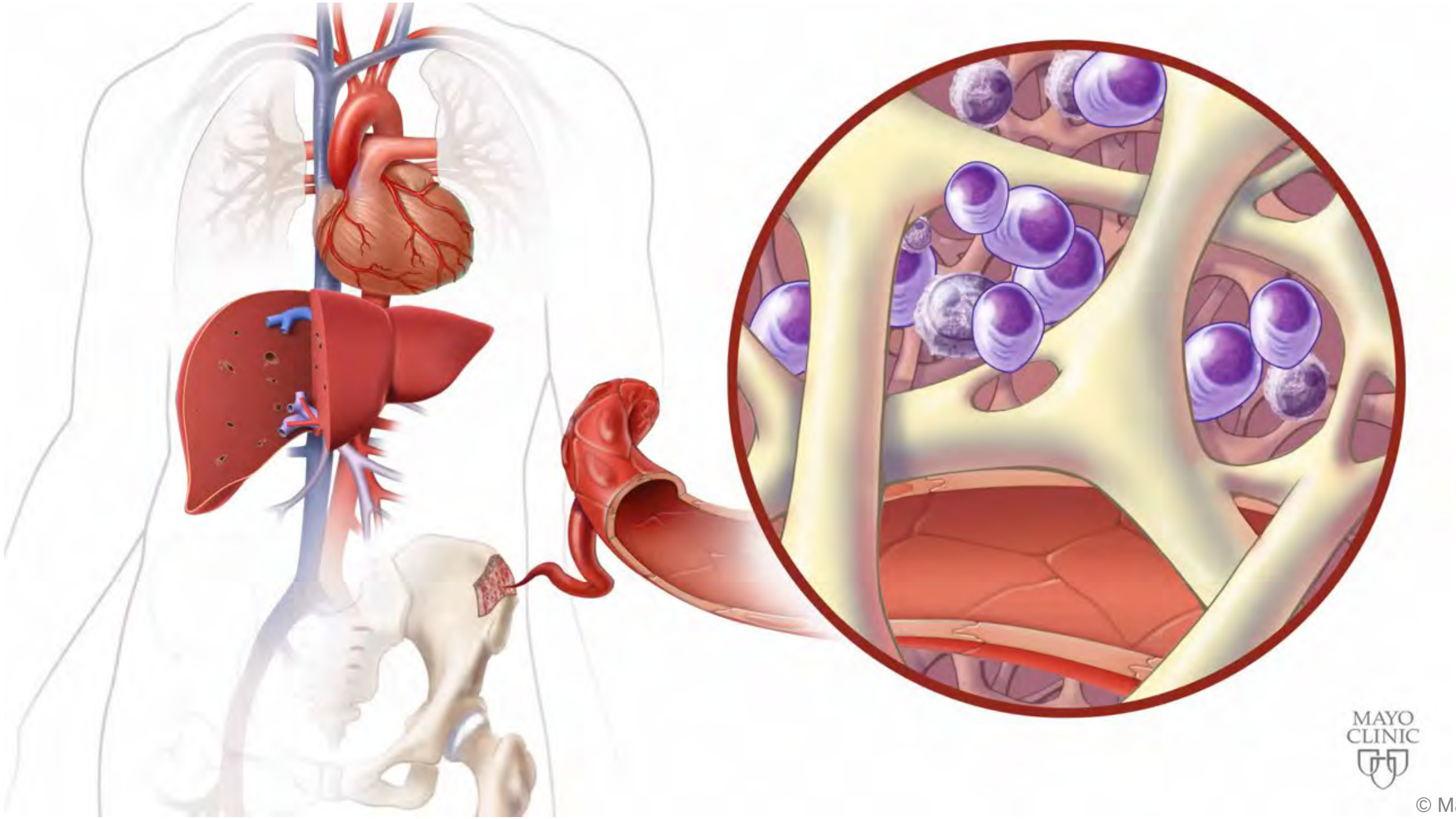


AL Amyloidosis

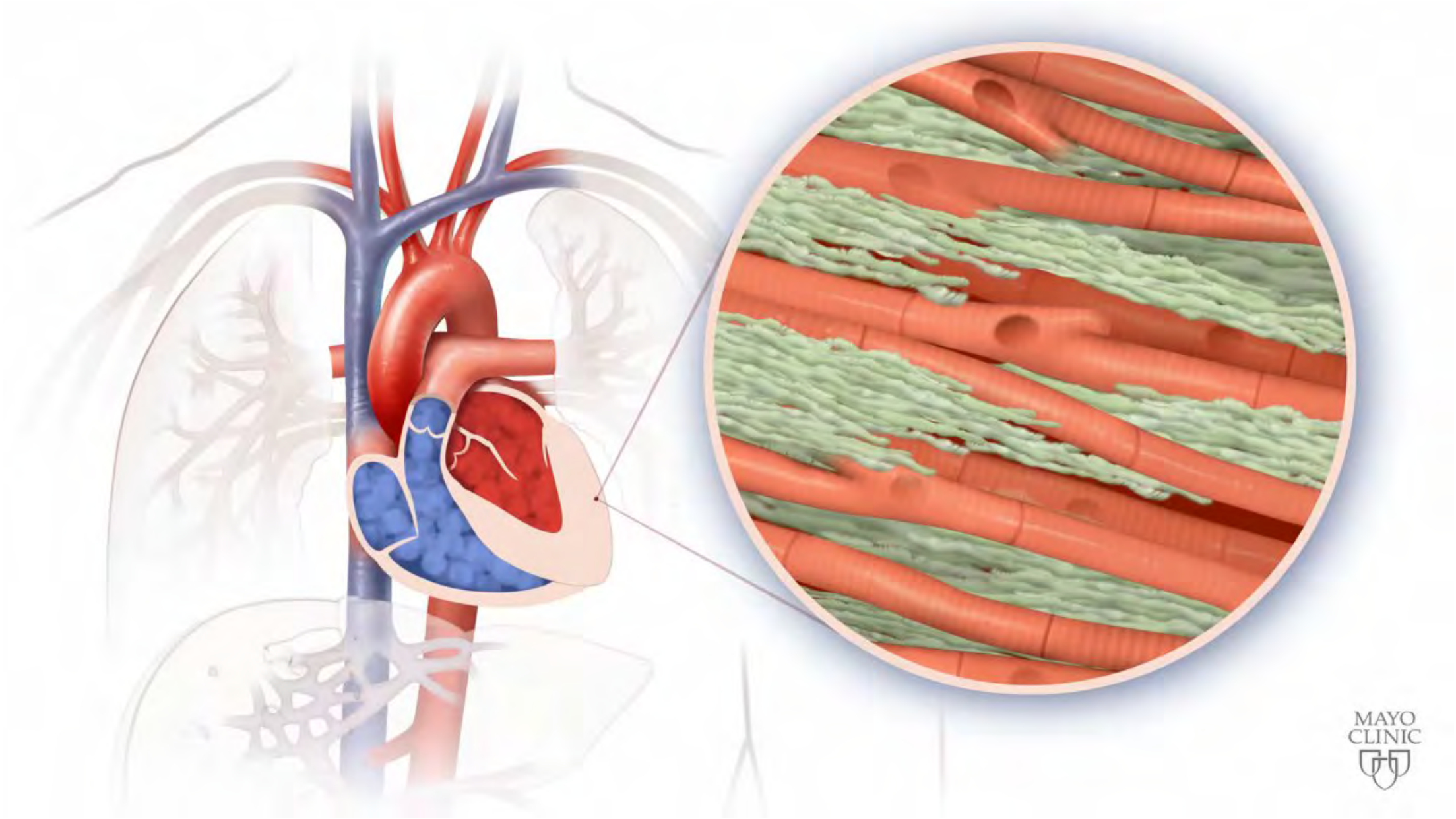
Protein: Immunoglobulin light chain
Protein Factory: Plasma Cells in bone marrow

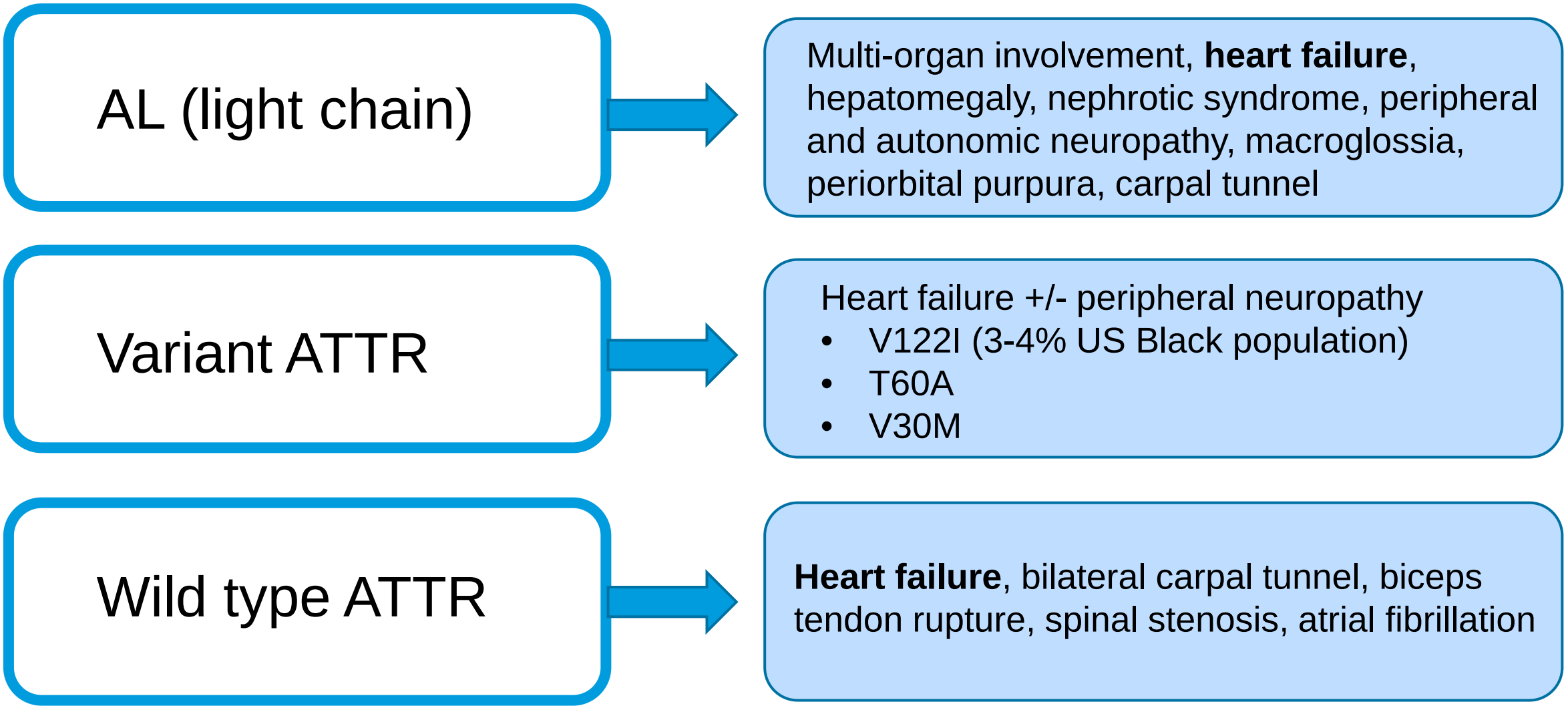
ATTR Amyloidosis

Protein: Transthyretin (TTR)
Protein Factory: Liver



© Mayo Clinic
Slide courtesy of Dr. Martha Grogan





Reference Link

Kittleson et al. 2023 ACC Expert Consensus Decision Pathway on Comprehensive Multidisciplinary Care for the Patient with Cardiac Amyloidosis. *JACC*. 2023

PREVALENCE

- Estimated annual incidence 1 in 75,000-100,000
- Prevalence 1 in 25,000
- 75% cardiac involvement
- 1 in 7 patients with multiple myeloma have concomitant AL amyloidosis

Reference Link

Bloom et al. Cardio-Oncology and Heart Failure: AL Amyloidosis for the Heart Failure Clinician: a Supplement to the Scientific Statement from the HFSA. *Journal of Cardiac Failure.* February 2025.

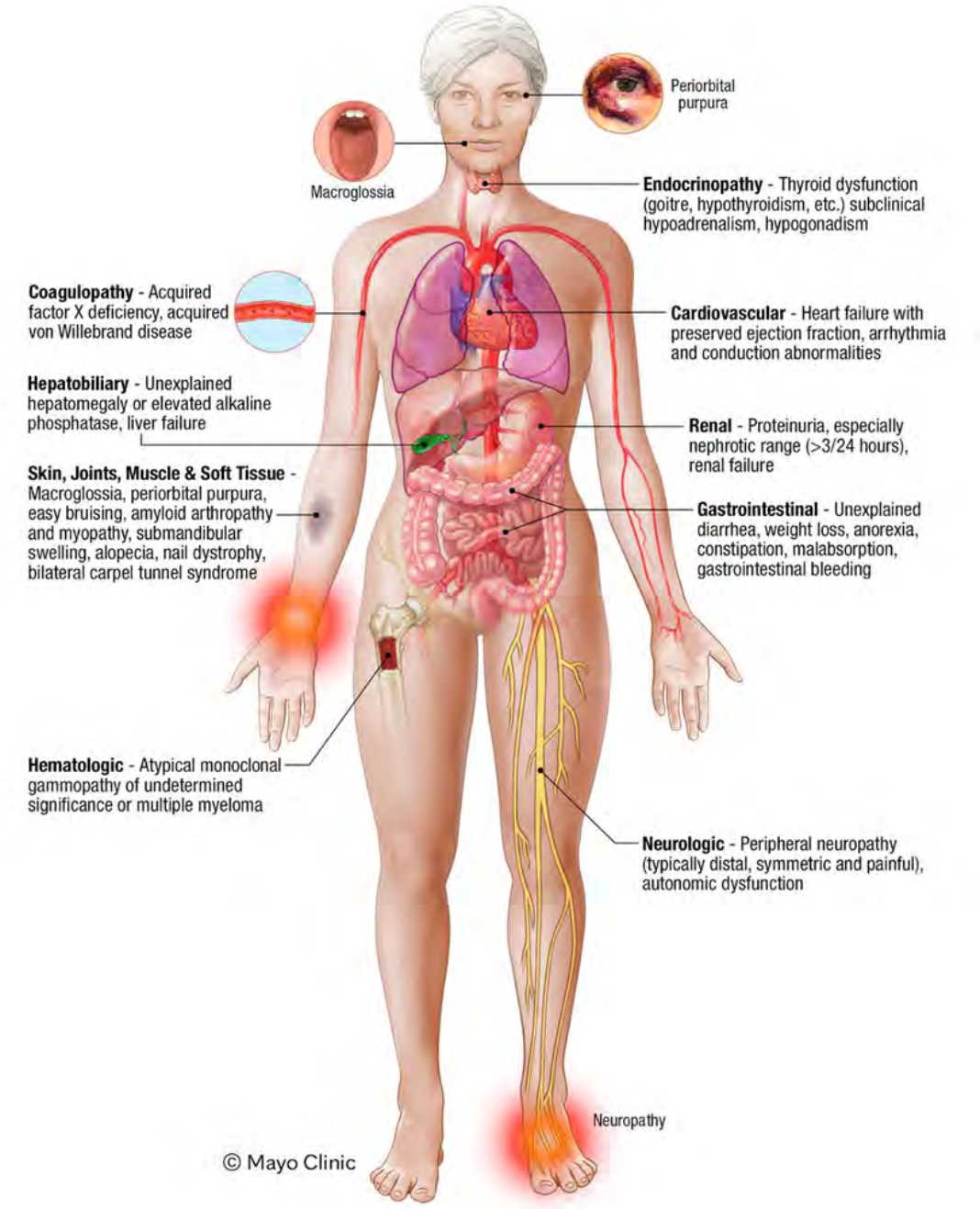
DIAGNOSTIC APPROACH

1. Left ventricular wall thickness ≥ 12 mm

2. ≥1 Clinical Clues

CLINICAL CLUES

- Heart failure ≥ 65 years
- Aortic stenosis in ≥ 65 years
- Autonomic dysfunction
- Peripheral polyneuropathy
- Bilateral carpal tunnel syndrome
- Ruptured biceps tendon
- Perioral/periorbital purpura
- Macroglossia
- Low voltage on ECG
- Decreased QRS voltage to mass ratio
- Pseudo Q waves on ECG
- Atrial Fibrillation
- Persistent elevation of cardiac biomarkers
- Intolerance to typical guideline directed medical therapy for heart failure

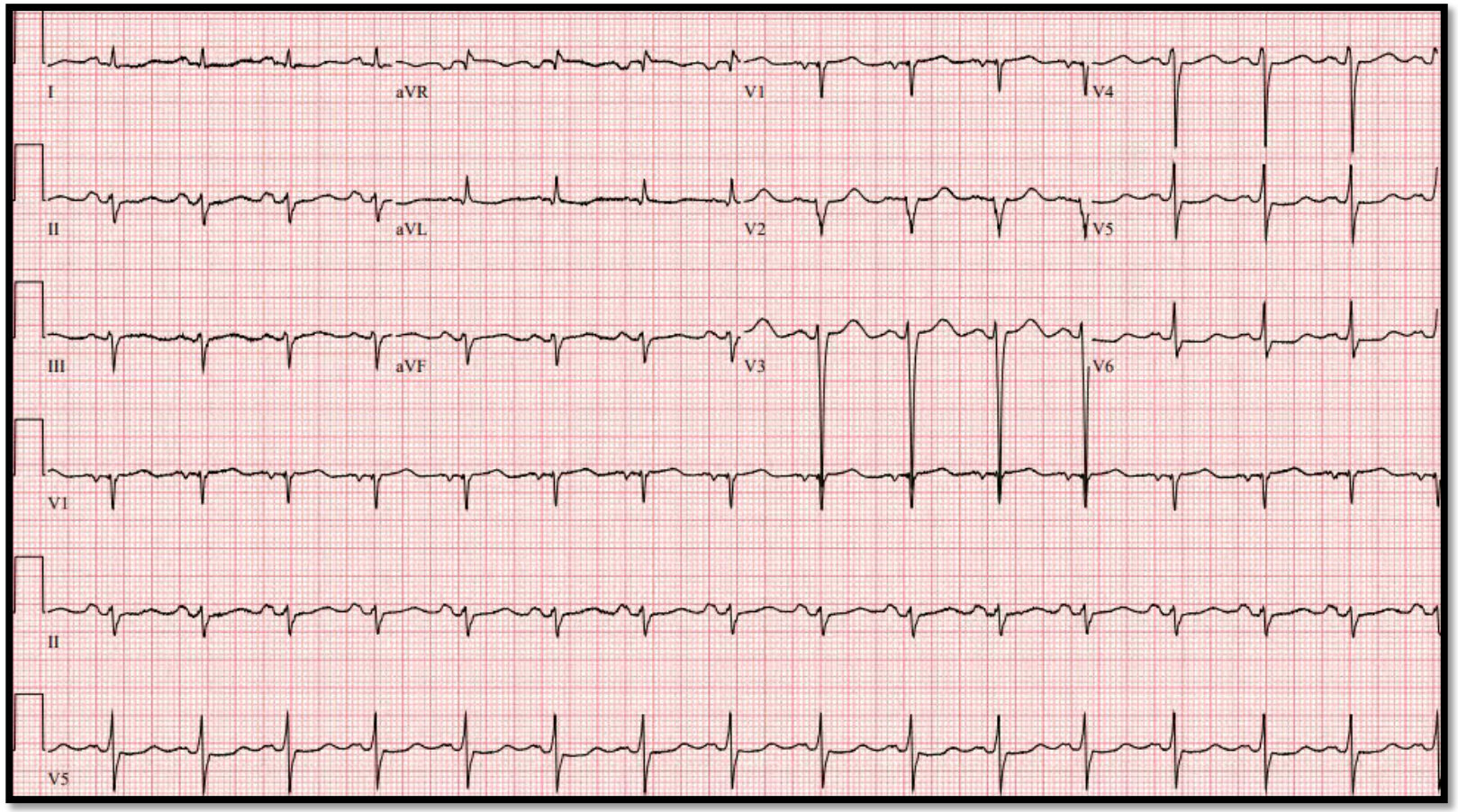


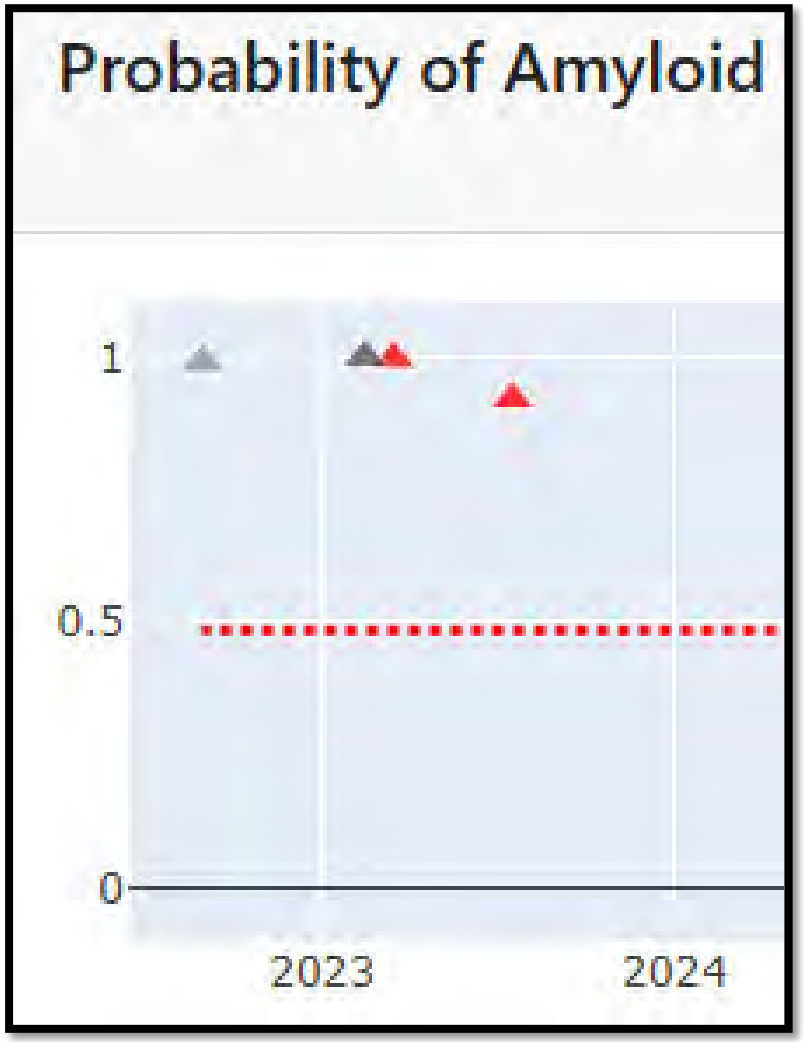
CASE PRESENTATION

- 55-year-old female with recent viral respiratory illness presented with progressive dyspnea on exertion
- Transthoracic echocardiogram: ejection fraction 25%
- Cardiac MRI: diffuse myocardial delayed enhancement
- Diagnosed with presumed myocarditis and initiated on GDMT

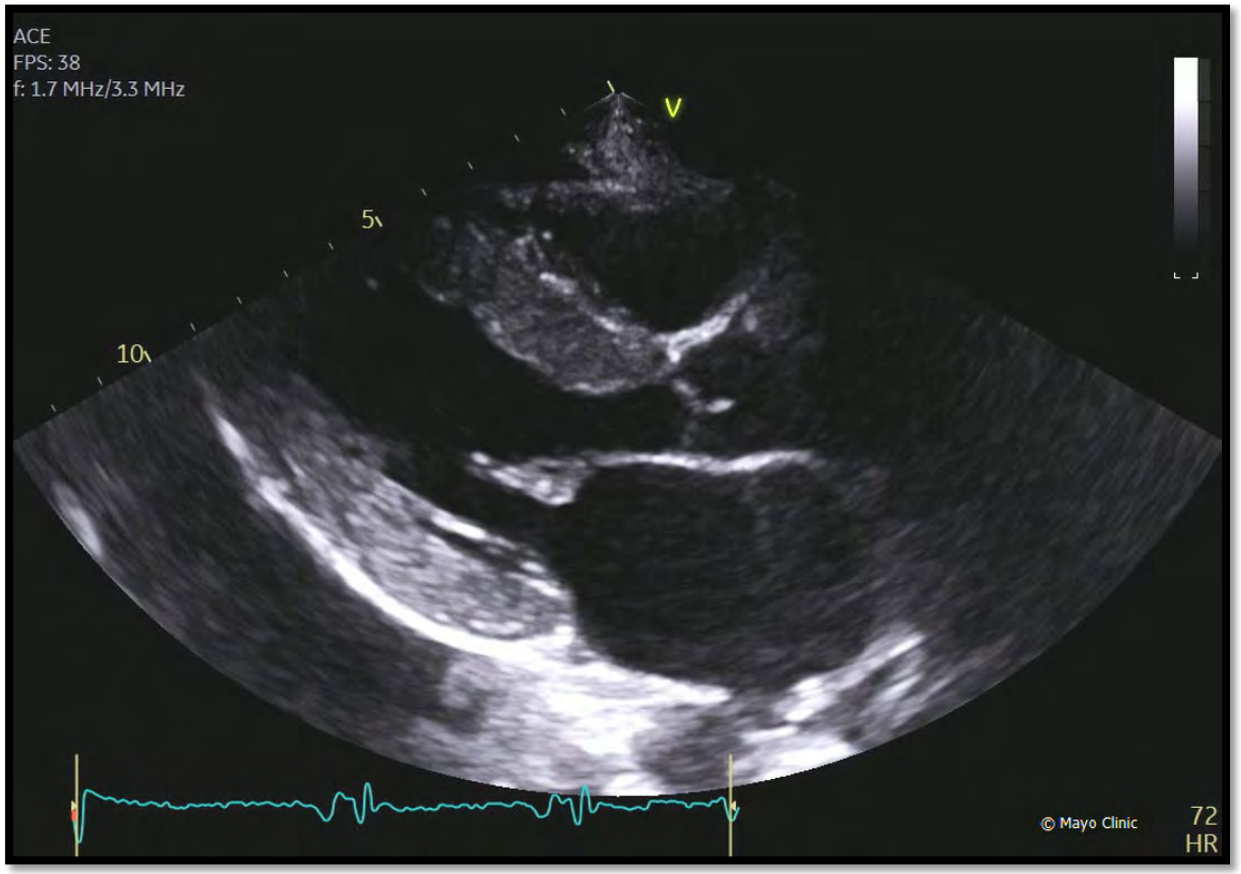
CASE CONTINUED

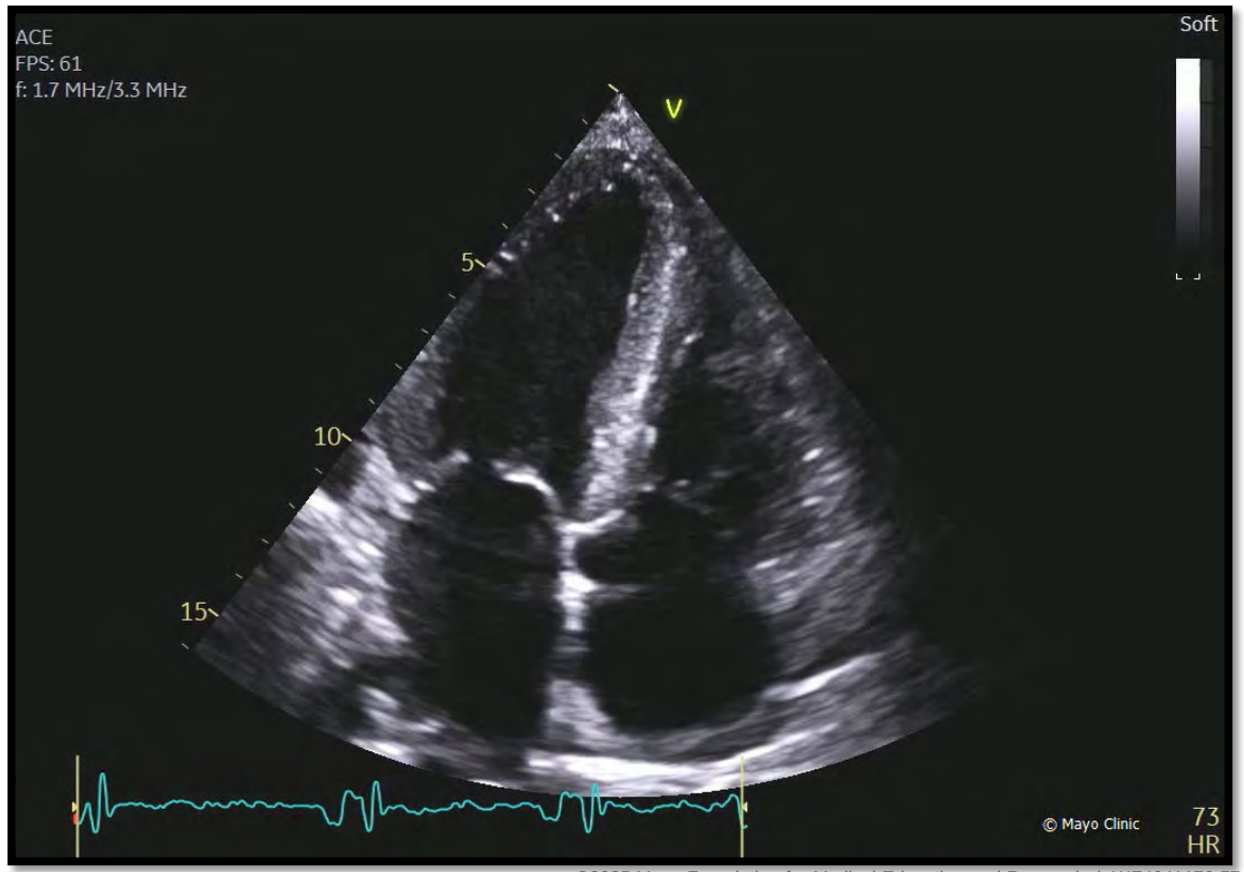
- Referred to our center due to progressive functional decline **6 months later**
- Not tolerating GDMT
- Recurrent pleural effusions requiring thoracenteses
- History **periorbital purpura** and paroxysmal **atrial fibrillation**

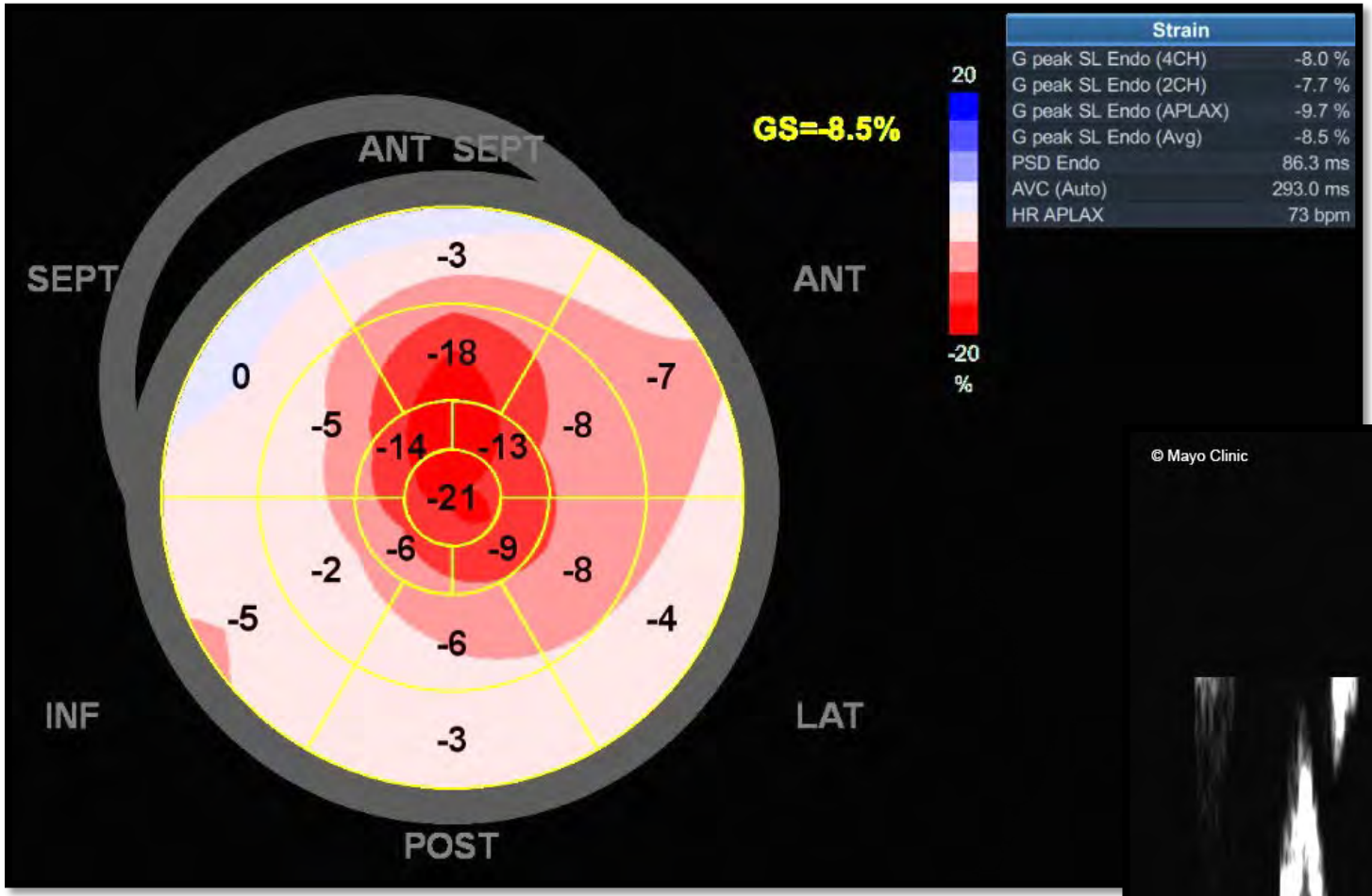


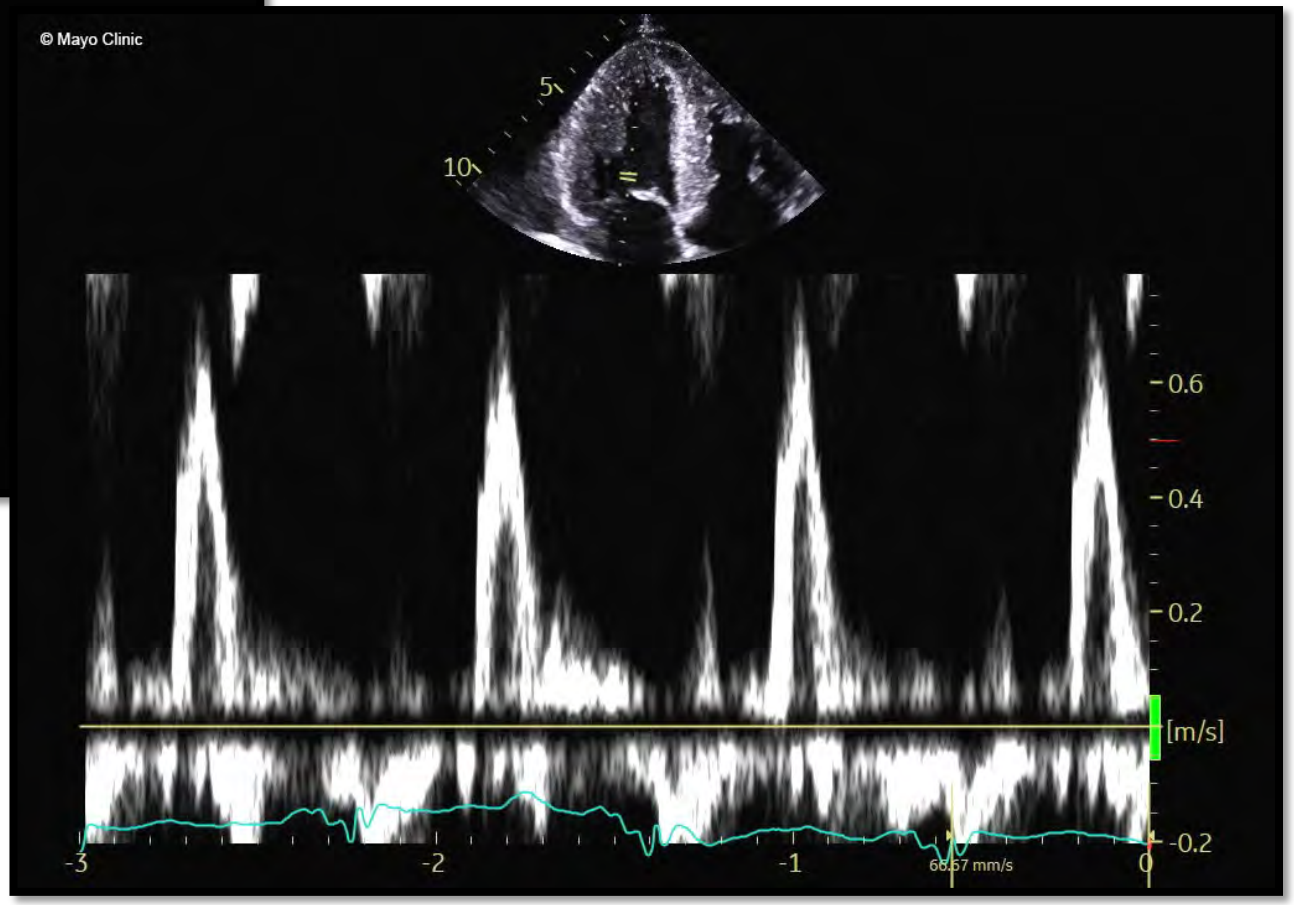


- High sensitivity troponin 115 ng/L
- NT proBNP 11918 pg/ML
- Creatinine 0.8 mg/dL









ASNC/AHA/ASE/EANM/HFSA/ISA/SCMR/SNMMI Expert Consensus Recommendations for Multimodality Imaging in Cardiac Amyloidosis: Part 1 of 2—Evidence Base and Standardized Methods of Imaging

SHARMILA DORBALA, MD, MPH, FASNC,[1] YUKIO ANDO, MD, PhD,[2] SABAHAT BOKHARI, MD,[3]
ANGELA DISPENZIERI, MD,[4] RODNEY H. F
OLIVIER GHEYSENS, MD, PhD,[7] JULIAN D
MAZEN A. HANNA, MDv,[9] BOUK
RAYMOND Y. KWONG, MD, MPH,[1]
EDWARD J. MILLER, MD, PhD,[14] JA
C. CRISTINA QUARTA, MD, PhD,[6] CLAUDIO R
RIEMER H.J.A. SLART, MD,[8] HEIN J. VERBE

*Boston, Massachusetts; Kumamoto, Japan; New York, New Y
Belgium; Groningen, and Amsterdam, The Netherlands; Cle
Ann Arbor, Michig*

ASNC/AHA/ASE/EANM/HFSA/ISA/SCMR/SNMMI Expert Consensus Recommendations for Multimodality Imaging in Cardiac Amyloidosis: Part 2 of 2—Diagnostic Criteria and Appropriate Utilization

SHARMILA DORBALA, MD, MPH, FASNC,[1] YUKIO ANDO, MD, PhD,[2] SABAHAT BOKHARI, MD,[3]
ANGELA DISPENZIERI, MD,[4] RODNEY H. FALK, MD,[1] VICTOR A. FERRARI, MD,[5] MARIANNA FONTANA, PhD,[6]
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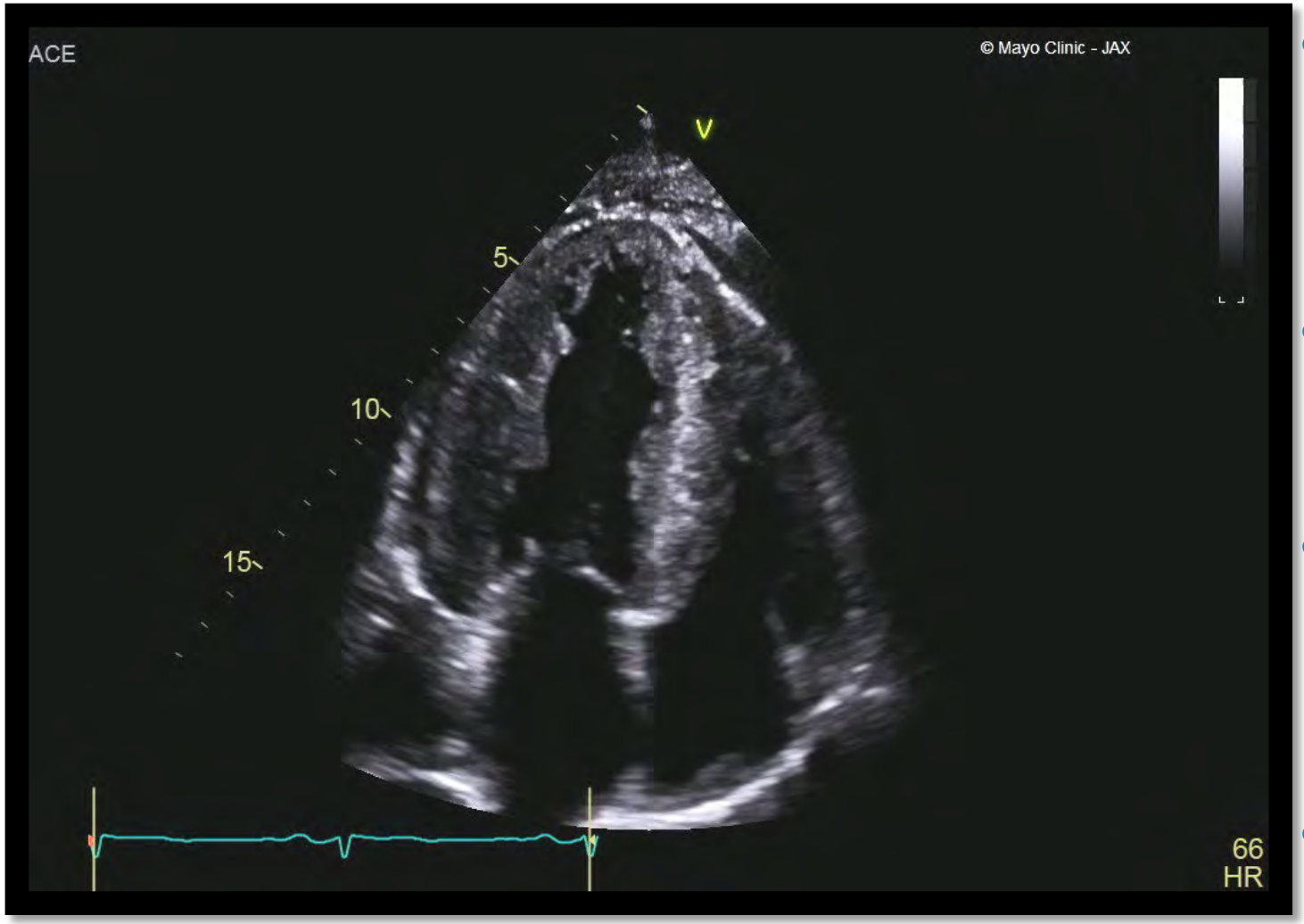
MAZEN A. HANNA, MD,[9] BOUKE P.C. HAZENBERG, MD, PhD,[10] ARNT V. KRISTEN, MD,[11] RAYMOND Y. KWONG, MD, MPH,[1]
MATHEW S. MAURER, MD,[3] GIAMPAOLO MERLINI, MD,[12,13] EDWARD J. MILLER, MD, PhD,[14] JAMES C. MOON, MD,[6]
VENKATESH L. MURTHY, MD, PhD,[15] C.CRISTINA QUARTA, MD, PhD,[6] CLAUDIO RAPEZZI, MD,[16]
FREDERICK L. RUBERG, MD,[17] SANJIV J. SHAH, MD,[18] RIEMER H.J.A. SLART, MD,[8] HEIN J. VERBERNE, MD, PhD,[19] AND
JAMIESON M. BOURQUE, MD, MHS, FASNC[20]

Boston, New York, Rochester, Philadelphia, Cleveland, New Haven, Ann Arbor, Chicago, and Charlottesville, USA; Kumamoto, Japan; London, United Kingdom; Leuven, Belgium; Groningen, and Amsterdam, Netherlands; Heidelberg, Germany; and Pavia, and Bologna, Italy

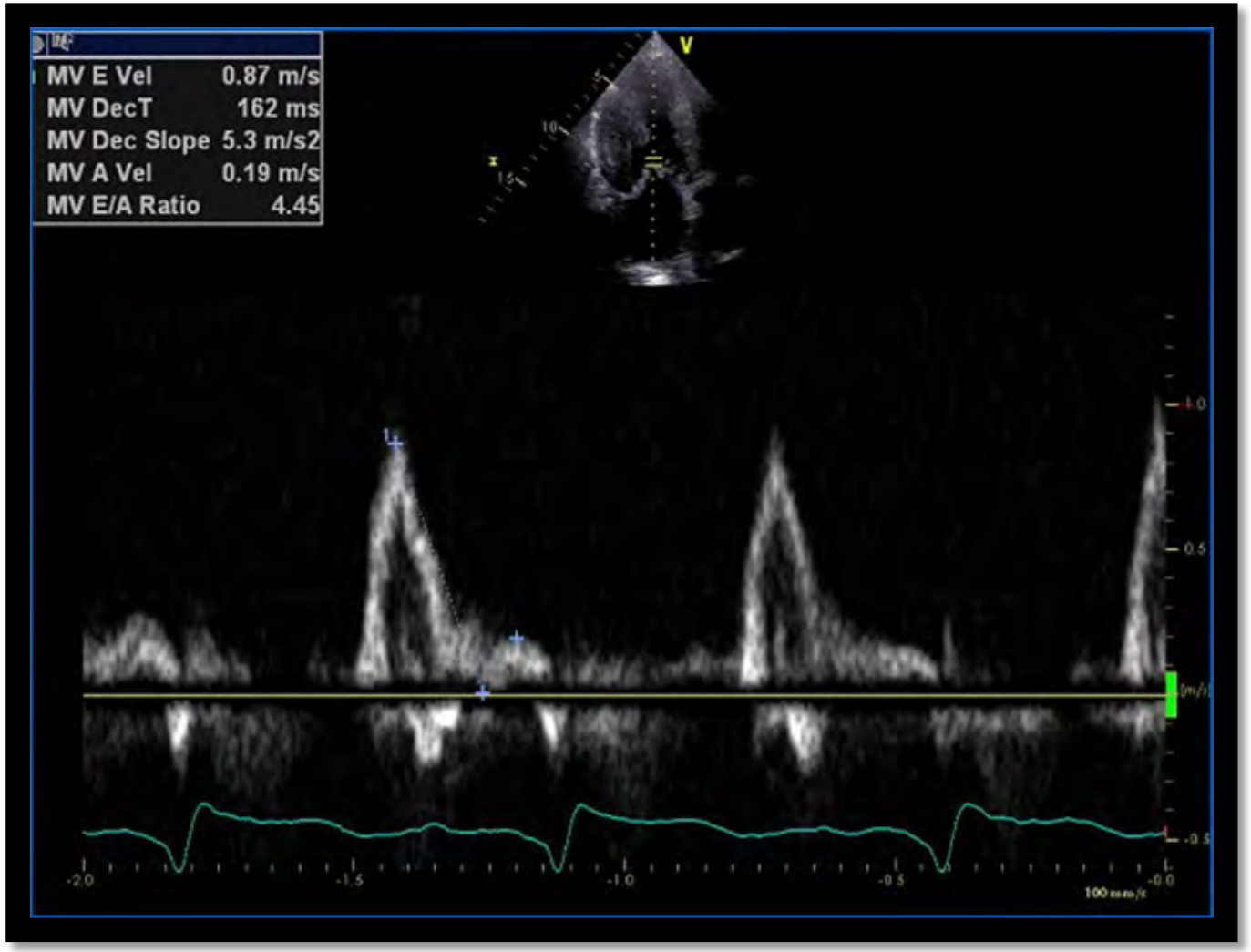
1. https://pubmed.ncbi.nlm.nih.gov/34196223/
2. https://pubmed.ncbi.nlm.nih.gov/31468377/

ECHOCARDIOGRAPHIC FEATURES

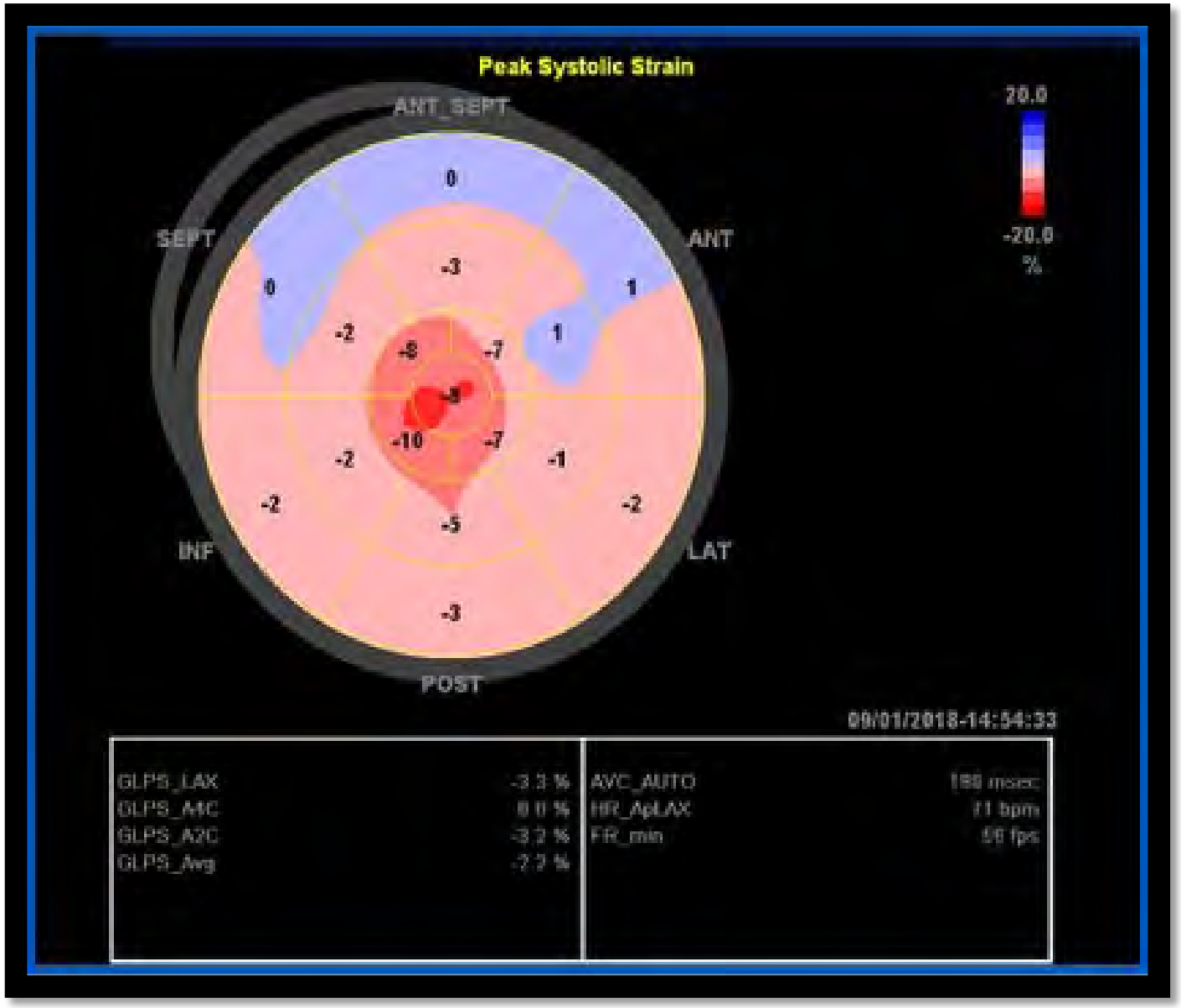


- Concentric biventricular wall thickness
- Bi-atrial enlargement
- Thickened valve leaflets and interatrial septum
- Pericardial effusion

ECHOCARDIOGRAPHIC FEATURES



- E/A ratio > 1.5
- Deceleration time < 150 ms
- Reduced A wave velocity
- 5-5-5 sign
  - All tissue Doppler velocities < 5 cm/sec



ORIGINAL ARTICLE

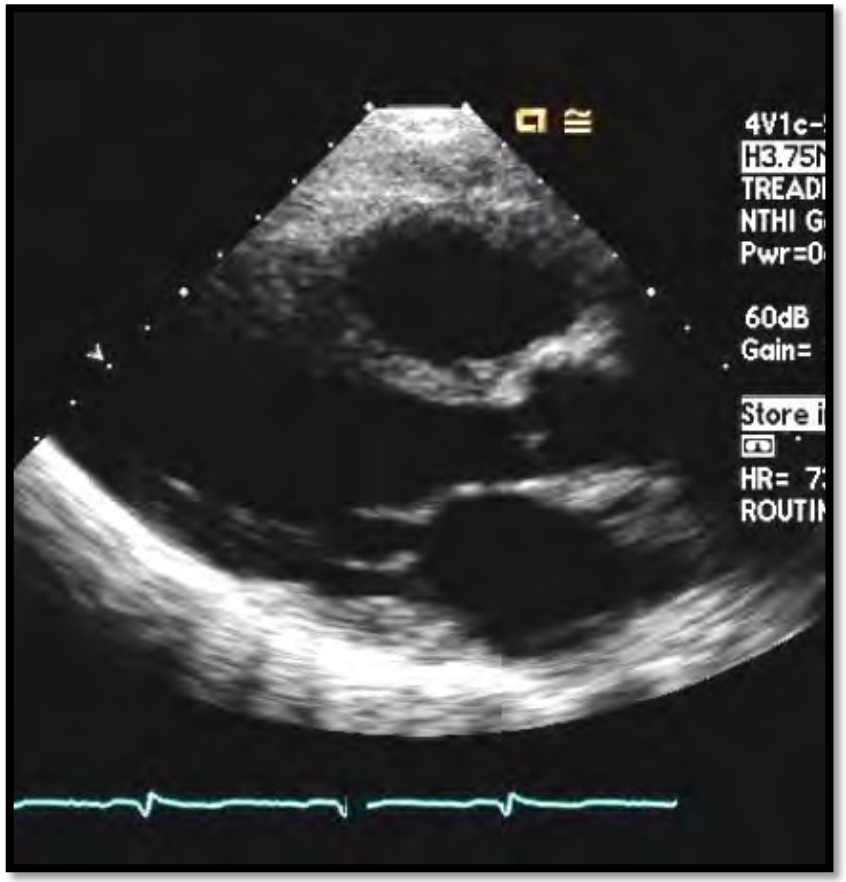
Relative apical sparing of longitudinal strain using two-dimensional speckle-tracking echocardiography is both sensitive and specific for the diagnosis of cardiac amyloidosis

Dermot Phelan, Patrick Collier, Paaladinesh Thavendiranathan, Zoran B Popović, Mazen Hanna, Juan Carlos Plana, Thomas H Marwick, James D Thomas

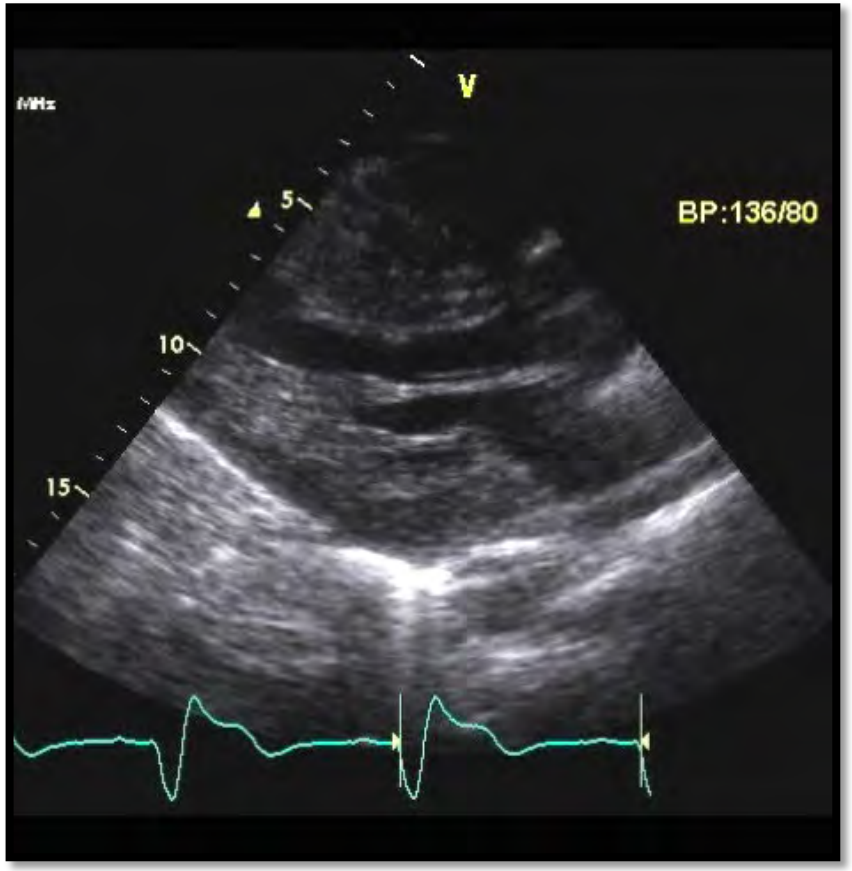
https://pubmed.ncbi.nlm.nih.gov/22865865/

CARDIAC AMYLOID: NOT ALL ABOUT WALL THICKENING

AL: End stage Heart Failure

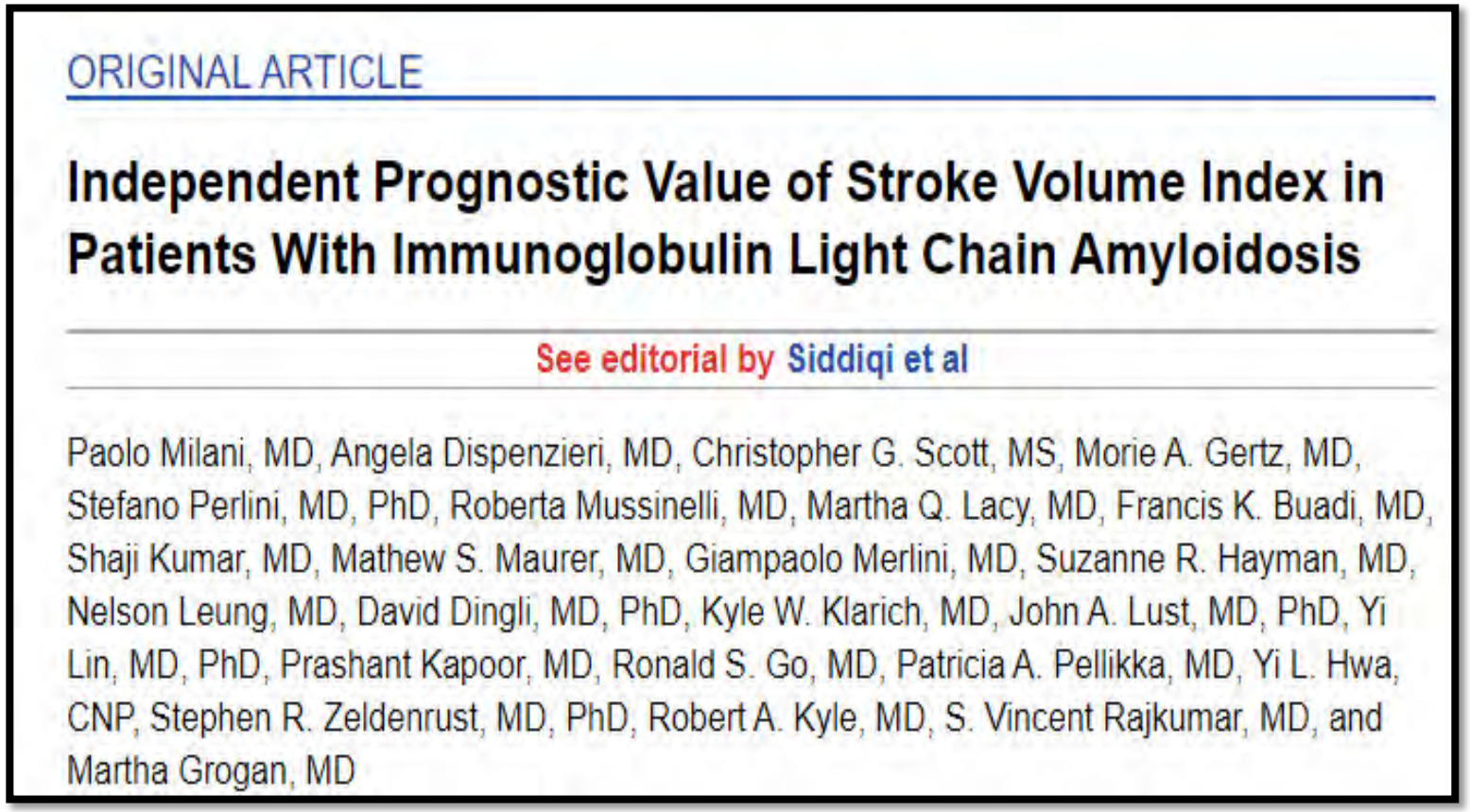


TTR: Walking 3 miles/day



ECHOCARDIOGRAPHIC PROGNOSIS

- Independent echo predictors of mortality
  - SVI < 33 mL/min
  - Cardiac index
  - LV strain -14%



ORIGINAL ARTICLE

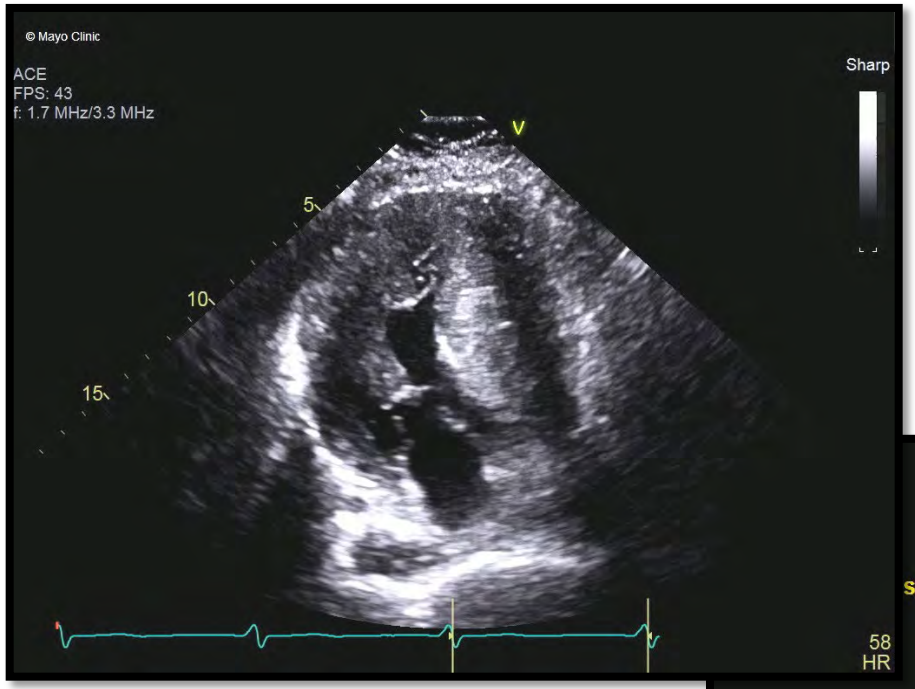
Independent Prognostic Value of Stroke Volume Index in Patients With Immunoglobulin Light Chain Amyloidosis

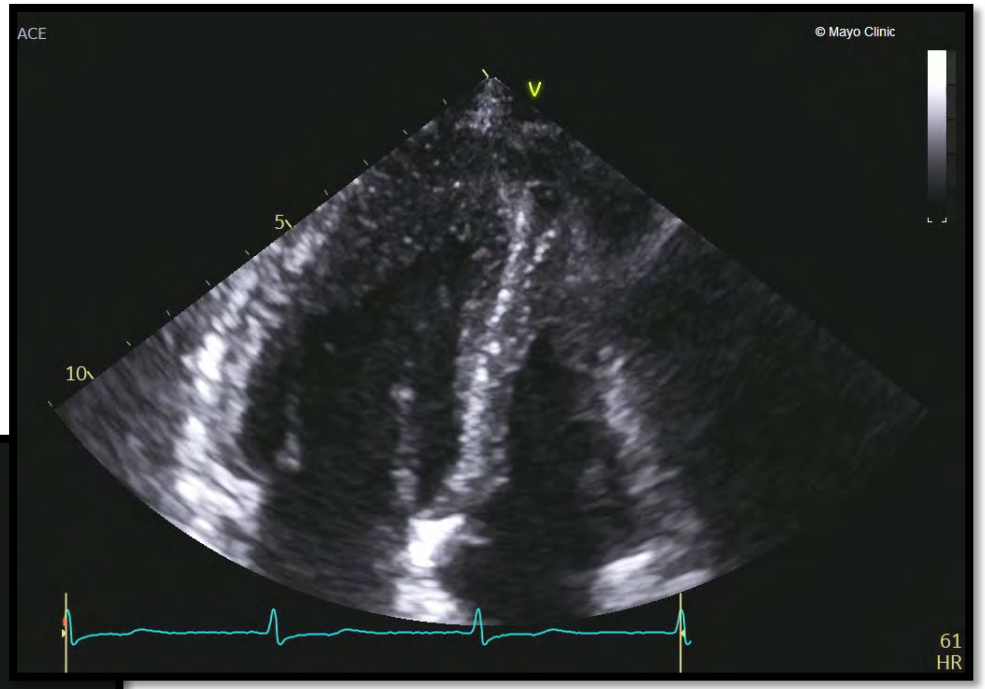
See editorial by Siddiqi et al

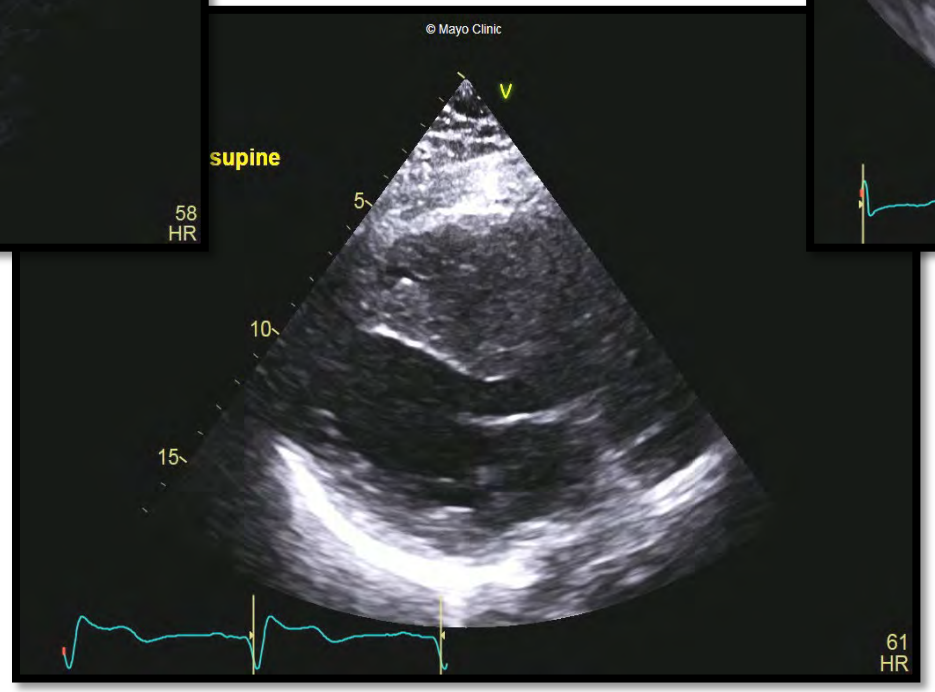
Paolo Milani, MD, Angela Dispenzieri, MD, Christopher G. Scott, MS, Morie A. Gertz, MD, Stefano Perlini, MD, PhD, Roberta Mussinelli, MD, Martha Q. Lacy, MD, Francis K. Buadi, MD, Shaji Kumar, MD, Mathew S. Maurer, MD, Giampaolo Merlini, MD, Suzanne R. Hayman, MD, Nelson Leung, MD, David Dingli, MD, PhD, Kyle W. Klarich, MD, John A. Lust, MD, PhD, Yi Lin, MD, PhD, Prashant Kapoor, MD, Ronald S. Go, MD, Patricia A. Pellikka, MD, Yi L. Hwa, CNP, Stephen R. Zeldenrust, MD, PhD, Robert A. Kyle, MD, S. Vincent Rajkumar, MD, and Martha Grogan, MD

https://pubmed.ncbi.nlm.nih.gov/29752392/

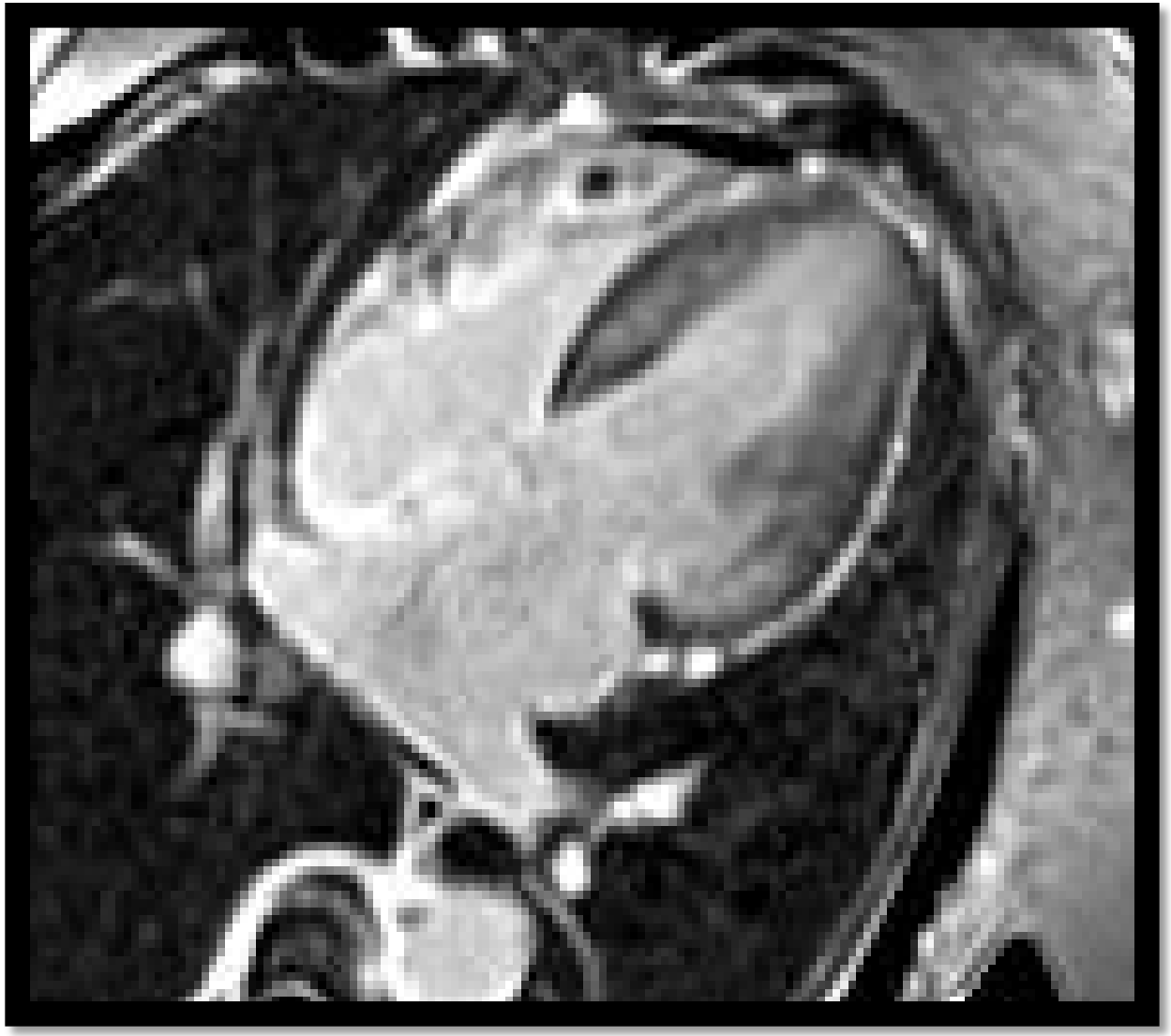
AMYLOID MIMICKERS

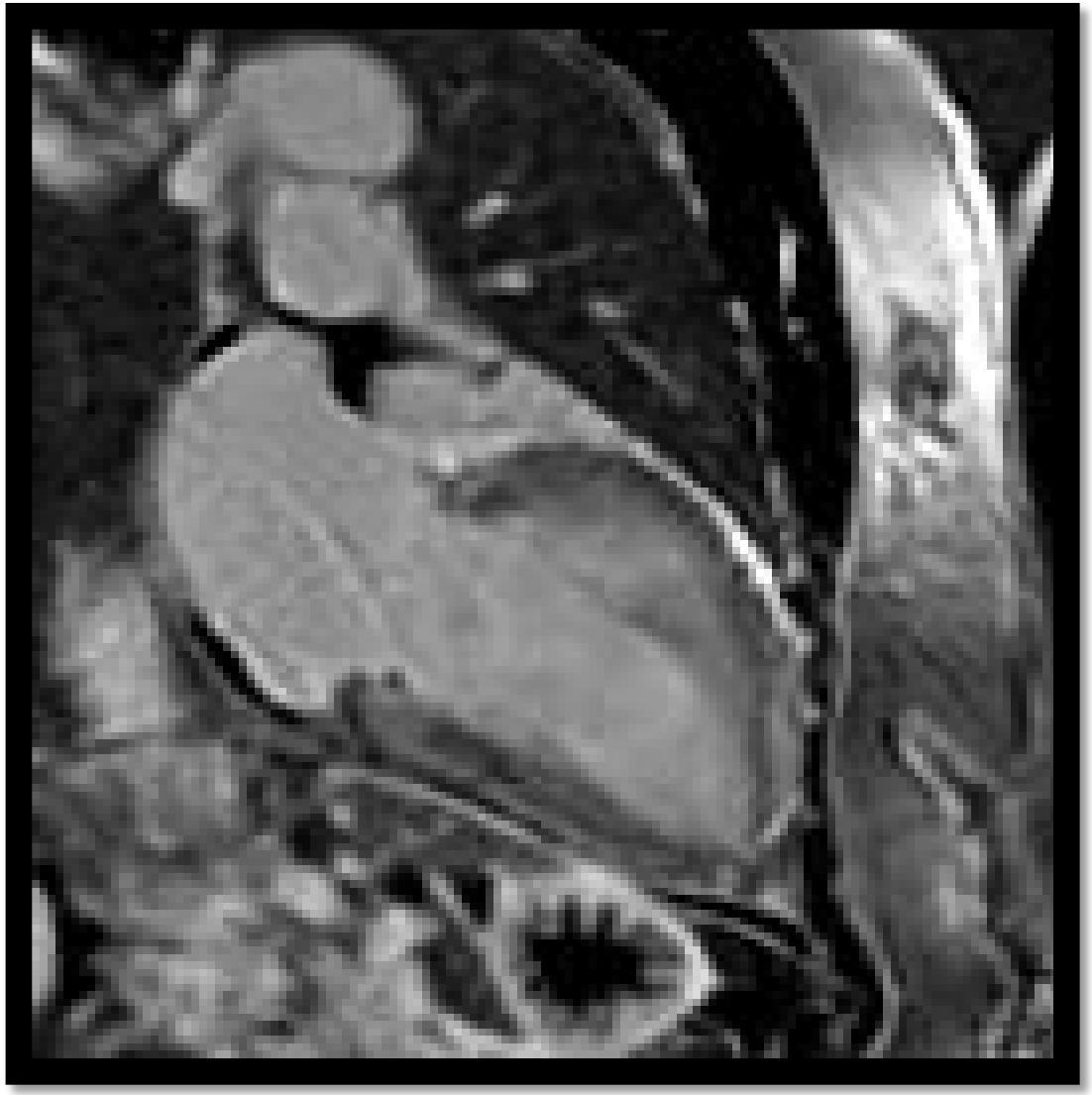






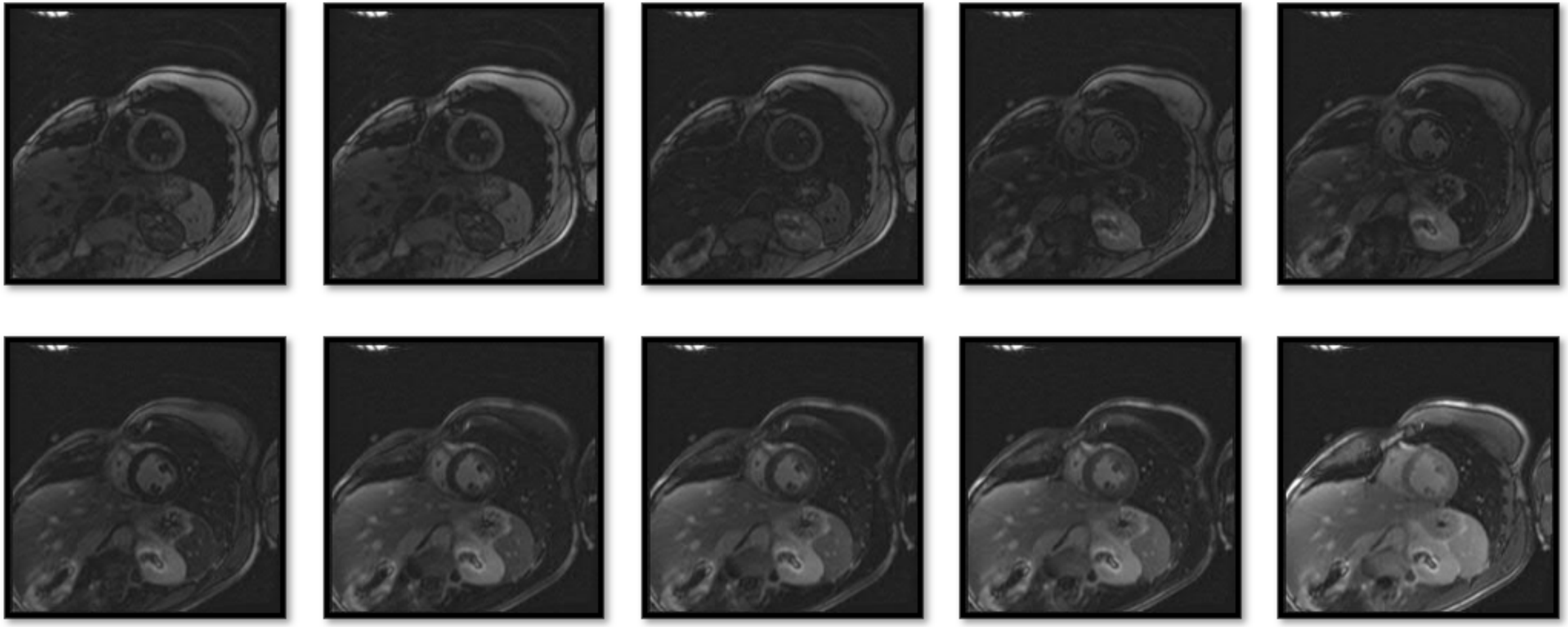
CARDIAC MAGNETIC RESONANCE



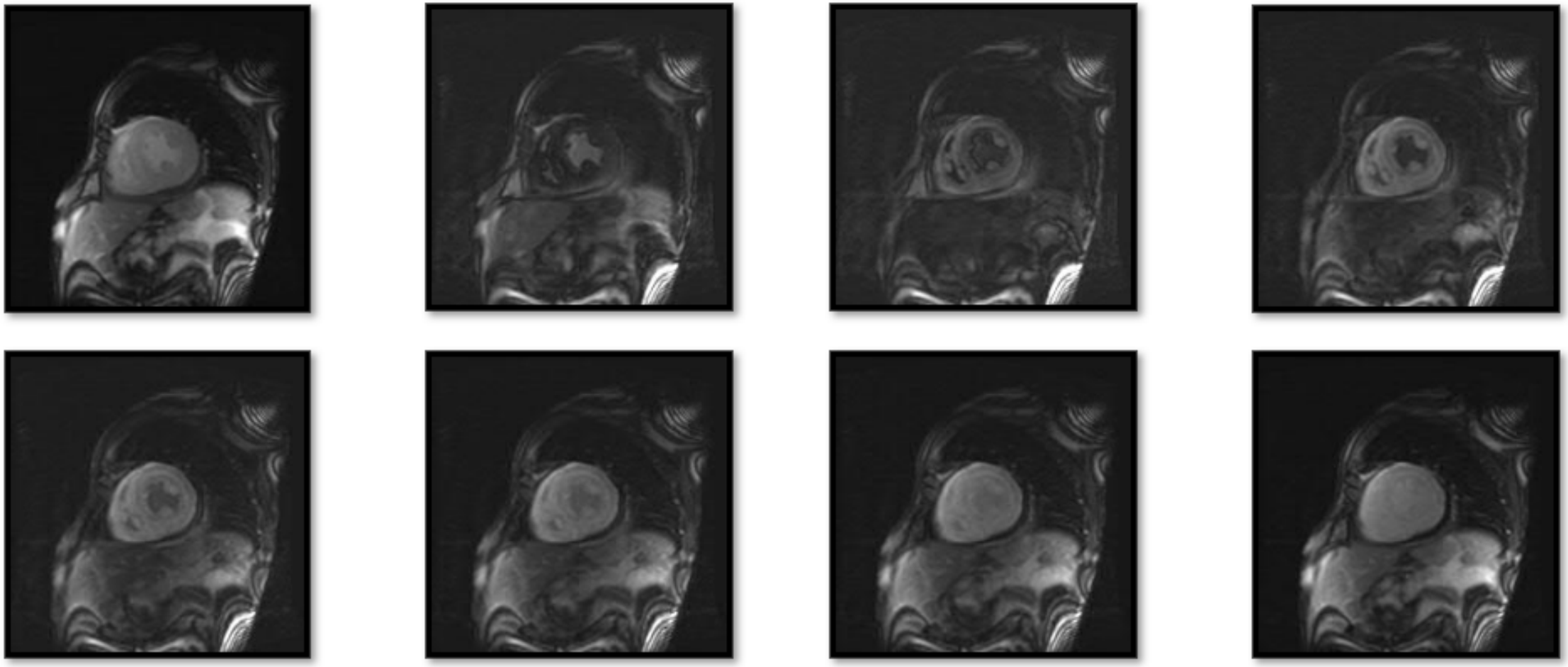


Slide courtesy of Dr. Jordan Ray

NORMAL NULLING PATTERN



ABNORMAL NULLING PATTERN



BACK TO THE CASE…

WHAT TO DO NEXT?

Blood tests to screen for amyloid?

1. CBC with differential
2. Prealbumin
3. Serum free light chains
4. Beta-2 microglobulin

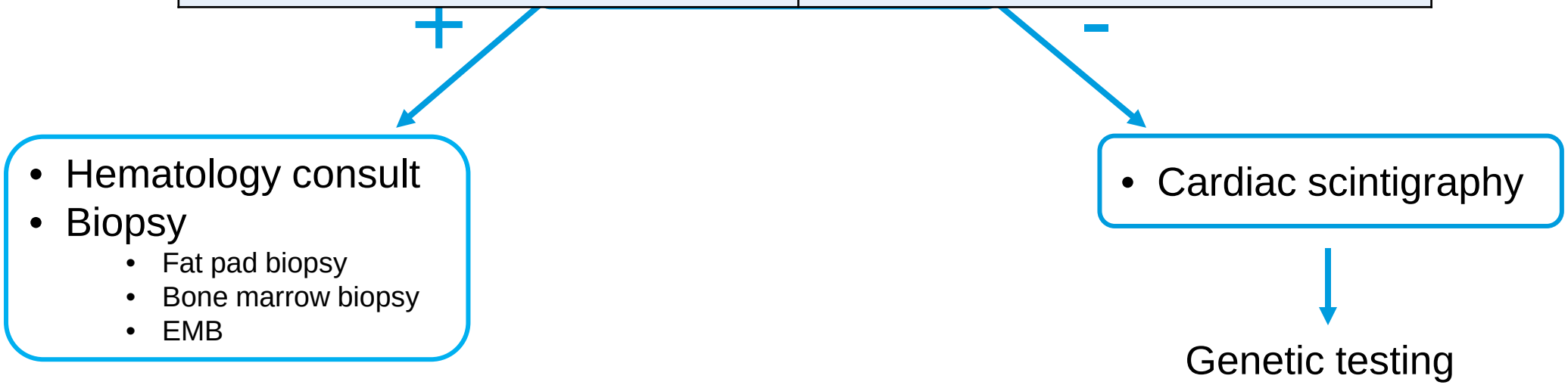
DIAGNOSTIC ALGORITHM

Estimated GFR	Free Light Chain Ratio
eGFR > 90 mL/min	0.26 – 1.65
eGFR 60 – 90 mL/min	0.26 – 2.00
eGFR 30 – 60 mL/min	0.26 – 2.50
eGFR < 30 mL/min	0.26 – 3.10

m free light chains

m immunofixation
SPEP alone

our urine
unofixation
JPEP alone



Reference Link

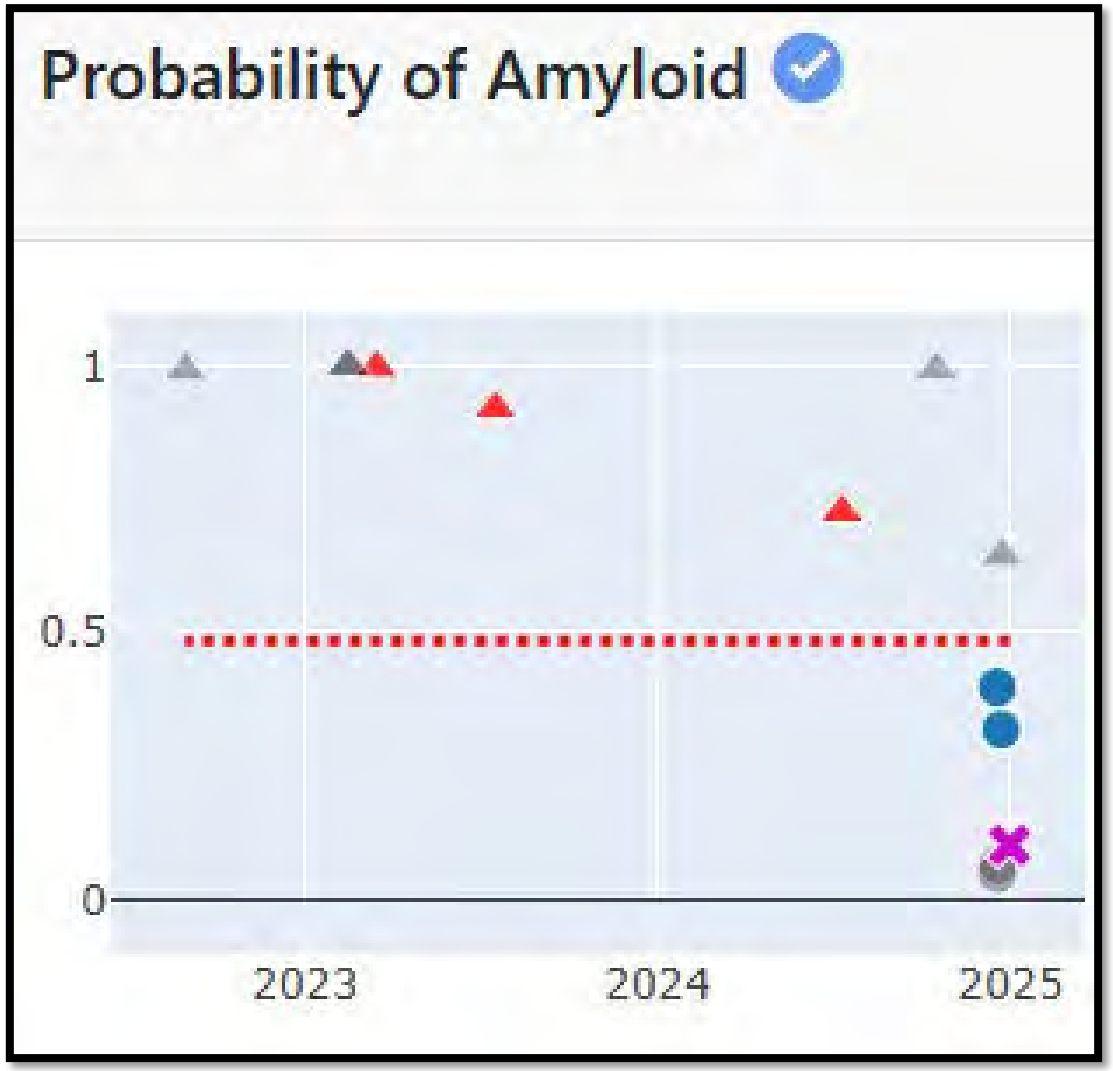
Kittleson et al. 2023 ACC Expert Consensus Decision Pathway on Comprehensive Multidisciplinary Care for the Patient with Cardiac Amyloidosis. JACC. 2023

CASE CONTINUATION

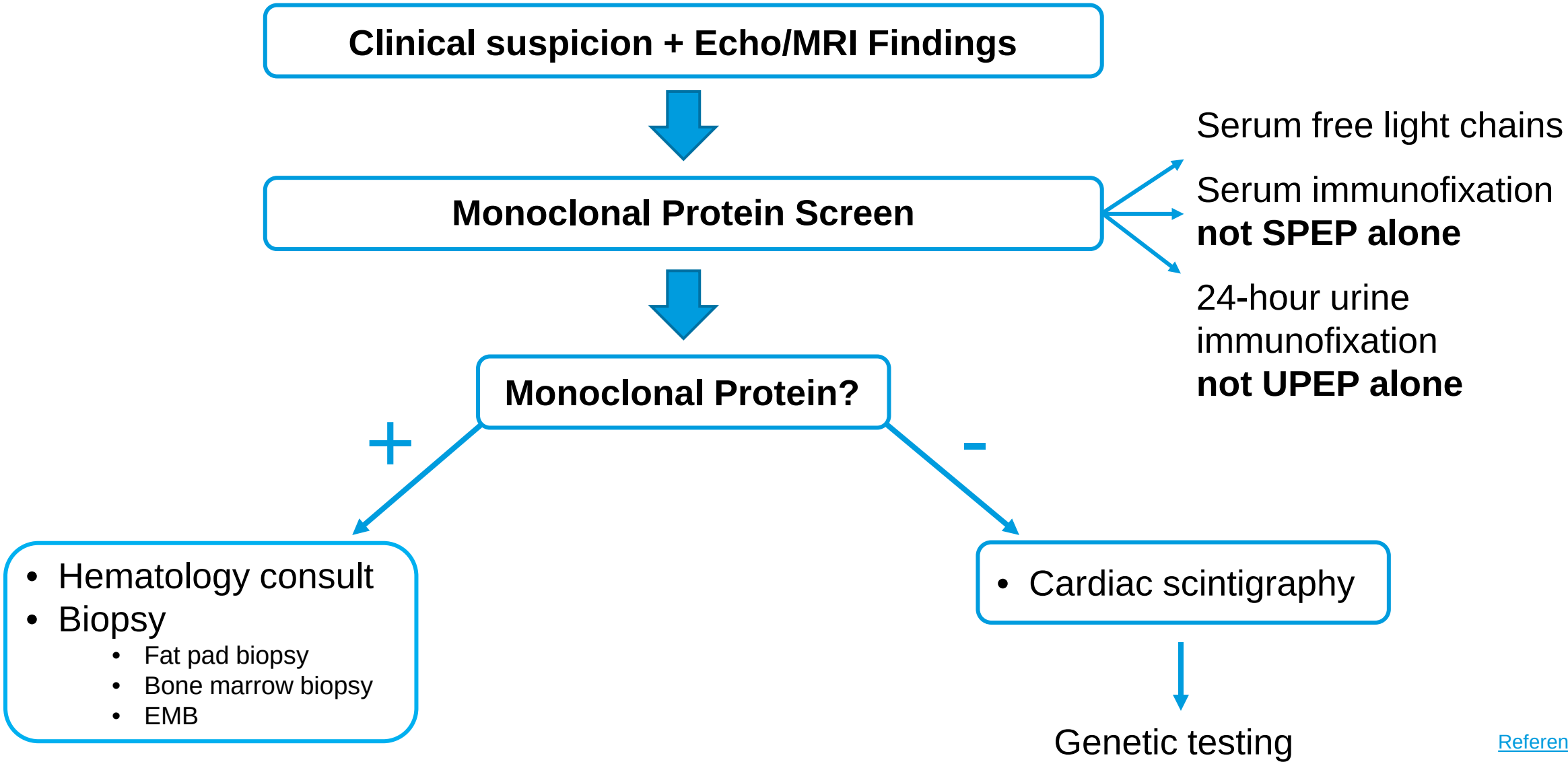
- Kappa free light chain 1.27 mg/dL, Lambda free light chain 5.84 mg/dL, and **Kappa/lambda FLC ratio 0.2**
- Serum immunofixation: **monoclonal IgG Lambda; M spike 1.5**
- Bone marrow biopsy: Atypical **plasmacytosis (10-15%)** with **amyloid deposits** detected by Congo red staining

CASE CONCLUSION

- Initiated on chemotherapy
- Achieved completed hematologic remission
- Underwent orthotopic heart transplantation



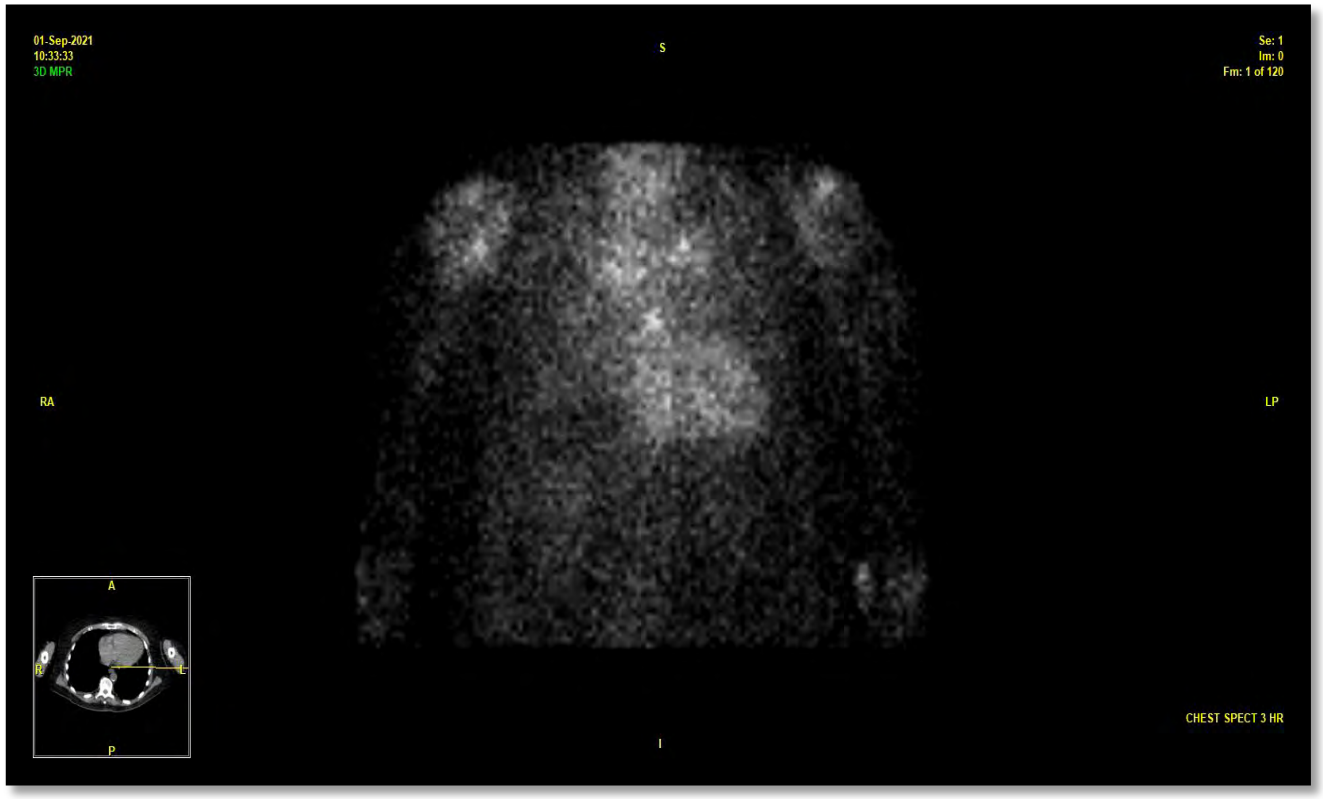
DIAGNOSTIC ALGORITHM



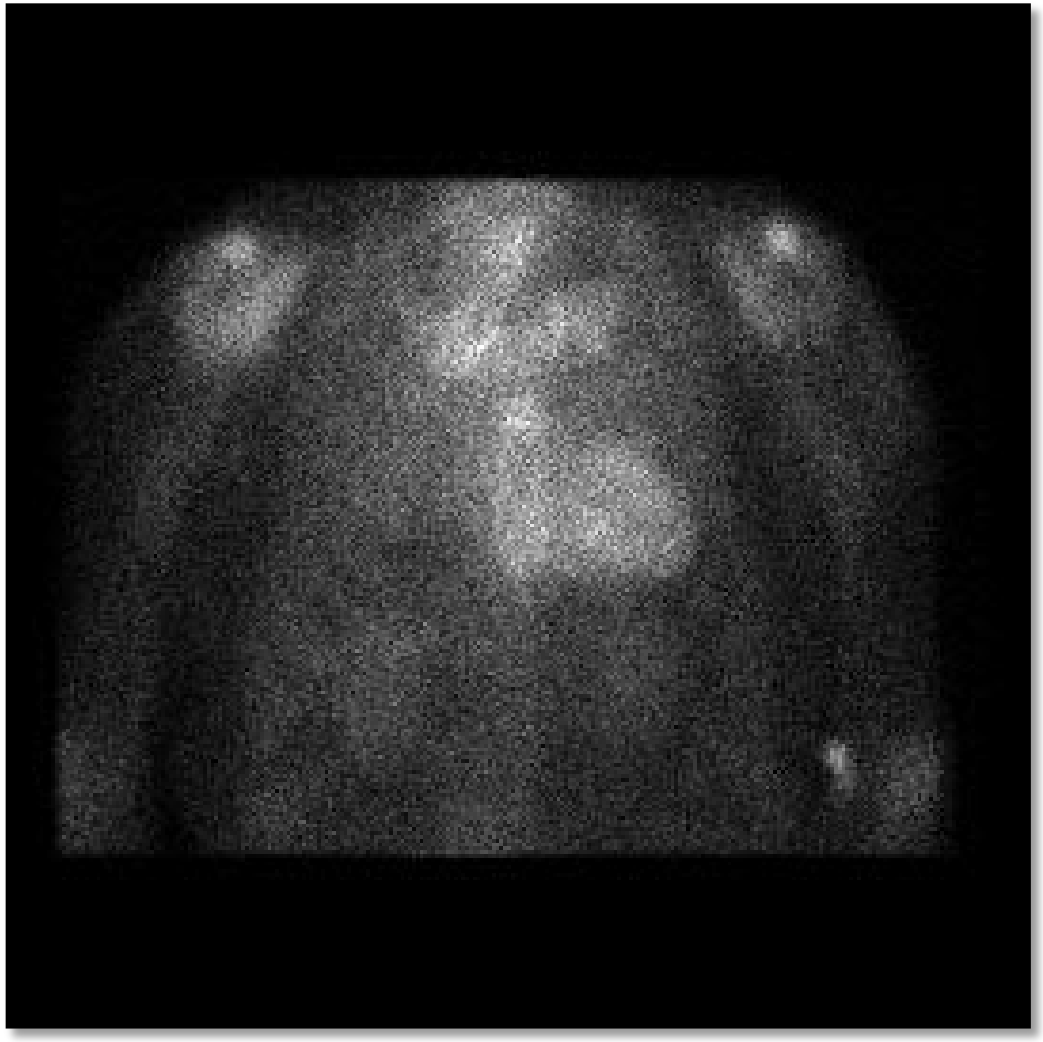
Reference Link

Kittleson et al. 2023 ACC Expert Consensus Decision Pathway on Comprehensive Multidisciplinary Care for the Patient with Cardiac Amyloidosis. JACC. 2023

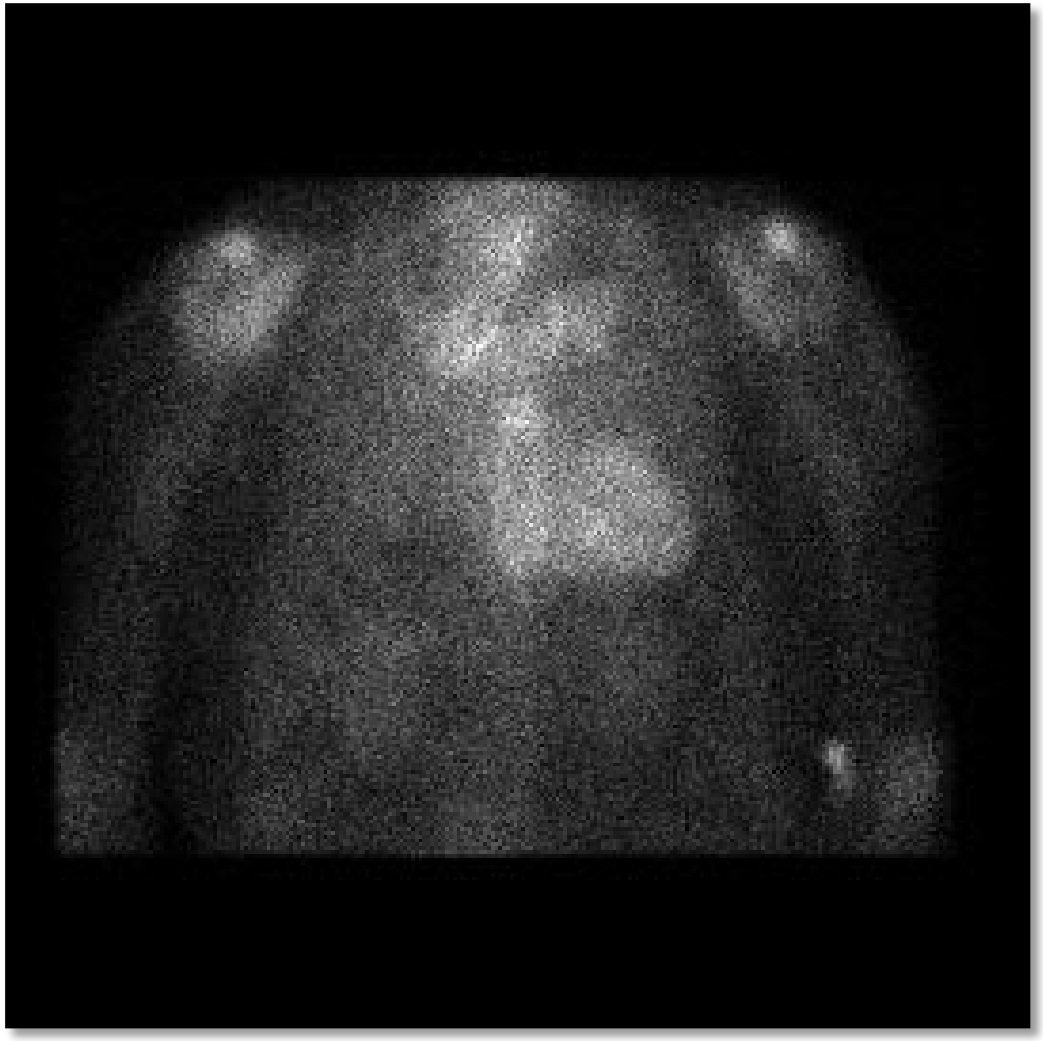
CARDIAC SCINTIGRAPHY



- ^{99m}Tc-labeled pyrophosphate (PYP)
- ^{99m}Tc-labeled 3,3-diphosphono-1,2-propanodicarboxylic acid (DPD)
- ^{99m}Tc-labeledhydroxymethylene diphosphonate (HMDP)



1 HOUR DELAY



3 HOUR DELAY

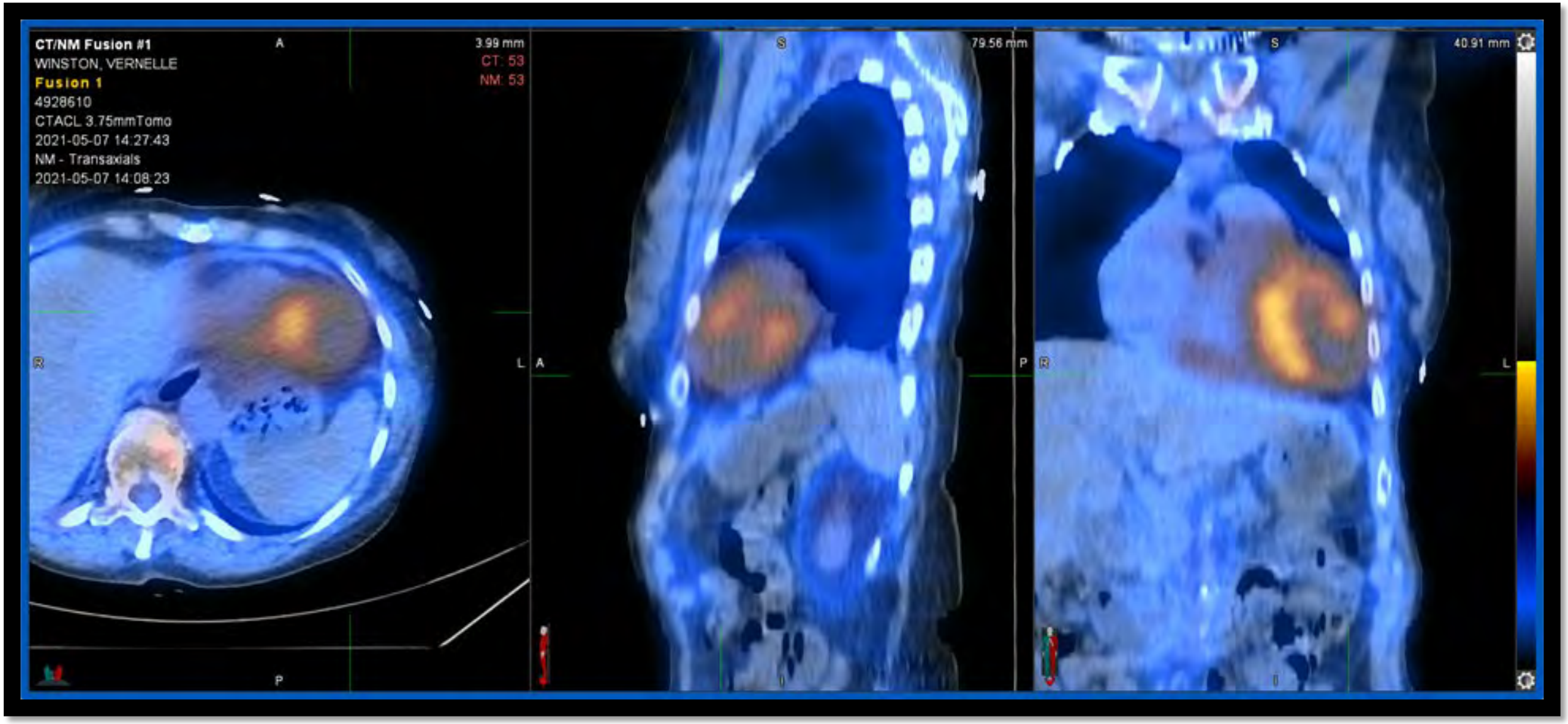
20% of biopsy proven AL patients had Grade 2-3 uptake

Ashutosh D. Wechalekar, MD, DM; John L. Berk, MD; Candida C. Quarta, MD, PhD;

Monoclonal gammopathy must be excluded to use cardiac scintigraphy

Philip N. Hawkins, PhD, FMedSci

https://pubmed.ncbi.nlm.nih.gov/27143678/



Slide courtesy of Dr. Julie Rosenthal

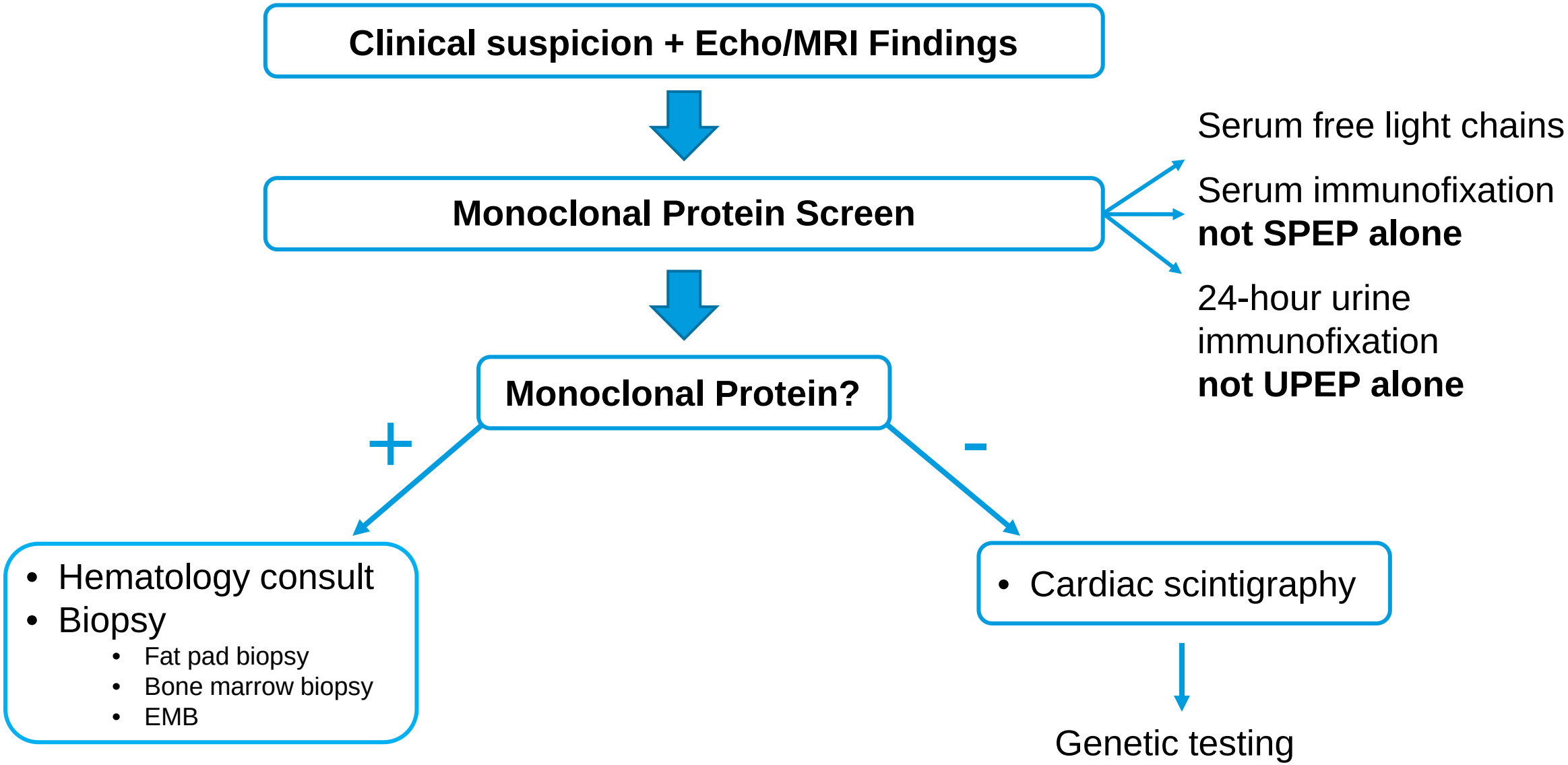
Table 4 Possible false positives and false negatives of bisphosphonate scintigraphy for detecting transthyretin cardiac amyloidosis

	Situation	How to suspect and confirm?
False positive	AL amyloidosis	Abnormal SPIE, UPIE or serum free light ratio. Requires histologic confirmation.
	Hydroxychloroquine cardiac toxicity	Interrogation. Requires histologic confirmation.
	AApoAI and AApoAII amyloidosis	Concomitant kidney disease present. Genetic testing.
	ApoAIV amyloidosis	Concomitant kidney disease present. Requires histologic confirmation.
	Aβ2M amyloidosis	Long-term dialysis (>9 years). Requires histologic confirmation.
	Blood pool	Cardiac dysfunction could be present. Use SPECT to detect uptake in myocardium. Delay acquisition.
	Rib fractures, valvular/annular calcifications	Use SPECT to detect uptake in myocardium.
	Recent myocardial infarction (<4 weeks)	Interrogation. Use SPECT to detect diffuse uptake in myocardium.
False negative	Phe84Leu ATTRv, Ser97Tyr ATTRv	Concomitant neuropathy. Familial disease. Genetic testing.
	Very mild disease	Requires histologic confirmation.
	Delayed acquisition	Shorter acquisition time interval.
	Premature acquisition	Prolong acquisition time interval.

AApoAI, apolipoprotein AI amyloidosis; AApoAII, apolipoprotein AII amyloidosis; AApoAIV, apolipoprotein A-IV amyloidosis; Aβ2M, β2-microglobulin amyloidosis; AL, light-chain amyloidosis; ATTRv, hereditary transthyretin amyloidosis; SPECT, single photon emission computed tomography; SPIE, serum protein electrophoresis with immunofixation; UPIE, urine protein electrophoresis with immunofixation.

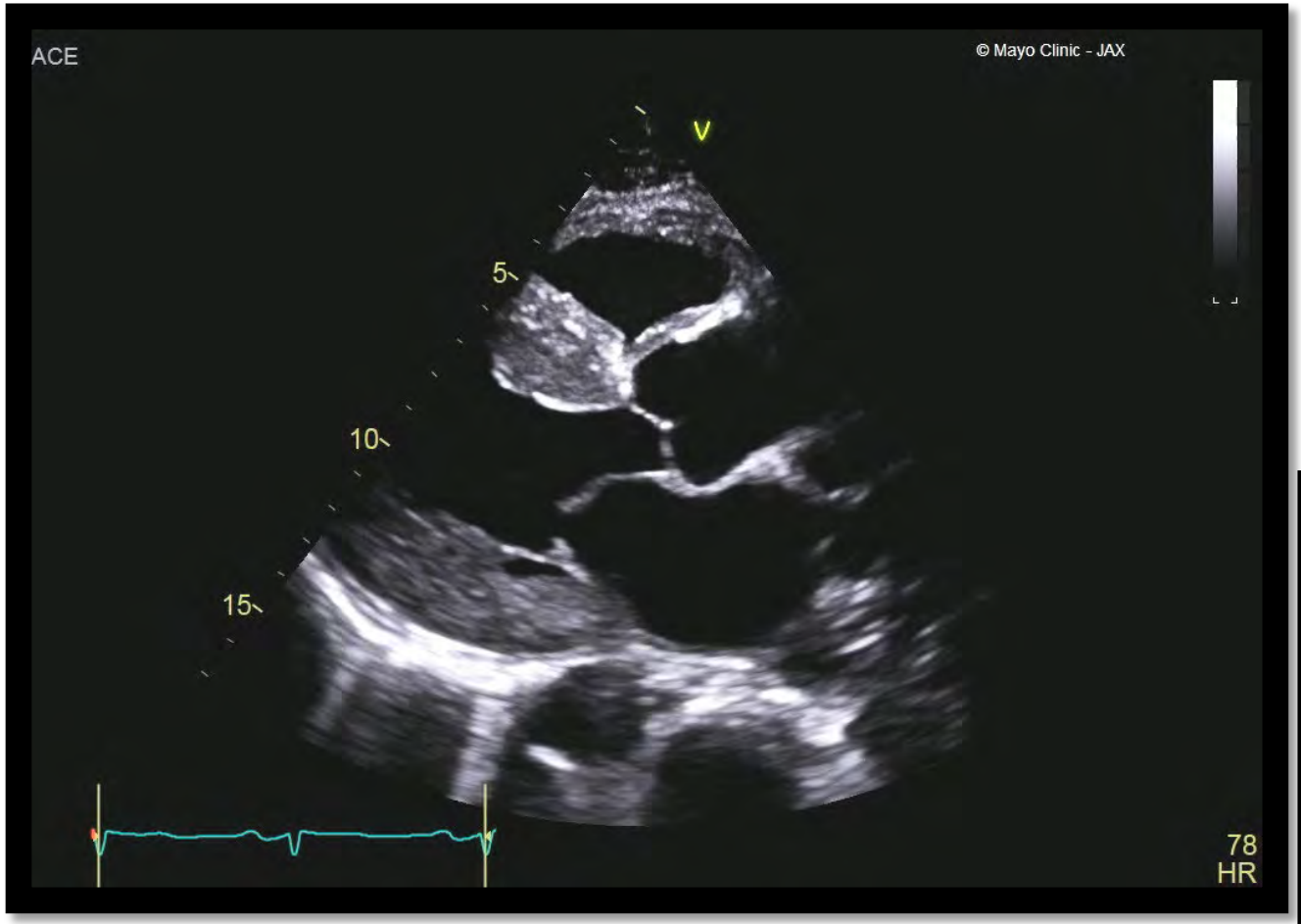
Garcia-Pavia et al. Diagnosis and treatment of cardiac amyloidosis. EHJ 2021

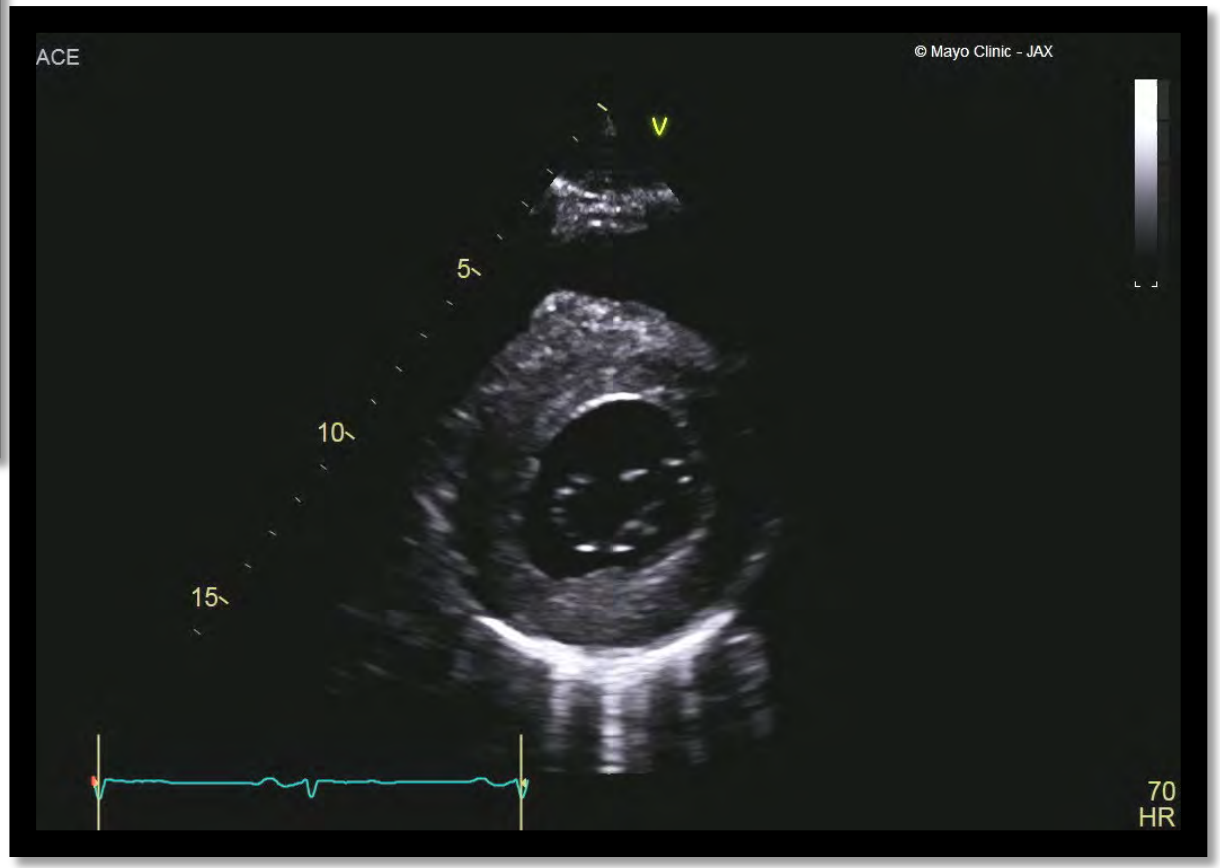
DIAGNOSTIC ALGORITHM

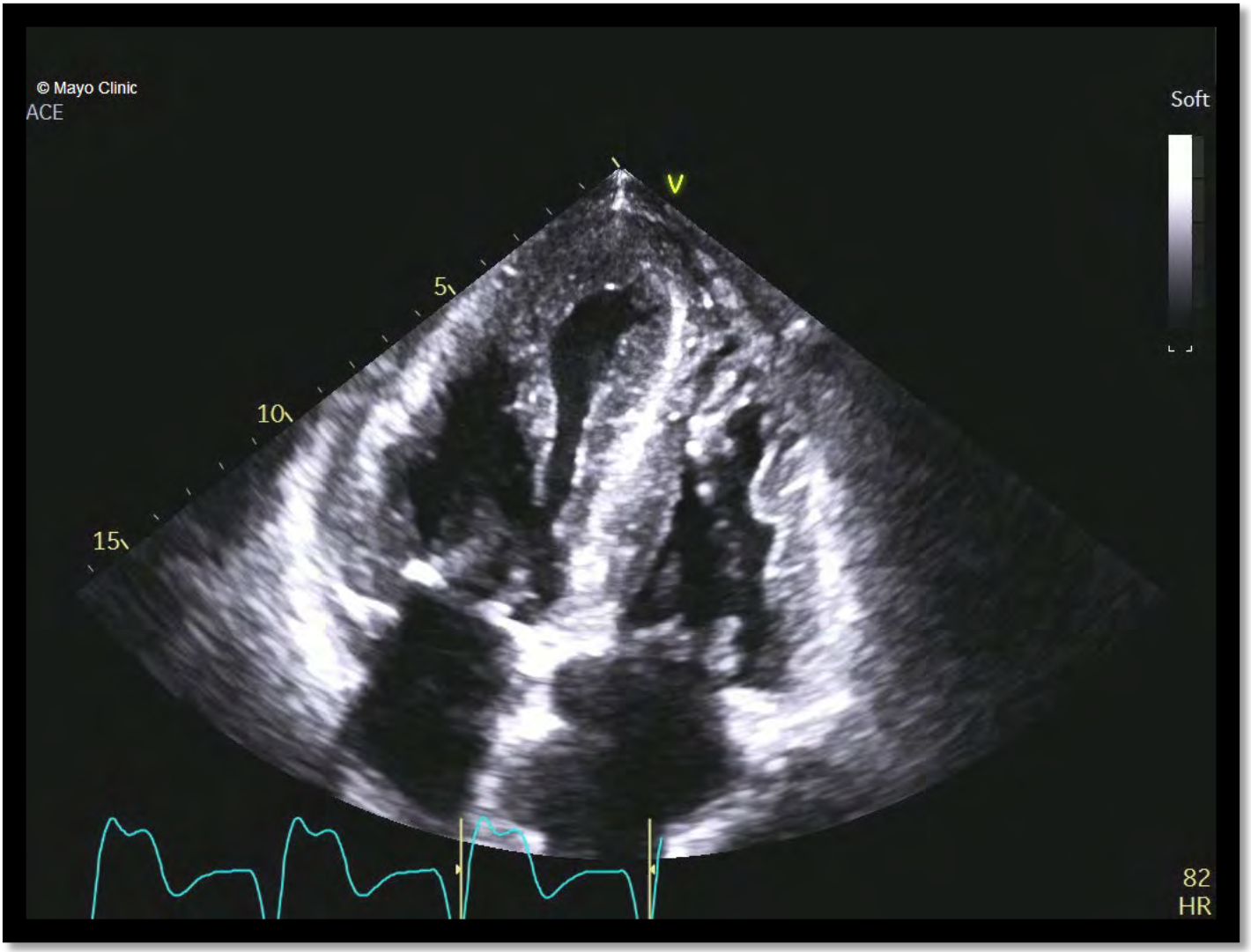


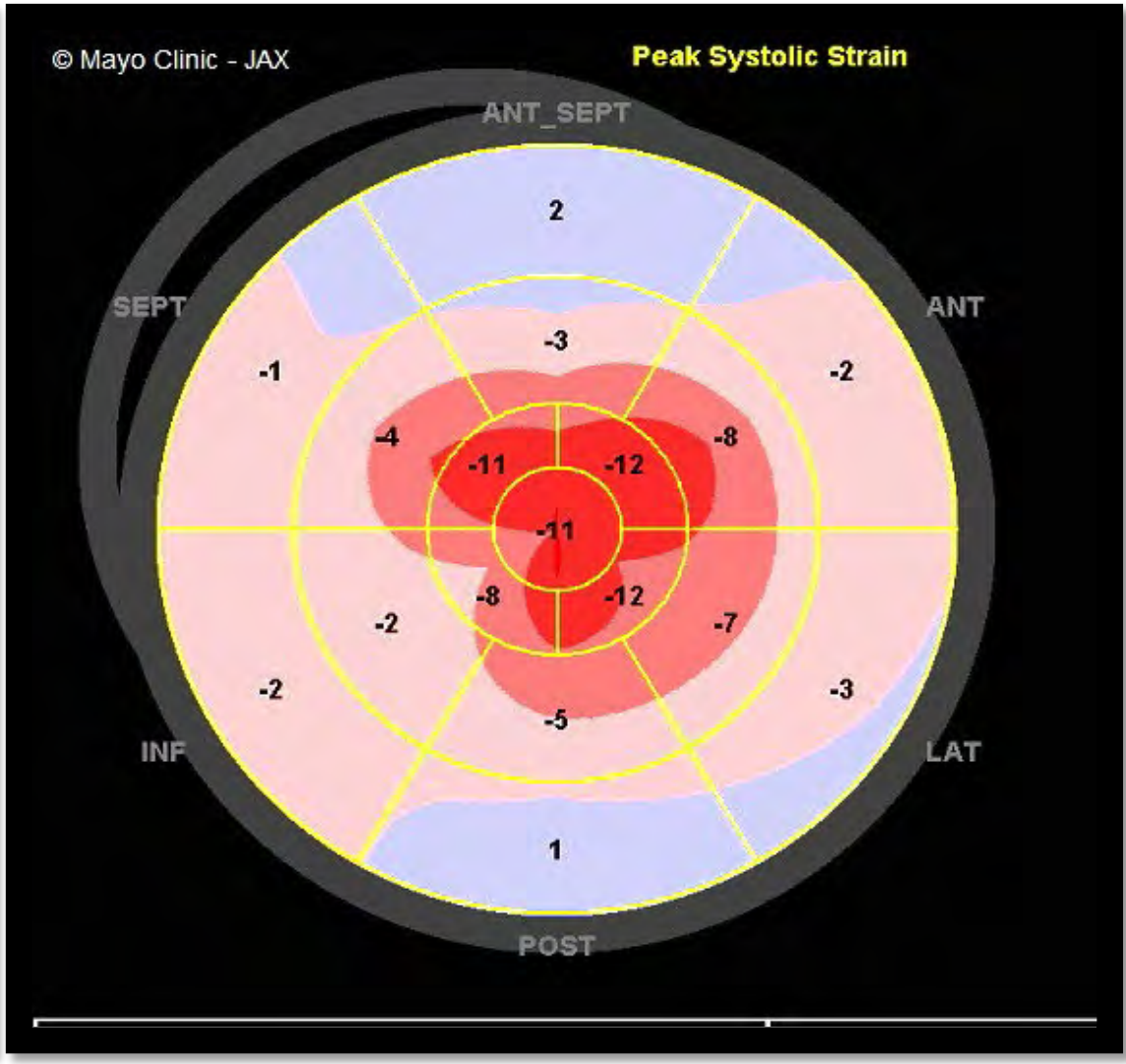
CASE PRESENTATION

- 67-year-old female presented to outside hospital with dyspnea
- **Atrial fibrillation** and recent diagnosis of influenza
- TTE completed → **increased left ventricular wall thickness**
- Cardiac scintigraphy → **Grade 3 uptake**









Next best step for diagnosis?

1. Cardiac MRI
2. Endomyocardial biopsy
3. Monoclonal protein screen
4. Start tafamidis

CASE CONTINUED

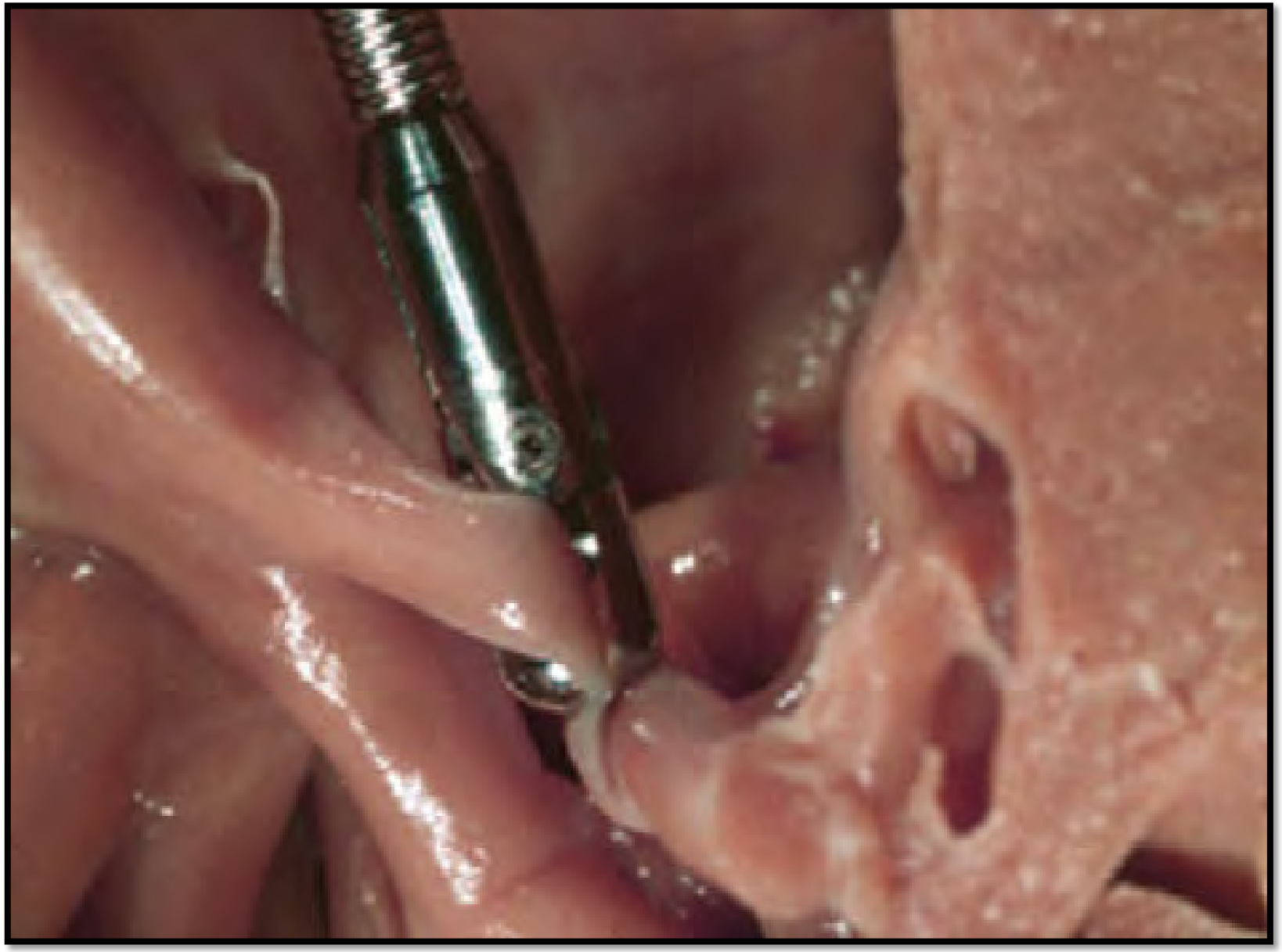
- Kappa free light chain 13.1 mg/dL, Lambda free light chain 1.07 mg/dL, **Kappa/lambda FLC ratio 12.2**
- Serum immunofixation: **Monoclonal IgG Kappa; M spike 3.8**
- High sensitivity **troponin 75**, **NT pro BNP 12168,** creatinine 1.4 mg/dL
- Urine IF: **Monoclonal IgG Kappa**

M — Must

G — Go

U — Under

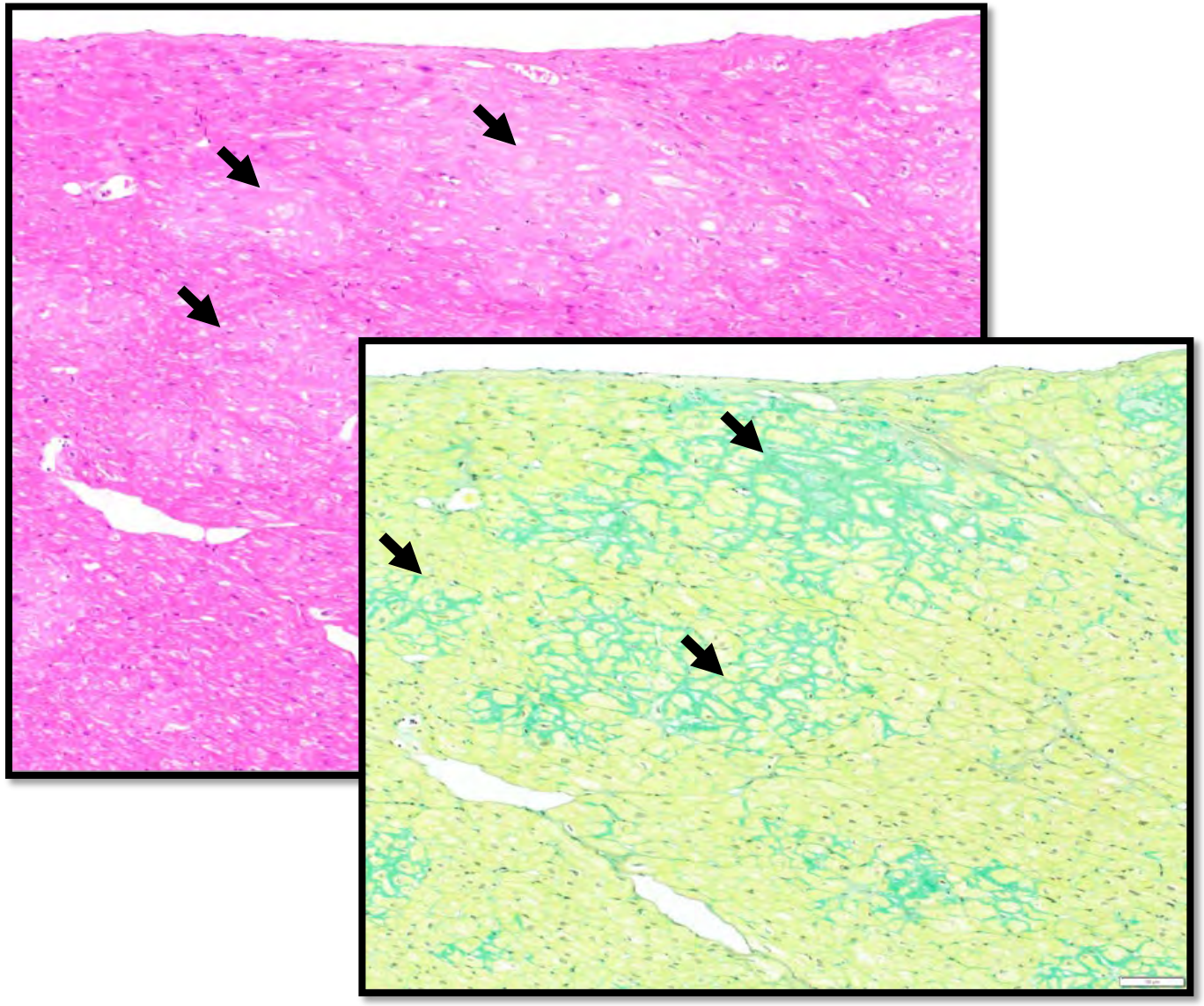
S — Skin

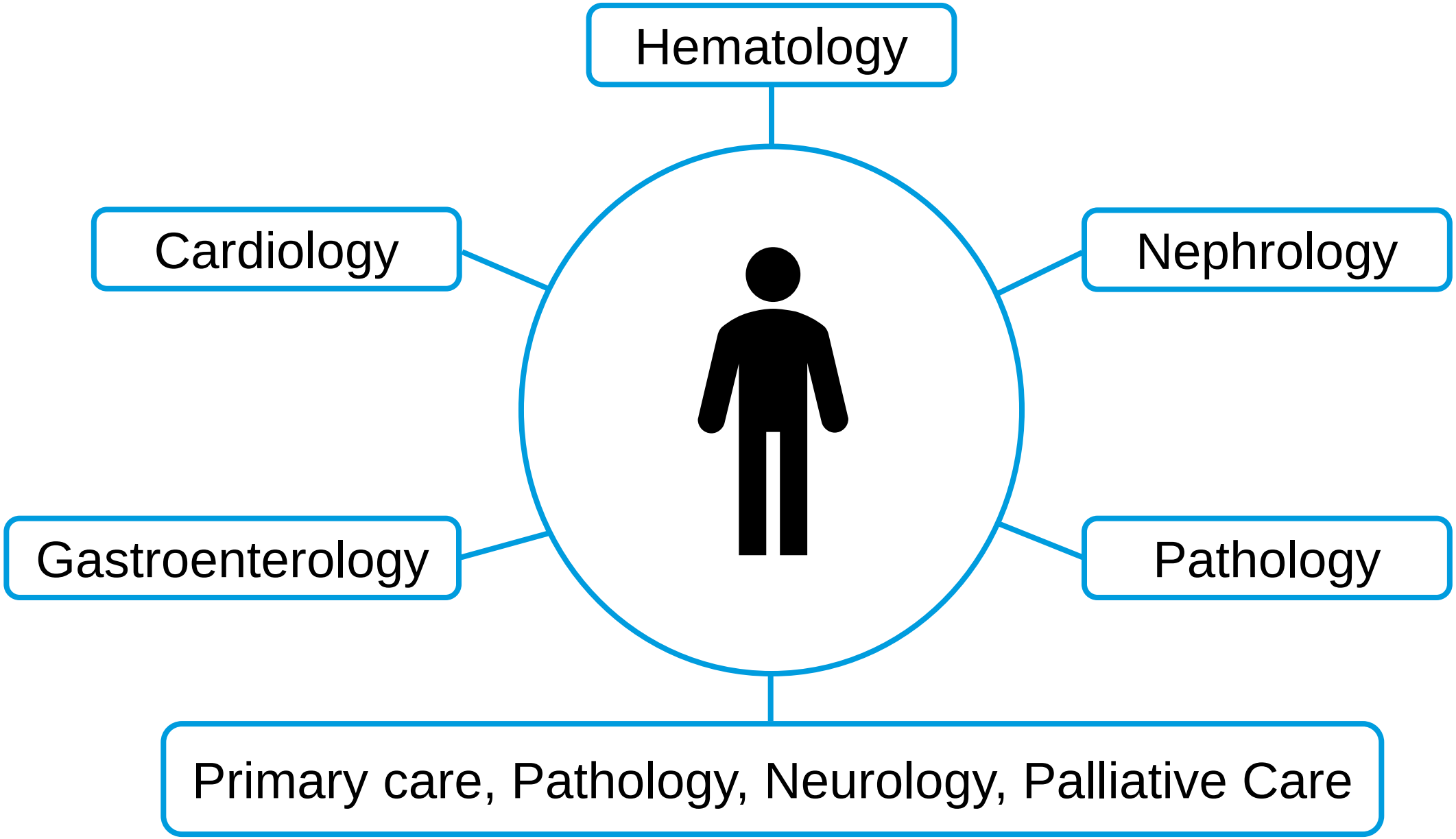


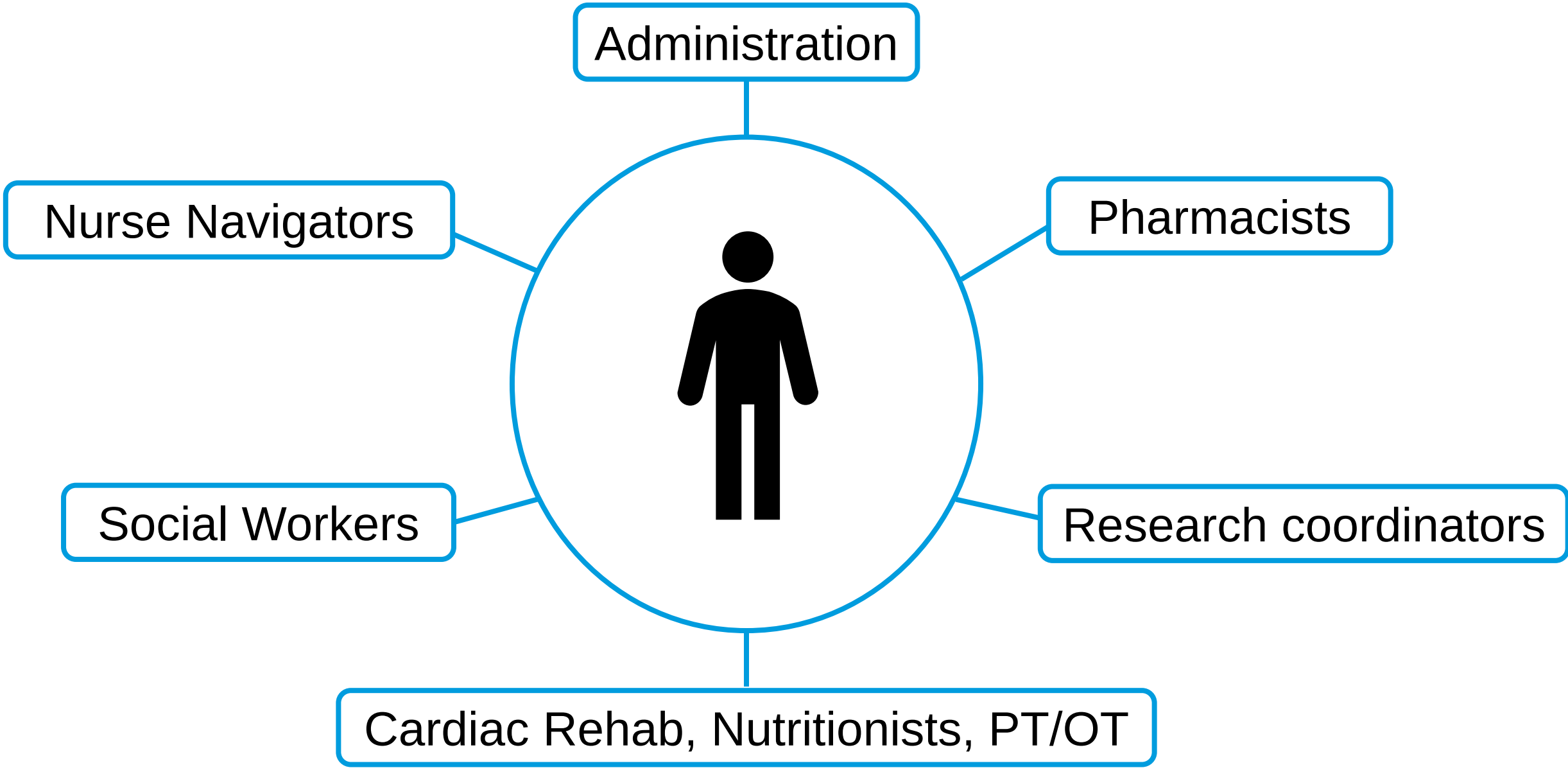
Reference Link Quarta CC, et al. EHJ. 2017; 38: 1905

Acronym courtesy of Dr. Dan Judge, shared by Dr. Martha Grogan

- Endomyocardial biopsy
- SAB and Congo Red positive for amyloid deposits
- Mass spectrometry→ AL amyloidosis







CHALLENGES

- Delayed diagnosis
- Complex diagnosis
- Multiorgan involvement and complex therapies

CHALLENGES

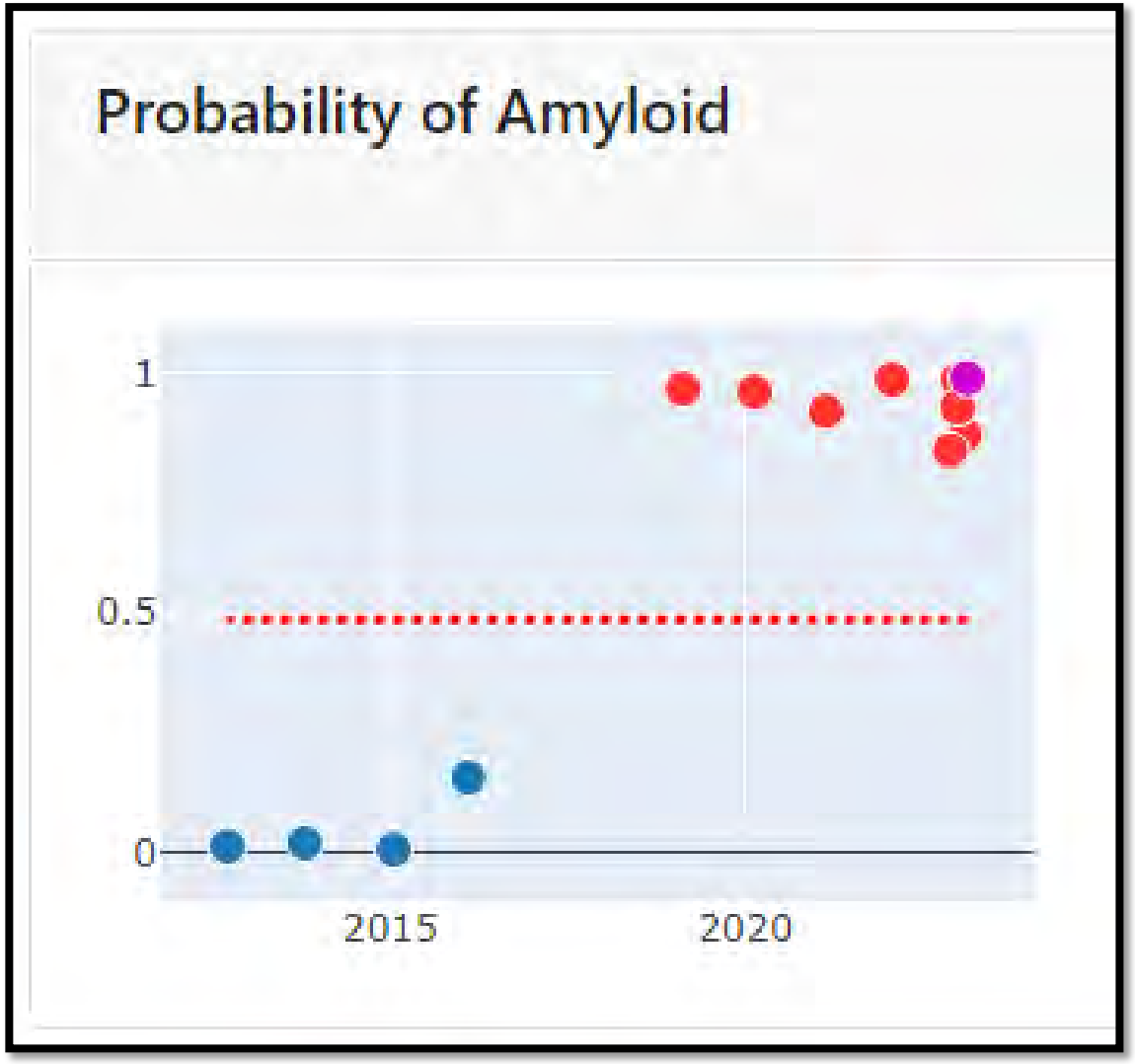
- Delayed diagnosis → **Education + screening tools**
- Complex diagnosis
- Multiorgan involvement and complex therapies

- 79-year-old male with hypertension and moderate mitral regurgitation → acutely dyspneic during routine scuba dive

ARTIFICIAL INTELLIGENCE

AI Dashboard

Show images for ECG 12 Lead



ORIGINAL ARTICLE

MAYO CLINIC

Artificial Intelligence–Enhanced Electrocardiogram for the Early Detection of Cardiac Amyloidosis

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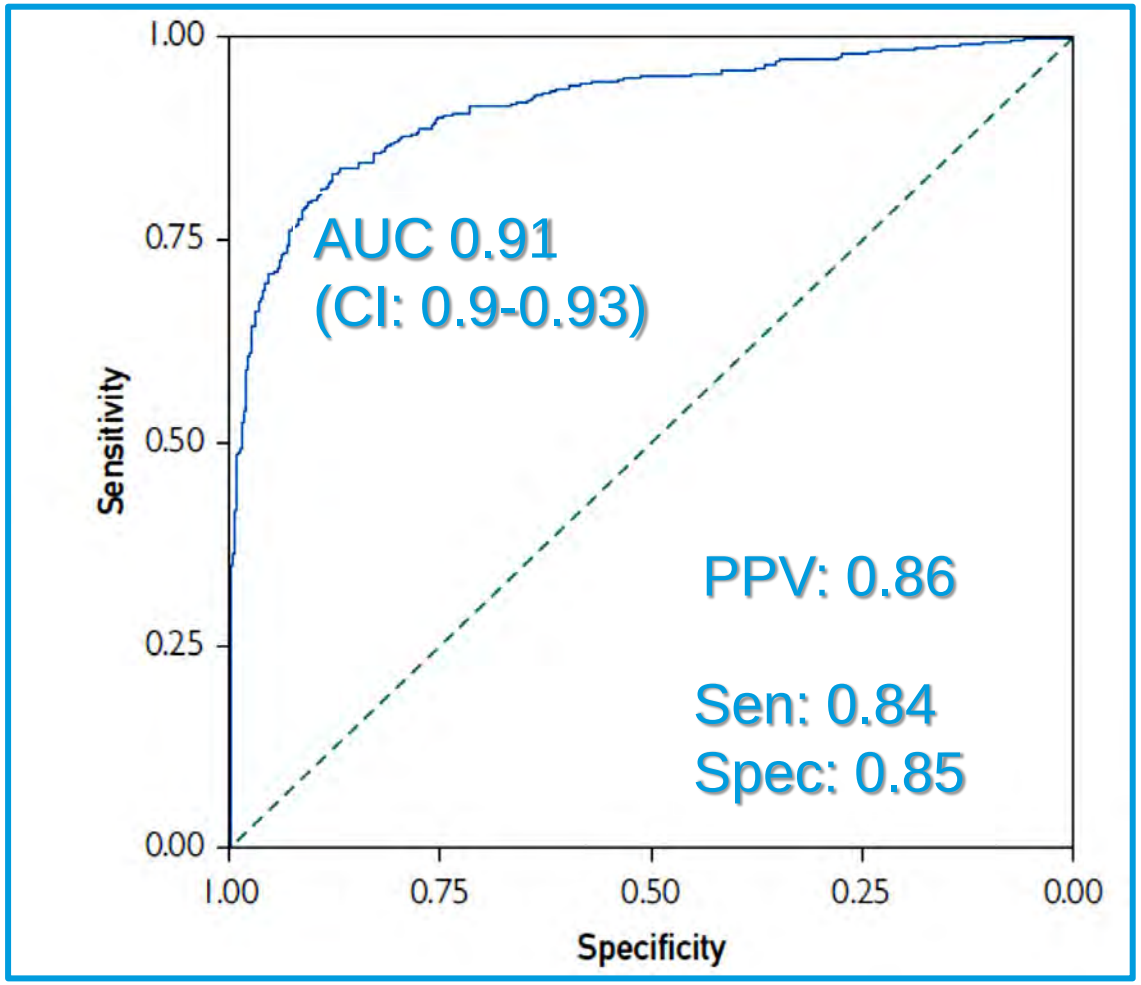
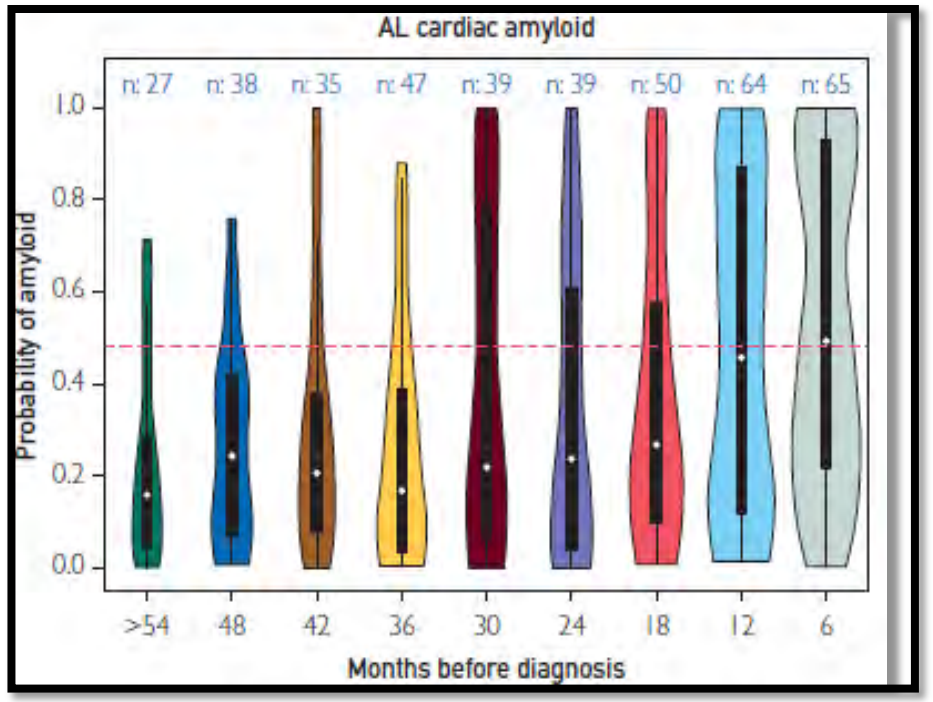
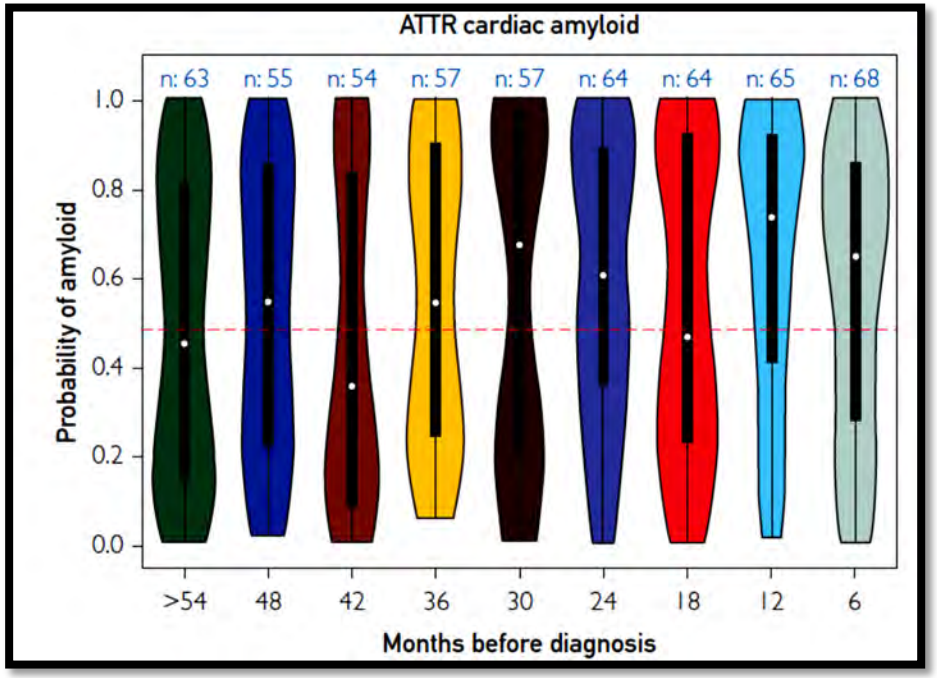
https://pubmed.ncbi.nlm.nih.gov/34218880/

AI EKG - MODEL







Grogan M, et al. Mayo Clin Proc. 2021; 96: 2768

BENEFITS OF SCREENING

- Screening ⇧ awareness & recognition
- Implementation of screening → improved diagnostic accuracy
- Earlier diagnosis
  - Initiation of therapy
  - Potential change in clinical course

CHALLENGES

- Delayed diagnosis
- Complex diagnosis → **Diagnostic algorithms**
- Multiorgan involvement and complex therapies

CHALLENGES

- Delayed diagnosis
- Complex diagnosis
- Multiorgan involvement and complex therapies → **Multidisciplinary approach**

Early Referral Alliances

General Cardiologists
Primary Care Clinicians
Advanced Practice Providers

Diagnostic Alliances

Hematologists
Pathologist
Cardiac Imagers
Pathologist

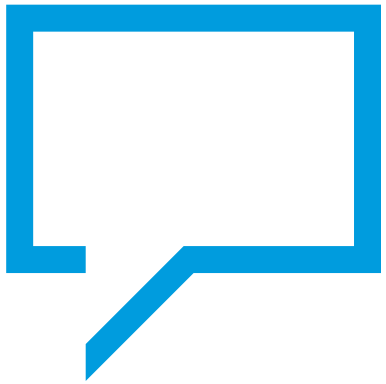
Follow-up Alliances

Nephrology
Gastroenterologist
Neurology
Pharmacists
Transplant Services
Palliative Care

SUMMARY

- Suspect amyloid: LV wall thickness ≥ 12 mm and clinical clues
- Know the diagnostic algorithm for cardiac amyloid: **Rule out AL first!**
- **AL amyloidosis is a medical emergency**
- Avoid diagnostic pitfalls (such as interpreting cardiac scintigraphy in the setting of abnormal monoclonal light chain testing)

QUESTIONS & ANSWERS



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Modern Management of AL Amyloid by Hematology

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Bone Marrow Transplant & Cellular Therapy Services

Memorial Sloan Kettering Cancer Center
Associate Professor of Clinical Medicine
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New York, New York

Patient QD

- 49M, previously physically active, developed dyspnea; stopped going to the gym

July 2019

- Hospitalized for asthma exacerbation + Pneumonia
  - Tx steroids, bronchodilators + diuresed

April 2020

- Unable to ambulate 20 yards→ cardiac evaluation
  - Nuclear stress test: LVEF 25%, no ischemia

August 2020

- Pulmonary evaluation → optimize asthma regimen
  - Thoracentesis with 1L clear fluid drained

October 2020

- Cardiology 2nd opinion
  - ECHO: Severe conc LVH, hypokinetic lat wall, LVEF 40%
  - ECG: NSR 91bpm, Low voltage, poor R wave progression
  - Cardiac MRI: Diffuse subendocardial LGE

Nov 2020

QD came to MSK

Dec 2020

- CBC normal, BUN 21, Cr 1.1, ALB 4.1, ALK Phos 222
- Free kappa 1.24mg/dl, free lambda 13.05mg/dl, k:l 0.10
- SPEP neg, IFE neg
- BNP 957, TROP 0.92
- 24hr Urine TP: none

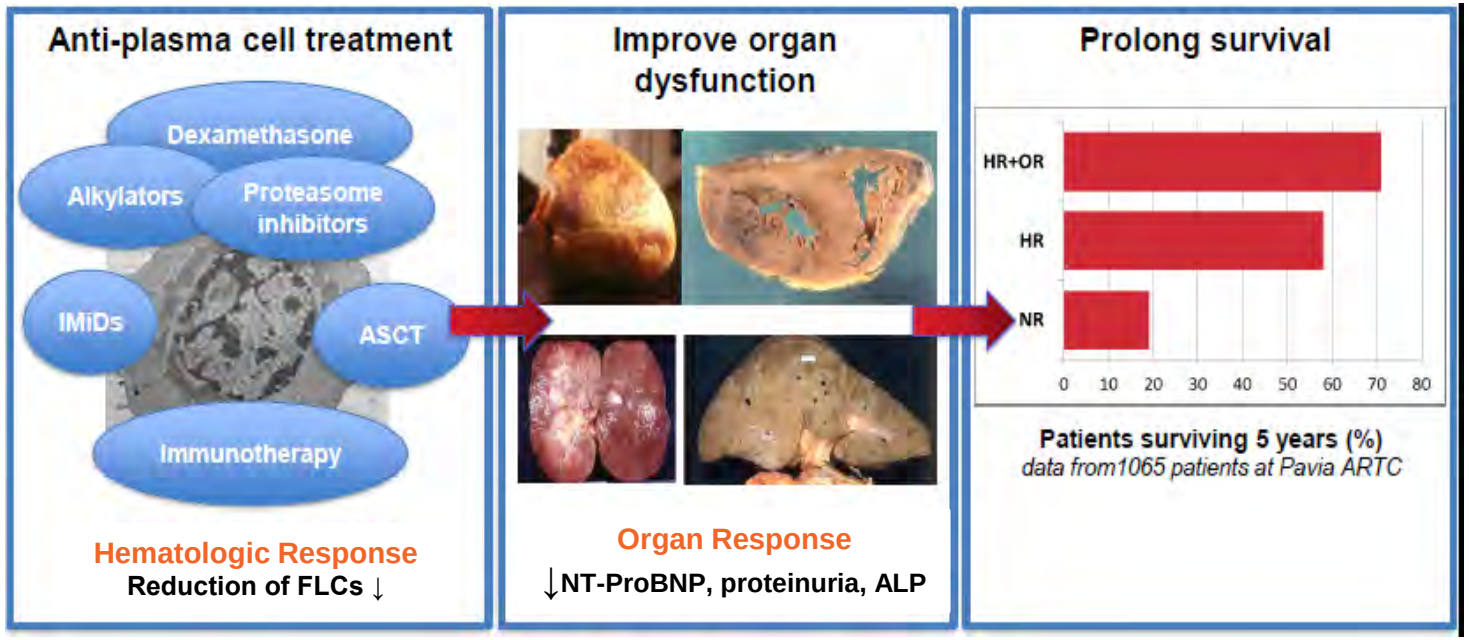
- ECHO: severely increased LV wall thickness (IVSd 1.9cm), mild global hypokinesis, LVEF 47%. + diastolic dysfunction, GLS 6%.
- Bone marrow: 10% lambda light chain restricted PCs, No evidence of amyloidosis. Translocation (11;14) by FISH.
- Fat pad biopsy: negative
- Endomyocardial biopsy: lambda light chain amyloidosis

Jan 2021

Mayo (2004) cardiac stage IIIA
Lambda light chain amyloidosis

Goal of treatment in AL Amyloidosis

- Target the diseased plasma cell clone to improve organ function and prolong survival



FLCs= monoclonal free light chains
HR= hematologic response
OR= organ response
NR= no response
CR= complete response
NT-ProBNP= N-terminal pro-B-type naturiuretic peptide
ALP= alkaline phosphatase

Deeper hematologic response
↑organ response
HR + OR = longer survival

Palladini et al. 2018

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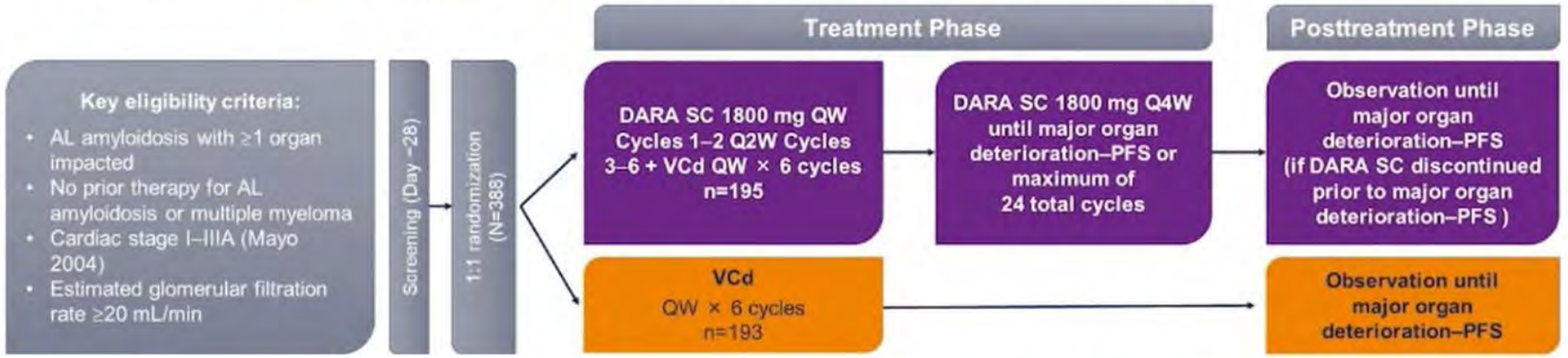
The first immunotherapy in AL Amyloidosis: Daratumumab

- ANDROMEDA is a randomized, open-label, active-controlled, phase 3 study of D-VCd vs VCd alone in patients with newly diagnosed AL amyloidosis



Primary endpoint: complete hematologic response (CR)
Secondary endpoints: major organ deterioration- PFS, organ response rate, time to response, overall survival, safety

D-VCd= Daratumumab- bortezomib, cyclophosphamide, dexamethasone
VCd= Bortezomib, cyclophosphamide, dexamethasone
PFS= Progression free survival

Kastritis et al. 2021

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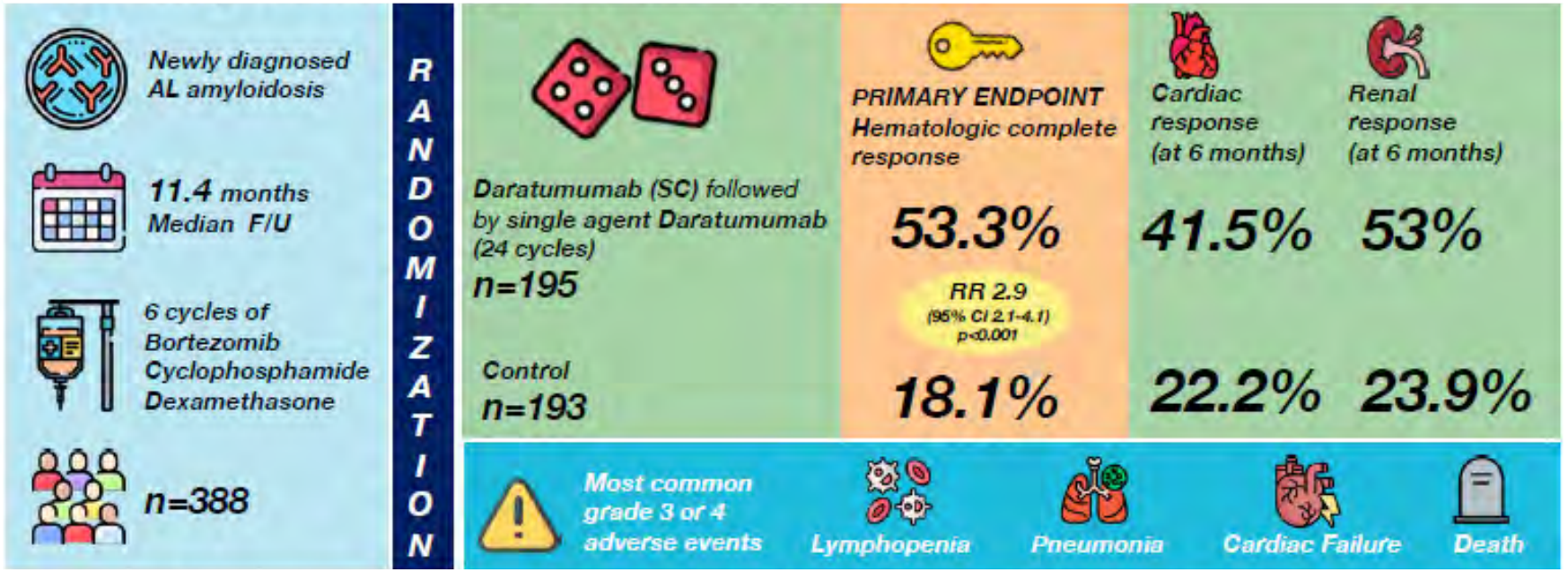
ANDROMEDA trial



In newly diagnosed AL amyloidosis, Dara-VCd versus VCd improved

- **hematologic complete response**
- **organ response**
- **major organ deterioration PFS**

Dara-VCd = first and only FDA-approved drug regimen for AL amyloidosis

5 years follow up: OS 76% vs 65%
HR 0.62 (95% CI: 0.42-0.90; P=0.012)

Kastritis et al. 2024
Lerma 2021.
Kastritis et al. 2021

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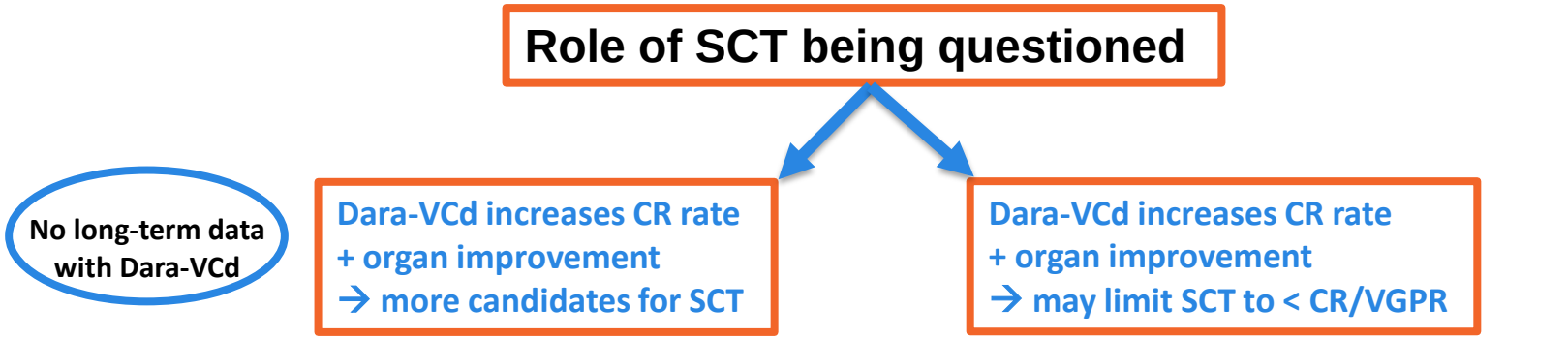
Implications of the ANDROMEDA trial

- **Dara-VCd is used as initial therapy for nearly all newly diagnosed patients with AL amyloidosis = new SOC**
- **With longer follow up, the hematologic CR rate in the dara-VCd arm is 59% (vs 19% in VCd)**
  - **similar to the CR rate with SCT + consolidation**

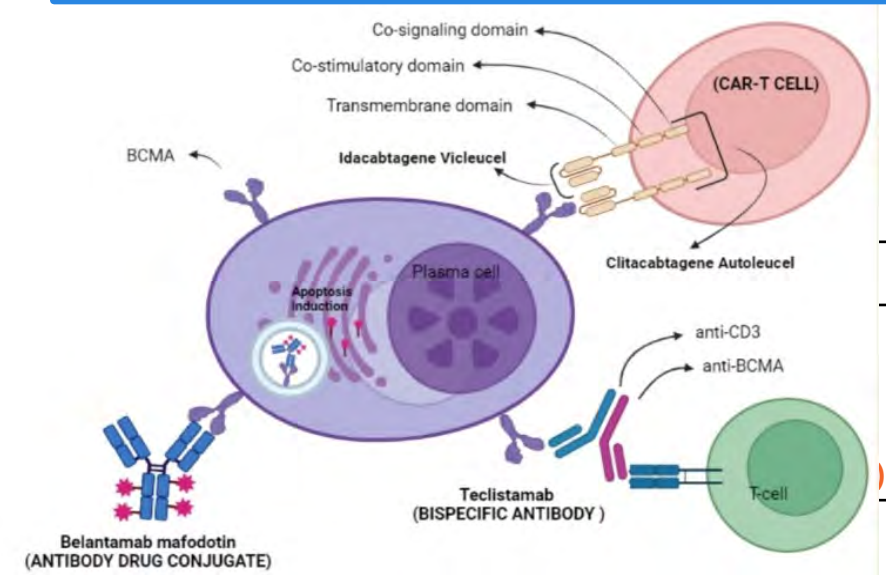


SWOG S2213: Phase III, Randomized Study in Newly Diagnosed AL

Kastritis et al. 2024
Crusoe et al. 2021

Salvage treatment options in AL

No SOC treatment beyond initial therapy



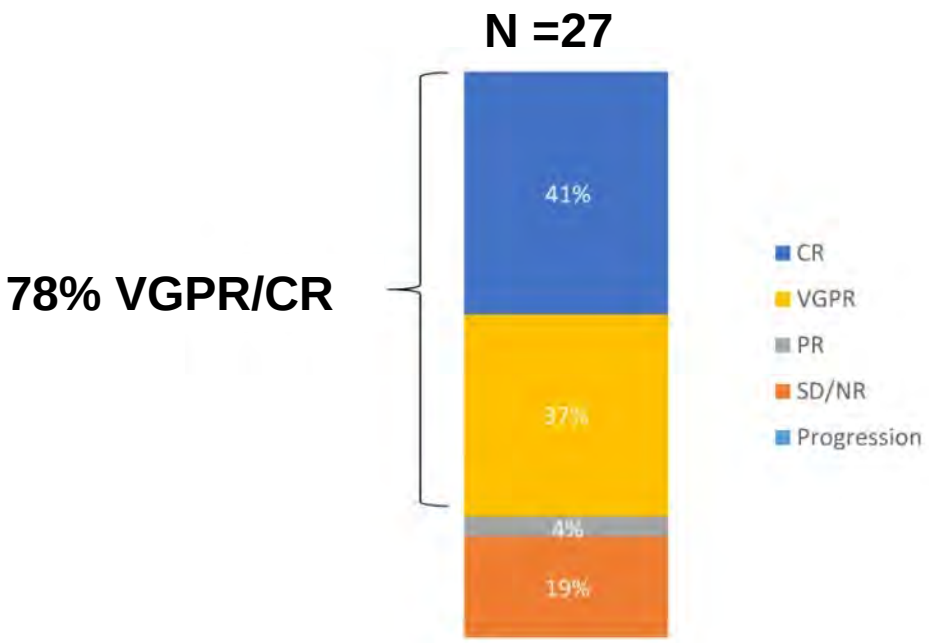
Proteasome inhibitors		Antibodies → plasma cells
• Bortezomib (Velcade) • Ixazomib (Ninlaro) • Carfilzomib (Kyprolis)	• • •	• Daratumumab (Darzalex) • Isatuximab (Sarclisa) • Elotuzumab (Empliciti)

Targeted therapy	Novel immunotherapy	CAR T cells	Amyloid-directed therapy
• Venetoclax (Venclexta) BCL-2 inhibitor • ~~Selinexor (Xpovio)~~ Blocks XPO-1, nuclear export protein	• Belantamab (Belamaf) Anti-BCMA antibody drug conjugate • Teclistimab (Tecvayli) Bispecific Ab (BCMA/CD3) • Talquetimab (Talvey) Bispecific Ab (GPRC5d/CD3) • Cevostamab Bispecific Ab (FCRH5/CD3)	• Ide-cel (ABECMA) Anti-BCMA CAR T • Cilta-cel (CARVYKTI) Anti-BCMA CAR T • MCARH109 Anti-GPRC5D CAR T	• NEOD001 (birtamimab) anti-LC antibody • CAEL-101 (anselamimab) anti-LC antibody

Novel therapies = Unique toxicities

“Targeted” therapy for AL amyloidosis

- 50% of patients with AL have the cytogentic abnormality **translocation (11;14)** which renders patients uniquely responsive to the BCL-2 inhibitor **Venetoclax**



Several clinical trials ongoing and/or planned

Reasonable 2nd line treatment for patients with t(11;14)

Premkumar et al. 2021.

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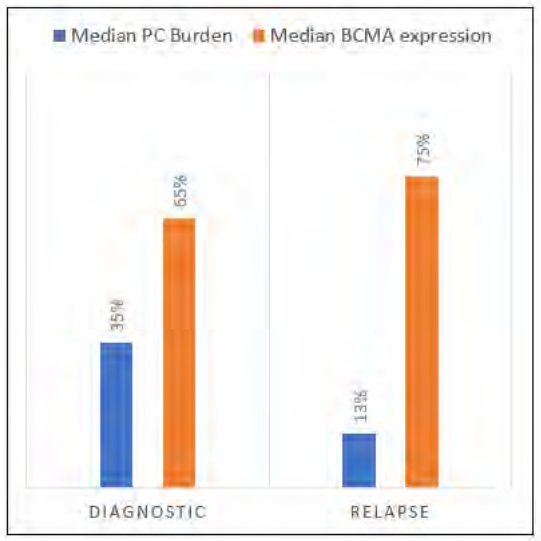
Chimeric antigen receptor (CAR) T cells

- Groundbreaking approach in the treatment of heme malignancies
- Impressive efficacy of **B-cell maturation antigen (BCMA)**-targeted CAR T cells in relapsed/refractory MM led to FDA-approval of 2 products (Abecma, Carvykti)

  ORR 73-98%, CR 33-82%
- **BCMA** also expressed on amyloidogenic plasma cells



Bal et al. ASH 2019.

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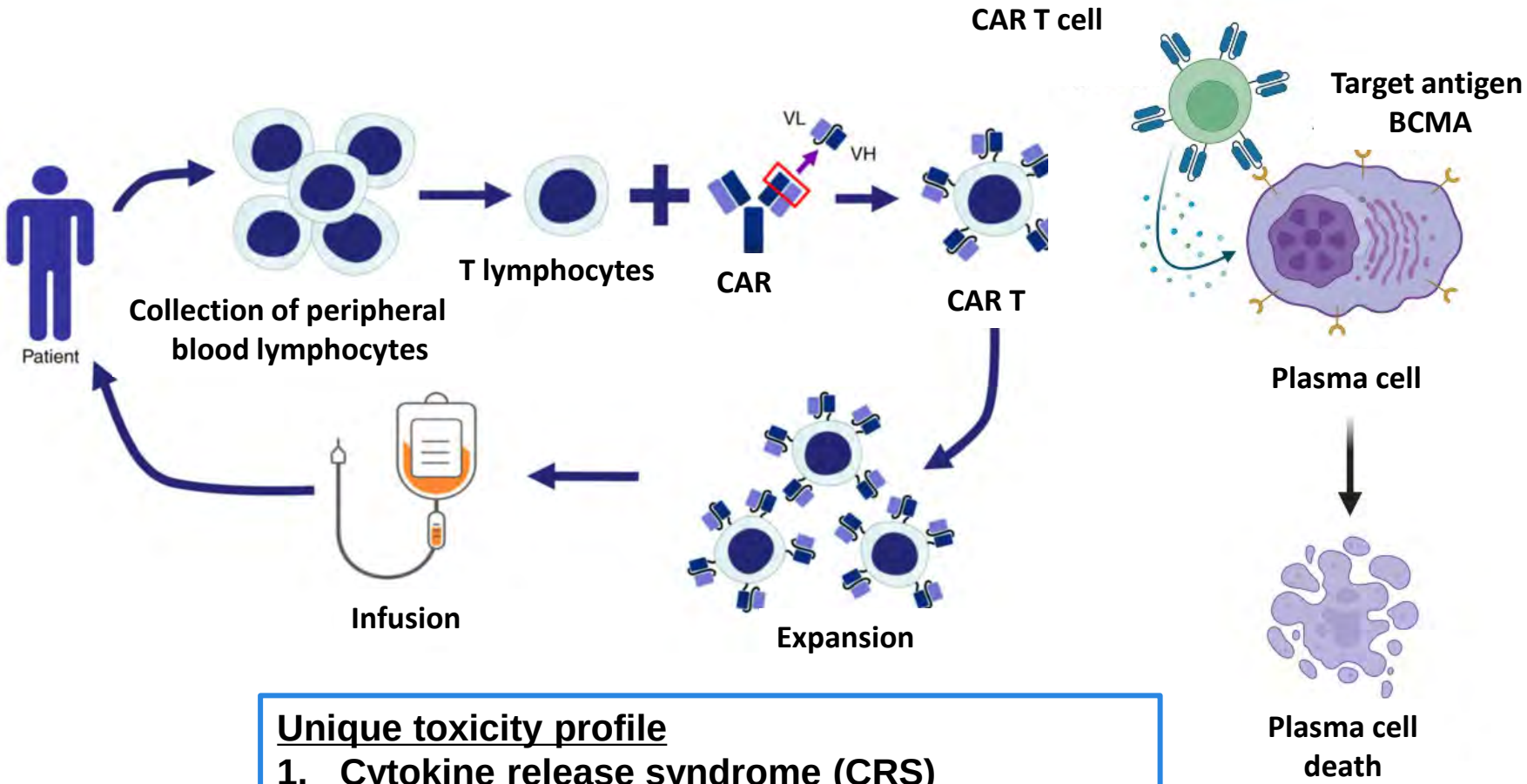
How do CAR T cells work?



Unique toxicity profile

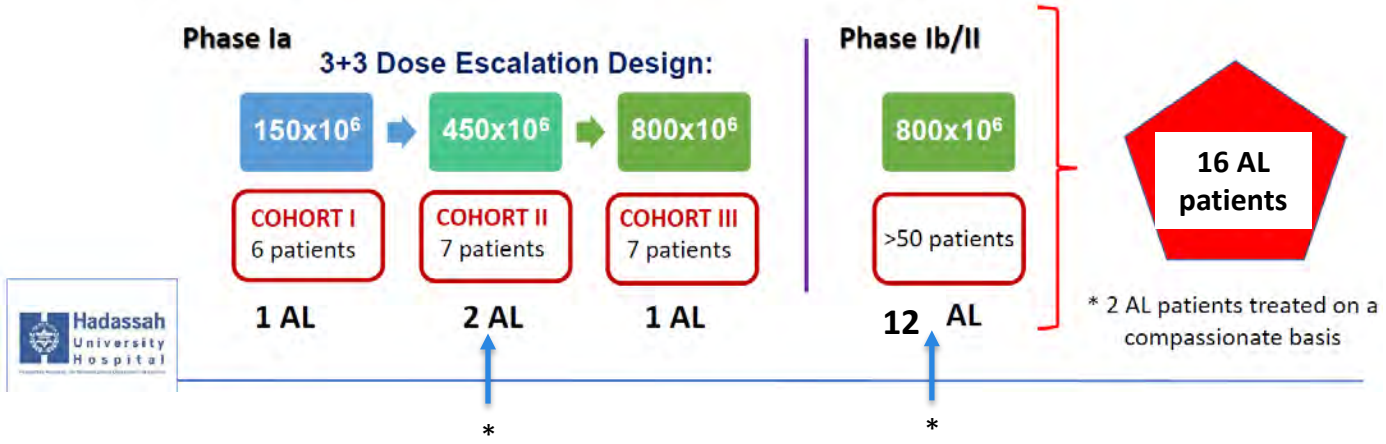
1. Cytokine release syndrome (CRS)
2. Immune effector cell neurotoxicity (ICANs)
3. Infections

Chen et al. 2022.
Holstein et al. 2023.

Phase 1b Dose Expansion Study of NXC-201 for the Treatment of Patients with Relapsed or Refractory AL Amyloidosis

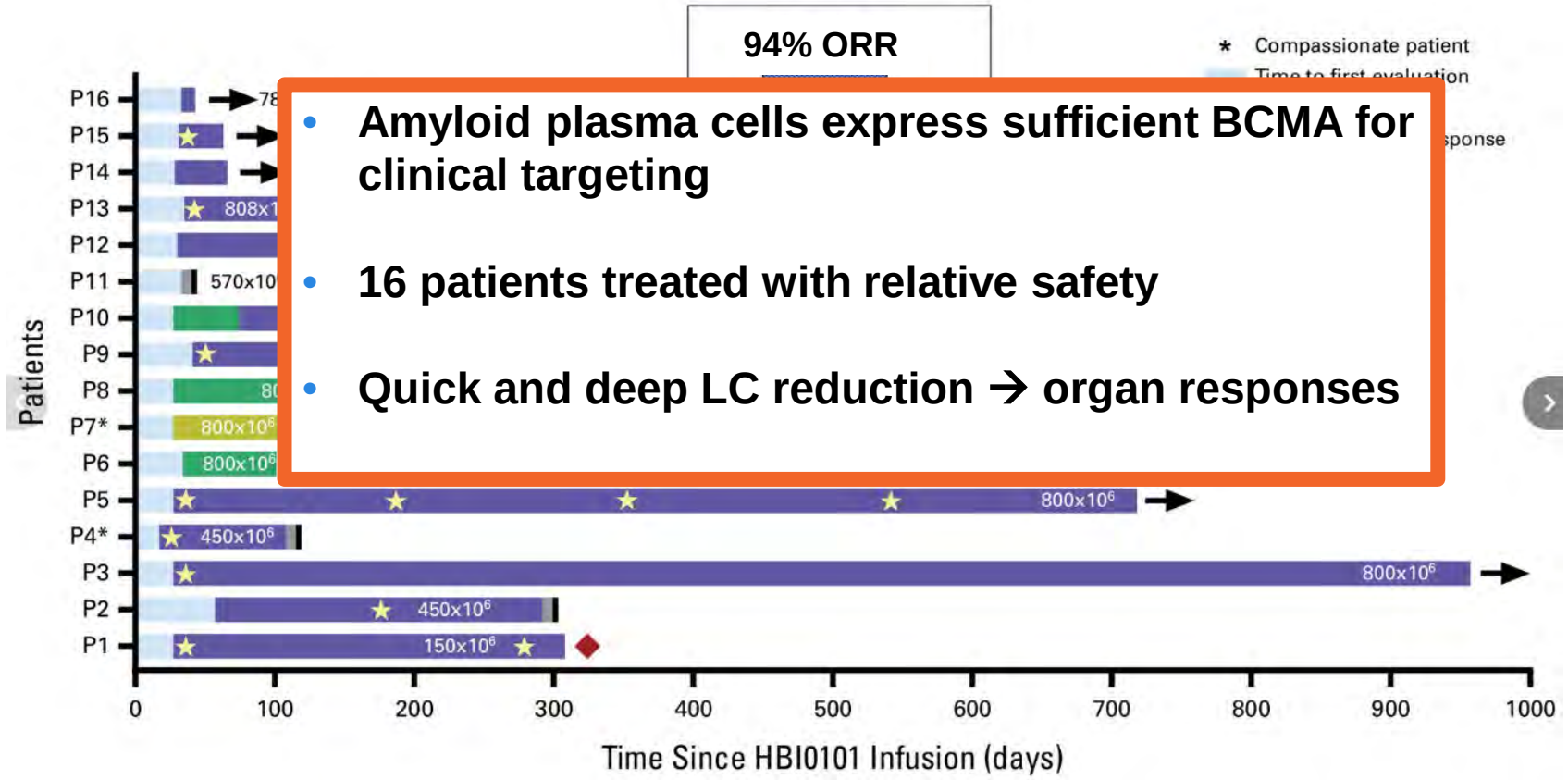
Clinical trial of HBI0101- NCT04720313

- A Phase Ia\Ib\2 Study of HBI0101 anti-BCMA CART in R/R MM and AL amyloidosis
- Phase Ia was designed as a dose-escalation 3X3 protocol. 20 pts.
- Phases Ib and 2 further tested 800 $X10^6$ cart cells, phase 2 is ongoing



Phase 1b Dose Expansion Study of NXC-201 for the Treatment of Patients with Relapsed or Refractory AL Amyloidosis

RESULTS- AL amyloidosis: Efficacy



- Amyloid plasma cells express sufficient BCMA for clinical targeting
- 16 patients treated with relative safety
- Quick and deep LC reduction → organ responses

Phase 1b dose expansion study of NXC-201 for relapsed or refractory AL amyloidosis

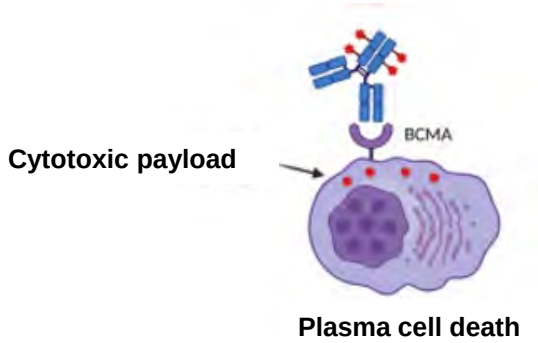
- 2 cohorts: 150 x 10^6 and 450 x 10^6
- Liberal inclusion criteria, after 1st line therapy < VGPR
- Correlative studies
  - Immune profiling, MRD testing
  - Remote monitoring → CRS signature

- N= 6 patients tx at MSK; 3 in each cohort
- 5/6 MRD negative by 12 color flow cytometry

Expansion open at MSK, UC Davis, Karmonos, Cleveland Clinic, Tufts and is actively accruing!

Other immunotherapeutic approaches

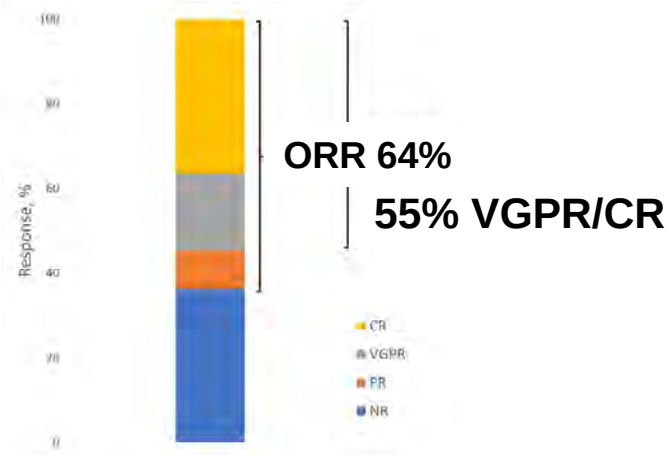
Belantamab mafadotin (Belamaf): antibody drug conjugate (ADC) directed against BCMA



- Drug = Auristatin F

Few retrospective series reported + 1 prospective trial underway in AL amyloidosis

N =11



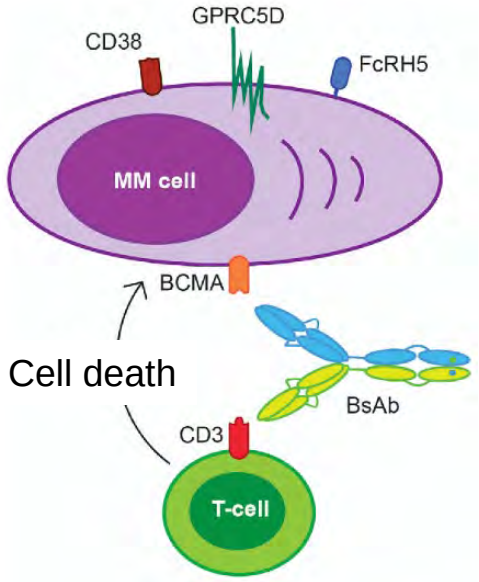
ORR 64%

55% VGPR/CR

***Ocular (eye) toxicity in up to 80% patients**

Khwaja et al. 2022
Zhang et al. 2022
Kastritis et al. 2022

Bispecific antibodies



FDA-approved bispecific Abs for MM

1. Teclistimab (BCMA)
2. Elranatamab (BCMA)
3. Talquetamab (GPRC5D)

ORR ~50-60%, CR ~30-40%

Toxicity profile

1. Cytokine release syndrome (CRS)
2. Immune effector cell neurotoxicity (ICANs)
3. Infections

Chakraborty R, Bhutani D, Maurer MS, Mohan M, Lentzsch S, D'Souza A. Safety and efficacy of teclistamab in systemic immunoglobulin light chain amyloidosis. *Blood Cancer J.* (2023) 13:1–4. doi:

7 patients, all achieved ≥ VGPR to Teclistimab, median 0.6 mos

Clinical trials in AL amyloidosis using the BCMA-directed products Teclistimab, Elranatamab, ABBV-383 are planned or have recently opened

Verkleij et al. 2022.
Holstein et al. 2023.
Chakraborty et al. 2023.

M24-209: An Open-Label Phase 1b Study Evaluating the Safety and Efficacy of ABBV-383 in AL Amyloidosis

Key Eligibility Criteria

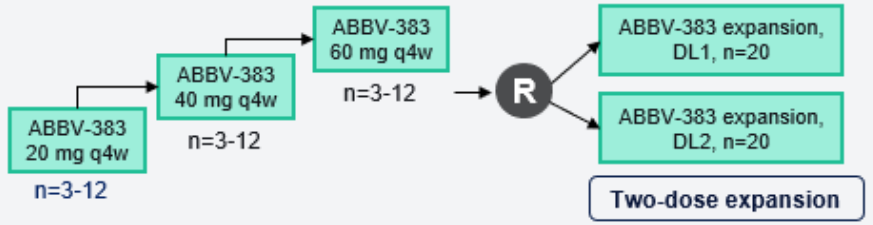
- Progressed on or after ≥1 prior therapy including PI **AND** anti-CD38 mAb
- ≥1 organ historically impacted
- Stage 1, 2, 3a & NT-proBNP <8,500 ng/L
- Measurable disease **dFLC ≥50 mg/L**

KEY OBJECTIVES

Primary:	*DLTs*
Secondary:	PK, Hematoloigc response, Organ response
Exploratory:	MRD

Phase 1 Dose Escalation and Safety Expansion Study

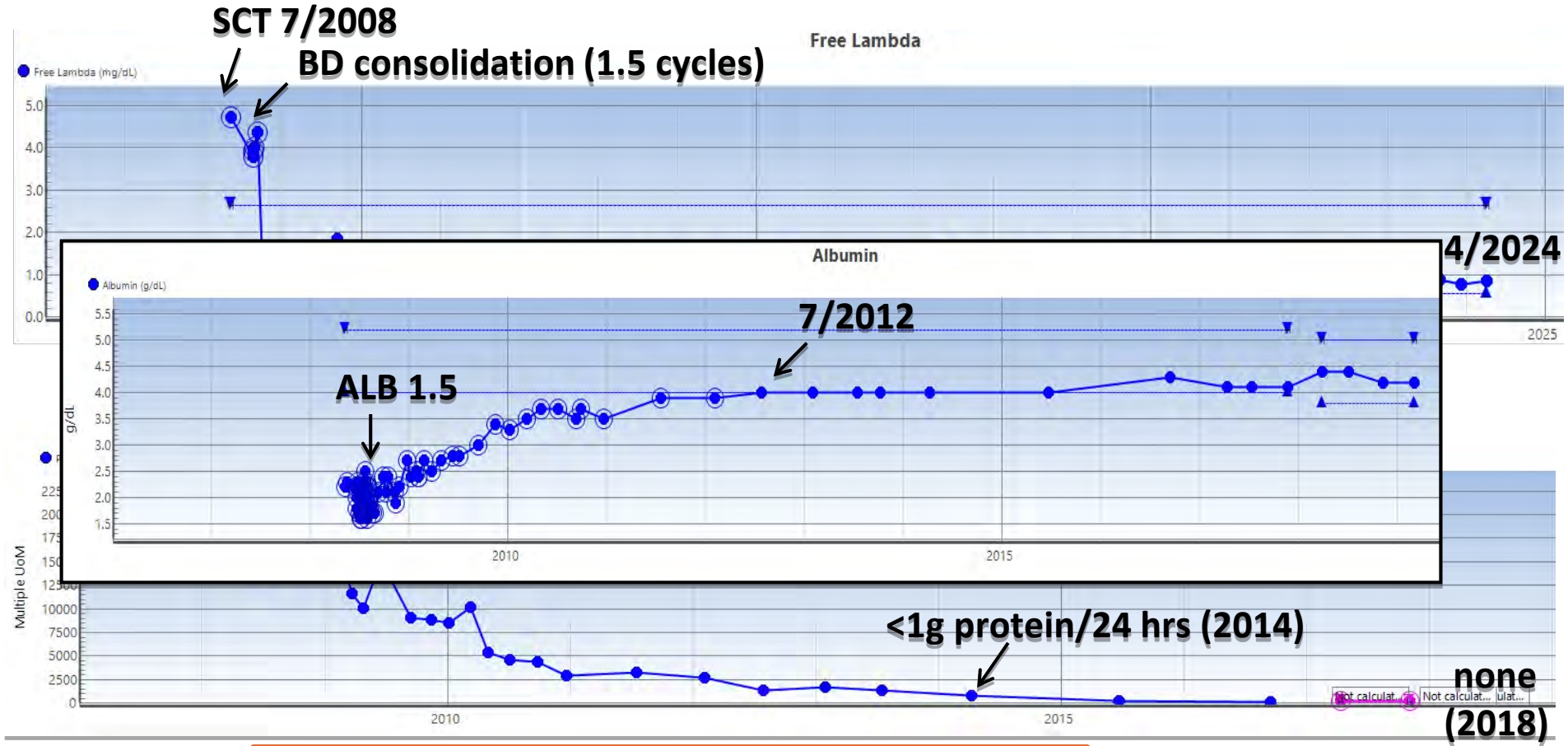
Relapsed/Refractory AL Amyloidosis (approx. n=76)



ABBV-383 (60mg IV Q4W)	
Schedule	Q4W
Route of Administration	Intravenous
Dosing	Day 1: Full dose No Step-Up dosing
CRS Monitoring Period (Day 1 of Cycle 1 only)	24-hours (Inpatient)

Hematologic response is necessary but not a guarantee for organ response

Organ response takes time!



Supportive care is essential!

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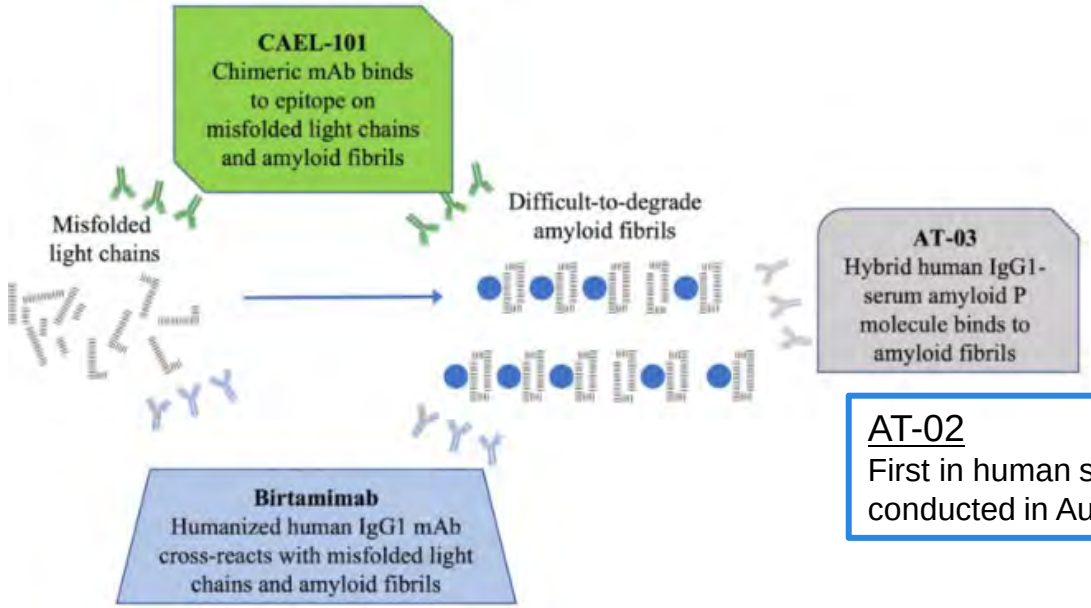
Amyloid-directed therapy

- **SOC treatment for AL amyloidosis targets pathologic plasma cells but does not address resident amyloid in organs/tissues**
- **Drugs in development to facilitate removal of amyloid fibrils**

CAEL-101 (Anselamimab)
Initial data in cardiac stage 3a/3b reported ~80% cardiac response.
- Phase III trials in patients with cardiac stage 3a/3b ongoing

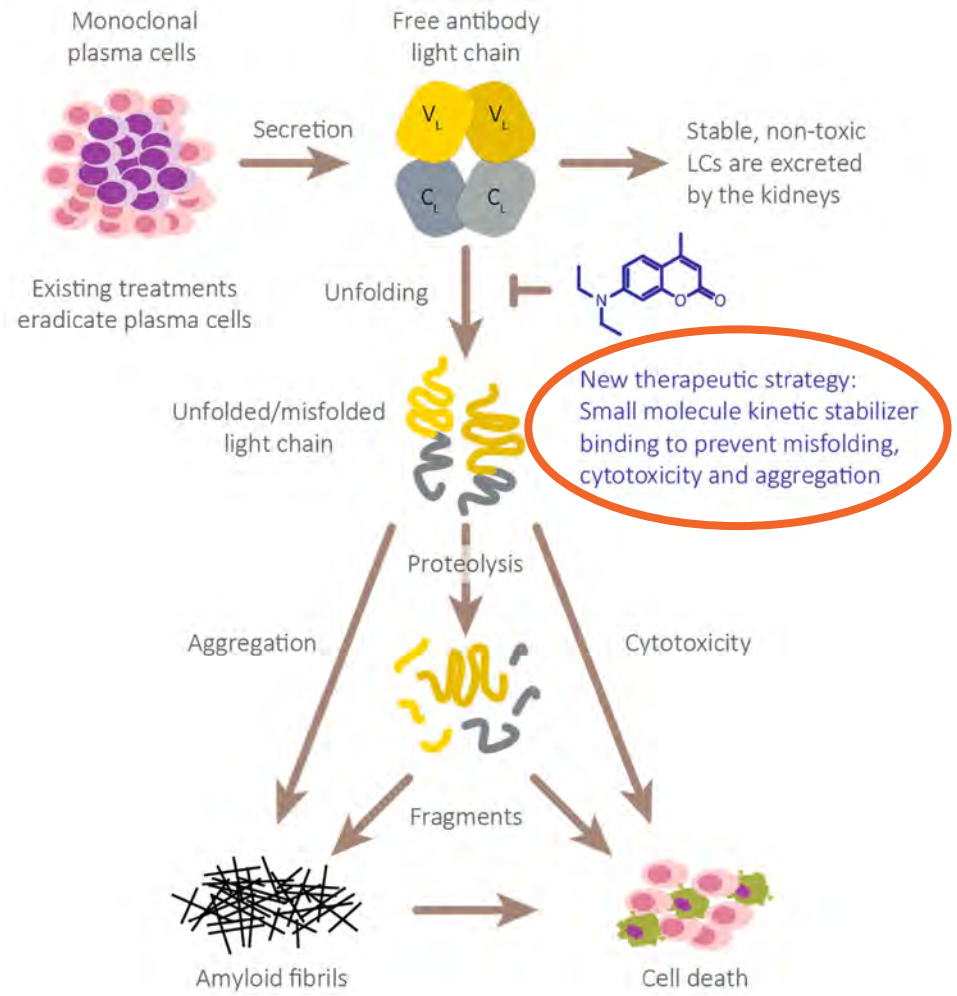


AT-02
First in human studies being conducted in Australia

NEOD001 (Birtamimab)
Initial phase ½ data suggested 57% cardiac and 60% renal response.
Yet, phase II *PRONTO* and phase III *VITAL* terminated early for futility.
Post-hoc analysis suggested possible benefit in stage IV patients.
- Phase III trial in patients with revised Mayo stage IV disease ongoing

Valent et al. 2022.
Gertz et al. 2016.
Gertz et al. 2023.

Novel approach: light chain stabilization



[Morgan et al. 2021](#).

Conclusions

- **SOC treatment for AL amyloidosis incorporates the monoclonal antibody daratumumab and has changed the treatment paradigm**
  - **May increase or decrease use of SCT in the upfront setting**
  - ***Organ responses take time*; not an indication to continue or change therapy when pt has achieved an optimal heme response**
- **Other immunotherapeutic approaches including BCMA-directed Studies in the salvage setting ongoing or planned**
  - **Unique toxicities**
- **Directly targeting amyloid deposits or stabilizing light chains are strategies being studied to reduce organ dysfunction or hasten organ recovery**
- **Patients who have advanced organ disease and have achieved a hematologic VGPR or CR may be candidates for organ transplantation**

Final thoughts…

Nothing replaces the importance of early diagnosis

Participation in clinical trials is essential

Thank you for your attention!

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Memorial Sloan Kettering Cancer Center

American Heart Association®

Disease Identification & Diagnosis: Case Based Panel Discussion

Disease Identification & Diagnosis: Case-Based Panel Discussion

Moderator

Mathew Maurer, MD
Professor of Medicine, Arnold and Arlene Goldstein Professor of Cardiology, NewYork-Presbyterian/Columbia University Irving Medical Center

Panelists

John O. Clarke, MD
Clinical Professor of Medicine, Division of Gastroenterology & Hepatology; Director, Esophageal Program; Vice-Chief, Education, Stanford Medicine

Heather J. Landau, MD
Director, Amyloidosis Program; Hematologist/Oncologist, Memorial Sloan Kettering Cancer Center

Mazen Hanna, MD
Co-Director, Amyloidosis Center; Cleveland Clinic

Jai Radhakrishnan, MD, MS
Professor of Medicine, Division of Nephrology, NewYork-Presbyterian/Columbia University Irving Medical Center

Initial Presentation

- 50-year-old male with an **IgA lambda MGUS** diagnosed 2010.
- He was feeling well and did moderate physical activity till Jan-23.
- Jan-23, he noted **dyspnea on exertion** after transitioning back to walking from crutches which he was using because he had broken his R patella in Sep-22.
- He thought the dyspnea was attributed to deconditioning but did not improve over the ensuing months.
- He had associated symptoms including **dizziness, fatigue** and an acute subjective **decrease in his production of saliva**.
- He experienced **onset of significant fatigue** in Mar-23 that has only progressed over the past few months, forcing him to take scattered naps throughout the day.
- He **lost 20lbs of weight unintentionally** over 6-8 months.

History of Present Illness

- In Jul-23, the patient experienced the onset of **gross painless hematuria**, which spontaneously resolved after 2 weeks.
- He also experienced the onset of insidiously progressive **nausea with decreasing appetite**.
- While traveling in Aug-23, he experienced a **recurrence of hematuria** with **dysuria** and **urgency** as well.
- He presented to an outside hospital in mid Aug-23 in mixed **hemorrhagic/septic shock** with **Staphylococcus epidermidis UTI**
  - He required 2 units of PRBCs and vasopressors for <24 hours.
  - A CT of his abdomen and pelvis without contrast was reportedly negative for osseous lesions but revealed a **posterior bladder mass.**
  - A cystoscopy with biopsy revealed **amyloid NOS.**
  - He was discharged 08/21/23 with rheumatologic laboratory assays (ANA, anti-Ro/La) pending; **Cr was 1.7** at the time, elevated from Sep-22.

Review of Systems

- No rash but notes **easy bruising.** He has **pruritus**.
- He denies difficulty hearing and vision issues but does wear glasses
- No chronic cough, no trouble swallowing.
- **Short of breath** walking 2 blocks, no orthopnea nor PND nor edema.
- He has **palpitations** and a **fast heart rate.** Pt had **near syncope** after her got up from a couch.
- He denies diarrhea but does have **constipation and nausea, low appetite.**
- He has lost **20 pounds in 8 weeks**. He has no blood in his stool, melena nor colitis.
- Had **hematuria** in the past. He has some dysuria. There is no history of renal stones.
- He has no history of CTS, spinal stenosis nor biceps tendon rupture.
- Pt denies numbness or tingling in lower extremities, but they feel “itchy”.
- No diabetes nor thyroid issues.
- Mood is described **anxious and depressed.**
- He has had **erectile dysfunction.**

Physical Exam

- **Appearance:** Underweight and ill-appearing
- **HEENT:** Anicteric scleral
- **Cardiovascular:** JVP < 6 cm, regular rate and rhythm, no murmurs nor gallop, no edema
- **Pulmonary:** normal breath sounds without wheezing or rales
- **Abdominal:** Non-distended, soft, scaphoid, no abdominal tenderness nor guarding
- **Musculoskeletal:** sarcopenic
- **General:** Skin is warm

Vital Sign	Value
BP	104/76 (Supine) 90/60 (Standing)
Pulse	97
RR	15
Temperature	Afebrile
Height	5 ft 5 in
BMI	18.9

Hematologic Tests Results

Bone Marrow Biopsy

- Involvement by plasma cell neoplasia/myeloma in a hypercellular bone marrow with background myeloid predominant progressively maturing trilineage hematopoiesis.
- Plasma cells: Increased at 23%, focally forming large clusters, atypical forms seen, consistent with involvement by plasma cell neoplasm
- No amyloid detected

Flow Cytometry

- Large, aberrant plasma cell population detected (12-13% of all nucleated events analyzed) with the following aberrant phenotype: CD138+, CD38+, CD200+, CD43+, CD20-, CD19-, CD22-, CD56-, CD117-, CD45-, CD81+/-, CD27+
- Kappa negative, lambda positive.
- Small polytypic B-cell population is detected.
- Hematogones are also noted.

Hematologic Tests *(cont.)*

1. Monosomy 13 in 88% cells.

2. Positive for IGH rearrangement in 82% cells.

3. Gain of 1q21 in 4% cells.
   This may represent a potential sub-clone.

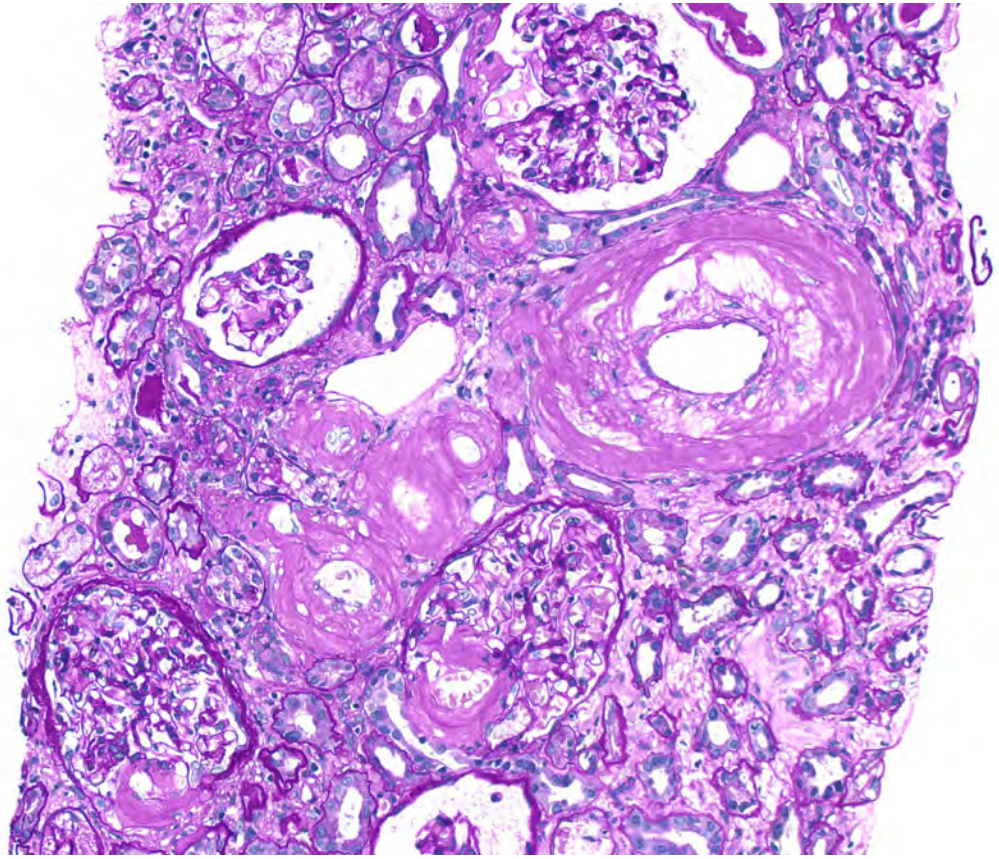
He does not have t(11;14)

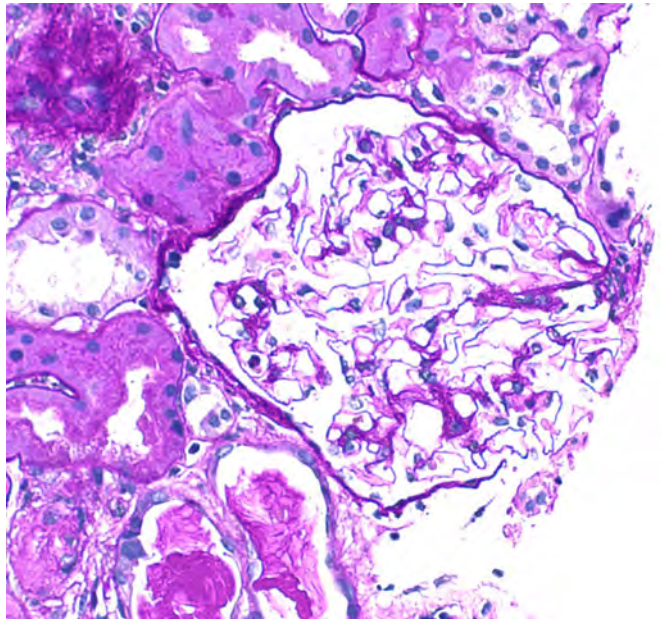
Initial Presentation to Amyloidosis Center

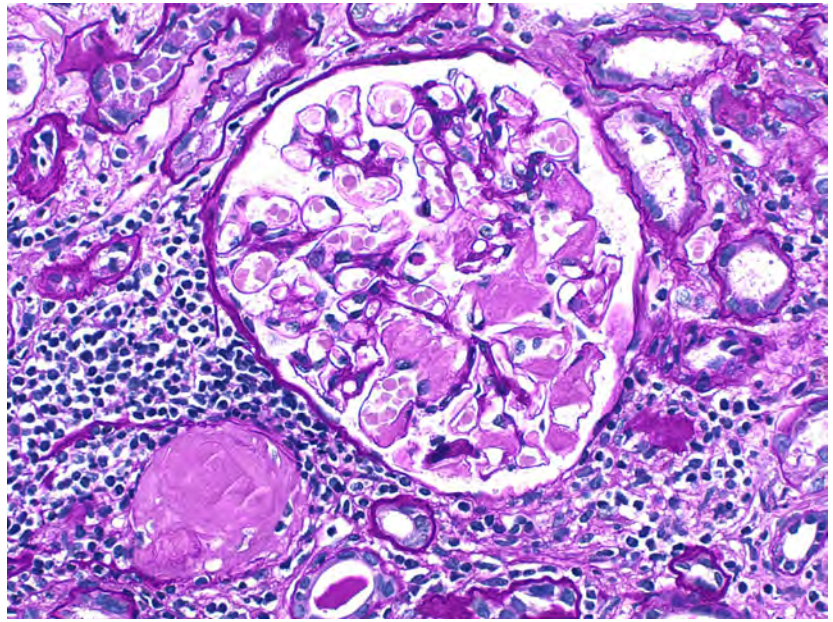
Test	Value
BMBx	Increased at 23% Lambda restricted PC
Fat Pad	Negative
PET-CT	Multiple Lytic Lesions
FLC lambda	15.07 mg/dl with difference of <18
NT-proBNP (pg/mL)	4931
hsTnT (ng/L)	48
ECHO	diastolic dysfunction
Cardiac MRI:	ECV 43%
Staging	Revised Mayo staging 3
ECOG PS	2 - Symptomatic, <50% confined to bed
KPS	60%

Test	Value
Hemoglobin [g/dL]	9.9
Albumin [g/dL]	2.6
Alkaline Phosphatase [IU/L]	60
AST/ALT [U/L]	22/14
B-2 Microglobulin [mg/L]	6.44
LDH [U/L]	203
Creatinine [mg/dL]	1.6
eGFR: [mL/min/m2]	53
Calcium [mg/dL]	8.9
Urine Protein -24 hours [mg]	4,043
Factor X Activity	60%

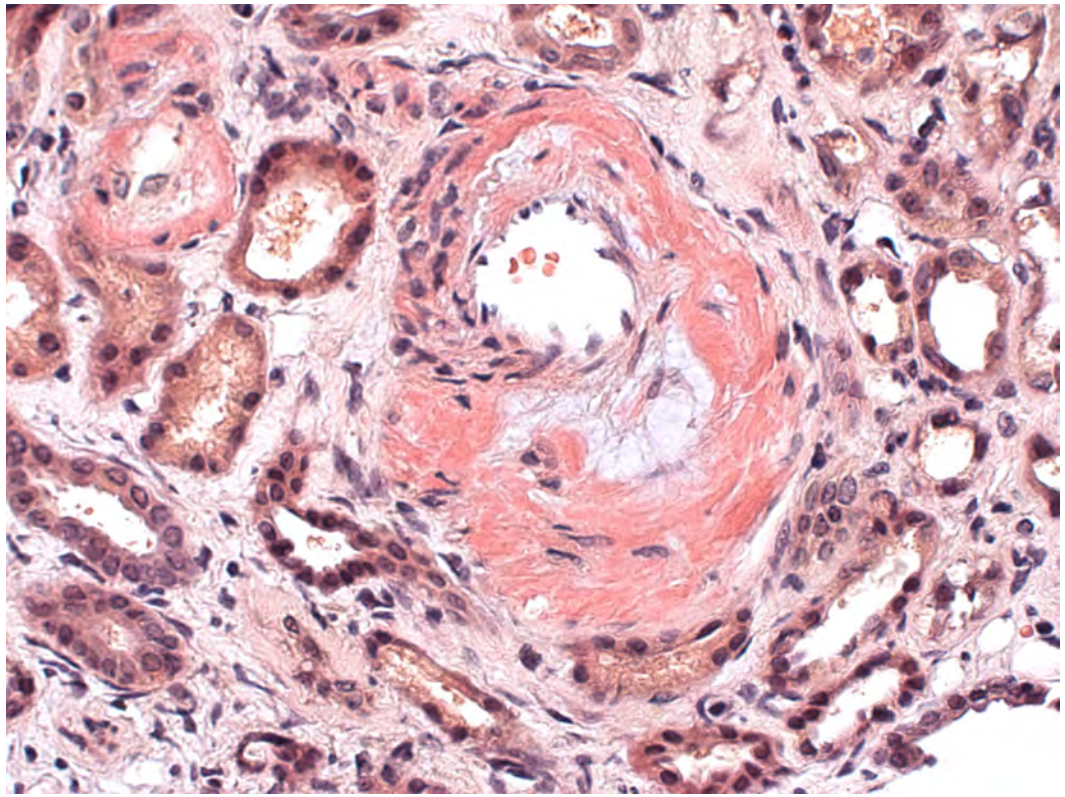
Renal Biopsy
Light Microscopy

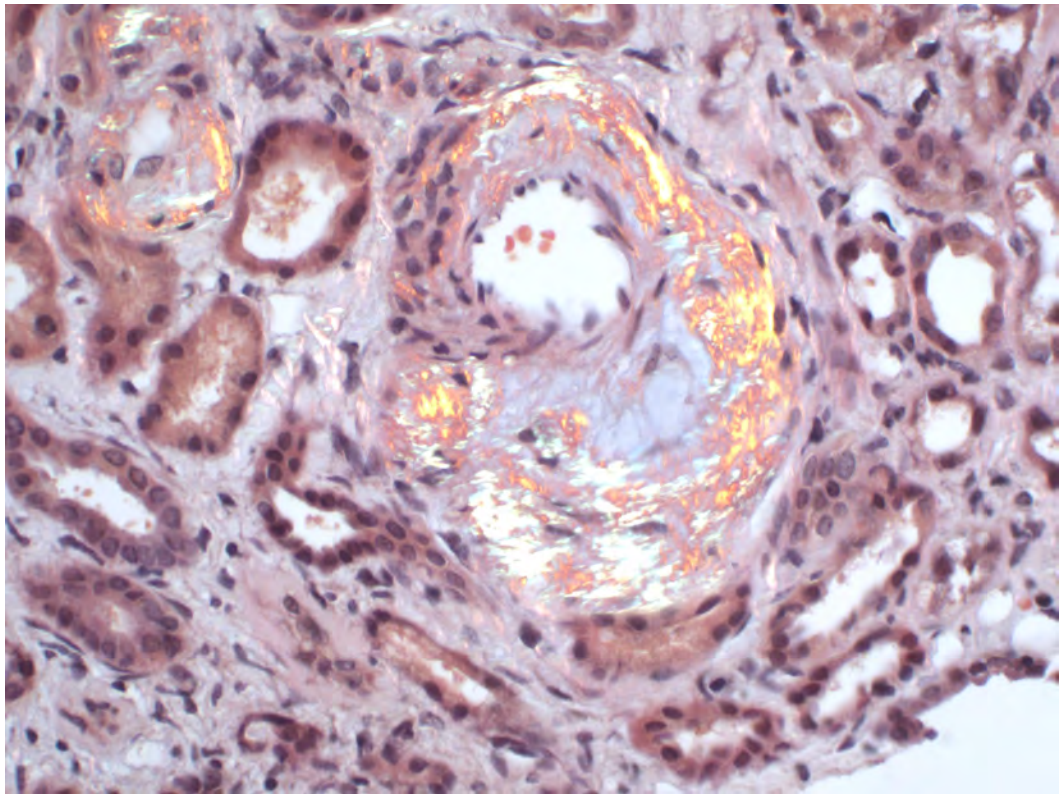




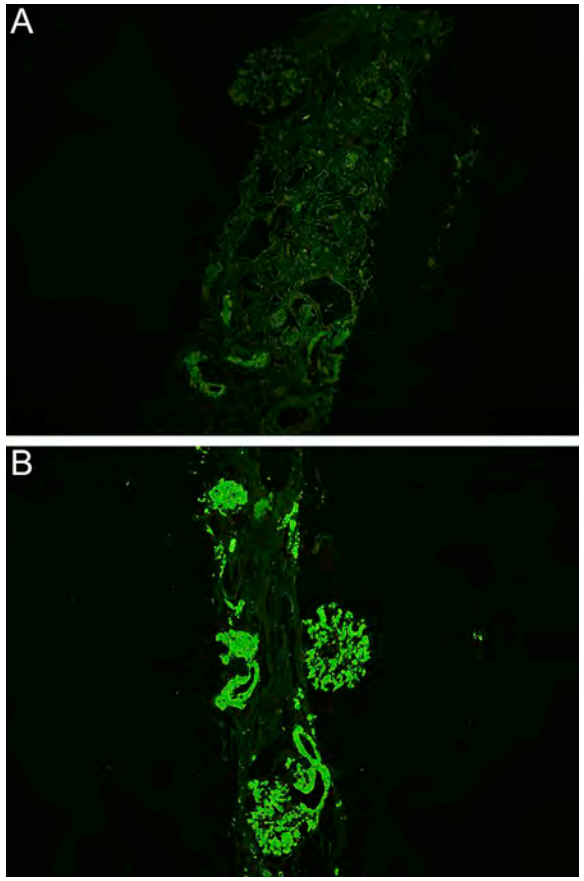


Congo Red



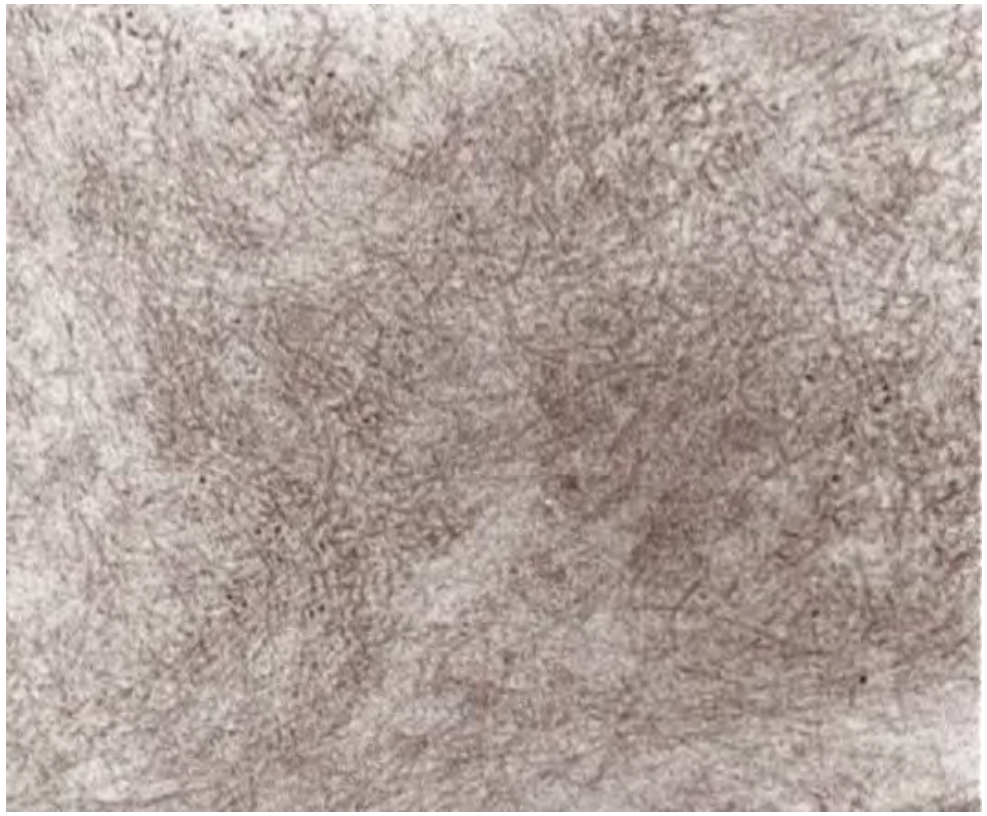


Immunofluorescence Microscopy



Lambda Light Chain Restriction

Electron Microscopy



Randomly-oriented fibrils
8-12 nm in diameter

Renal Biopsy Results

Fat Pad Biopsy

- No Amyloid Detected

Renal Biopsy

- AL-lambda amyloidosis with predominant involvement of blood vessels. ***see comment below***
- Tubular atrophy and interstitial fibrosis, moderate.
- Arterio- and arteriolosclerosis with hyalinosis, severe.

*The immunofluorescence findings of 3+ smudgy staining for lambda in the distribution of amyloid deposits, without significant staining for kappa, supports a diagnosis of AL-lambda amyloidosis. The predominant involvement of the blood vessels suggests lack of autoregulation as a likely contributing factor to the patient's recent history of AKI. There is also less prominent glomerular and interstitial involvement by amyloid.

Gastrointestinal Results

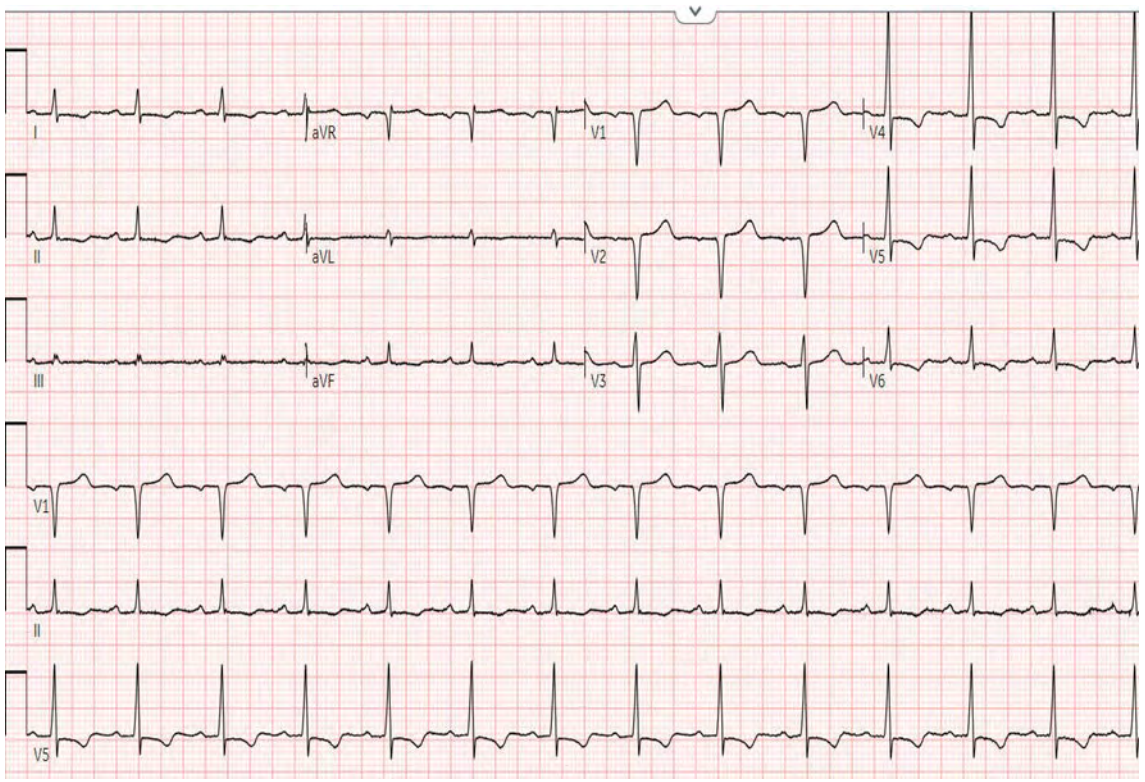
Gastric Emptying Study

Time Point	Normal % of the radiotracer remaining in the stomach	Patient Result % of the radiotracer remaining in the stomach
63 Minutes	30-90%	95.8 %
119 Minutes	Upper Limit 60%	78.4%
180 Minutes	Upper Limit 30%	55.6%
240 Minutes	Upper Limit 10%	32.3%

IMPRESSION: Delayed gastric emptying suspicious for gastroparesis.

Cardiac Results:

Electrocardiogram



Echocardiogram

- LV wall thickness is mildly increased (12 mm)
- There is concentric remodeling of the left ventricle.
- Left ventricular systolic function is normal with an EF of 60 to 65%.
- The LV mass index is 104.4 g/mÂ².
- There is an apical sparing pattern of LV global longitudinal strain
- The absolute value of global longitudinal strain (GLS) is 12.4 % (nl greater than or = 18%. Values between 16% and 18% are borderline).
- Right Ventricle: Right ventricular size is normal. The right ventricular systolic function is normal.
- Left Atrium: There is mild left atrial enlargement. The LA Volume is 64.2 ml. Left atrium volume index is 39.6 ml/mÂ².

Cardiac Test Results *(cont.)*

Cardiac MRI Results	
LV Wall thickness	ANTEROSEPTAL: 1.5 cm INFEROLATERAL: 1.3 cm
LV EDD	4.4 cm
End Diastolic Volume	130 ml (113-196), 80 ml/m^2 (62-97)
End Systolic Volume	60 ml (29-74), 37 ml/m^2 (15-37)
Cardiac output	5.06 L/min, 3.10 L/min/m^2
LV mass	204 g (107-184), 125 g/m^2 (57-91)
Stroke Volume	69 ml (75-131), 42 ml/m^2 (41-65)
Ejection Fraction	53 % (58-76)

Right Heart Catheterization Results
RA 5/4 (3)
PA 23/10 (15)
PCW 10/9 (7)
Fick CO: 5.01 CI: 3.13
PA sat 64%
TCO: 3.13; TCI 1.74

Cardiac MRI Summary

- Low grade diffuse myocardial enhancement with associated Increased myocardial extracellular volume fraction (ECV 46% [normal < 33%])
- Myocardial tissue properties are consistent with cardiac amyloid.
- Normal right ventricular size. Normal right ventricular systolic function.
- Mild bi-atrial enlargement.
- Bicuspid, non-stenotic aortic valve (non-coronary/right coronary cusp fusion). Mild aortic regurgitation.
- Small circumferential pericardial effusion

Treatment for Light Chain Amyloidosis

Initiated 09/21/2023

Medication	Dosing
Daratumumab	1800mg SC weekly for 2 cycles, q2wk C3-6, q4wk thereafter
Bortezomib	ECOG 2 will start at 1.0mg/m2 SC weekly
Cyclophosphamide	ECOG 2 will start at 300mg/m2 IV weekly
Dexamethasone	10mg weekly

Baseline Labs:

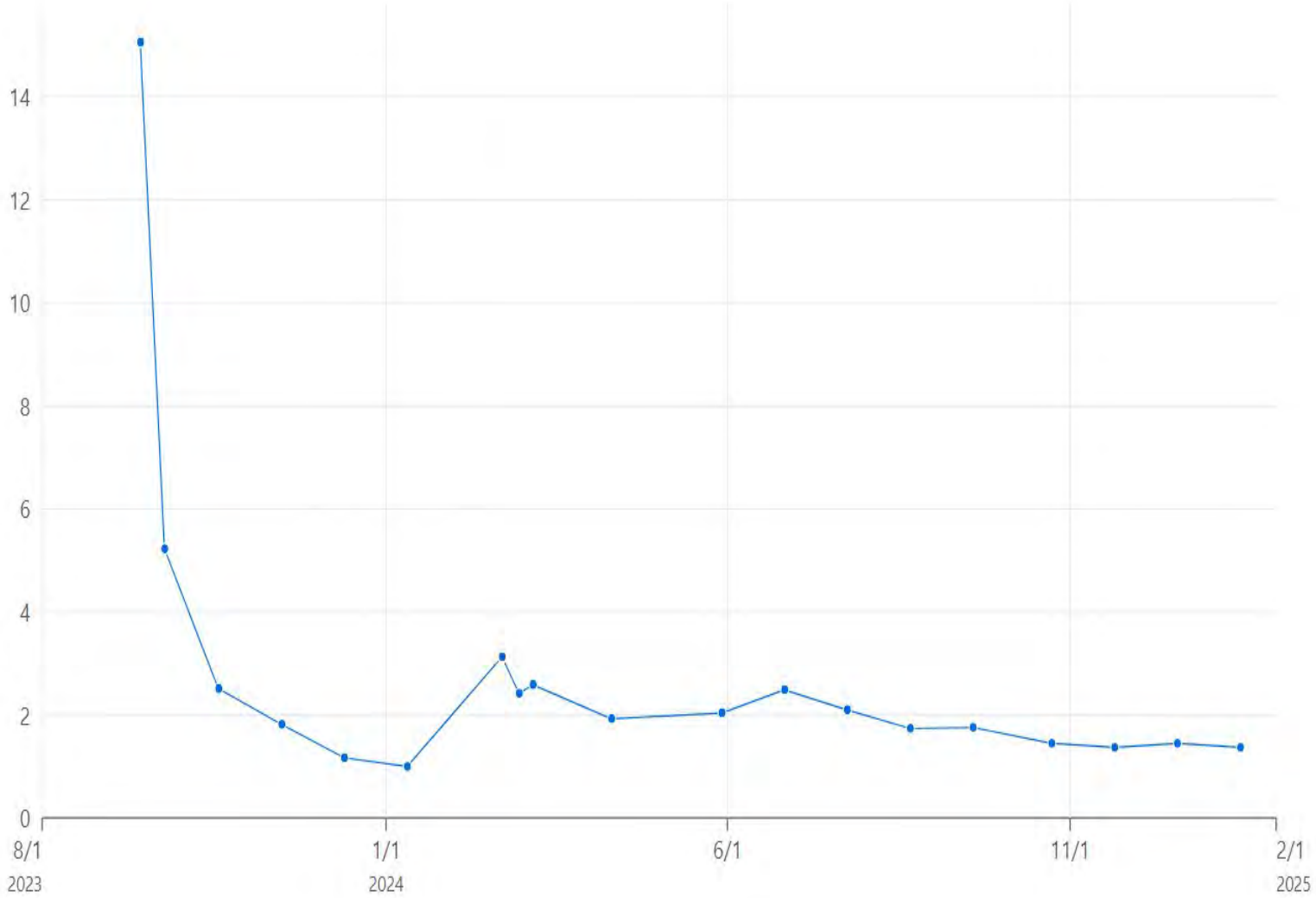
Test	Value
NT-proBNP (pg/mL)	4931
hsTnT (ng/L)	48
eGFR: [mL/min/m2]	53

Note:

Bortezomib and Cytoxan were omitted since 1/11/24 due to toxicity, currently on daratumumab and dexamethasone

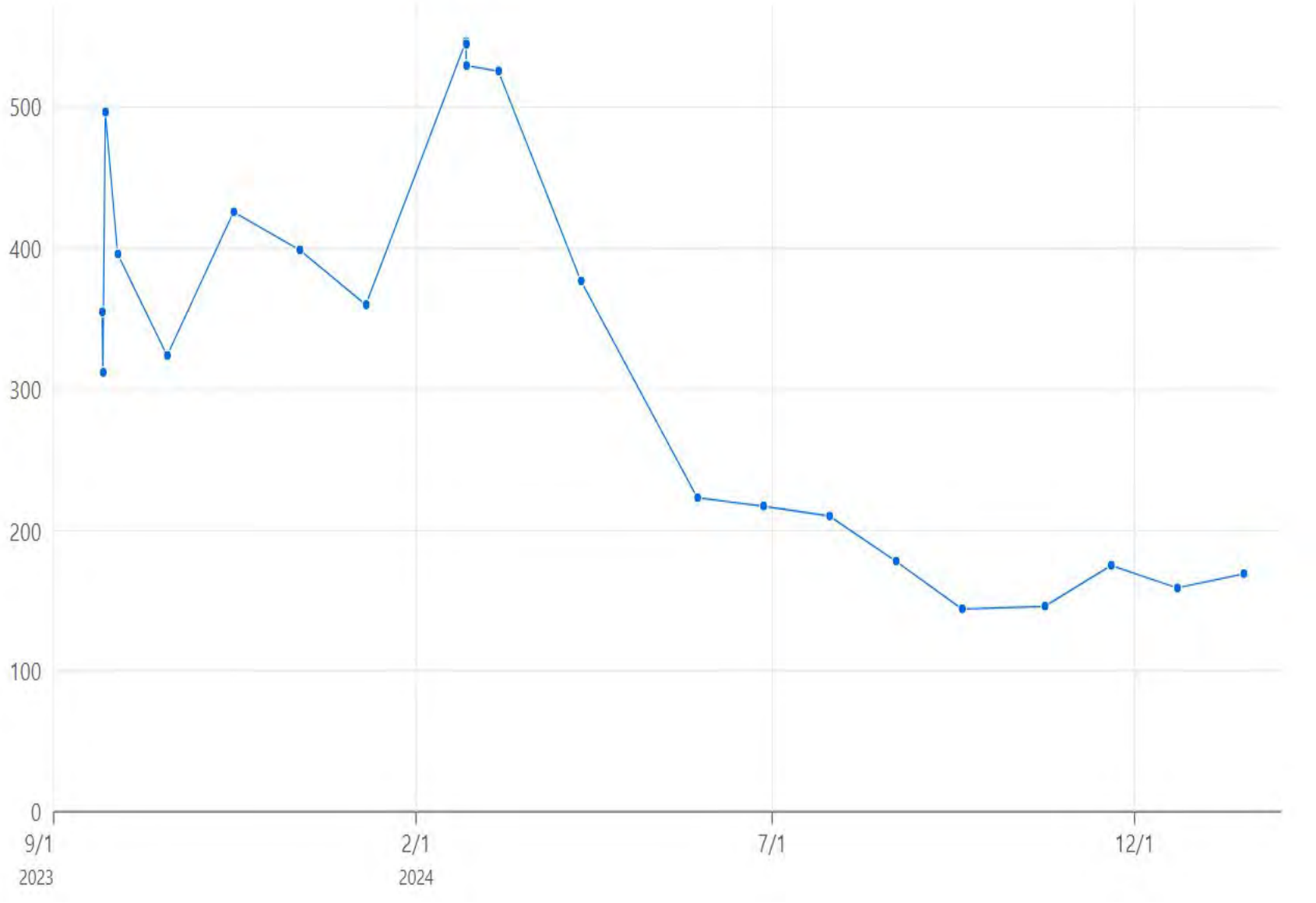
Course of Light Chains & Cardiac Biomarkers

Lambda Light Chains



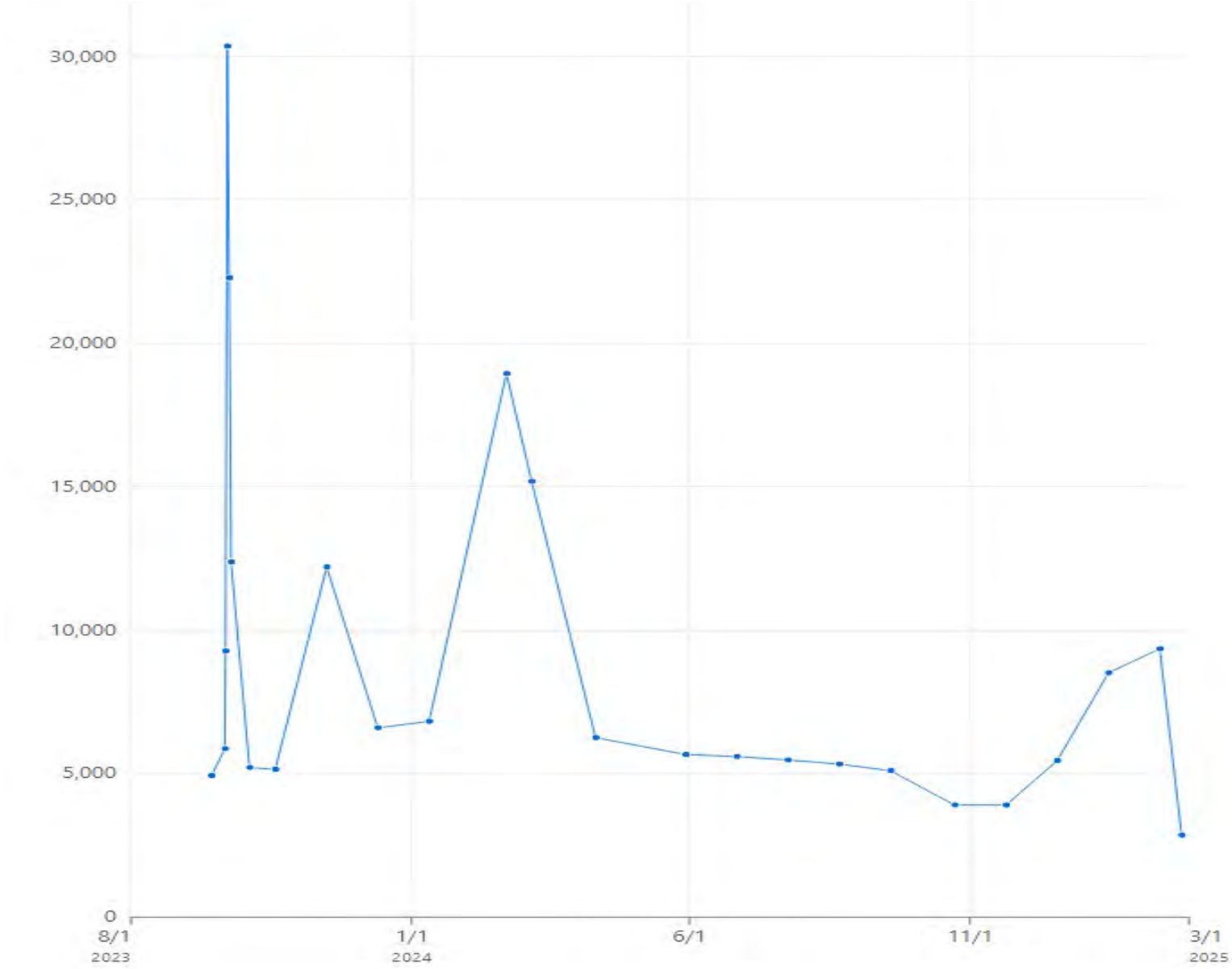
Course of Light Chains & Cardiac Biomarkers

Hs Troponin T



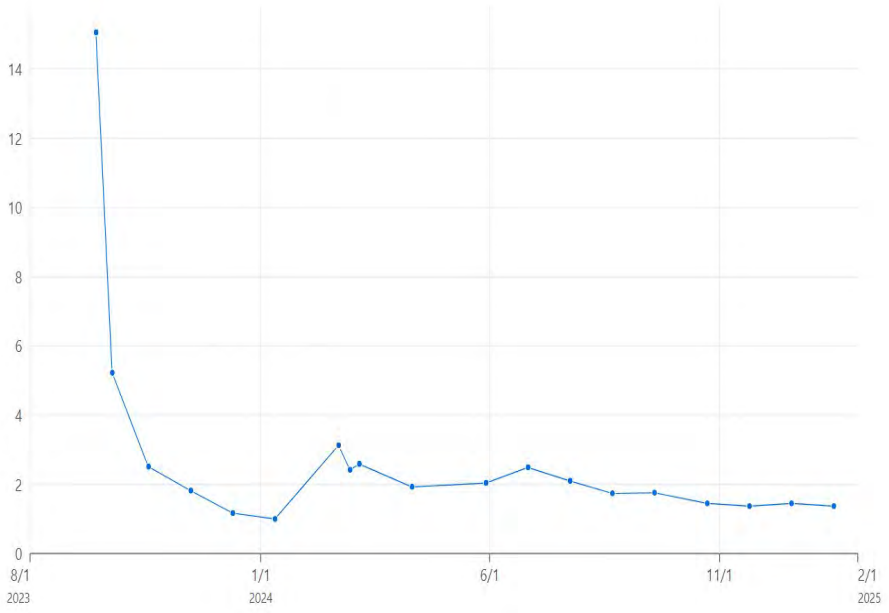
Course of Light Chains & Cardiac Biomarkers

NTproBNP

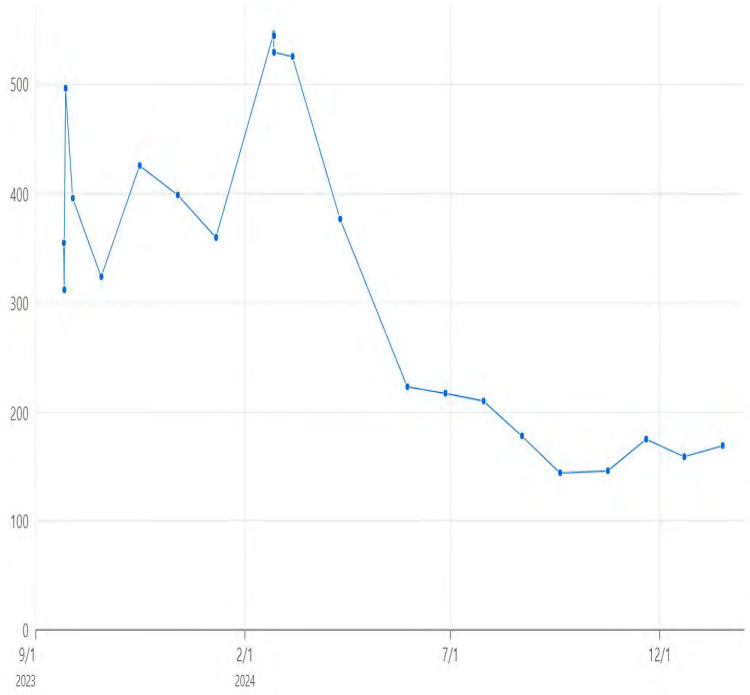


Course of Light Chains & Cardiac Biomarkers

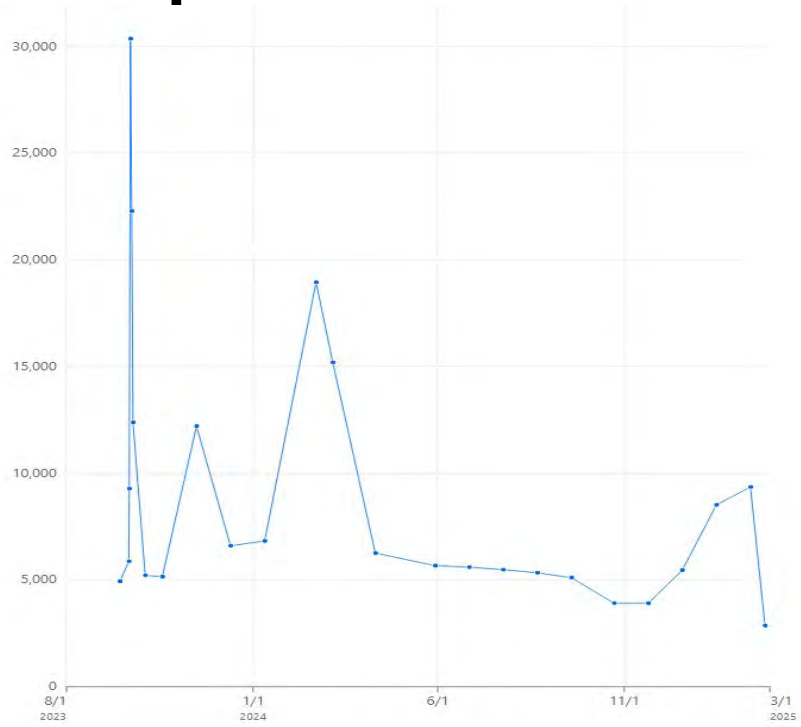
Lambda Light Chains



Hs Troponin T

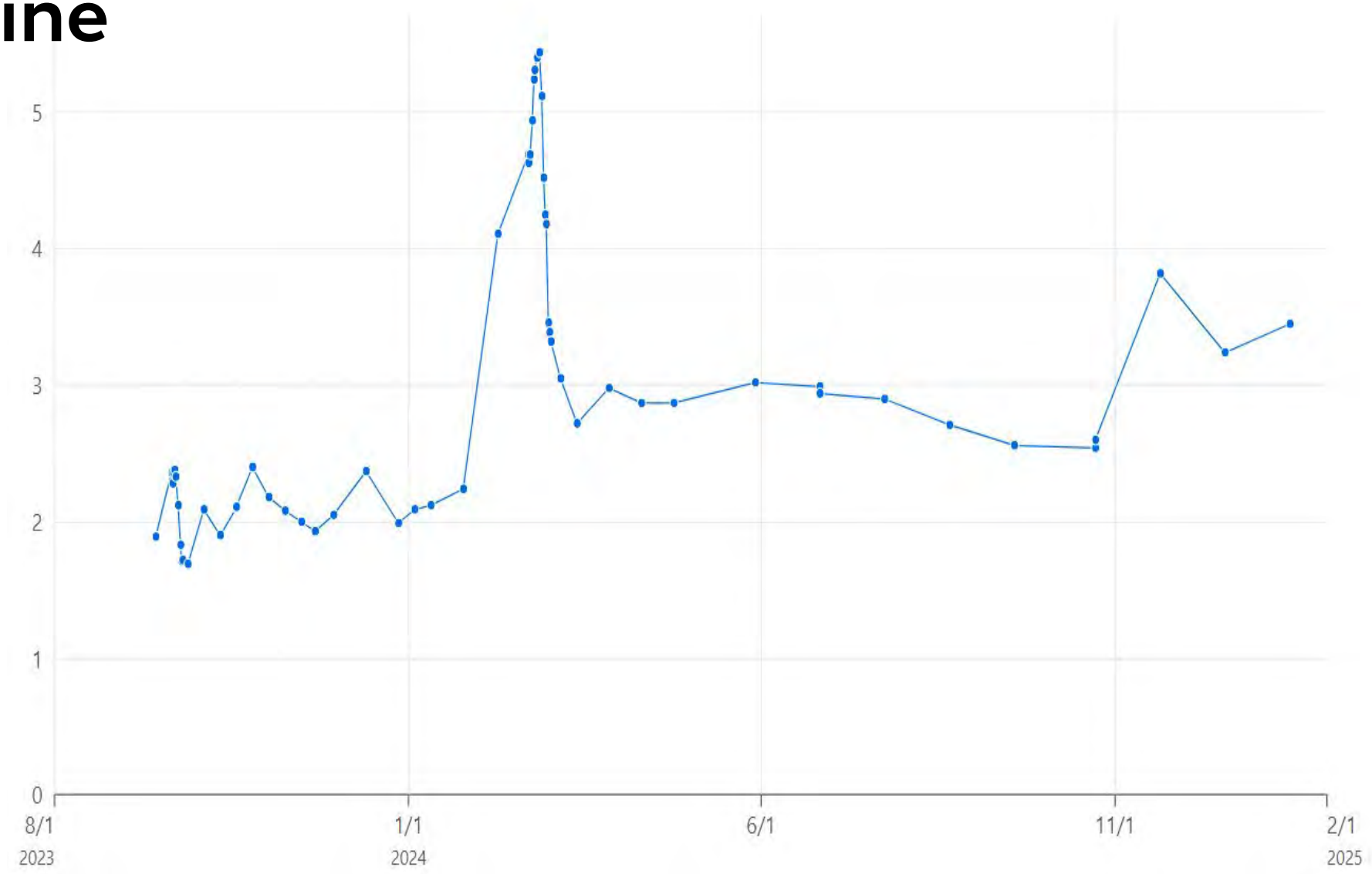


NTproBNP



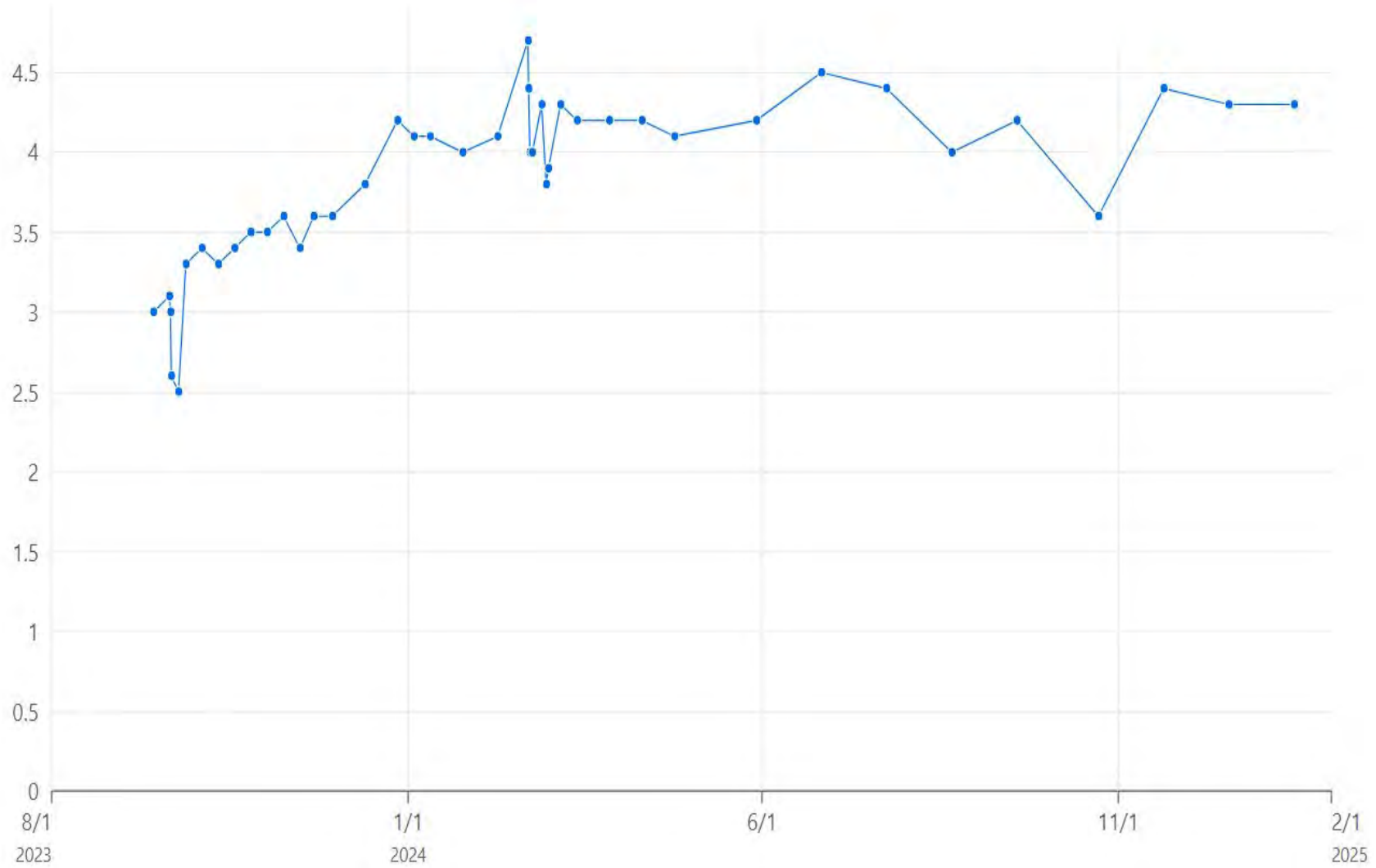
Course of Renal Parameters

Creatinine



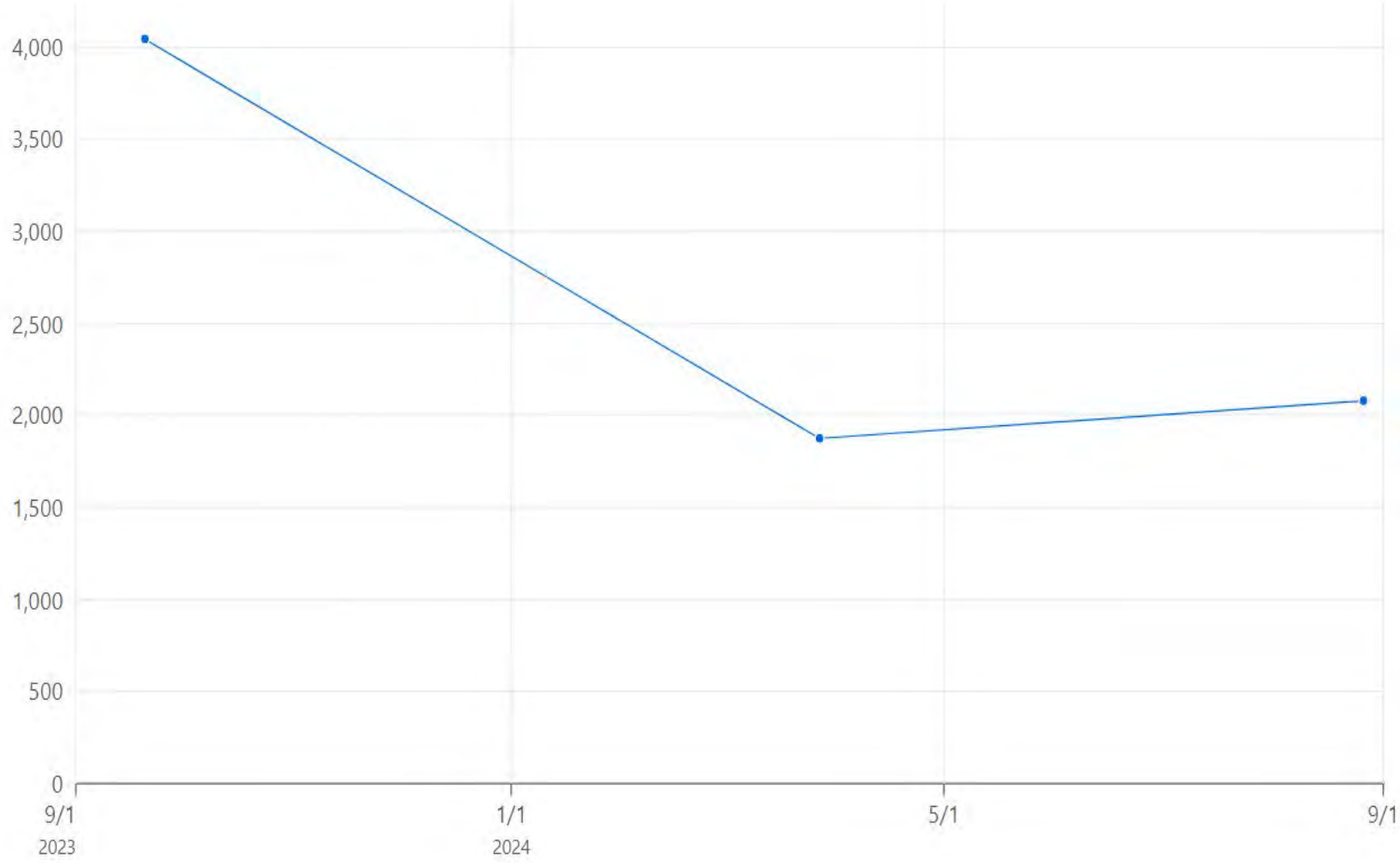
Course of Renal Parameters

Albumin



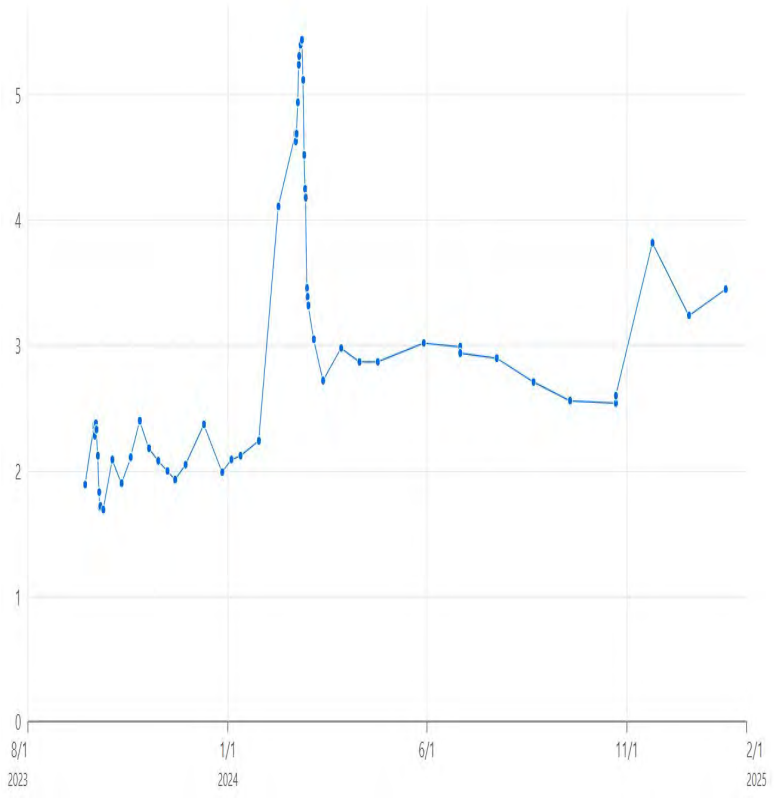
Course of Renal Parameters

Urinary Protein

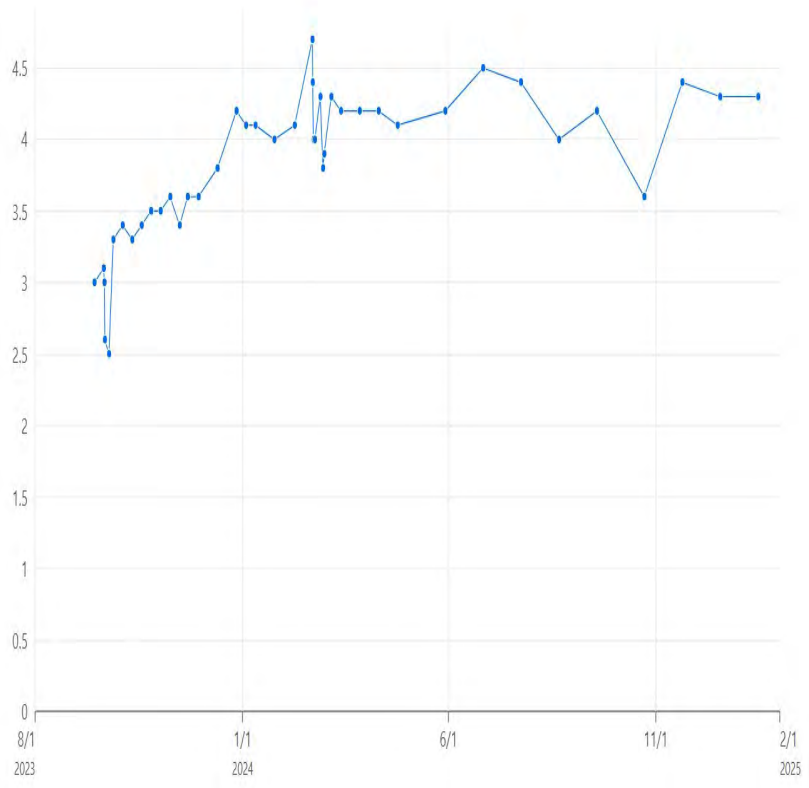


Course of Renal Parameters

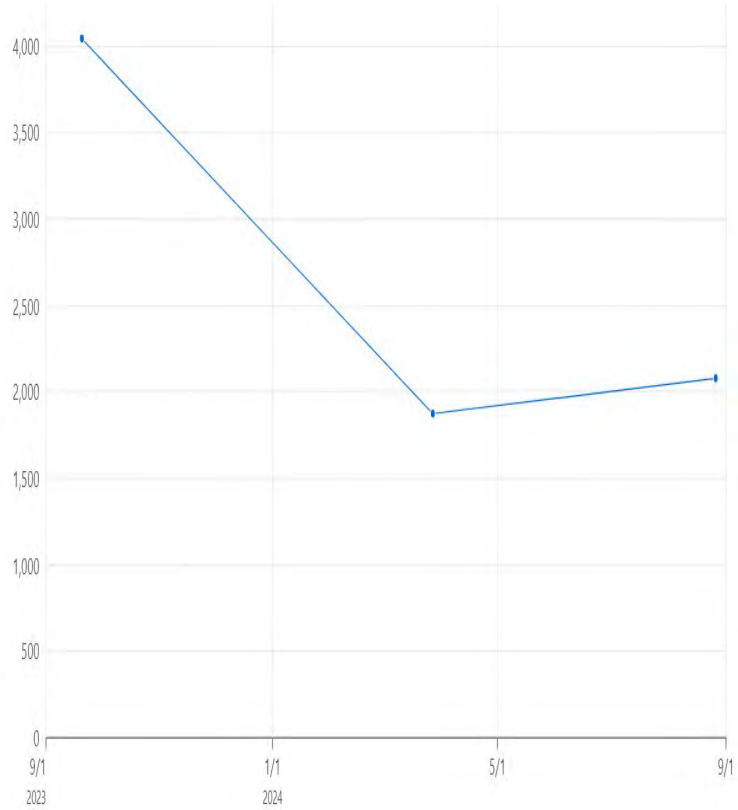
Creatinine



Albumin



Urinary Protein



Key Takeaways

- ✓ Early diagnosis
- ✓ Multi-Disciplinary Management
- ✓ Controlling light chains while minimizing toxicity

Q & A

Moderator

Mathew Maurer, MD
Professor of Medicine, Arnold and Arlene Goldstein Professor of Cardiology, NewYork-Presbyterian/Columbia University Irving Medical Center

Panelists

John O. Clarke, MD
Clinical Professor of Medicine, Division of Gastroenterology & Hepatology; Director, Esophageal Program; Vice-Chief, Education, Stanford Medicine

Heather J. Landau, MD
Director, Amyloidosis Program; Hematologist/Oncologist, Memorial Sloan Kettering Cancer Center

Mazen Hanna, MD
Co-Director, Amyloidosis Center; Cleveland Clinic

Jai Radhakrishnan, MD, MS
Professor of Medicine, Division of Nephrology, NewYork-Presbyterian/Columbia University Irving Medical Center

Break

10 MINUTES

Welcome Back!
& Upcoming Sessions:

Addressing & Overcoming Disparities in AL Amyloidosis Care and Research
Kevin M. Alexander, MD, FACC

Multidisciplinary Care Approaches
Yevgeniy Brailovsky, DO, MSc, FACC, FACP,
Julie Rosenthal, MD
Brett Sperry, MD

Multidisciplinary Care Approaches: Panel Discussion
Moderated by Mathew Maurer, MD,
Panel: Yevgeniy Brailovsky, DO, MSc, FACC, FACP, Julie Rosenthal, MD, Brett Sperry, MD, Naim Bideiwy, FNP-C, MSN, & Tammy Reideler, MSN, RN

Q&A and Closing Remarks

American Heart Association®

Addressing & Overcoming Disparities in AL Amyloidosis Care and Research

Kevin M. Alexander, MD

Assistant Professor of Medicine
Advanced Heart Failure and Transplant Cardiology

Stanford Amyloid Center

Stanford Medicine

@KMAlexanderMD

Disclosures

- Consulting/advisory board: Alexion, Alnylam, Arbor Biotechnologies, Novo Nordisk, Pfizer
- Clinical trials: CARDIO-TTRansform, Coramitug phase II, MAGNITUDE, DepleTTR
- Grant funding: AHA, Eidos, NIH
- Clinical Events Committee: ATTRibute-CM, LIBREXIA, REACT-AF

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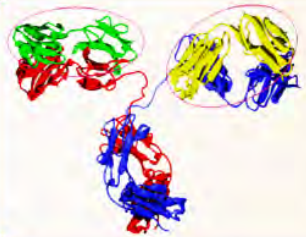
Prevalance of Cardiac Amyloidosis

Estimated US Cases

1,000s

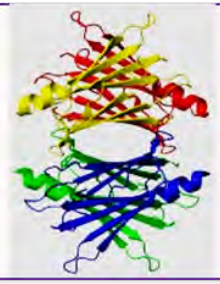


Light chain amyloidosis (AL)
- Immunoglobulin light chain produced from plasma cells
- Multiple organs (heart, kidneys, peripheral nervous system)

100,000s

Wild-type transthyretin (ATTRwt) amyloidosis
- Late onset (> 60 y/o)
- Important cause of heart failure with preserved ejection fraction
- Primarily cardiac involvement

10,000s



Hereditary or variant ATTR (ATTRv) amyloidosis
- Mutated TTR (point mutation)
- Multiple organs (heart, peripheral nervous system, GI)

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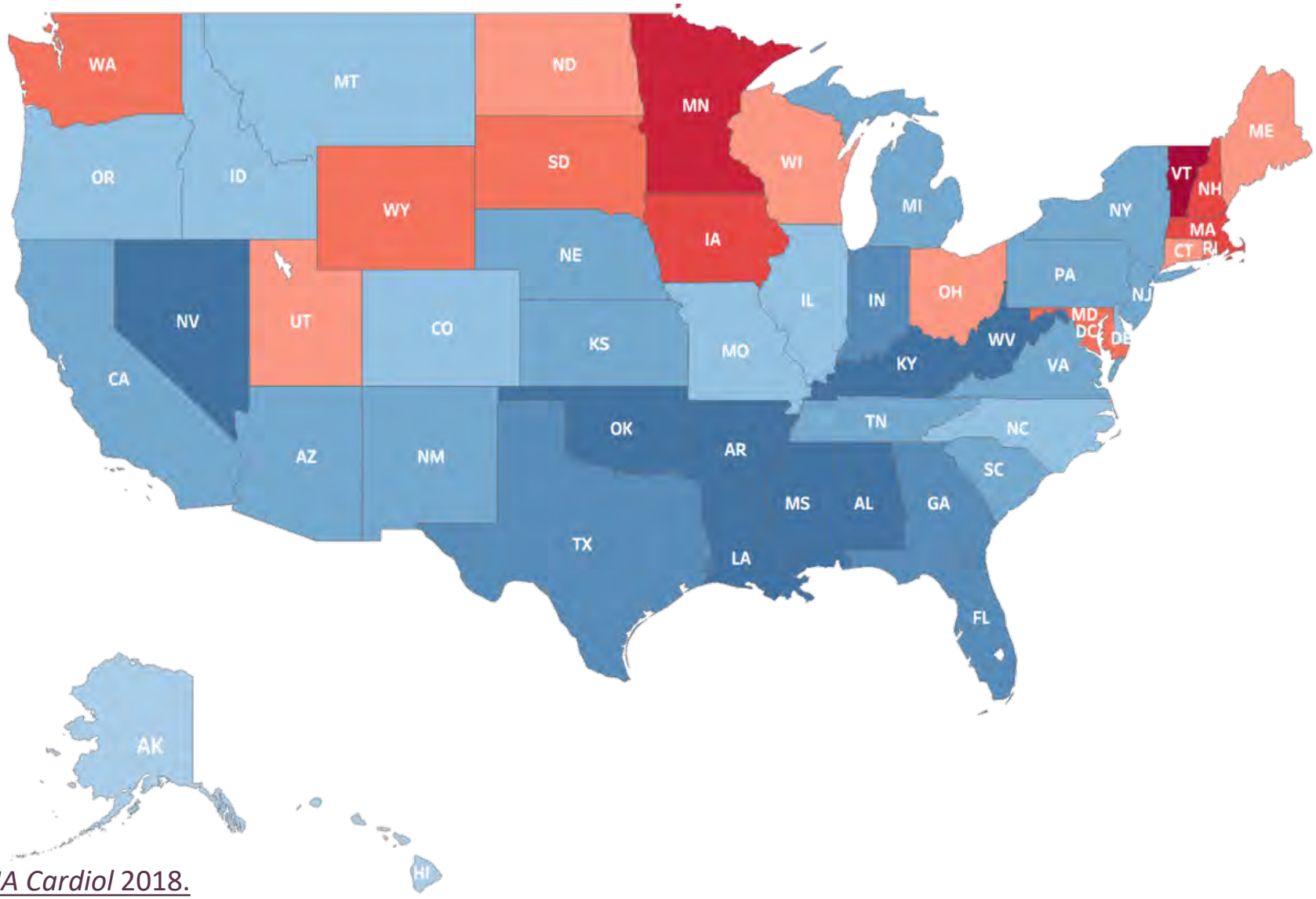
Cardiac Amyloidosis is Under-recognized



Alexander et al., *JAMA Cardiol* 2018.

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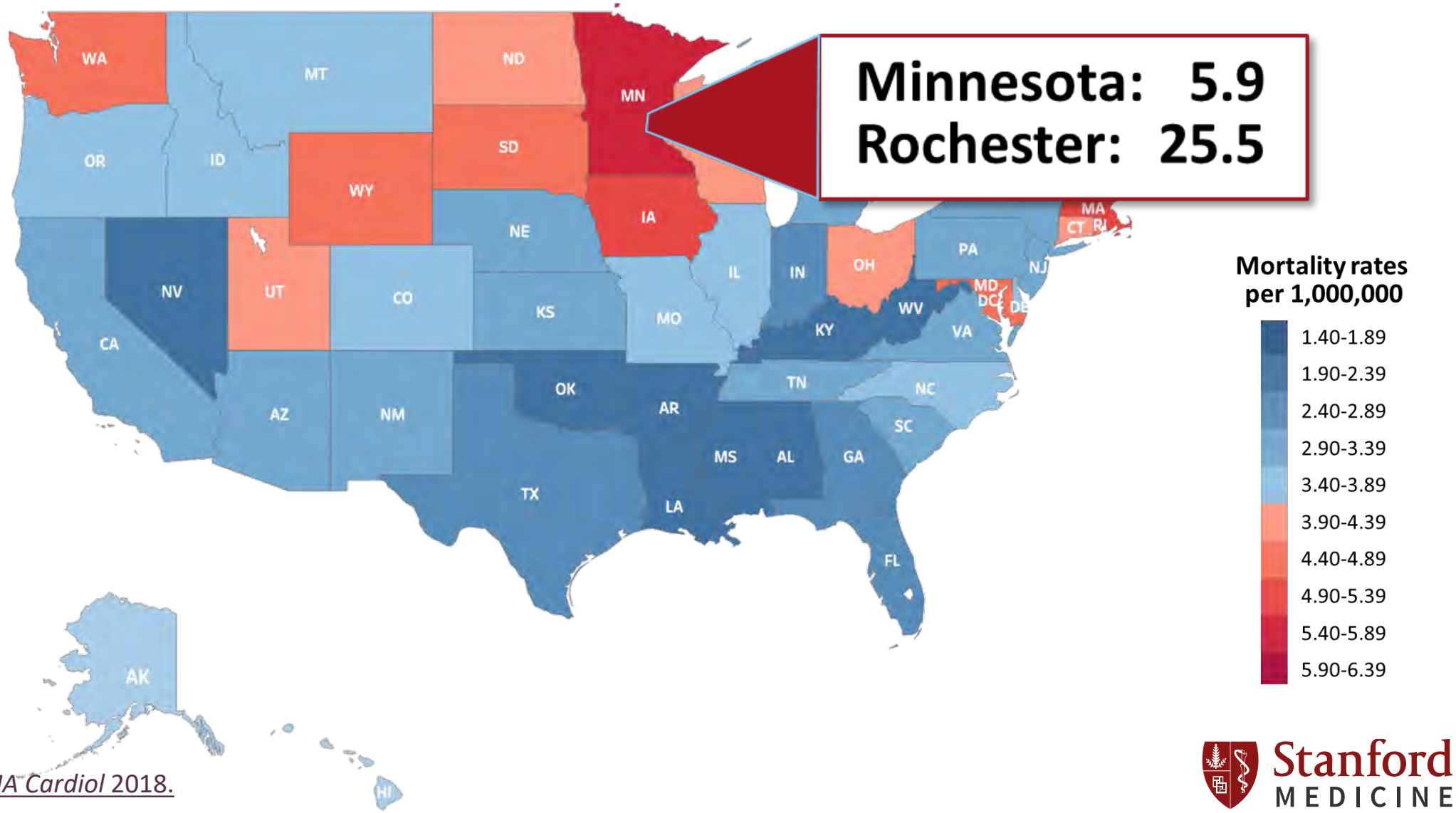
Cardiac Amyloidosis is Under-recognized



Alexander et al., *JAMA Cardiol* 2018.

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High Reported Amyloidosis Mortality Near Amyloid Centers

	County	Number of Deaths	Age-adjusted Death Rate Per 1,000,000 (95% CI)
	Mower County, MN	31	31.73 (21.41-45.30)
MAYO	Olmsted County, MN	62	25.45 (19.46-32.69)
	Johnson County, IA	23	14.81 (9.28-22.42)
	Linn County, IA	49	13.54 (10.02-17.90)
BU/BWH	Suffolk County, MA	133	12.84 (10.65-15.03)
	Chittenden County, VT	29	12.51 (8.38-17.97)
	St. Louis City, MO	65	12.00 (9.24-15.32)
VCU	Albemarle County, VA	22	11.83 (7.42-17.91)
	Black Hawk County, IA	27	10.86 (7.15-15.79)
Hopkins	District of Columbia	101	10.47 (8.42-12.52)
Stanford	San Francisco County, CA	163	10.38 (8.78-11.99)
	La Crosse County, WI	21	10.38 (6.34-16.03)
MAYO	Ramsey County, MN	87	10.32 (8.26-12.75)
Cleveland Clinic	Cuyahoga County, OH	291	10.26 (9.08-11.45)
BU/BWH	Norfolk County, MA	132	9.73 (8.06-11.40)
	National	26 591	4.95 (4.89-5.01)

Alexander et al., *JAMA Cardiol* 2018.

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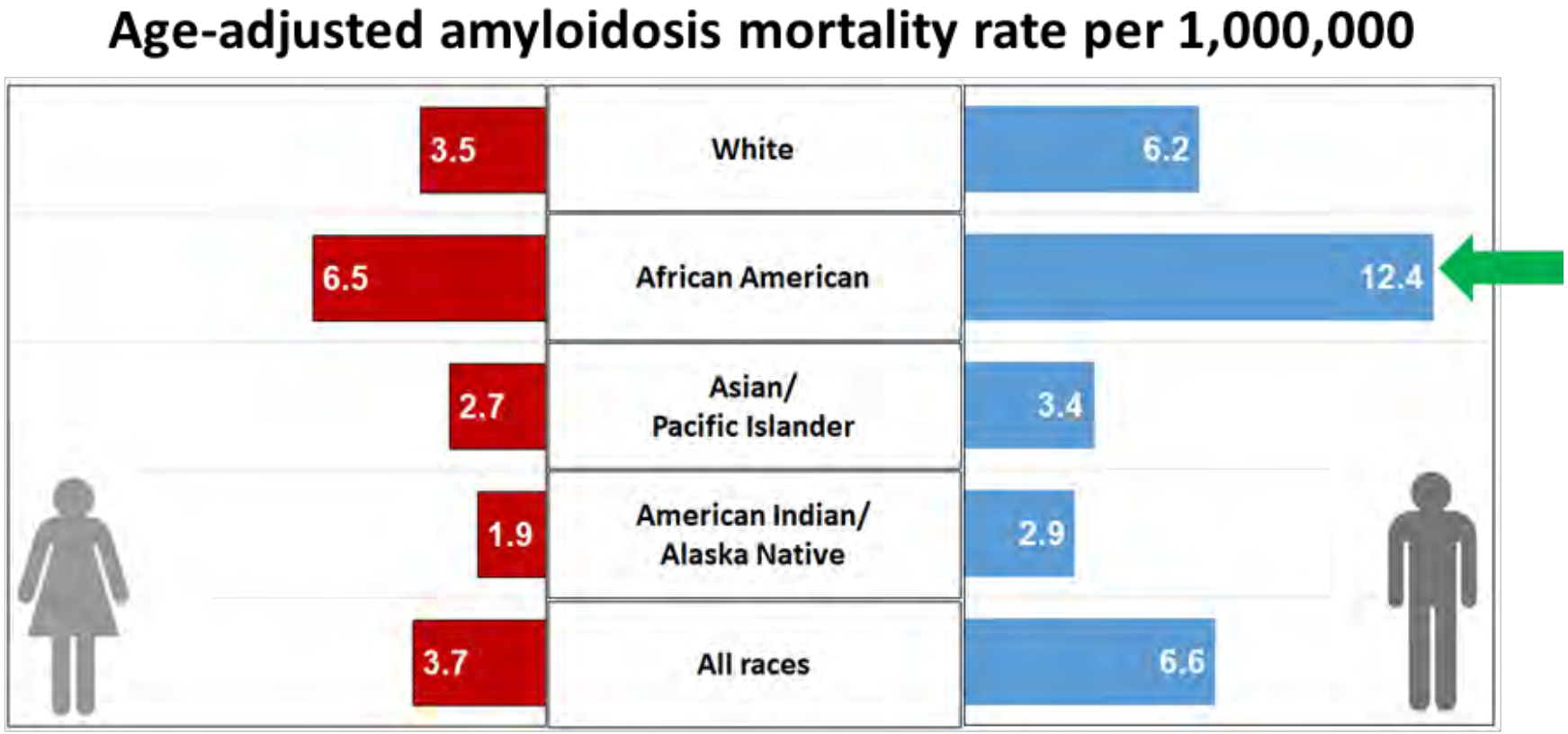
Cardiac Amyloidosis Disproportionately Affects Black Individuals



Alexander et al., *JAMA Cardiol* 2018.

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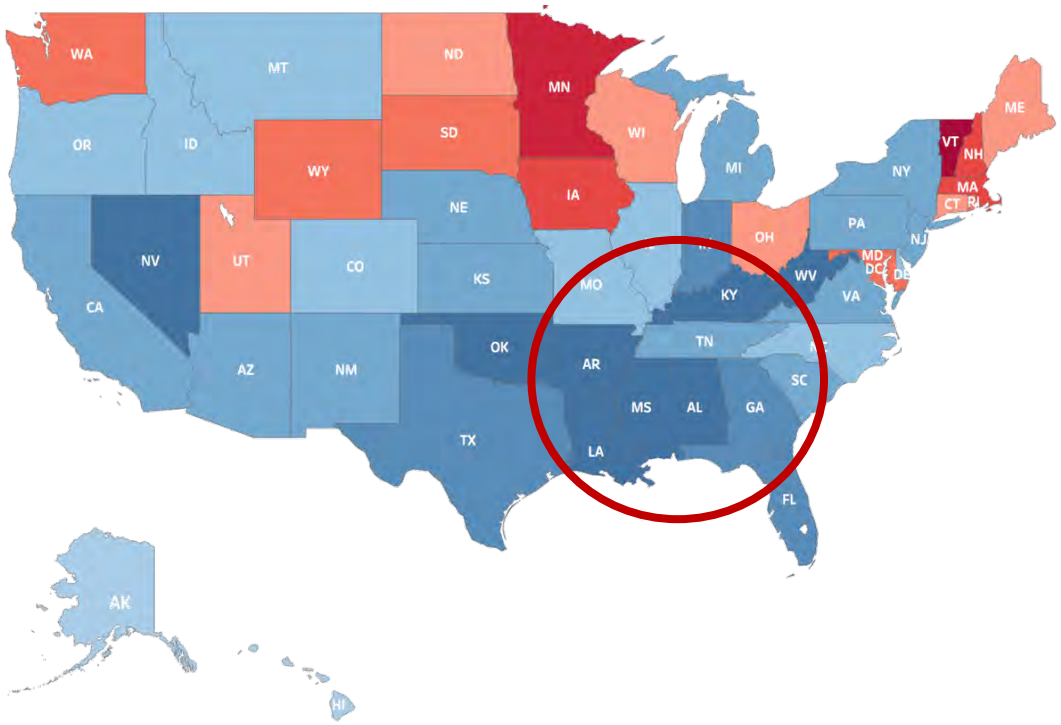
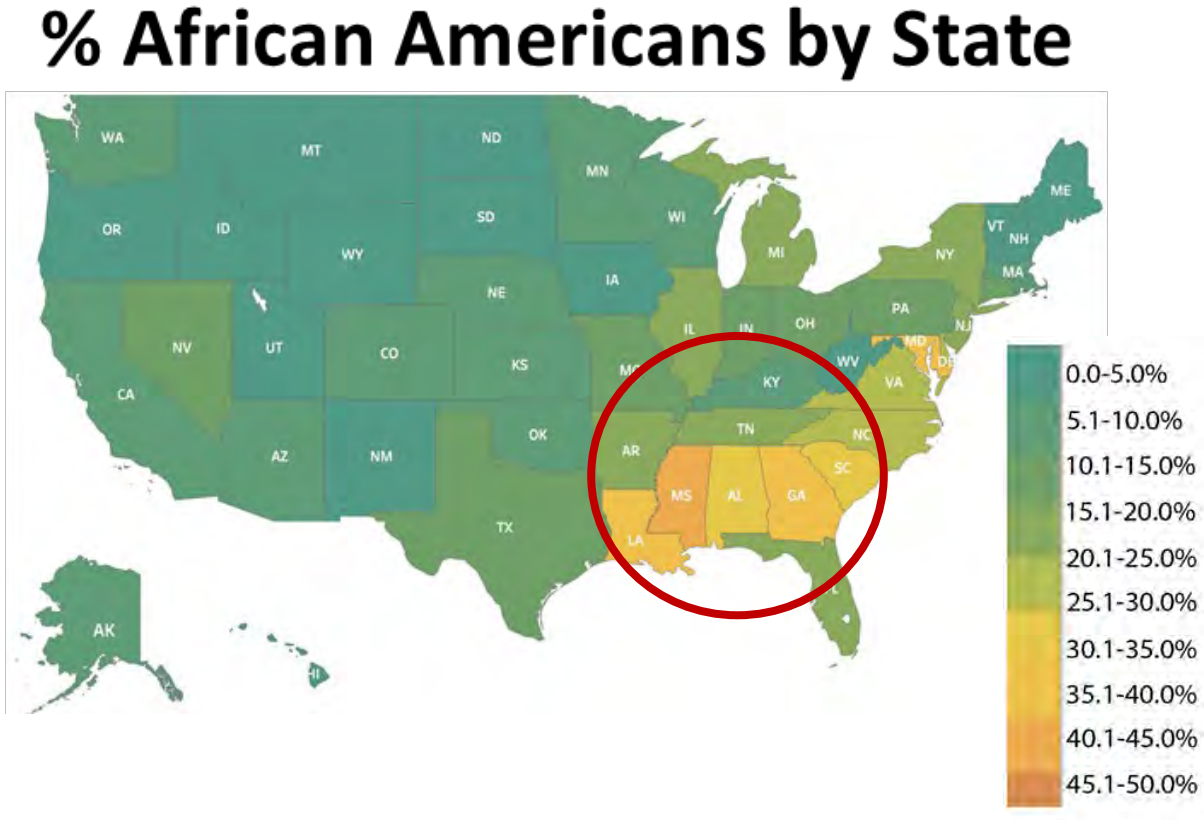
Cardiac Amyloidosis Is Disproportionately Underdiagnosed Among Black Individuals





Alexander et al., *JAMA Cardiol* 2018.

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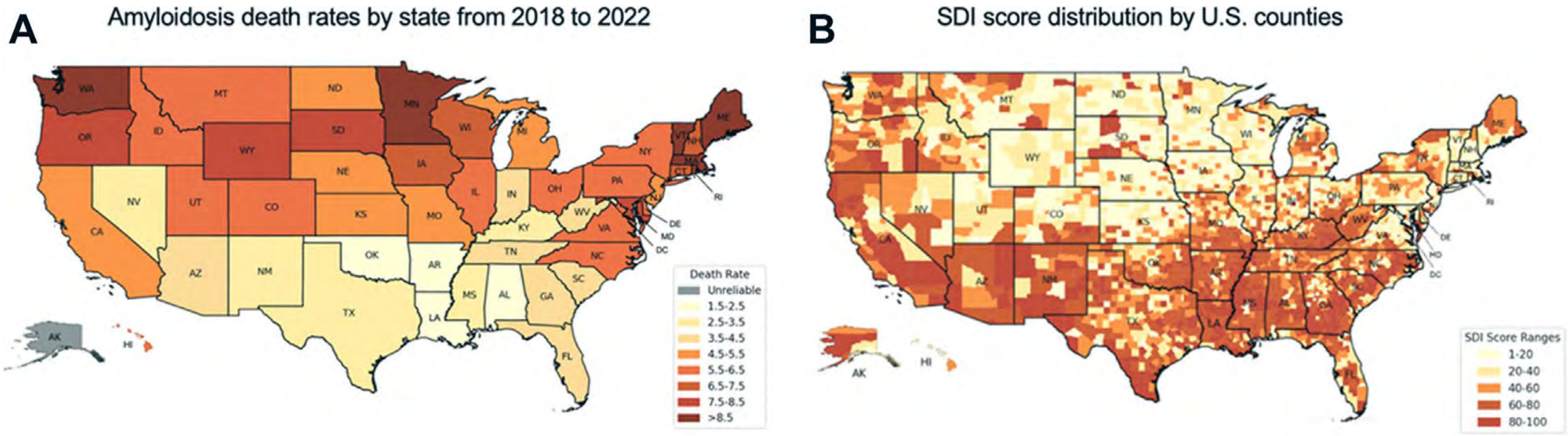
Cardiac Amyloidosis Is Disproportionately Underdiagnosed in Socially Vulnerable Areas



Fahad et al., *JACC HF* 2025.

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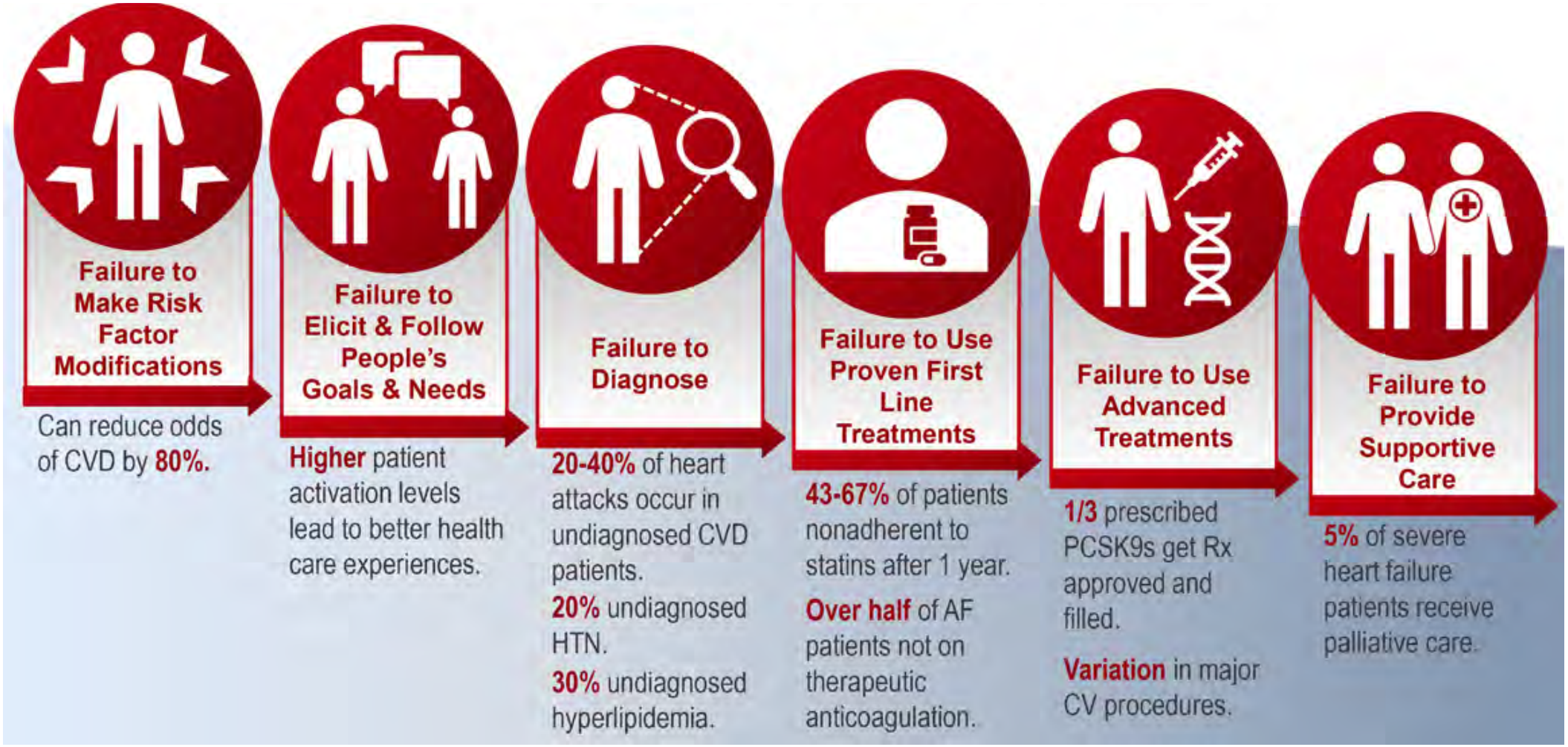
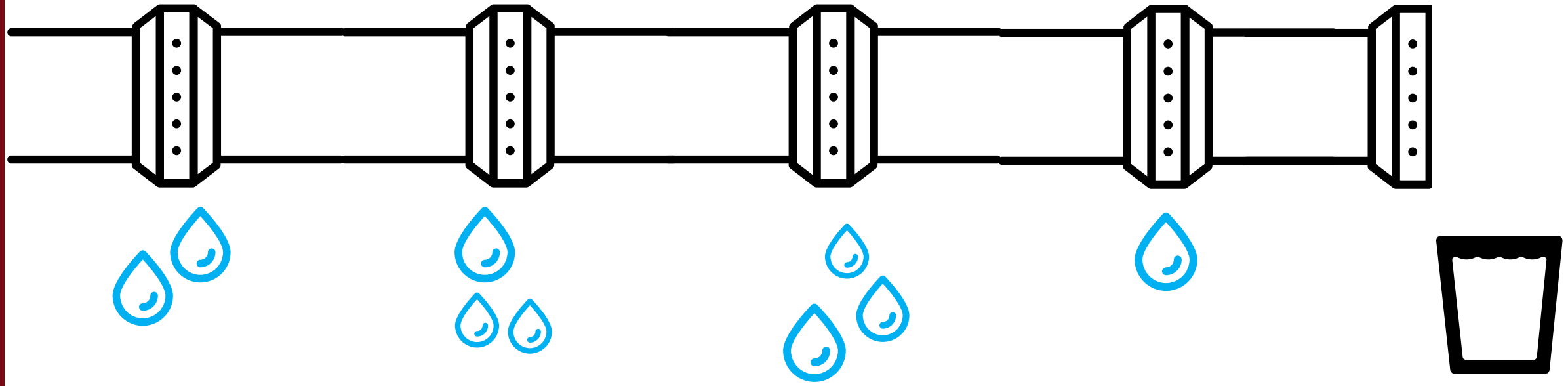
Challenges in Preventing and Treating CV Disease



McClellan M et al., *Circulation* 2019.

Challenges in Treating Cardiac Amyloidosis

Limited Disease Awareness



Spencer-Bonilla G et al., *Curr CV Risk Rep* 2021.

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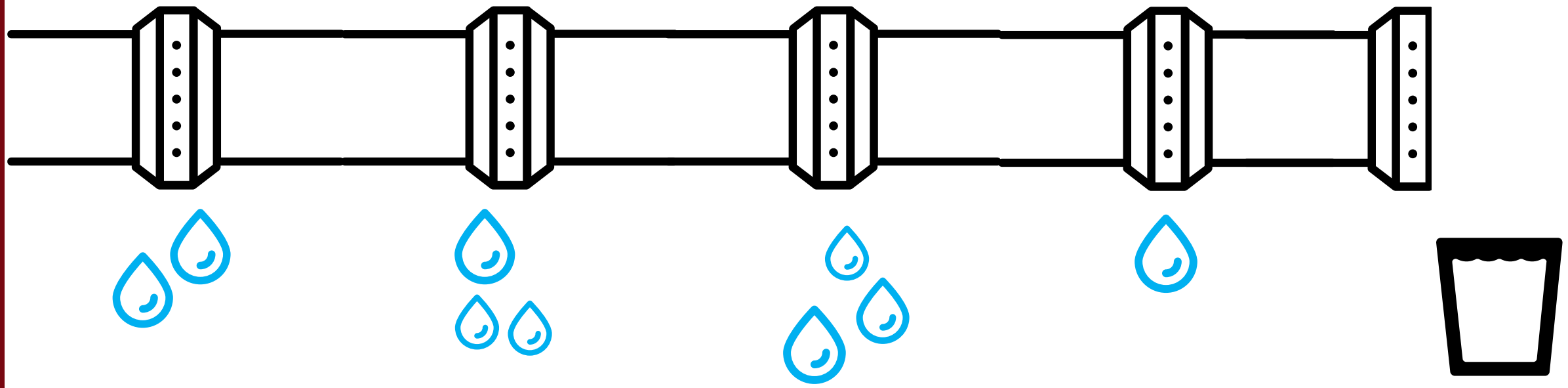
Challenges in Treating Cardiac Amyloidosis

Under-recognition in Certain Groups



Spencer-Bonilla G et al., *Curr CV Risk Rep* 2021.

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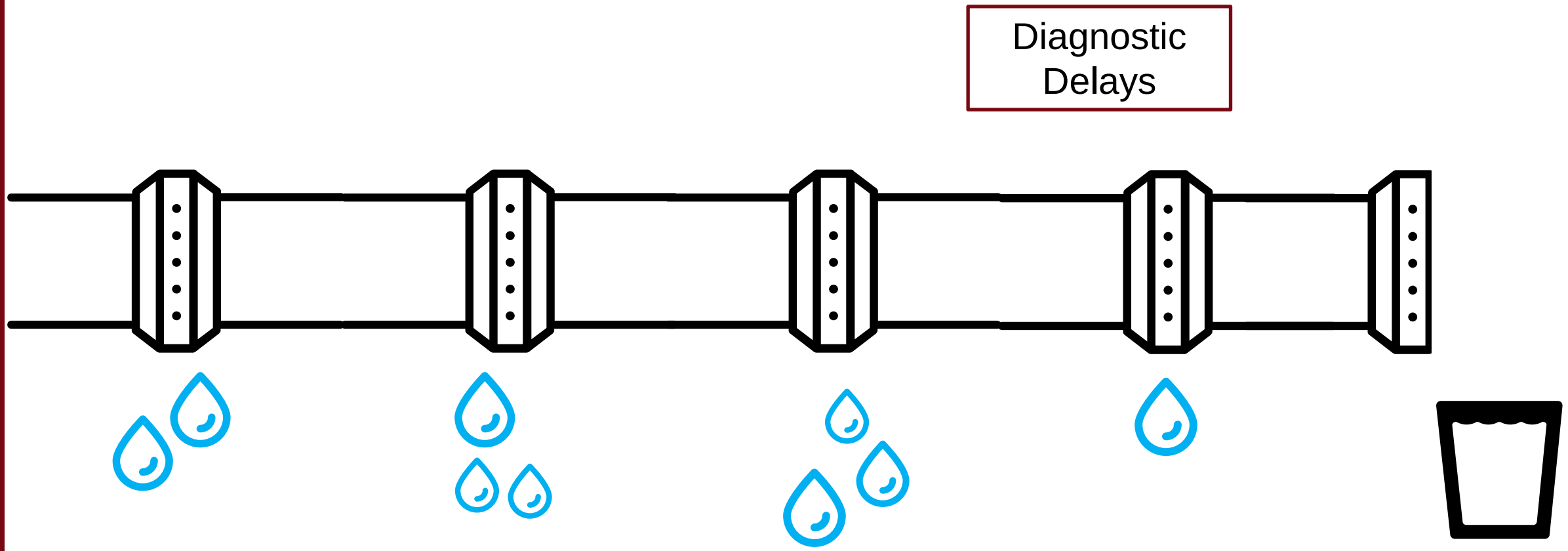
Challenges in Treating Cardiac Amyloidosis



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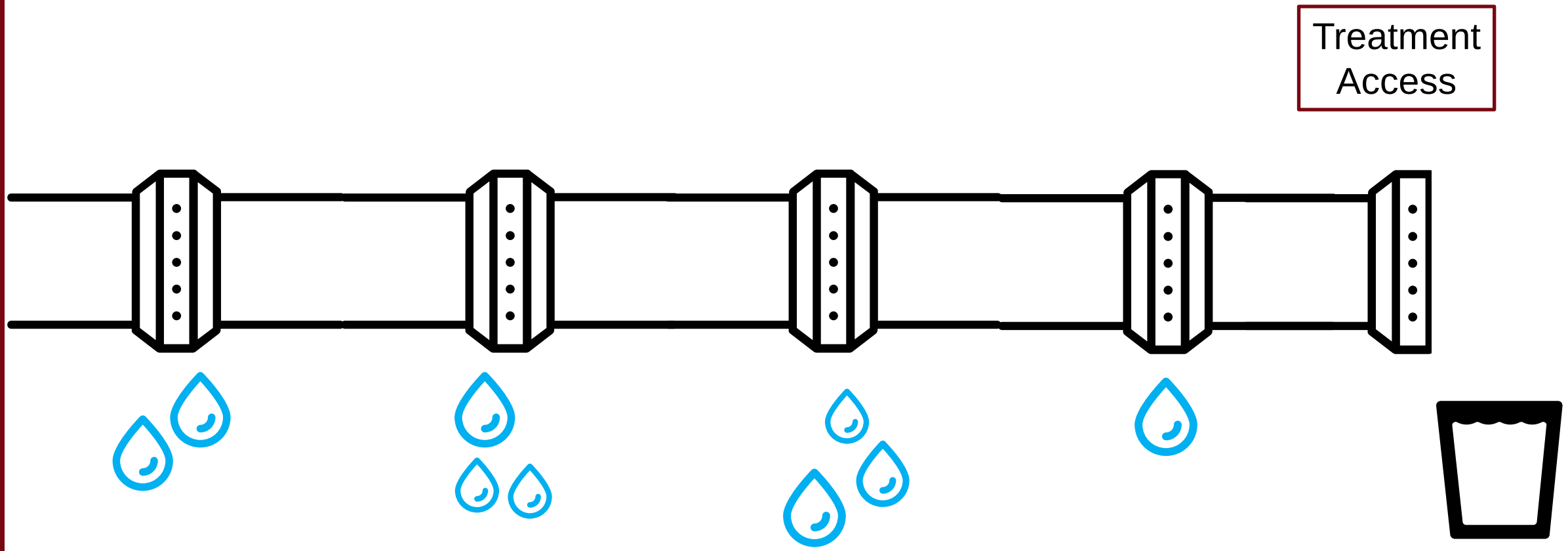
Challenges in Treating Cardiac Amyloidosis



Spencer-Bonilla G et al., *Curr CV Risk Rep* 2021.

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Potential Interventions to Improve AL Amyloidosis Care

- Telemedicine
- AI/machine learning for disease detection (ECG, TTE, EHR)
- Strengthened partnerships between academic centers and community practices

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Clinical Trial Considerations

- Visit and test frequency
- Remote data collection
- Budget for travel
- Diversify the clinical trial staff and pipeline
- Education on clinical trials
- Include patients in guiding clinical trial design (e.g., PCORI model)

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Research on Diversity in Clinical Trials: AHA Strategically Focused Research Network

Awardees named for $20 million Strategically Focused Research Network on the Science of Diversity in Clinical Trials

Partner	Advance	Create	Develop	Train
with diverse groups to overcome long-established barriers	the science of diversity for greater health equity	an open access Diversity in Clinical Trials Toolkit	a Clinical Trials Network to connect sponsors & stakeholders	and develop clinical trial leaders

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Conclusions

- AL Amyloidosis is a rare disease with numerous challenges for timely diagnosis and treatment.
- General health disparities can be magnified in rare disease.
- Multiple approaches are needed to improve AL Amyloidosis outcomes in diverse populations and to increase clinical trial access.

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American Heart Association®

Multidisciplinary Care Approaches

Multidisciplinary Care Approaches

Yevgeniy Brailovsky, DO, MSc, FACC, FACP
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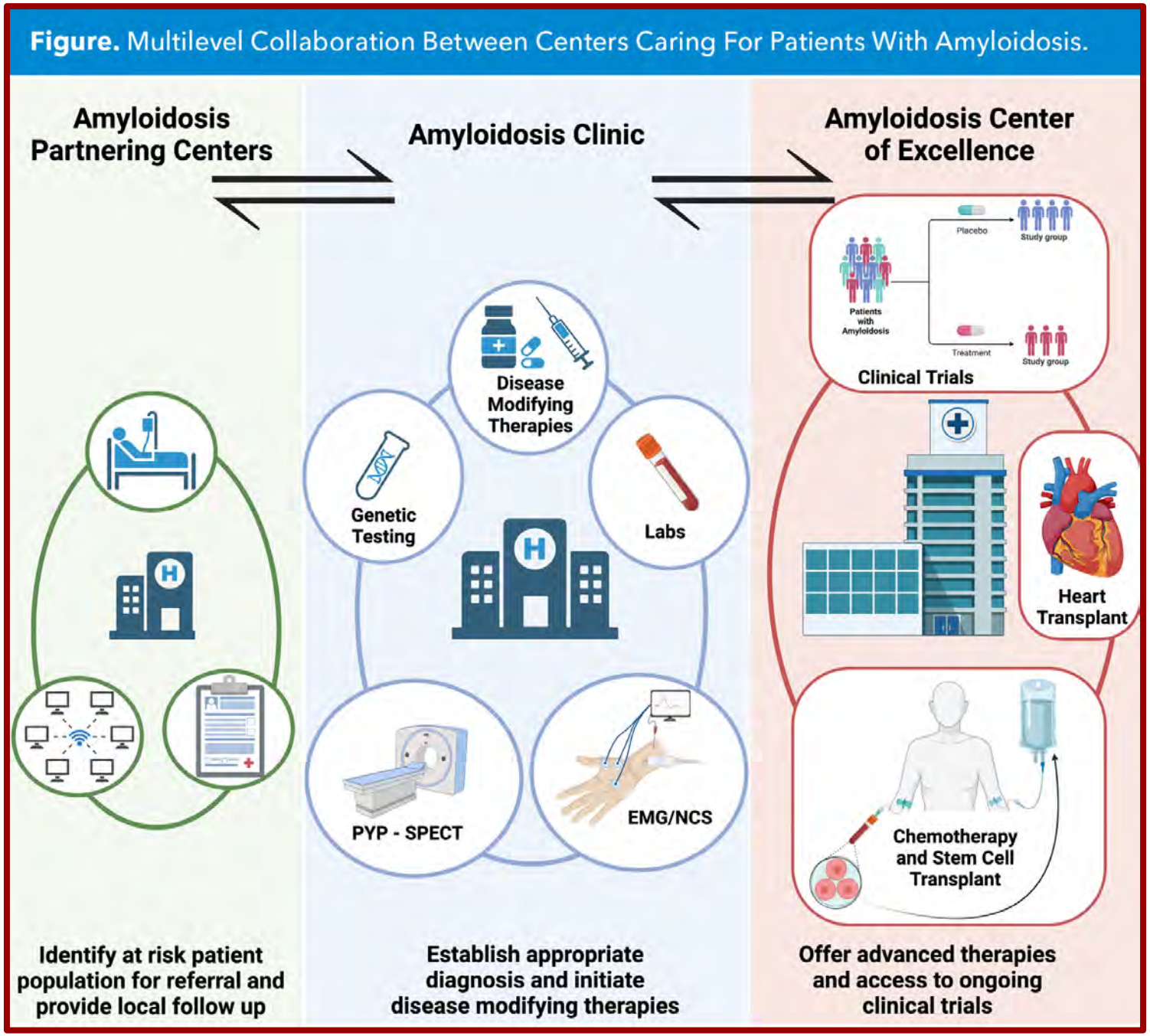
Julie Rosenthal, MD
Director, Cardiac Amyloidosis Program; Assistant Professor of Medicine, Cardiology,
Mayo Clinic Hospital - Arizona

Brett Sperry, MD
Associate Professor of Medicine, Cardiology,
Saint Luke's Community Hospital - Kansas City



Brailovsky Y et al. ACC Magazine. 2025

Outline:

1. **Identifying Stakeholders**
2. How to Achieve Institutional Support
3. Growing a Center of Excellence

Identifying Stakeholders

Identifying Stakeholders

Building your Amyloidosis team of excellence

Why?

The field of Amyloidosis is rapidly evolving and has been galvanized by advancements in:

1. Disease awareness
2. Diagnostics
3. Disease targeted therapeutics

Multiple touch points within your Cardiology practice

What?

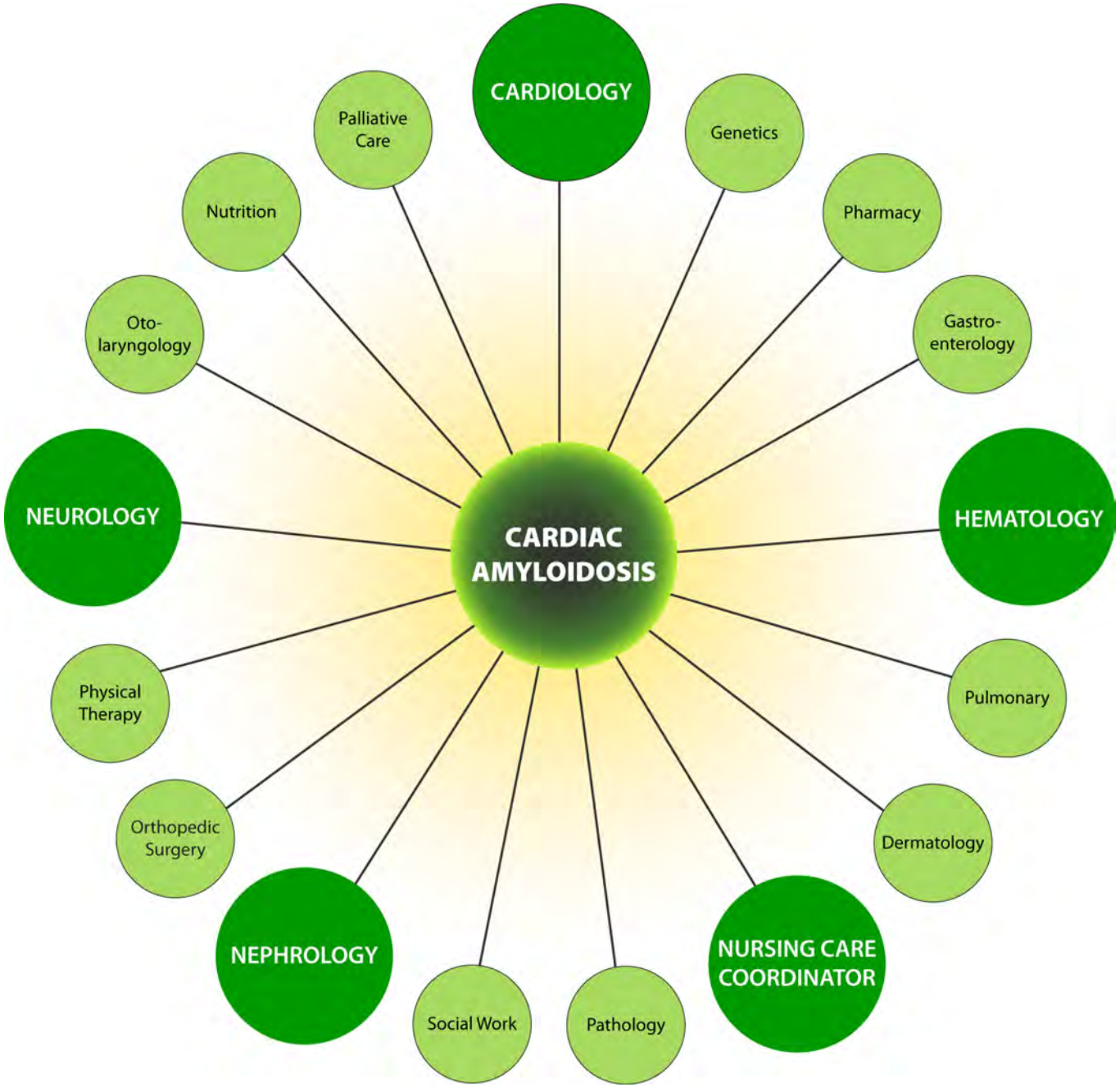
Amyloidosis is a multi-system disease, with no boundaries!

- Abnormal protein deposition leading to organ dysfunction

- Common causes of multiple cardiac complications:
  1. Heart failure
  2. Arrhythmias
  3. Valvular heart disease

Who?

1. Patients
2. Cardiology & Non-Cardiology Partners
3. **Comprehensive Care Team**
    - Confirm/exclude diagnosis
    - Develop therapeutic plan: disease targeted & supportive care
    - Provide: Advanced Therapeutics & Clinical Trials



Comprehensive Care Team

Deliver:

- Integrative
- Efficient
- Coordinated care

Advance:

- Program development
- Quality
- Outcomes

Sperry BW et al. Heart Fail Rev 2021.

Outline:

1. Identifying Stakeholders
2. **How to Achieve Institutional Support**
3. Growing a Center of Excellence

How to Achieve Institutional Support

Why do you need to create a center?

Requires specialized knowledge.

- Many cardiology and other healthcare professionals lack this knowledge.
- **You can become an expert!**

Multidisciplinary care is needed.

- There are several types of Amyloidosis with various multisystem manifestations
- Need for ancillary help:
  - Clinical and research coordinators,
  - Pharmacy,
  - Genetic counselors

Develop Overarching Program Goals

- ✓ **Mission statement**
- ✓ **Multidisciplinary meetings**
- ✓ **Dedicated amyloid clinic time**
- ✓ **Dedicated administrative time**
- ✓ **Identify gaps in your Amyloidosis team**
  - Focus recruitment efforts to those positions!

Sperry BW et al. Heart Fail Rev 2021.

Create Institutional Buy-In

Amyloid consults generate significant downstream revenue.

- Referrals and Follow-up Visits
- Procedures/Imaging
  - Biopsies, CMRI, Nuclear Scintigraphy, Echo, RHC, CPET
- Pharmacy Revenue
- Heart/Bone Marrow Transplantation

Sperry BW et al. Heart Fail Rev 2021.

PROFORMA - Amyloidosis Program - FY2023

Physician Revenue							
	#/yr	CPT	RVU	Charge	Payment	Total Charges	Total Payments
Level 5 consult							
Level 5 follow up/yr							
Echo interpretation							
Nuclear interpretation							
Cardiac MRI interpretation							
Right heart catheterization							
CPET							
EMG/NCS							
Heart biopsy							
Kidney biopsy							
Fat pad biopsy							
Bone marrow biopsy							
Physician Revenue						**$ -**	**$ -**

Hospital Revenue							
Echo							
Nuclear							
Cardiac MRI							
Right heart catheterization							
CPET							
EMG/NCS							
Heart biopsy							
Kidney biopsy							
Fat pad biopsy							
Bone marrow biopsy							
Heart transplant							
Stem cell transplant							
Pharmacy revenue - drug 1							
Pharmacy revenue - drug 2							
Pharmacy revenue - drug 3							
Hospital Revenue						**$ -**	**$ -**

Expenses							
Salary Expense							
Benefits							
Total Expense							**$ -**
Net Profit/(Loss)							**$ -**

Create Institutional Buy-In

Amyloid consults generate significant downstream revenue.

- Referrals and Follow-up Visits
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- Pharmacy Revenue
- Heart/Bone Marrow Transplantation

More resources are needed than standard cardiac patients.

- Care Coordination
- Patient Assistance Paperwork
- 2x as many patient contacts/messages as other HF patients!
- Clinical Trials

Sperry BW et al. Heart Fail Rev 2021.

Outline:

1. Identifying Stakeholders
2. How to Achieve Institutional Support
3. **Growing a Center of Excellence**

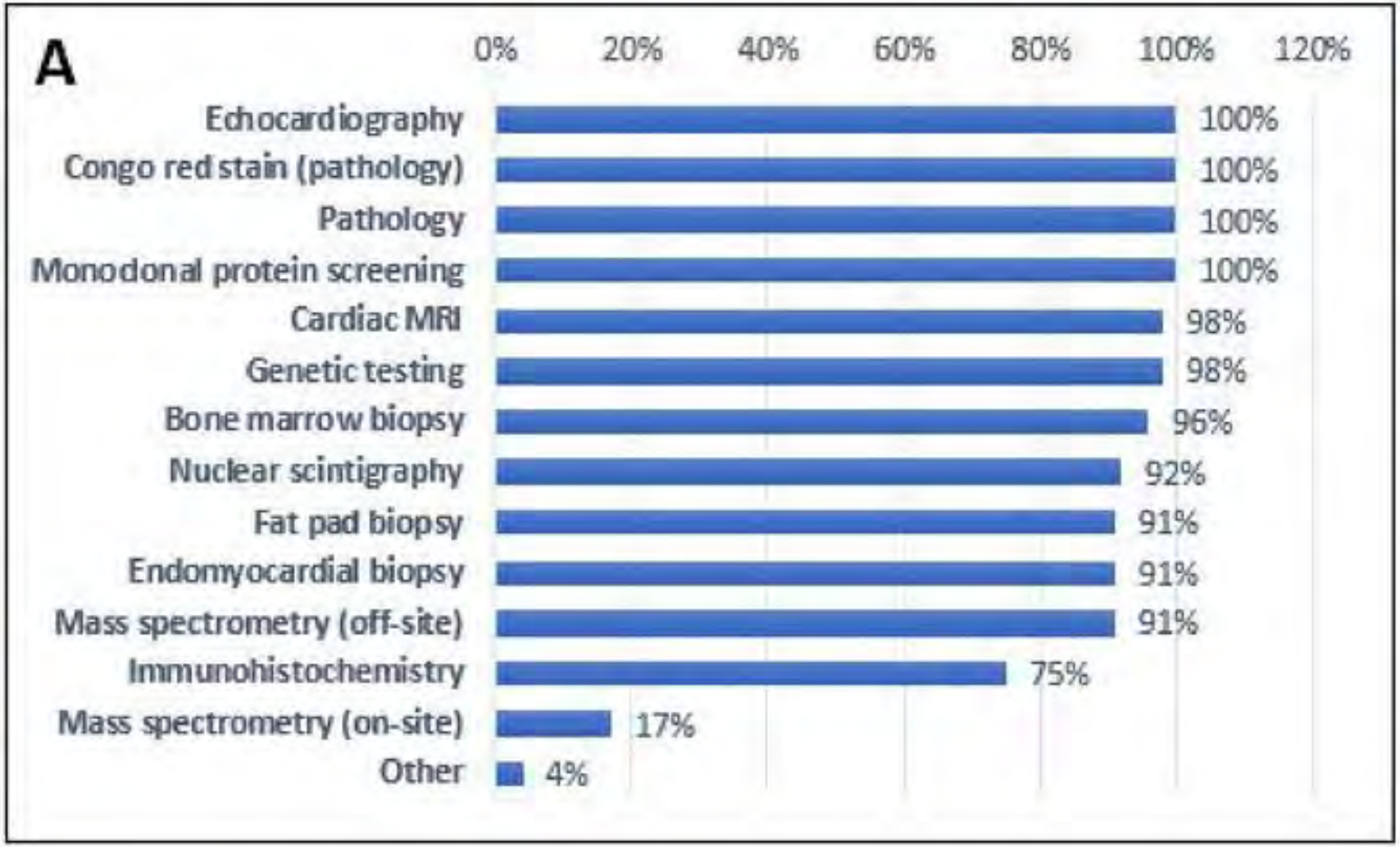
Growing a Center of Excellence

What is an Amyloidosis Center of Excellence?

Provide care for patients with suspected and confirmed diagnosis of Amyloidosis across the entire spectrum of disease.

1. Deliver rapid, multidisciplinary approach to diagnosis
    - Labs, imaging, biopsy capabilities
2. Initiate state-of-the art therapies (Specialty Pharmacy)
    - ATTR: TTR stabilizers, RNA silencers
    - AL: CyBorD-Dara, Autologous Stem Cell transplant, CART-T, Bi-specifics,…
    - Heart transplant in selected patients
3. Provide access to available clinical trials in this rapidly evolving field
4. Provide educational resources and access to support groups
5. Partner with community

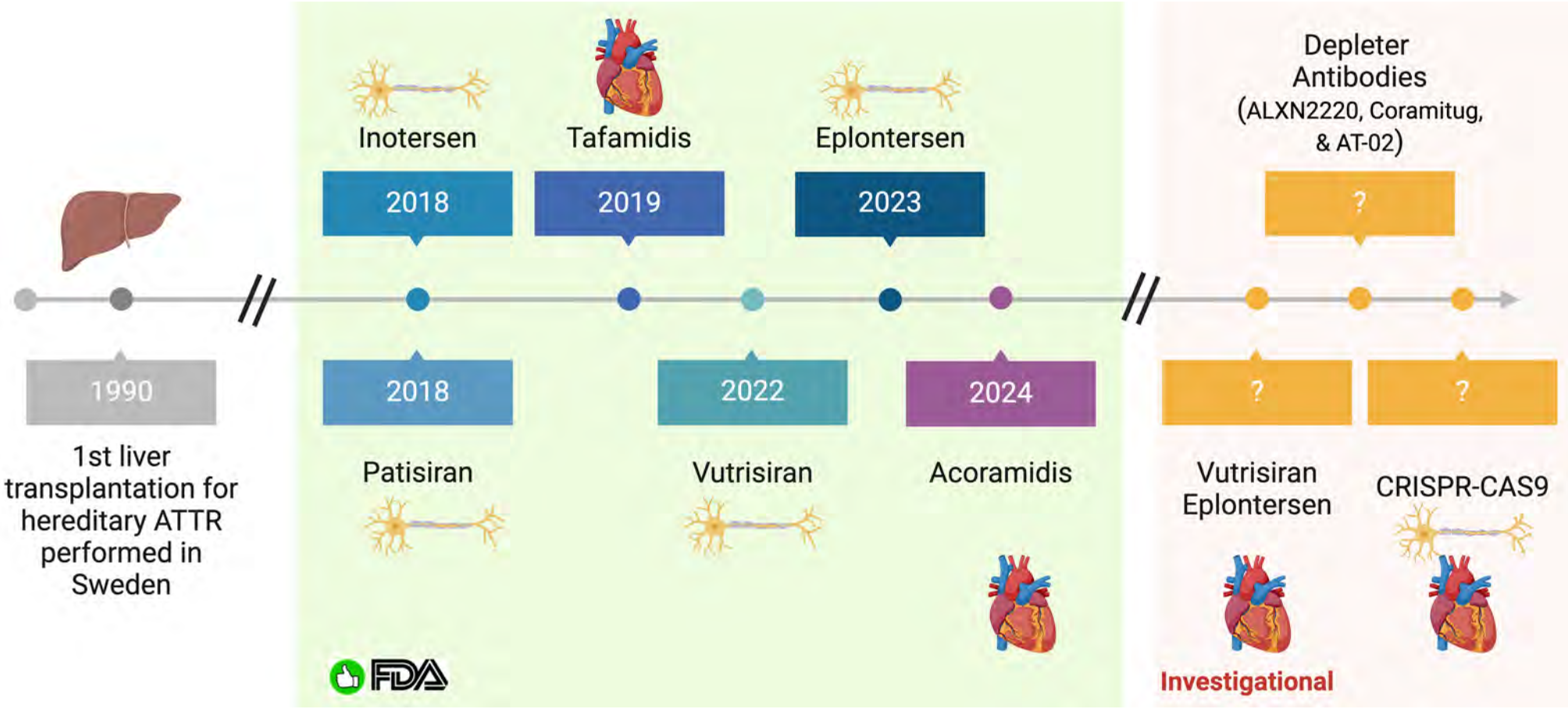
Are there a minimum requirement for diagnostic capabilities?



Cheng R, et al. Heart 2024;110:823–830.

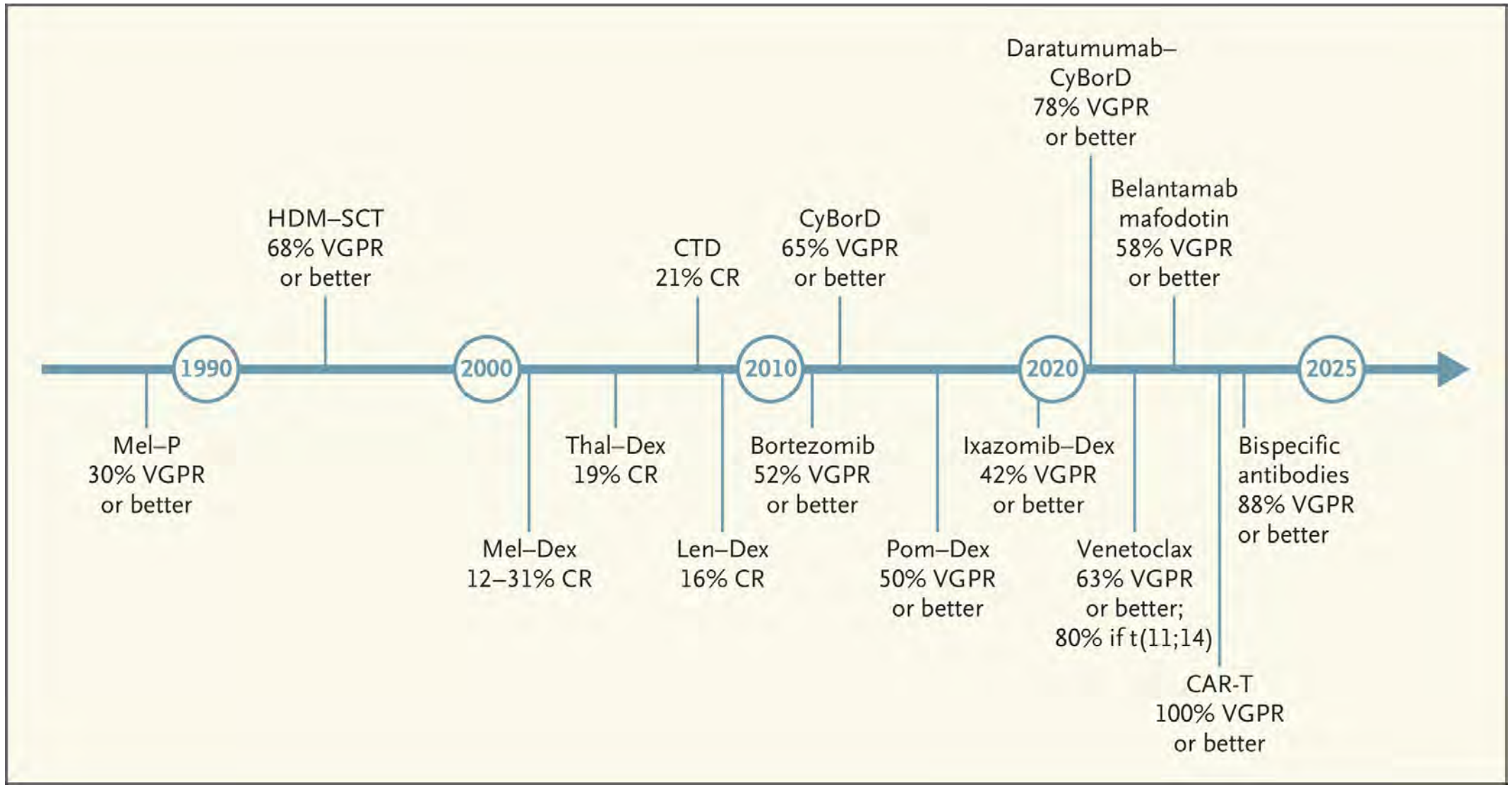
Progress in Therapeutic Arena of ATTR

$$$



Specialty Pharmacy is an invaluable resource!

Progress in Therapeutic Arena of AL



N Engl J Med 2024;390:2295-2307

Team will vary by institution.

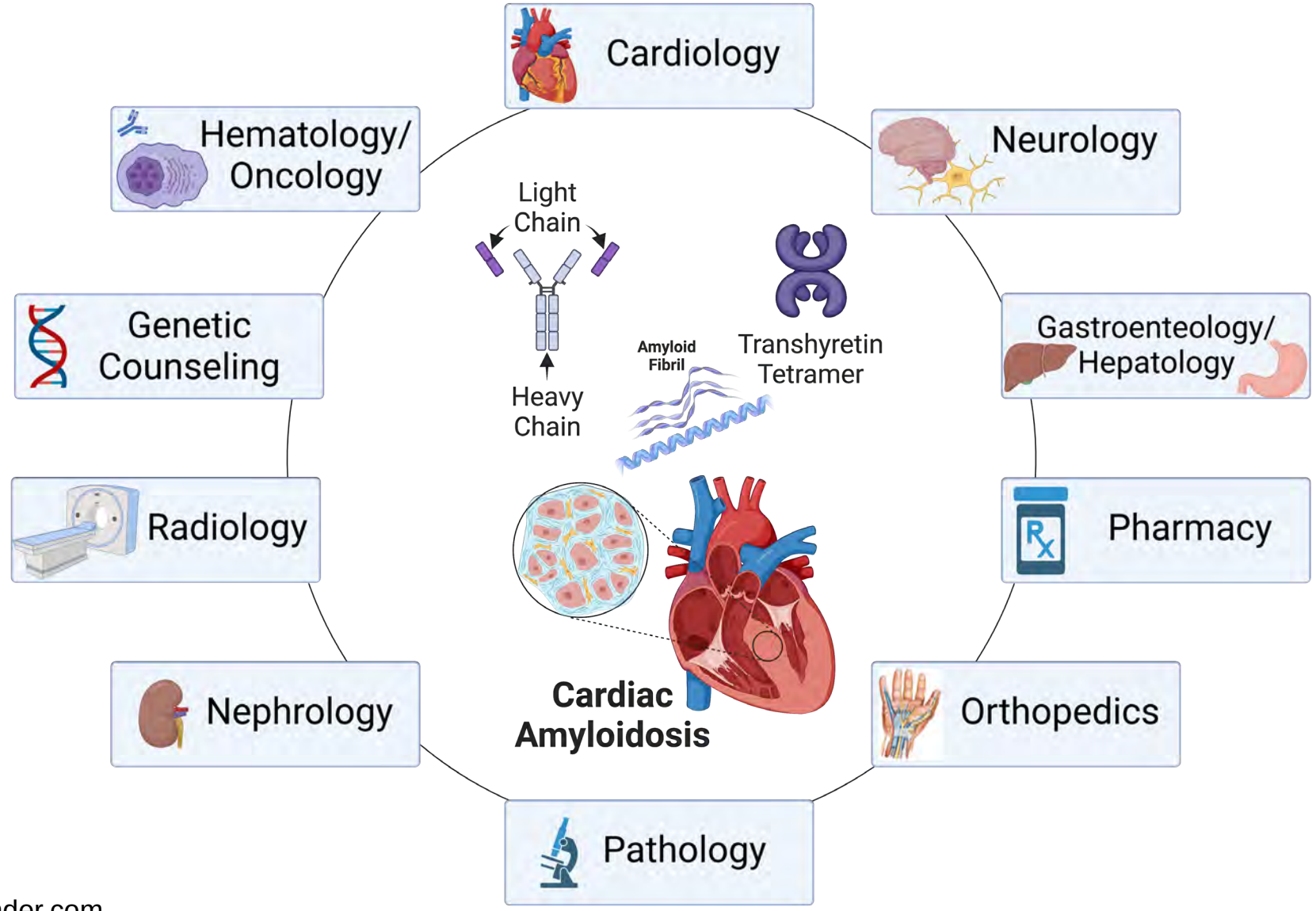
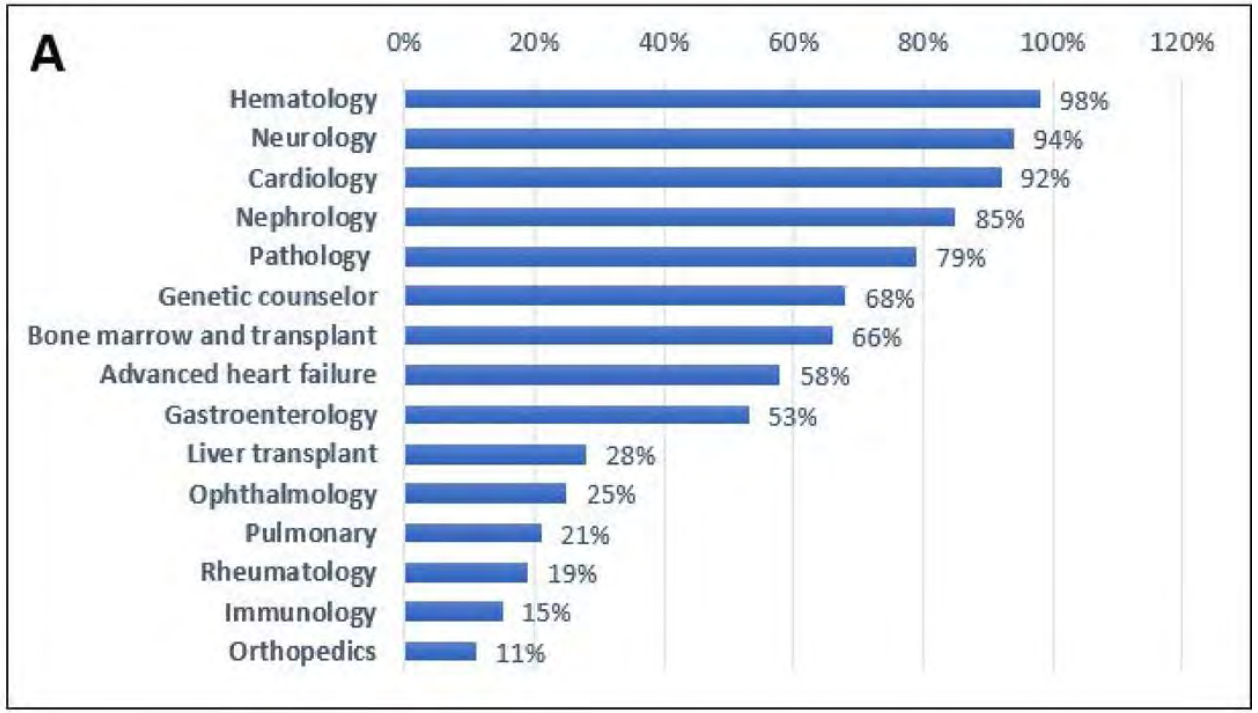
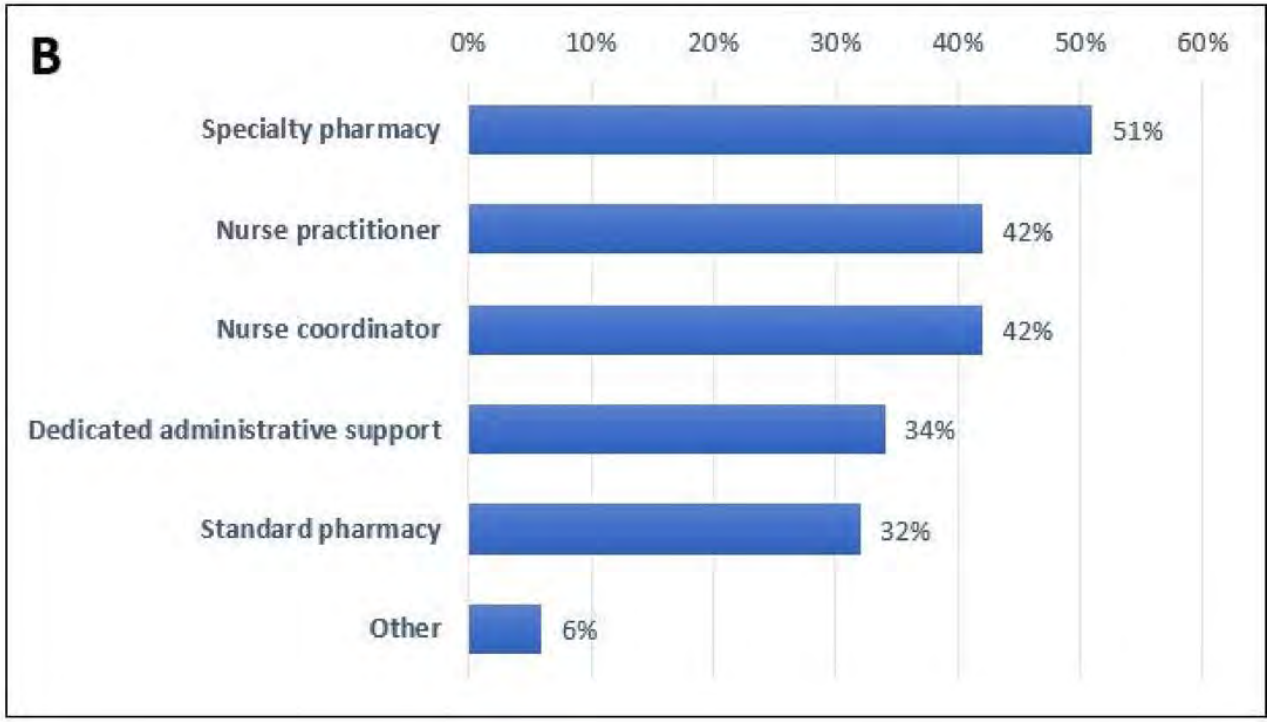


Figure created with Biorender.com

Brailovsky et al, J Am Coll Cardiol Case Rep. 2023 Mar, 10 101759

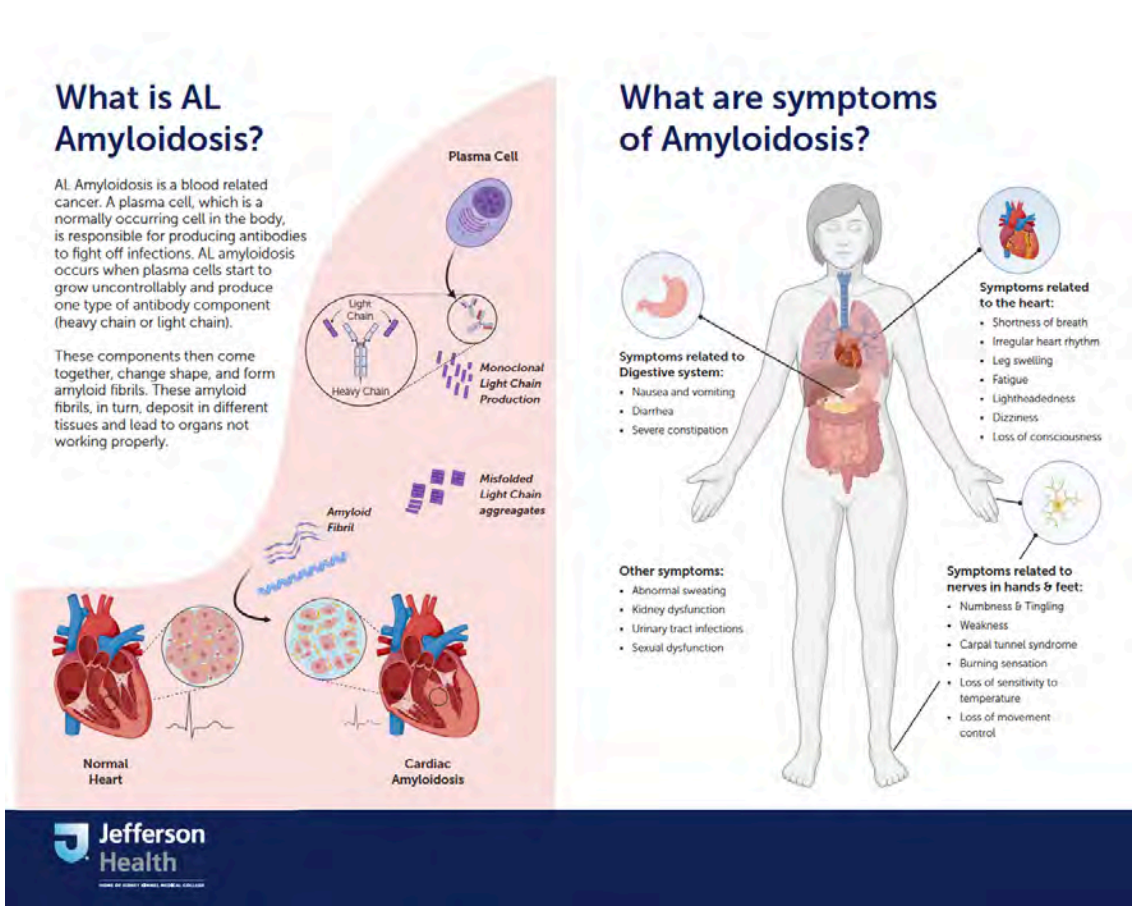
Team will vary by institution. Are there a minimum requirements?

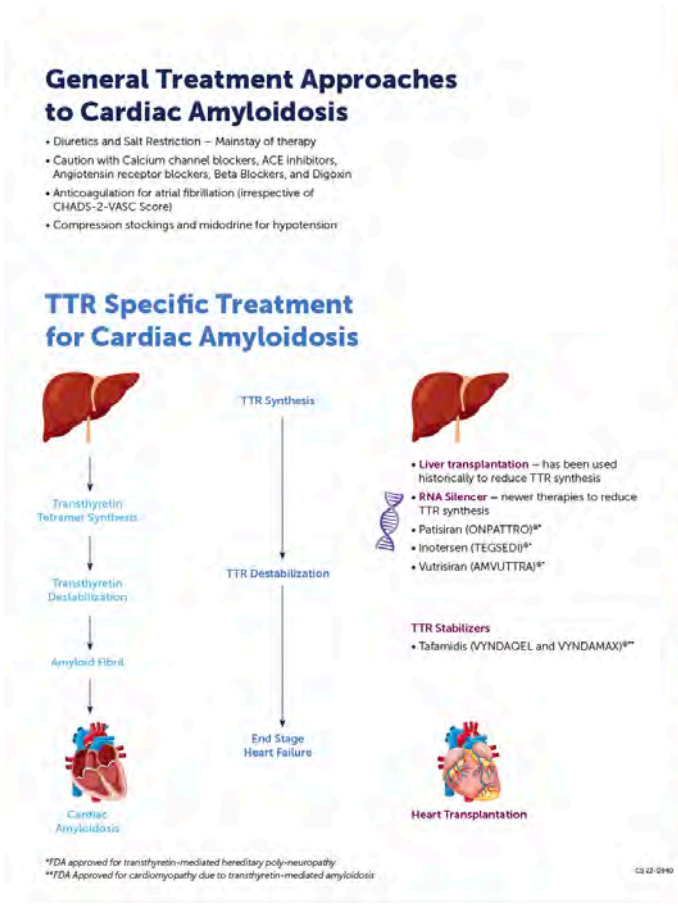


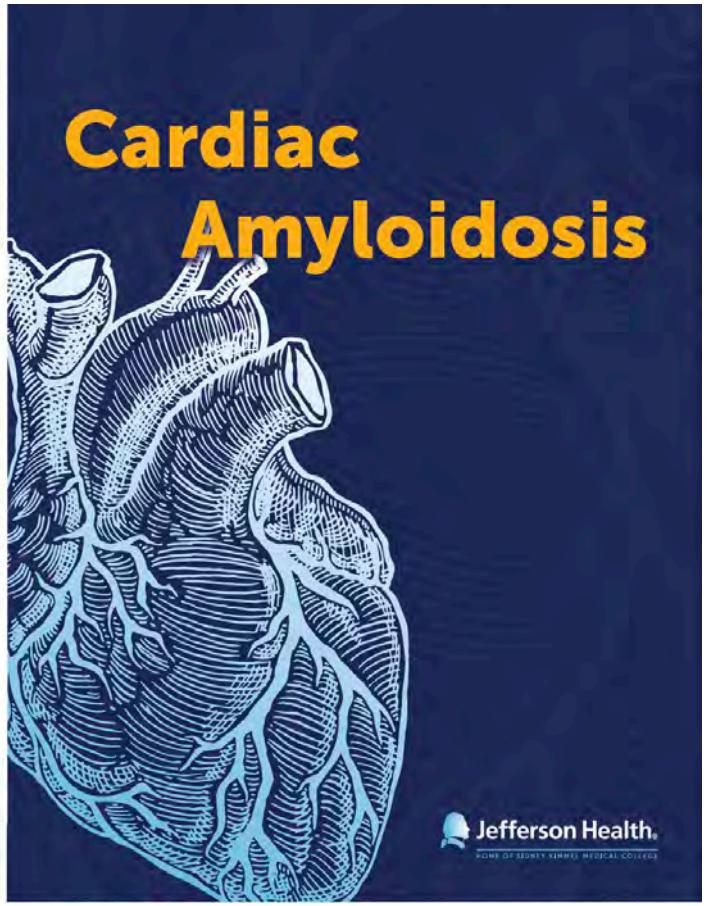


Cheng R, et al. Heart 2024;110:823–830.

Develop Educational Resources





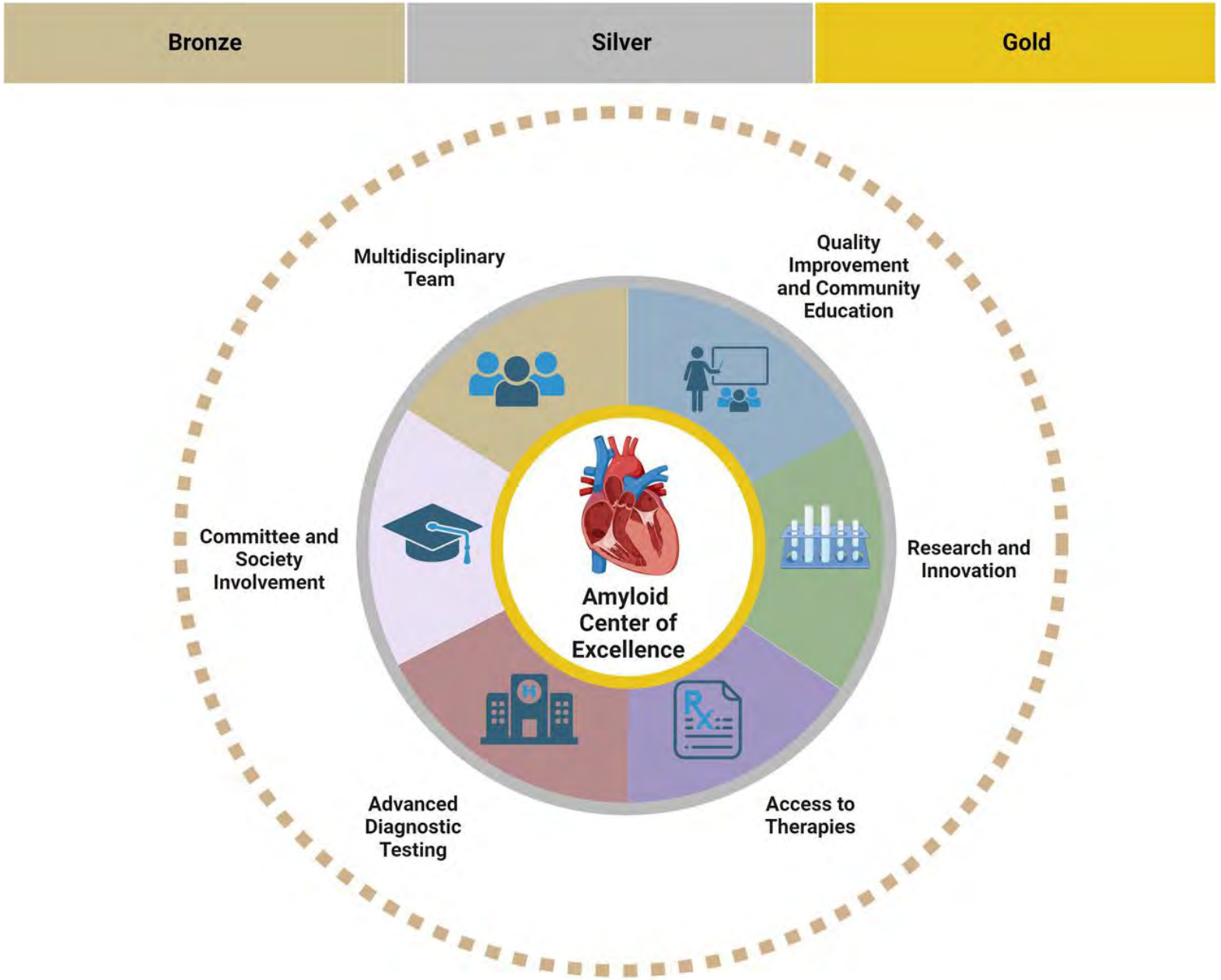


Amyloid Center of Excellence Designations

	Bronze	Silver	Gold
Diagnosis of amyloidosis			
Identify clinical red flags to initiate diagnostic evaluation	X	X	X
Order monoclonal protein screens	X	X	X
Interpret abnormal monoclonal protein screen	X	X	X
Refer for bone scintigraphy	X	X	X
Perform and interpret bone scintigraphy		X	X
Arrange amyloid typing (eg, mass spectrometry)	X	X	X
Perform and interpret cardiac MRI		X	X
Refer for genetic testing	X	X	X
Perform and interpret genetic testing for amyloidosis, offer counselling		X	X
Surrogate site biopsy (such as fat pad biopsy)	X	X	X
Affected organ biopsy		X	X
Treatment of amyloidosis			
Prescribe tafamidis*	X	X	X
Prescribe and administer patisiran/vutrisiran*		X	X
Administer anti-plasma cell therapy*		X	X
Clinical trial access—at least one type of amyloidosis*		X	X
Clinical trial access—more than one type of amyloidosis*			X
Access to stem cell transplantation*			X
Access to solid organ transplantation*			X
Access to palliative care services (particularly for light chain amyloidosis)		X	X
Education and outreach			
Community and professional education	X	X	X

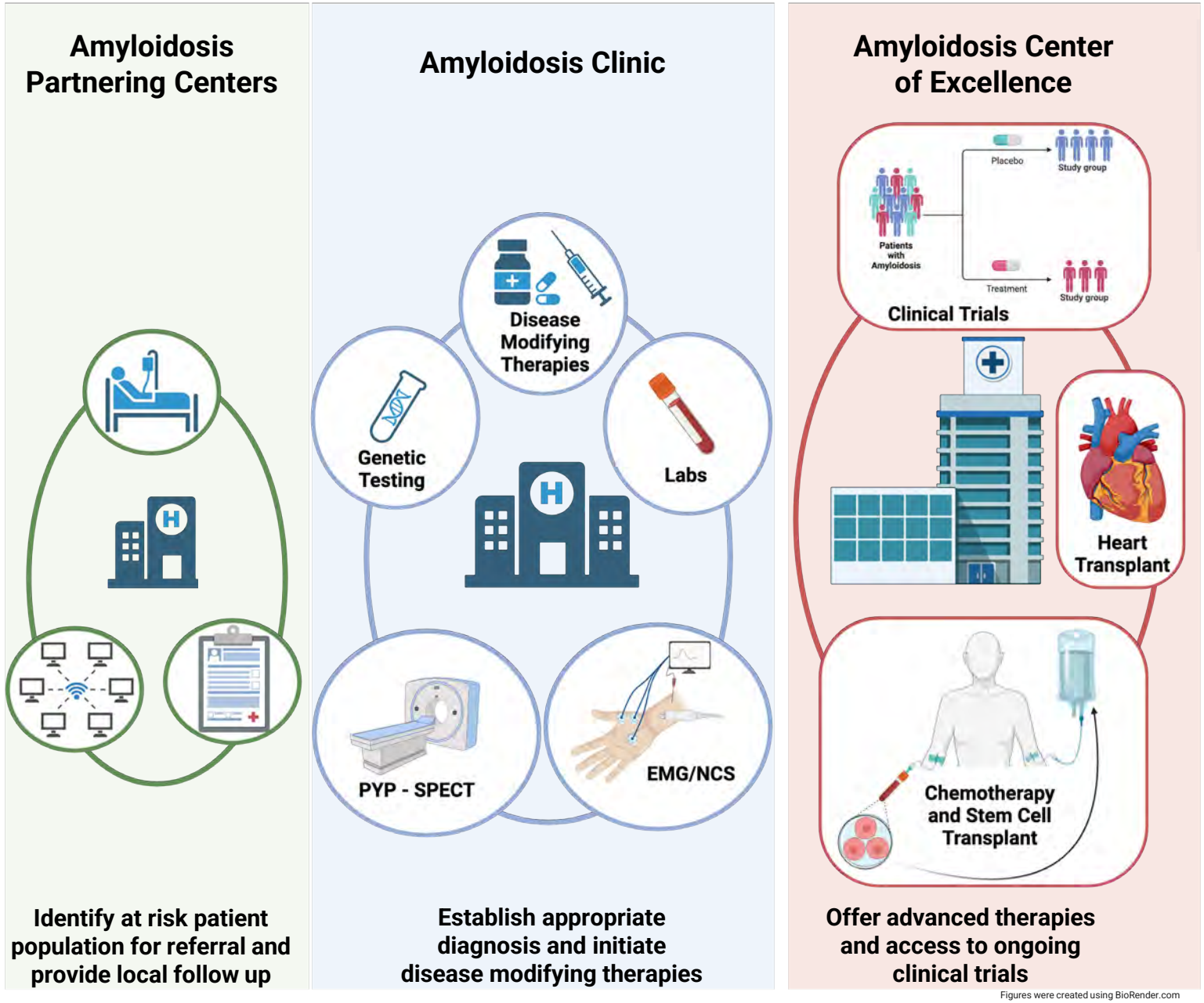
Cheng R, et al. Heart 2024;110:823–830.

Proposed Model for an Amyloid Center of Excellence



Cheng R, et al. Heart 2024;110:823–830.

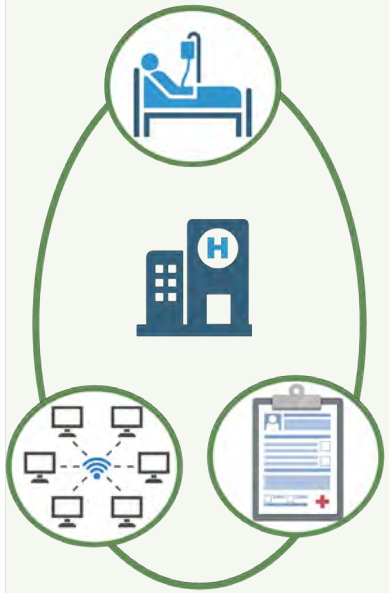
Partner with the Community



Figures were created using BioRender.com

Brailovsky Y et al. ACC Magazine. 2025

Amyloidosis Partnering Centers

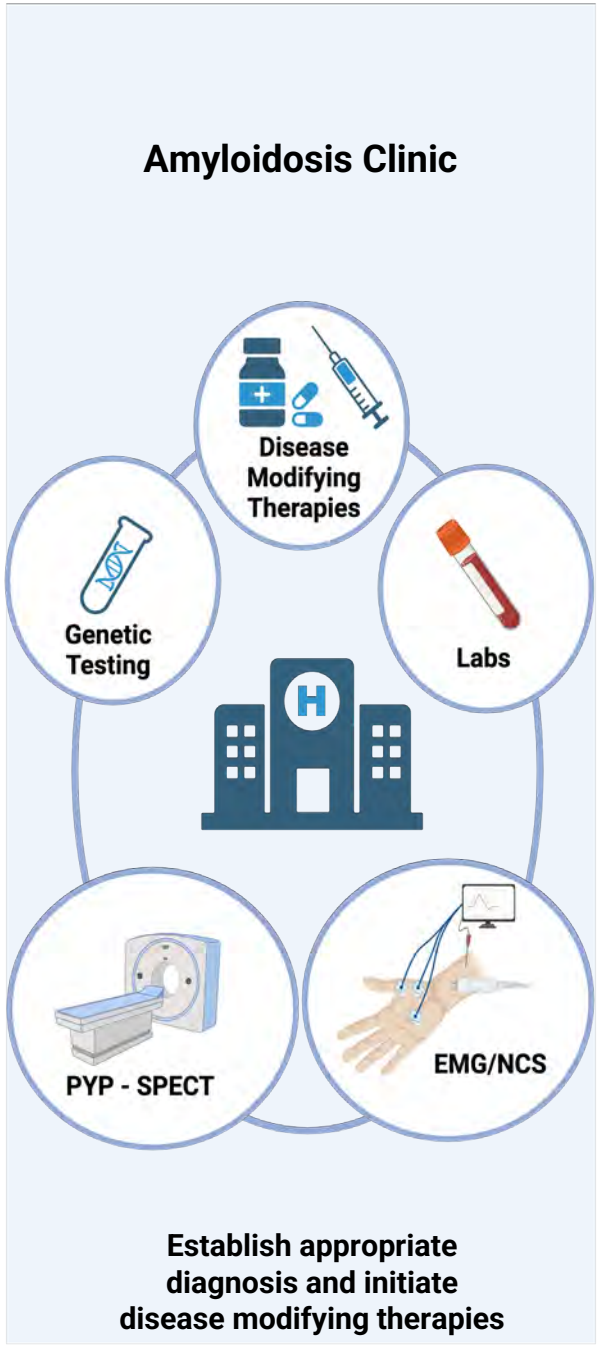


Identify at risk patient population for referral and provide local follow up

Find the Patients

- Majority of patients with amyloidosis are likely outside of large centers
- Develop practices to identify patients with early signs of amyloidosis
- Identify systems for expedited referral to amyloidosis clinics/centers of excellence
- Feedback loop to continue local follow up and promote clinician education

Brailovsky Y et al. ACC Magazine. 2025

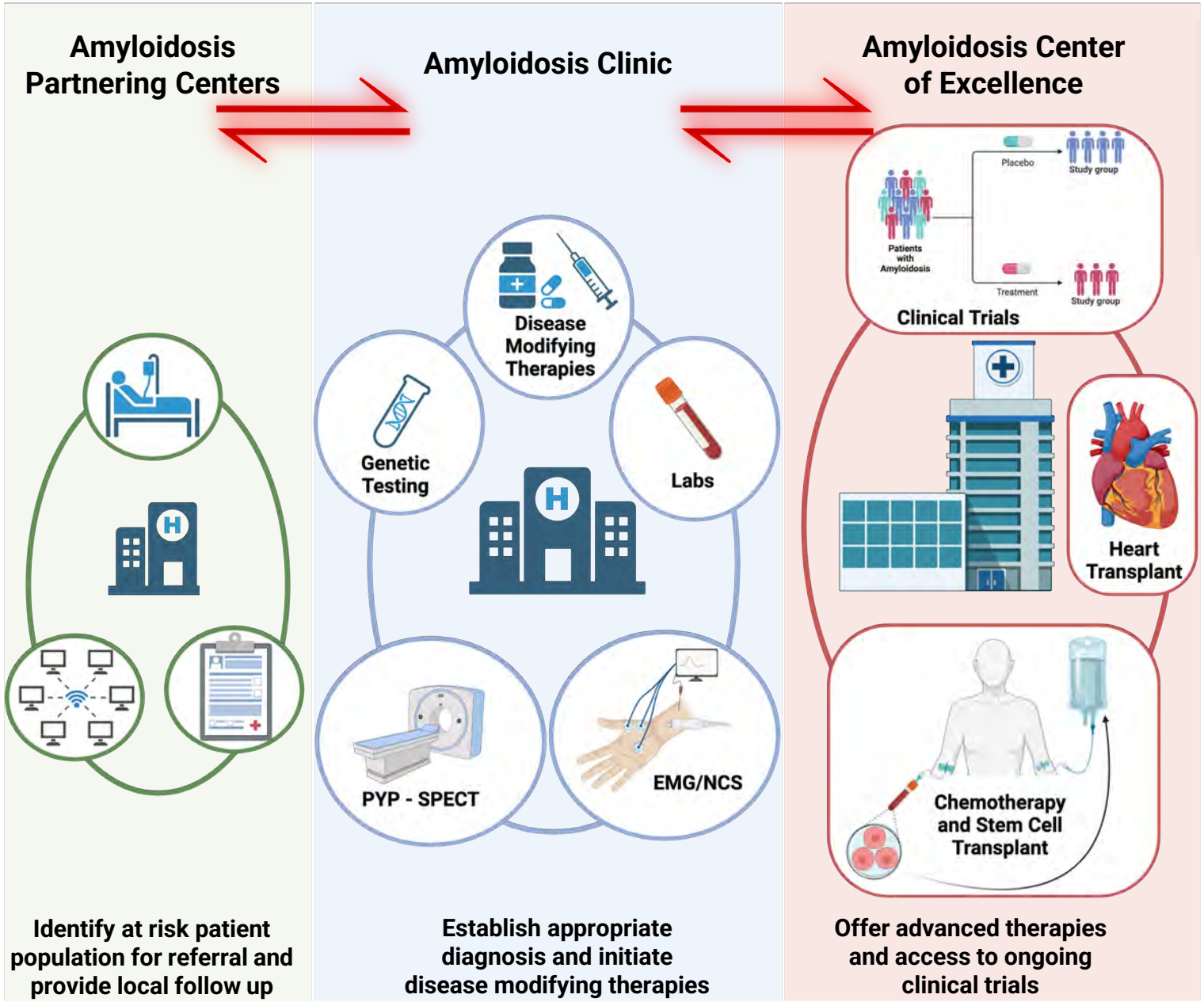


Establish the Diagnosis and Initiate Approved Therapies

- Multiple state of the art therapies are available
- The cost of therapy is still high
- Specialty pharmacy is key
- Identify patients who may be eligible/interested in clinical trials
- Refer patients for advanced therapies (Heart transplant, ASCT)

Brailovsky Y et al. ACC Magazine. 2025

Partner with the Community



Brailovsky Y et al. ACC Magazine. 2025

Q & A

Moderator

Mathew Maurer, MD
Professor of Medicine,
Arnold and Arlene Goldstein Professor of Cardiology,
NewYork-Presbyterian/Columbia University Irving Medical Center

Panelists

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NewYork-Presbyterian/Columbia University Irving Medical Center

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Mayo Clinic Hospital - AZ

Brett Sperry, MD
Associate Professor of Medicine, Cardiology,
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Naim Essam Bideiwy, FNP-C, MSN
Cardiology; NewYork-Presbyterian/Columbia University Irving Medical Center

Tammy Reideler, MSN, RN, OCN
Acute Leukemia and Amyloidosis Nurse Navigator;
Mayo Clinic Hospital - FL

Continuing the Conversation

POST-FORUM SURVEY: Coming Soon!

Your feedback will help us evaluate today's impact on closing gaps and overcoming barriers in AL Amyloidosis care, advancing clinical knowledge, practice, and patient outcomes.

MARK YOUR CALENDARS: May 14, 2025 | 1-2p ET

Join us for the follow-up National Webinar where we will discuss:

- ✓ Key takeaways from today's forum
- ✓ Insights from the pre & post forum surveys
- ✓ Launch of **AL Amyloidosis Educational Toolkit**, featuring resources for diagnosis, clinical management, and patient advocacy

Scan the QR code to Register!

The registration link can also be found in the chat!

American Heart Association®

Thank you for joining us today!

Recordings of today's sessions will be enduring resources in a few weeks on www.heart.org

We look forward to seeing you on the May 14th Webinar!