CRACKING THE CODE: MODERN APPROACHES TO CARDIAC AMYLOID

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Northwell℠
Cardiovascular Institute

DISCLOSURES

- Sub-investigator for the clinical trials presented herein, conducted at Northwell Health.
- No other relevant financial or non-financial conflicts of interest to disclose.

OBJECTIVES

- Pathophysiology
- Manifestations
- Diagnostic strategies
- Current management
- Emerging therapies

HISTORY

- “Amyloid degeneration” was first defined by Rudolph Virchow in 1857

The American Journal of
PATHOLOGY
Discoveries in Basic and Translational Pathobiology

AMYLOIDOSIS OF LUNGS AND HEART *

HENRY W. FERRIS, M.D.

(*From the Department of Pathology, Cornell University Medical College, New York, N. Y.*)

REPORT OF CASE

CASE 2. *Clinical History:* F. V., a white male, 52 years of age, was admitted to the medical service of the New York Hospital March 21, 1935. There was no history of significant disease in the family. A number of years before, he was treated for gonorrhea, complicated by urethral stricture. His general health since then had been good, however, until about 1 year before admission when he noted dyspnea on exertion and became more easily fatigued. These symptoms increased in severity during the next 9 months, and 3 months before admission he commenced to have night sweats and noticed some swelling and pulsation of the liver. There was also a chronic cough wi amount of mucus. He was treated with digitalis and

Physical Examination: The patient was well developed and nourished, but was moderately dyspneic. The percussion note was flat over the base of the right lung and breath sounds were absent in that location, as well as in the right axilla. The remainder of the lower lobe and the middle lobe were filled with moist râles. Similar râles were heard in the left lower lobe. The left border of the heart extended almost to the left anterior axillary line. The heart sounds were regular (70 per minute) and of tic-tac quality. A faint, soft systolic murmur was heard over the precordium. The systolic blood pressure was 125 and the diastolic 75 mm. Hg. The abdomen was slightly distended with the suggestion of a fluid wave. The liver edge was palpable a hand's breadth below the costal margin and was smooth and firm. There was slight swelling of the ankles.

Heart: The heart weighed 650 gm. In both auricular appendages were masses of friable thrombus, lightly adherent to the endocardium. The valve measurements were normal. The myocardium was firm in consistence with a homogeneous, glassy cut surface. The right ventricle was 0.7 cm. and the left 2 to 2.5 cm. in thickness. There were a few atheromatous plaques in the intima of the coronary

Ferris HW. Amyloidosis of Lungs and Heart. Am J Pathol. 1936 Sep;12(5):701-718.5. PMID: 19970296; PMCID: PMC1911015.

CARDIAC AMYLOIDOSIS: IS IT REALLY RARE?

- 16.8% of patients with HFpEF have ATTR
- 16% of patients undergoing TAVR for severe AS have ATTR
- 11.7% of patients referred for TEER for severe MR were noted to have concomitant cardiac amyloidosis
- 9% of patients initially labelled as HCM had cardiac amyloidosis

1. Garcia-Pavia P, Garcia-Pinilla JM, Lozano-Bahamonde A, Yun S, Garcia-Quintana A, Gavira-Gomez JJ, Aibar-Arregui MA, Barge-Caballero G, Villota JN, Bernal L, Tarilonte P. Prevalence of transthyretin cardiac amyloidosis in patients with heart failure with preserved ejection fraction: the PRACTICA study. Revista Española de Cardiología (English Edition). 2025 Apr 1;78(4):301-10.
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3. Dona C, Nitsche C, Koschutnik M, Heitzinger G, Mascherbauer K, Kammerlander AA, Dannenberg V, Halavina K, Rettl R, Duca F, Traub-Weidinger T. Unveiling cardiac amyloidosis, its characteristics, and outcomes among patients with MR undergoing transcatheter edge-to-edge MV repair. Cardiovascular Interventions. 2022 Sep 12;15(17):1748-58.
4. Maurizi N, Rella V, Fumagalli C, Salerno S, Castelletti S, Dagradi F, Torchio M, Marceca A, Meda M, Gasparini M, Boschi B, Girolami F, Parati G, Olivotto I, Crotti L, Cecchi F. Prevalence of cardiac amyloidosis among adult patients referred to tertiary centres with an initial diagnosis of hypertrophic cardiomyopathy. Int J Cardiol. 2020 Feb 1;300:191-195. doi: 10.1016/j.ijcard.2019.07.051. Epub 2019 Jul 17. PMID: 31371117.

THE EVOLVING PARADIGM

Historical View:

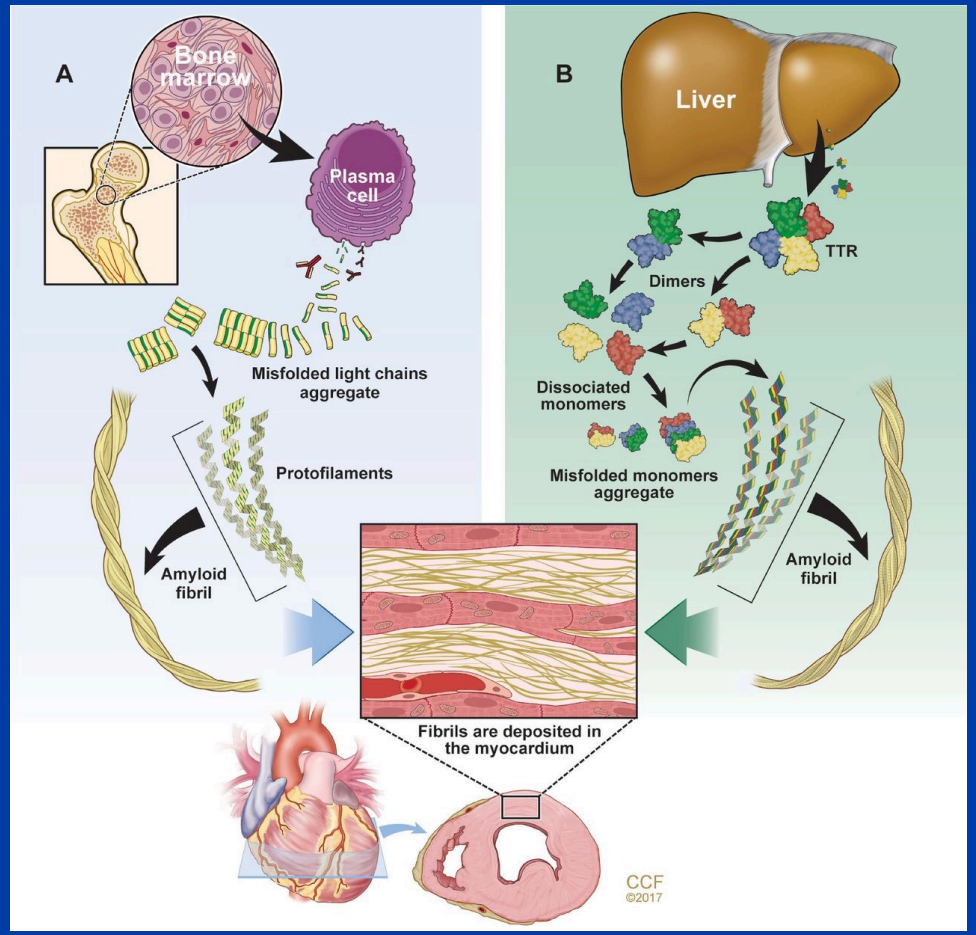
A rare, terminal condition with limited diagnostic tools and no effective treatments

Modern Reality (2026):

A frequently underdiagnosed cause of Heart Failure (HFpEF) and Polyneuropathy, now manageable with transformative, targeted therapies.

CRACK IT EARLY.....!

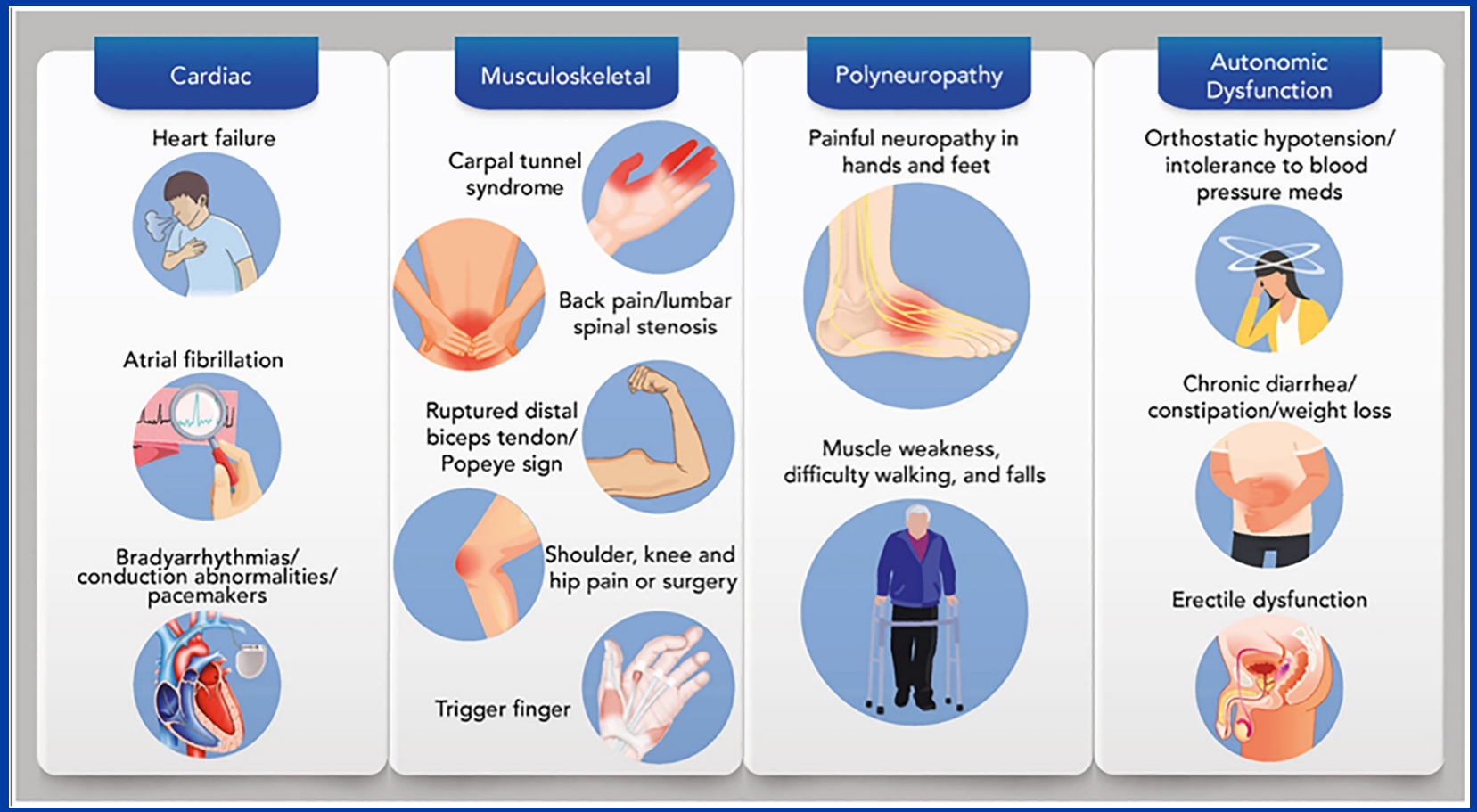
PATHOPHYSIOLOGY



- What is amyloid? Extracellular deposition of misfolded protein
- Two dozen proteins known to form amyloid fibrils in vivo
- Two predominant types affecting the heart:
  - AL (light chain) —plasma cell dyscrasia
  - ATTR — transthyretin
    - ATTRwt (wild-type, formerly senile)
    - ATTRv (hereditary/variant)

Cleveland Clin. J. Med. 84(12 Suppl. 3):12–26

CLINICAL MANIFESTATIONS

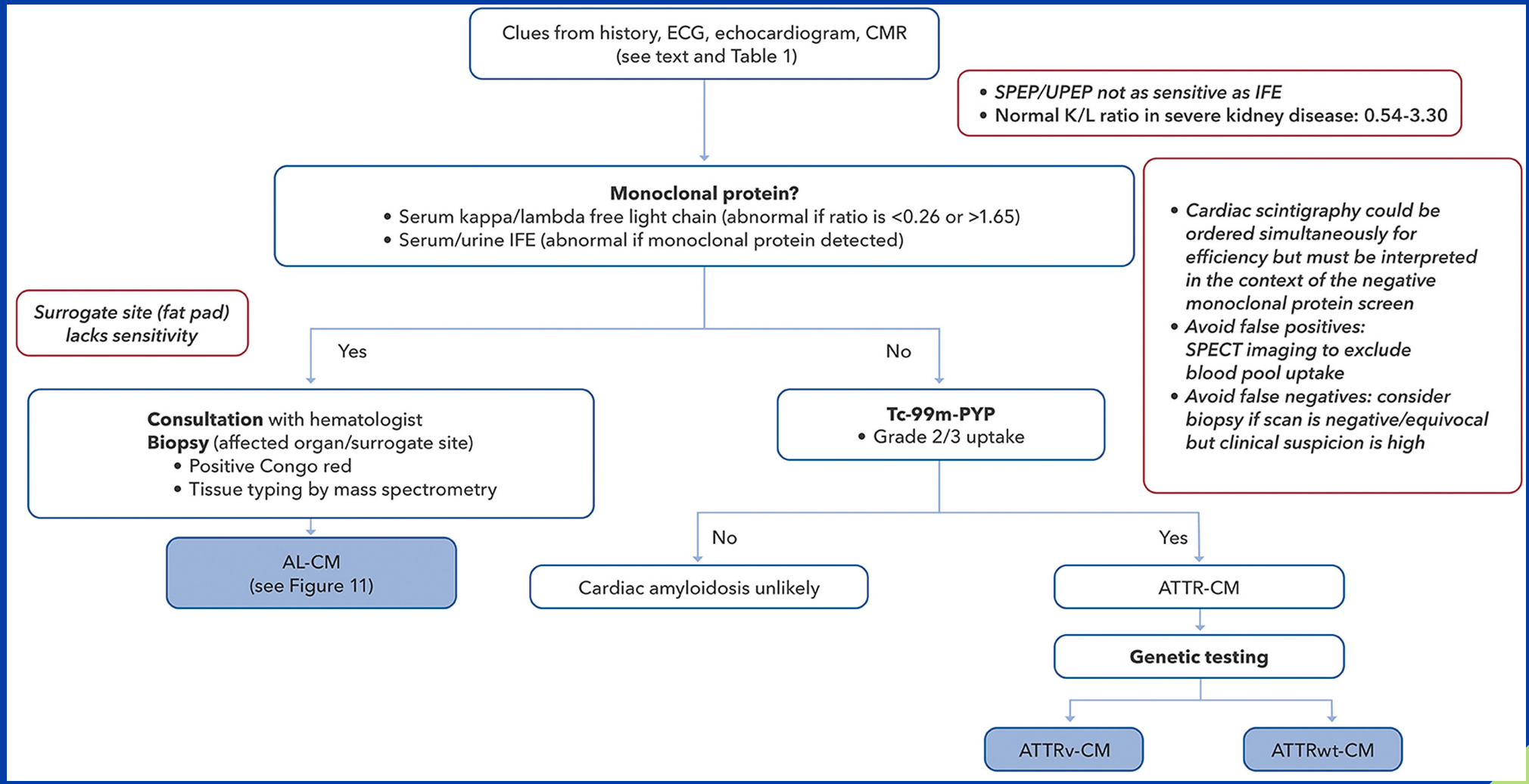


Cardiac Red Flags:

- HFpEF without hypertension, particularly old men
- Intolerance to neurohormonal antagonists
- Elevated biomarkers (NT-proBNP / BNP and troponin) out of proportion to clinical scenario
- Low flow – low gradient aortic stenosis
- Low voltage on EKG despite LVH on echo

J Am Coll Cardiol. 2023;81(11):1076-1126

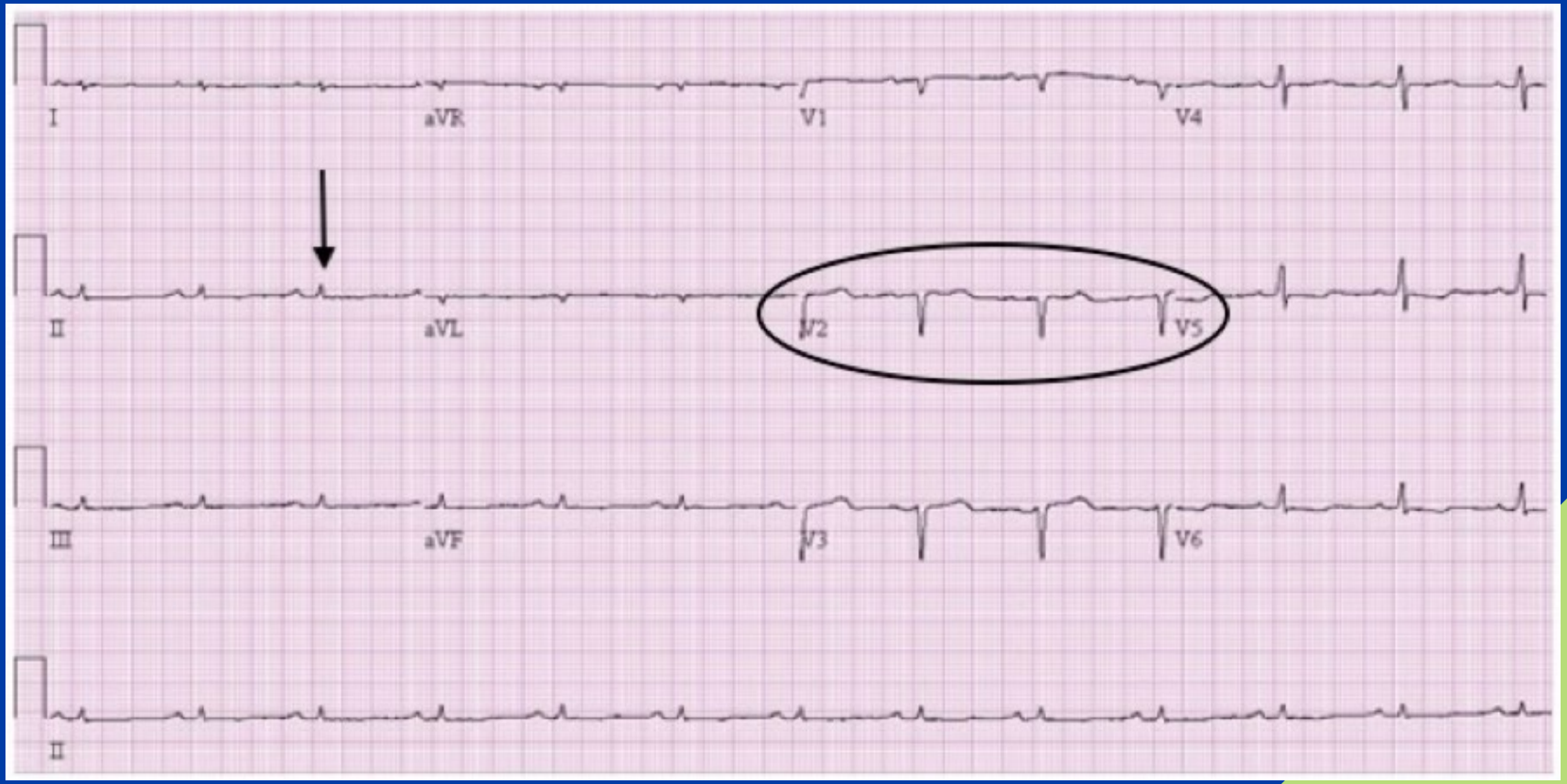
DIAGNOSIS



Writing Committee: Kittleson MM, Ruberg FL, Ambardekar AV, Brannagan TH, Cheng RK, Clarke JO, Dember LM, Frantz JG, Hershberger RE, Maurer MS, Nativi-Nicolau J, Sanchorawala V, Sheikh FH. 2023 ACC Expert Consensus Decision Pathway on Comprehensive Multidisciplinary Care for the Patient With Cardiac Amyloidosis: A Report of the American College of Cardiology Solution Set Oversight Committee. J Am Coll Cardiol. 2023 Mar 21;81(11):1076-1126. doi: 10.1016/j.jacc.2022.11.022. Epub 2023 Jan 23. Erratum in: J Am Coll Cardiol. 2023 Mar 21;81(11):1135. doi: 10.1016/j.jacc.2023.02.013. PMID: 36697326.

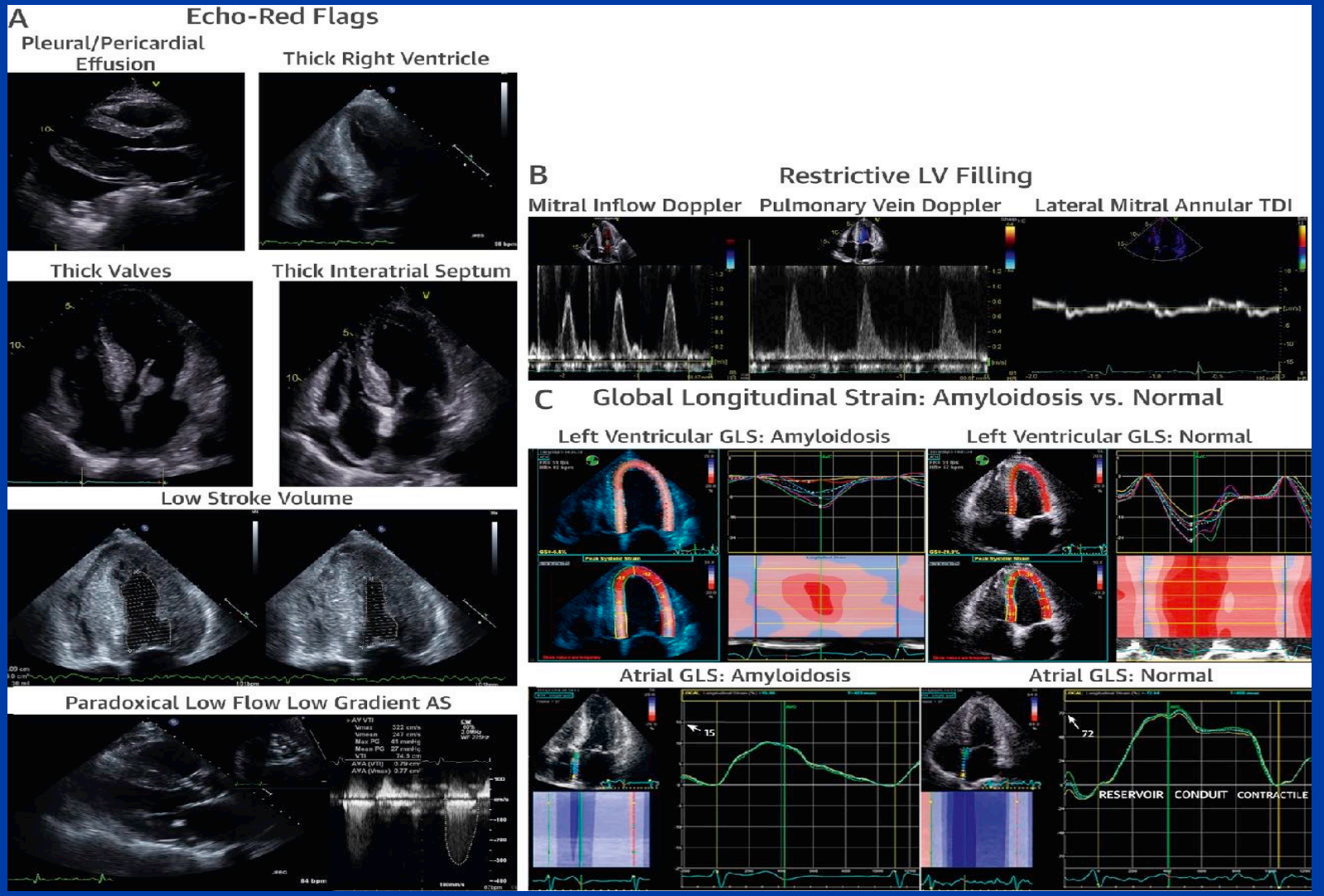
DIAGNOSTIC CLUES: EKG

- Low voltage (45% in AL, 18-45% in ATTR)
- Pseudoinfarct pattern
- Increased PR interval
- RBBB pattern
- Discordance between LV thickness noted on echo and ECG voltage



Maurer MS, Elliott P, Comenzo R, Semigran M, Rapezzi C. Addressing Common Questions Encountered in the Diagnosis and Management of Cardiac Amyloidosis. Circulation. 2017 Apr 4;135(14):1357-1377. doi: 10.1161/CIRCULATIONAHA.116.024438. PMID: 28373528; PMCID: PMC5392416.

DIAGNOSIS: ECHOCARDIOGRAM



DIAGNOSIS: CARDIAC MRI

Morphological and Functional Markers	Late Gadolinium Enhancement (LGE)	Parametric Mapping (T1 & ECV)
• Appearance (increased wall thickness) • Diastolic function	Diffuse subendocardial-> transmural	Increased ECV Increased T1 values

DIAGNOSIS: RULE OUT AL

- Serum Kappa / lambda free light chain (abnormal if ratio is <0.26 or >1.65)
- Serum IFE (abnormal if monoclonal protein detected)
- Urine IFE (abnormal if monoclonal protein detected)

DIAGNOSIS: NUCLEAR IMAGING

- Three Technetium labeled nuclear agents:
  - 99mTc-pyrophosphate [99mTc-PYP]
  - 99mTc-3,3-diphosphono- 1,2-propanodicarboxylic acid [99mTc-DPD]
  - 99mTc-hydroxymethylene diphosphonate [99mTc- HMDP].

- Bind avidly to TTR deposits in the heart

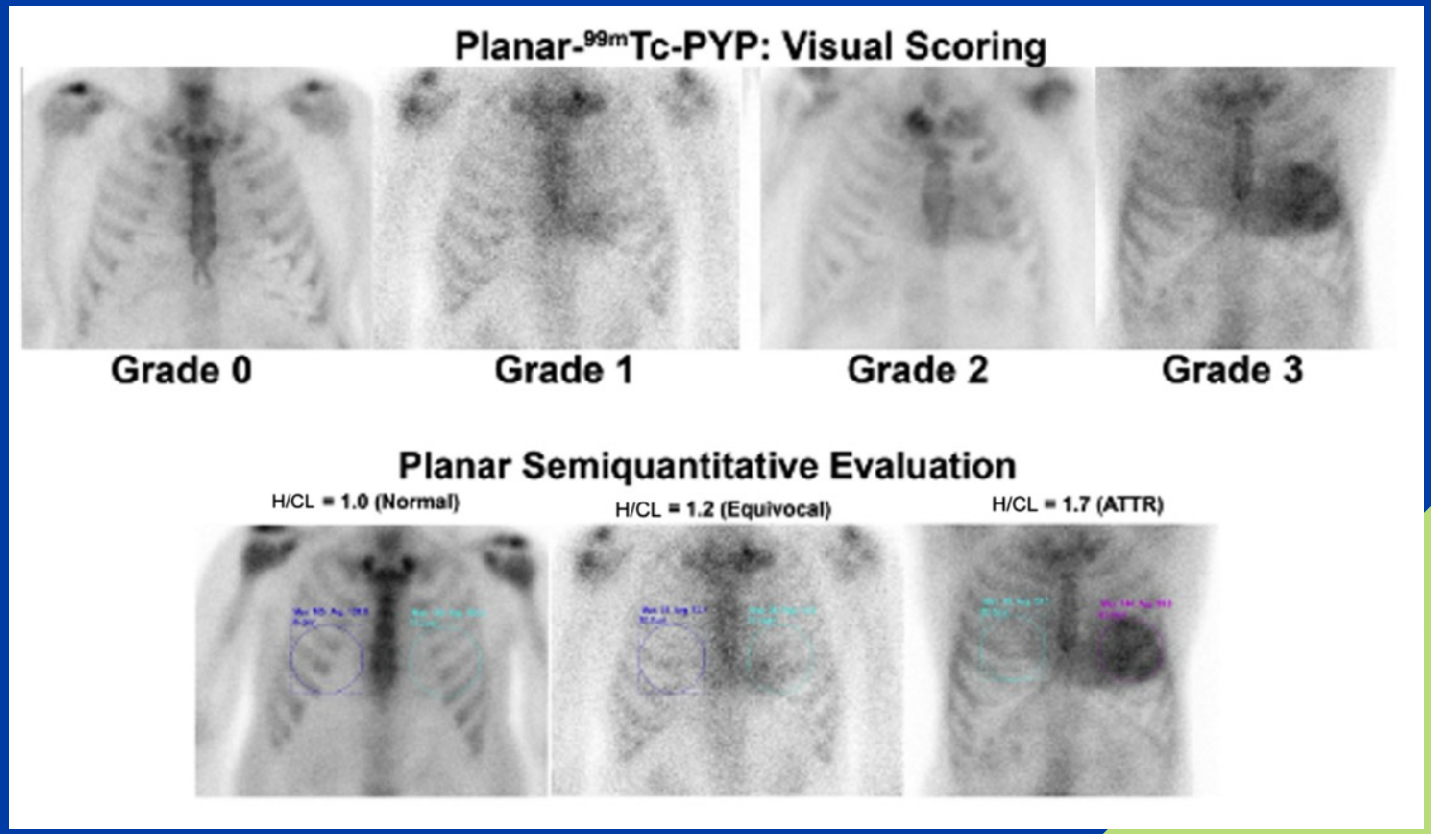
- Injection is followed by planar and SPECT imaging at 1 and 3 hrs

DIAGNOSIS: NUCLEAR IMAGING

Planar imaging (2D)

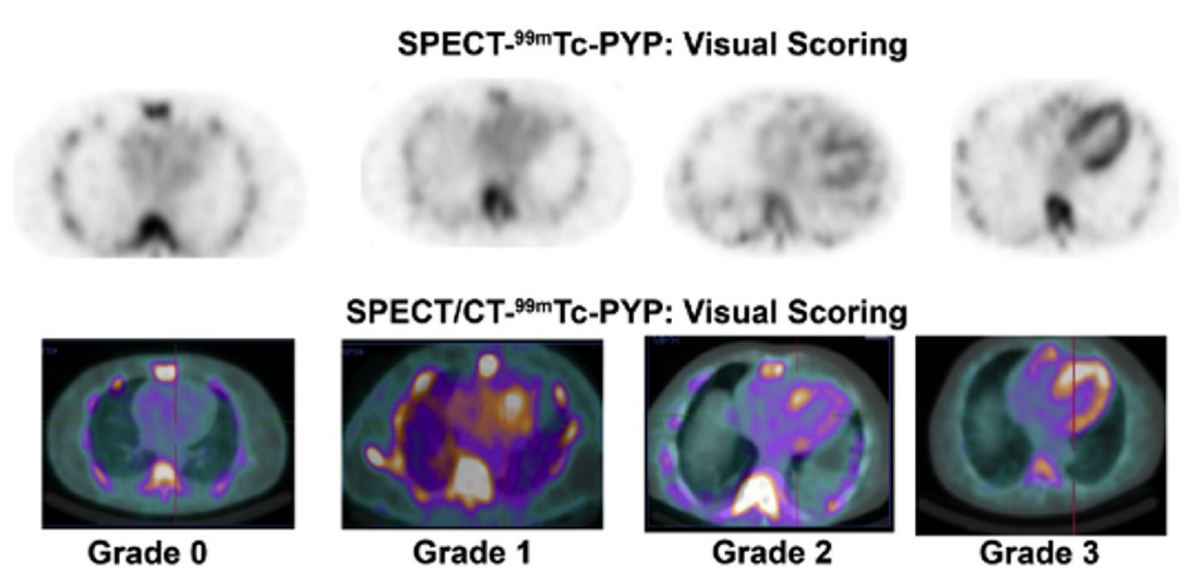
Perugini Scale:

Grade	Description
Grade 0	No myocardial uptake and normal bone uptake.
Grade 1	Mild myocardial uptake, but significantly less than bone uptake.
Grade 2	Myocardial uptake equal to or greater than bone uptake.
Grade 3	Intense myocardial uptake with much-reduced or absent bone uptake.



DIAGNOSIS: NUCLEAR IMAGING

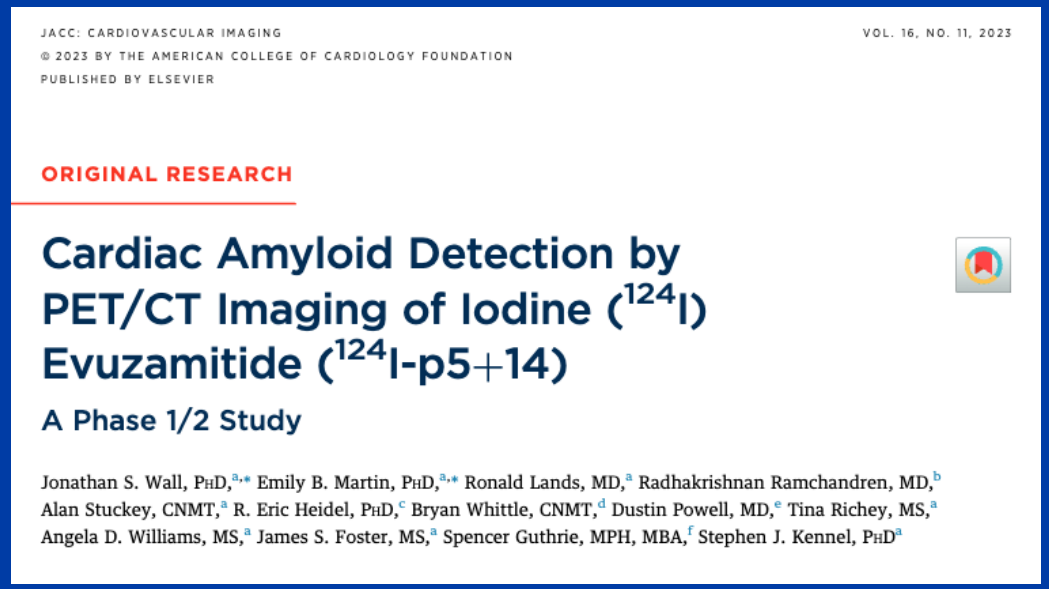
SPECT / SPECT CT (3D)



Feature	Planar Imaging	SPECT	SPECT/CT
Dimension	2D (Flat)	3D (Slices)	3D (Slices) + Anatomy
Primary Use	Initial Perugini Scoring	Confirming Myocardial Location	Highest precision; clearing artifacts
False Positives	High (due to blood pool)	Low	Lowest
Vessel/Rib Overlap	Significant	Minimized	Eliminated

Non-ATTR causes of positive PYP scan: AL amyloidosis, blood pooling, rib fracture, hydroxychloroquine toxicity, acute MI, other rare causes of CA

DIAGNOSIS: NUCLEAR IMAGING



JACC: CARDIOVASCULAR IMAGING VOL. 16, NO. 11, 2023

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ORIGINAL RESEARCH

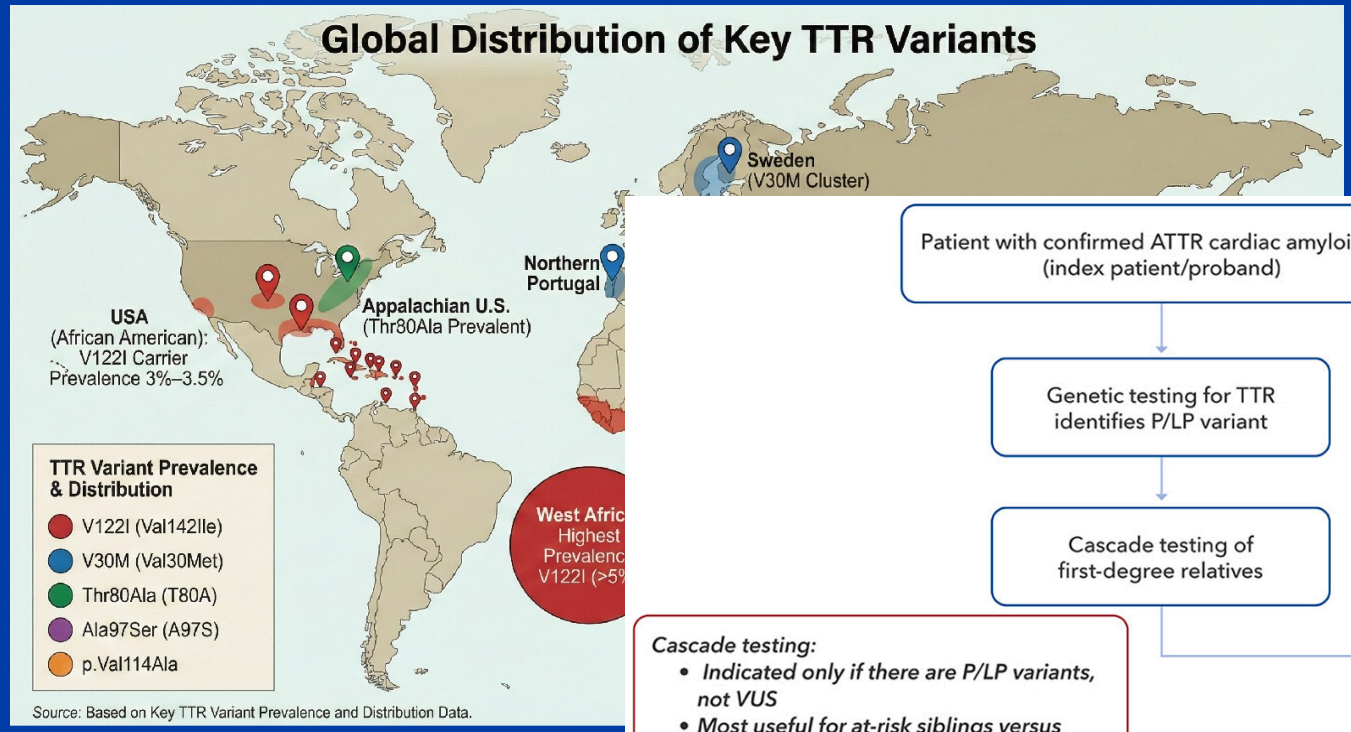
Cardiac Amyloid Detection by PET/CT Imaging of Iodine (^{124}I) Evuzamitide (^{124}I-p5+14)

A Phase 1/2 Study

Jonathan S. Wall, PhD,[a,*] Emily B. Martin, PhD,[a,*] Ronald Lands, MD,[a] Radhakrishnan Ramchandren, MD,[b] Alan Stuckey, CNMT,[a] R. Eric Heidel, PhD,[c] Bryan Whittle, CNMT,[d] Dustin Powell, MD,[e] Tina Richey, MS,[a] Angela D. Williams, MS,[a] James S. Foster, MS,[a] Spencer Guthrie, MPH, MBA,[f] Stephen J. Kennel, PhD[a]

- Evuzamitide (specifically 124I-evuzamitide, also known as AT-01)
- FDA Breakthrough Designation: In August 2024, the FDA granted 124I-evuzamitide Breakthrough Therapy Designation
- Pan-Amyloid Detection: It can identify multiple types of amyloid deposits, including AL (light chain) and ATTR (transthyretin), in the heart, kidneys, liver, and spleen.
- High Sensitivity: Clinical trials reported a 96.2% sensitivity for detecting cardiac involvement, making it significantly more accurate than many current non-invasive methods.
- Early disease detection

DIAGNOSIS: GENETIC TESTING



Patient with confirmed ATTR cardiac amyloidosis (index patient/proband)

Genetic testing for TTR identifies P/LP variant

- *Ensure gene panel includes TTR*
- *Avoid overly broad screening, which may uncover variants in other genes that are coincidental but not clinically relevant*

Cascade testing of first-degree relatives

Cascade testing:

- *Indicated only if there are P/LP variants, not VUS*
- *Most useful for at-risk siblings versus offspring, given age-dependent penetrance of ATTRv-CM*
- *Be prepared to counsel on incomplete penetrance, variable expressivity, implications for life, disability, and long-term care insurance – especially for offspring likely decades away from disease manifestations*
- *Engage a genetic counselor if possible*

Individual undergoes genome-wide testing

TTR variant identified (secondary finding)

Identification of asymptomatic TTR variant gene carriers

Genetic screening:

- *Ongoing assessment is required after a P/LP TTR variant is identified*
- *Start clinical assessment 10 years before the age of onset of the proband (if one exists; see Figure 6)*

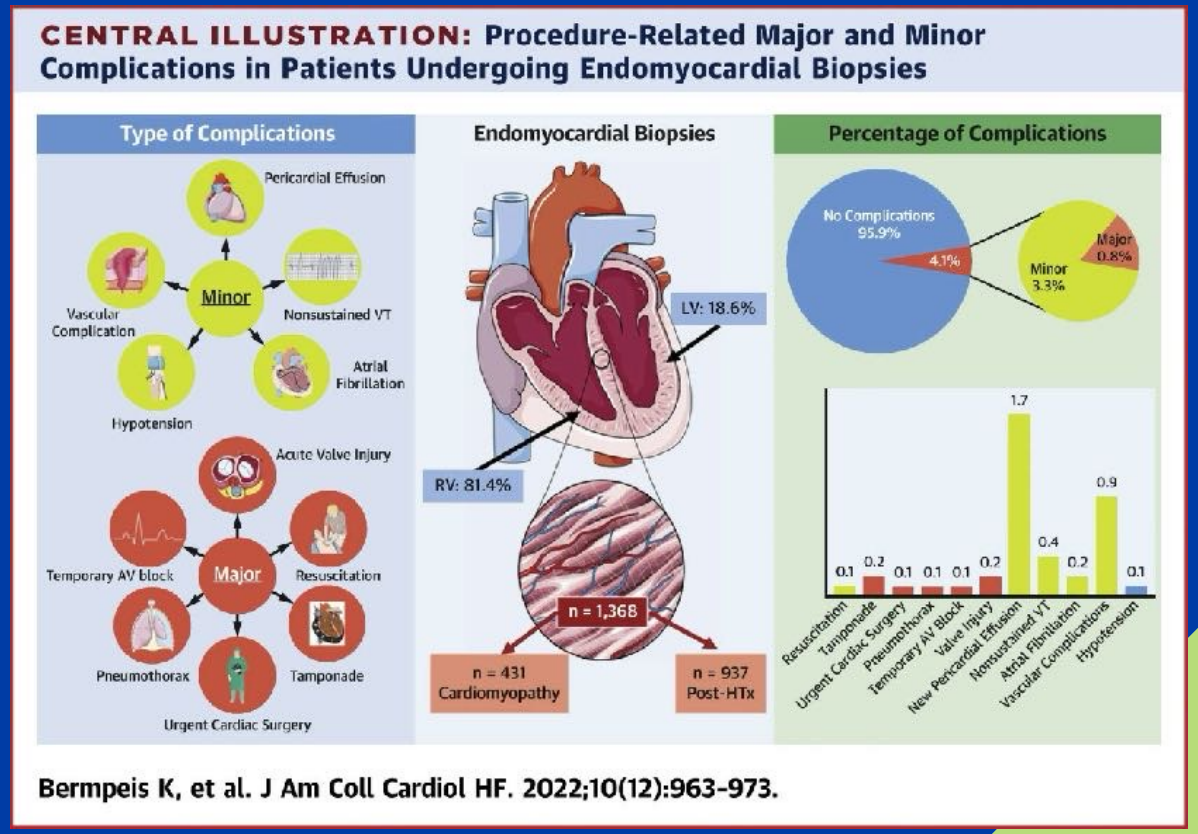
DIAGNOSIS: NON-INVASIVE DIAGNOSIS OF ATTR-CA

Currently the accepted definition of a noninvasive diagnosis of ATTR-CM requires **all** of the following:

- Unexplained heart failure or carrier status of a pathogenic TTR mutation
- Echocardiographic and/or cardiac MRI findings suggestive of cardiac amyloidosis
- **The absence of a monoclonal gammopathy by serum free light chain assay and serum and urine Immunofixation**
- The presence of ≥ grade 2 uptake on (^{99m}Tc-PYP, ^{99m}Tc-DPD, ^{99m}Tc-HDMP) ***confirmed by SPECT imaging***

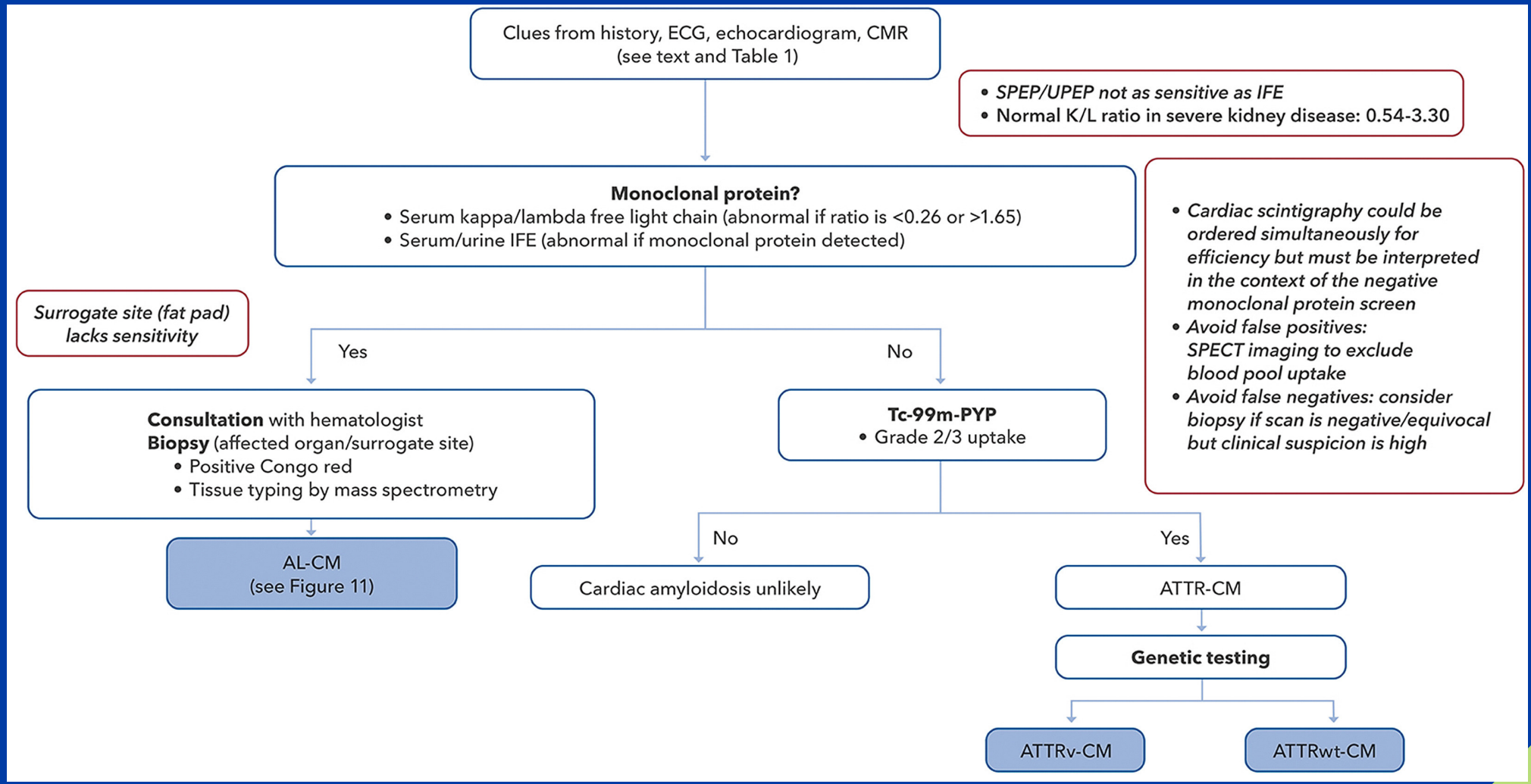
DIAGNOSIS: ROLE OF ENDOMYOCARDIAL BIOPSY

- Remains gold standard for diagnosis
- Important to consider in patients with high likelihood despite negative non-invasive testing
- Relatively safe
- Highly sensitive and specific
- Risk of major complications < 0.5 %



Bermpeis K, et al. J Am Coll Cardiol HF. 2022;10(12):963-973.

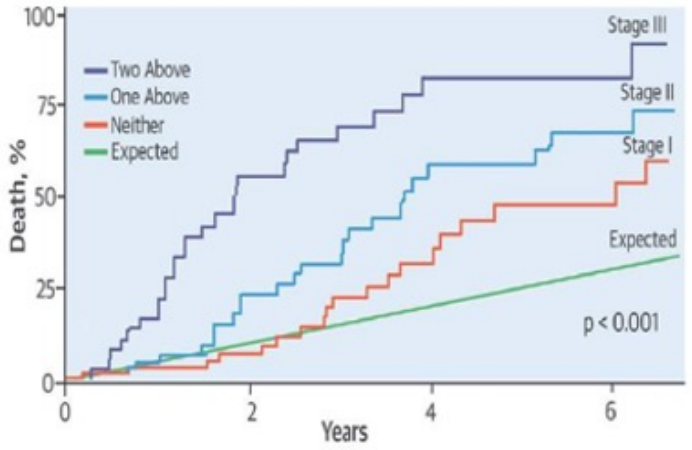
DIAGNOSIS



Writing Committee: Kittleson MM, Ruberg FL, Ambardekar AV, Brannagan TH, Cheng RK, Clarke JO, Dember LM, Frantz JG, Hershberger RE, Maurer MS, Nativi-Nicolau J, Sanchorawala V, Sheikh FH. 2023 ACC Expert Consensus Decision Pathway on Comprehensive Multidisciplinary Care for the Patient With Cardiac Amyloidosis: A Report of the American College of Cardiology Solution Set Oversight Committee. J Am Coll Cardiol. 2023 Mar 21;81(11):1076-1126. doi: 10.1016/j.jacc.2022.11.022. Epub 2023 Jan 23. Erratum in: J Am Coll Cardiol. 2023 Mar 21;81(11):1135. doi: 10.1016/j.jacc.2023.02.013. PMID: 36697326.

MANAGEMENT: RISK STRATIFICATION

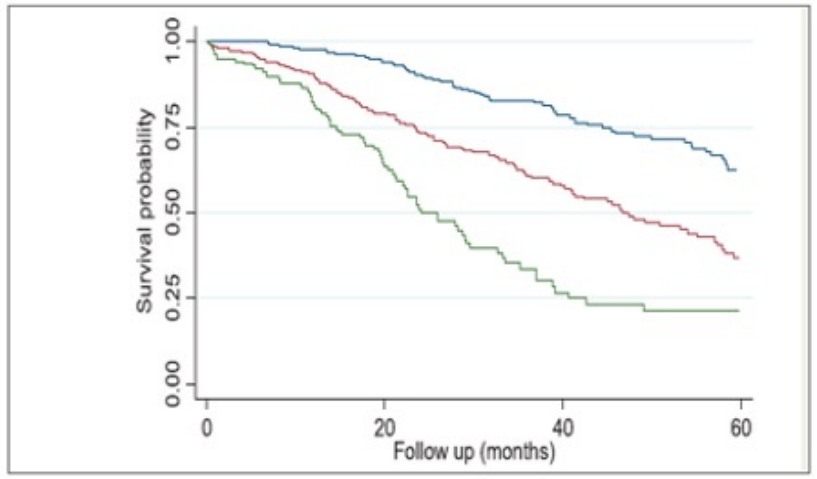
Mayo Staging 2012
ATTRwt Cardiac Amyloidosis



JACC.2016;68(10):1014-20

Stage I: NT-proBNP ≤3000 ng/L & Troponin T<0.05
Stage II: NT-proBNP >3000 ng/L or Troponin T>0.05
Stage III: NT-proBNP >3000 ng/L & Troponin T>0.05

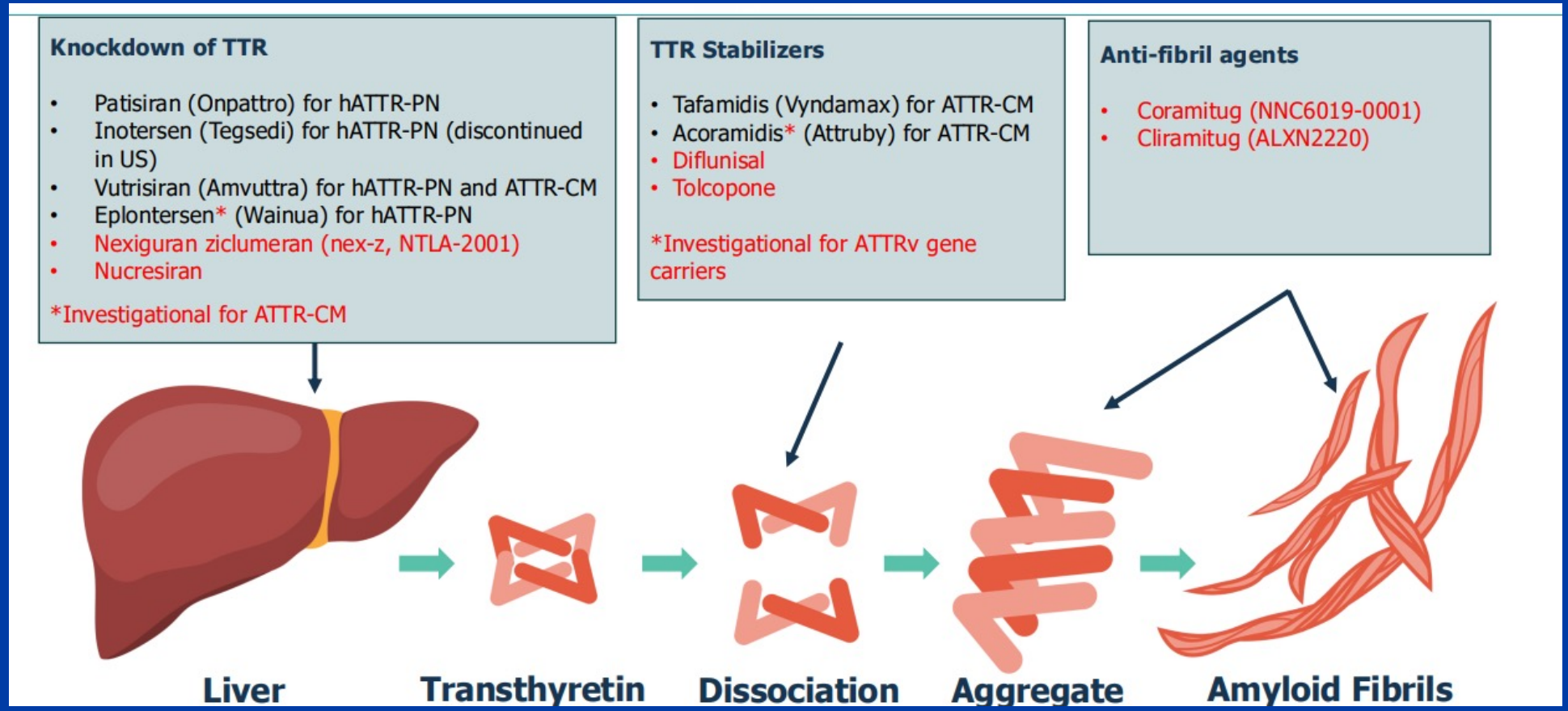
UK NAC Staging System (2017)
ATTR Cardiac Amyloidosis



EHJ. 2018;39(30):2799-2806

Stage I: NT-proBNP ≤3000 ng/L & eGFR ≥45ml/min
Stage II: NT-proBNP>3000 ng/L or eGFR <45ml/min
Stage III: NT-proBNP>3000 ng/L & eGFR <45ml/min

MANAGEMENT: PHARMACOTHERAPY



Amyloid Research Consortium: Master Template

MANAGEMENT: STABILIZER - TAFAMIDIS

- Mechanism of action: Stabilizer that blinds to thyroxine binding site of TTR, thus stabilizing tetramers and decreasing amyloid deposits
- Most effective early in disease process
- Dose:
  - Tafamidis (Vyndamax): 61 mg once daily.
  - Tafamidis meglumine (Vyndaqel): 80 mg once daily – discontinued in USA on 12/31/2025

Attach

VYNDAMAX attaches to the TTR protein.

Stabilize

VYNDAMAX stabilizes TTR, helping it stay together.

Maintain

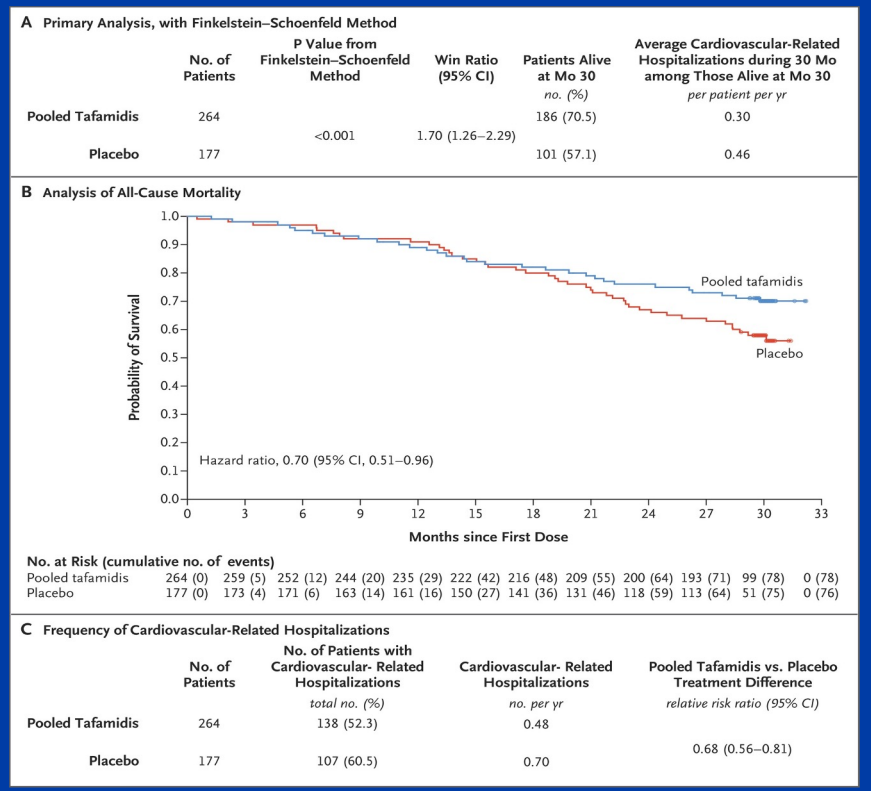
By stabilizing TTR, VYNDAMAX slows the breakdown and buildup of dangerous deposits, which can help to slow the progression of ATTR-CM.

MANAGEMENT: STABILIZER - TAFAMIDIS

Tafamidis Treatment for Patients with Transthyretin Amyloid Cardiomyopathy

Mathew S. Maurer, M.D., Jeffrey H. Schwartz, Ph.D., Balarama Gundapaneni, M.S., Perry M. Elliott, M.D., Giampaolo Merlini, M.D., Ph.D., Marcia Waddington-Cruz, M.D., Arnt V. Kristen, M.D., Martha Grogan, M.D., Ronald Witteles, M.D., Thibaud Damy, M.D., Ph.D., Brian M. Drachman, M.D., Sanjiv J. Shah, M.D., et al., for the ATTR-ACT Study Investigators*

- Multi-center, double blind, phase three placebo- controlled trial
- 441 patients
- 2:1:2 ratio to receive 80 mg of tafamidis, 20 mg of tafamidis, or placebo for 30 months
- Primary outcome: all-cause mortality and CV-hospitalizations (hierarchically assessed)
- Secondary outcomes:
  - from baseline to month 30 for the 6-minute walk test
  - Score on KCCQ-OS



A Primary Analysis, with Finkelstein–Schoenfeld Method

	No. of Patients	P Value from Finkelstein–Schoenfeld Method	Win Ratio (95% CI)	Patients Alive at Mo 30 *no. (%)*	Average Cardiovascular-Related Hospitalizations during 30 Mo among Those Alive at Mo 30 *per patient per yr*
Pooled Tafamidis	264	<0.001	1.70 (1.26–2.29)	186 (70.5)	0.30
Placebo	177			101 (57.1)	0.46

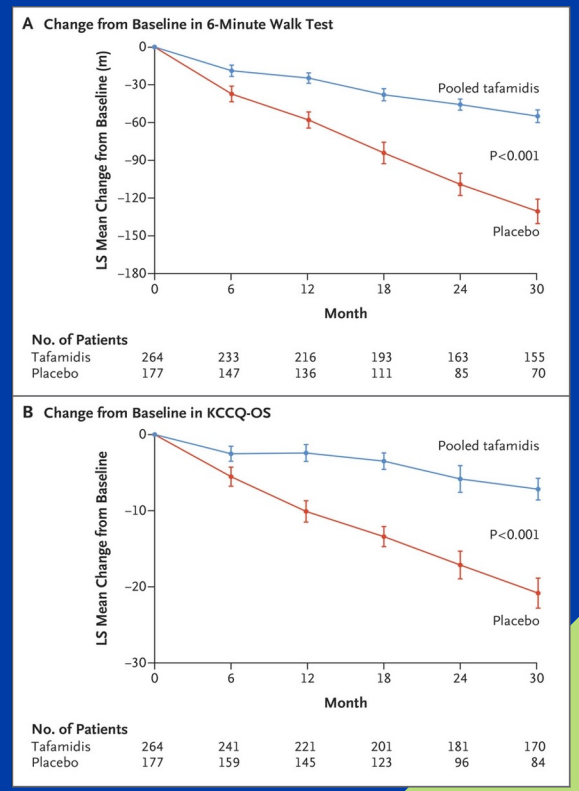
B Analysis of All-Cause Mortality

No. at Risk (cumulative no. of events)

Pooled tafamidis	264 (0)	259 (5)	252 (12)	244 (20)	235 (29)	222 (42)	216 (48)	209 (55)	200 (64)	193 (71)	99 (78)	0 (78)
Placebo	177 (0)	173 (4)	171 (6)	163 (14)	161 (16)	150 (27)	141 (36)	131 (46)	118 (59)	113 (64)	51 (75)	0 (76)

C Frequency of Cardiovascular-Related Hospitalizations

	No. of Patients	No. of Patients with Cardiovascular- Related Hospitalizations *total no. (%)*	Cardiovascular- Related Hospitalizations *no. per yr*	Pooled Tafamidis vs. Placebo Treatment Difference *relative risk ratio (95% CI)*
Pooled Tafamidis	264	138 (52.3)	0.48	0.68 (0.56–0.81)
Placebo	177	107 (60.5)	0.70	



A Change from Baseline in 6-Minute Walk Test

No. of Patients

Tafamidis	264	233	216	193	163	155
Placebo	177	147	136	111	85	70

B Change from Baseline in KCCQ-OS

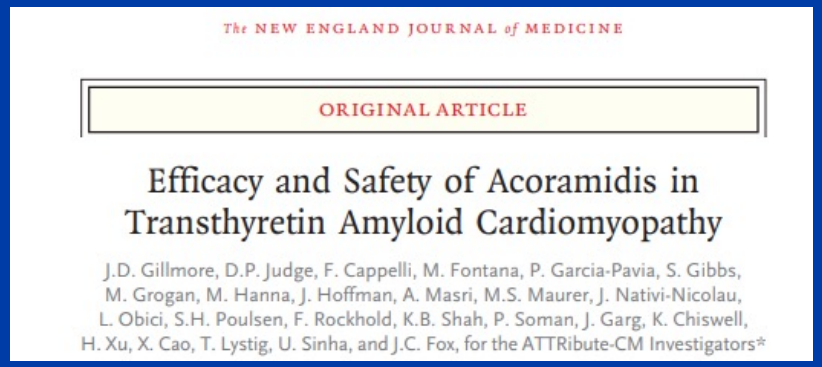
No. of Patients

Tafamidis	264	241	221	201	181	170
Placebo	177	159	145	123	96	84

MANAGEMENT: STABILIZER - ACORAMADIS

- Mechanism of action: Stabilizer that binds TTR at thyroxine-binding sites and slows dissociation of the TTR tetramer into its constituent monomers, thus reducing amyloid deposits.
- Dose: 712 mg twice daily.

MANAGEMENT: STABILIZER - ACORAMADIS

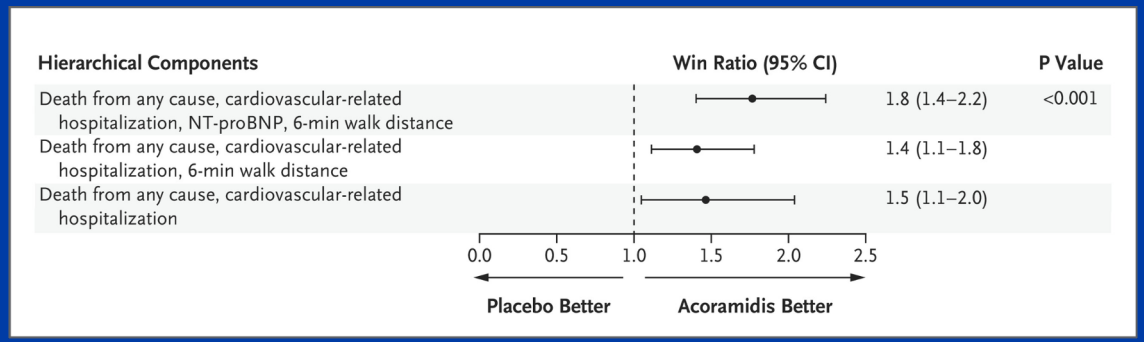

The NEW ENGLAND JOURNAL of MEDICINE

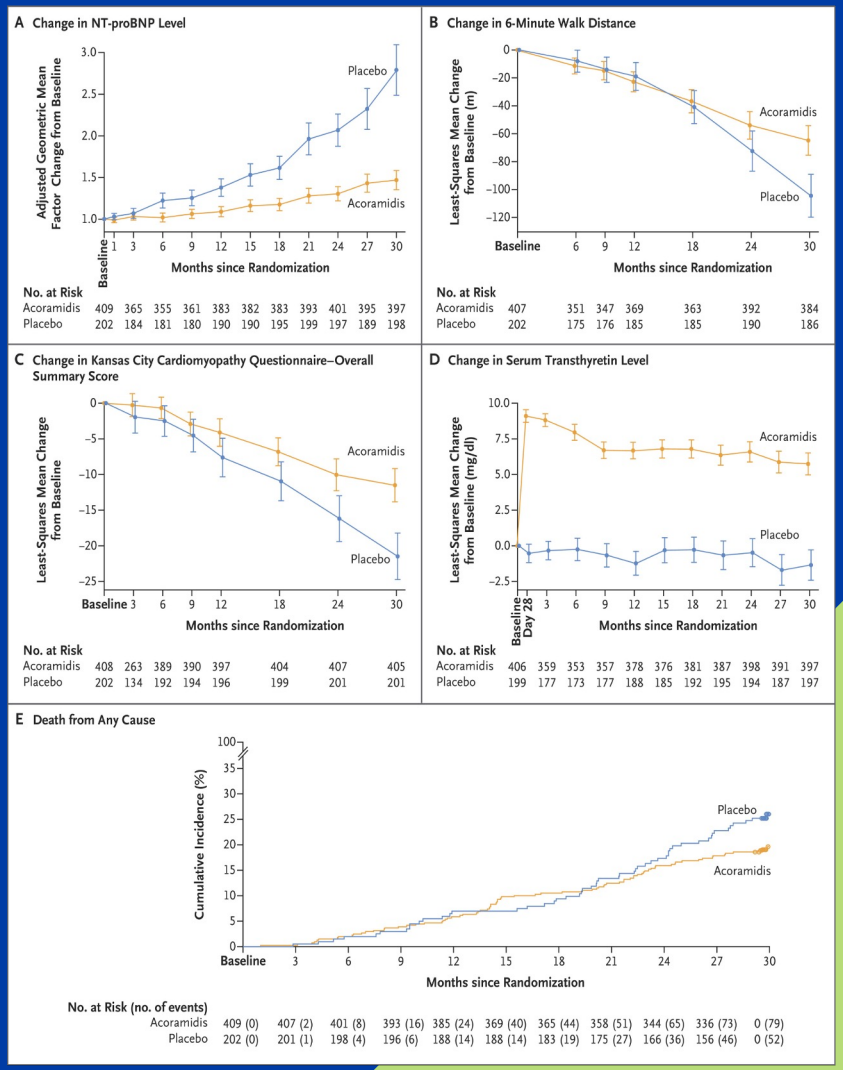
ORIGINAL ARTICLE

Efficacy and Safety of Acoramidis in Transthyretin Amyloid Cardiomyopathy

J.D. Gillmore, D.P. Judge, F. Cappelli, M. Fontana, P. Garcia-Pavia, S. Gibbs, M. Grogan, M. Hanna, J. Hoffman, A. Masri, M.S. Maurer, J. Nativi-Nicolau, L. Obici, S.H. Poulsen, F. Rockhold, K.B. Shah, P. Soman, J. Garg, K. Chiswell, H. Xu, X. Cao, T. Lystig, U. Sinha, and J.C. Fox, for the ATTRibute-CM Investigators*

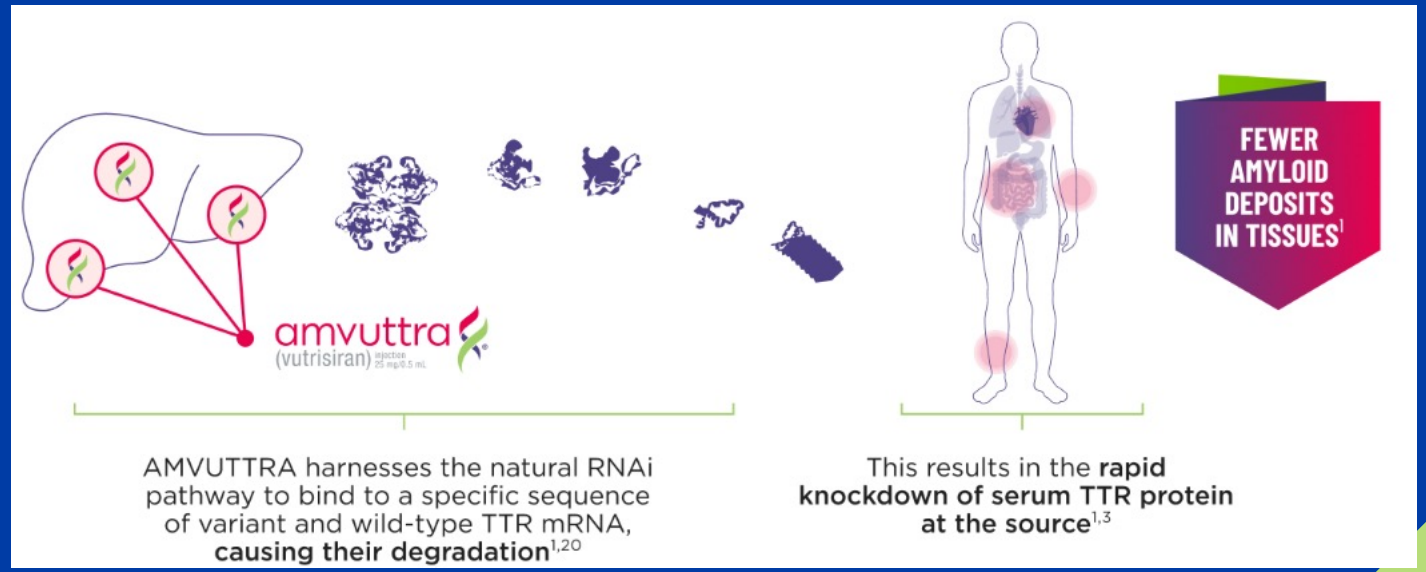
- Multi-center, double blind, phase three placebo- controlled trial
- 441 patients
- 2:1 randomized to receive acoramidis 800 mg vs placebo
- 30 month
- Primary outcome: hierarchical analysis included death from any cause, cardiovascular-related hospitalization, the change from baseline in the NT-proBNP level, and the change from baseline in the 6-minute walk distance.





MANAGEMENT: SILENCER - VUTRISIRAN

- Mechanism of action: double-stranded small interfering ribonucleic acid (siRNA)-N-acetylgalactosamine (GalNAc) conjugate that causes degradation of mutant and wild-type transthyretin (TTR) messenger RNA (mRNA) through RNA interference, which results in a reduction of serum TTR protein and TTR protein deposits in tissues.
- **Dose:** 25 mg once every 3 months.
- Provide vitamin A supplementation at the recommended daily allowance during therapy. If patients develop ocular symptoms consistent with vitamin A deficiency (eg, night blindness), refer to an ophthalmologist.



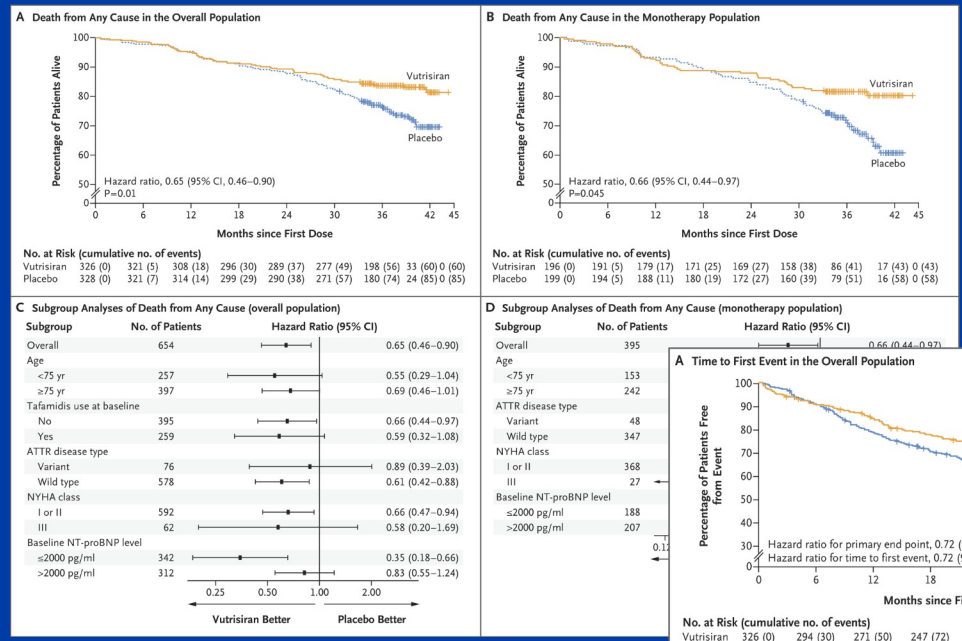
MANAGEMENT: SILENCER - VUTRISIRAN

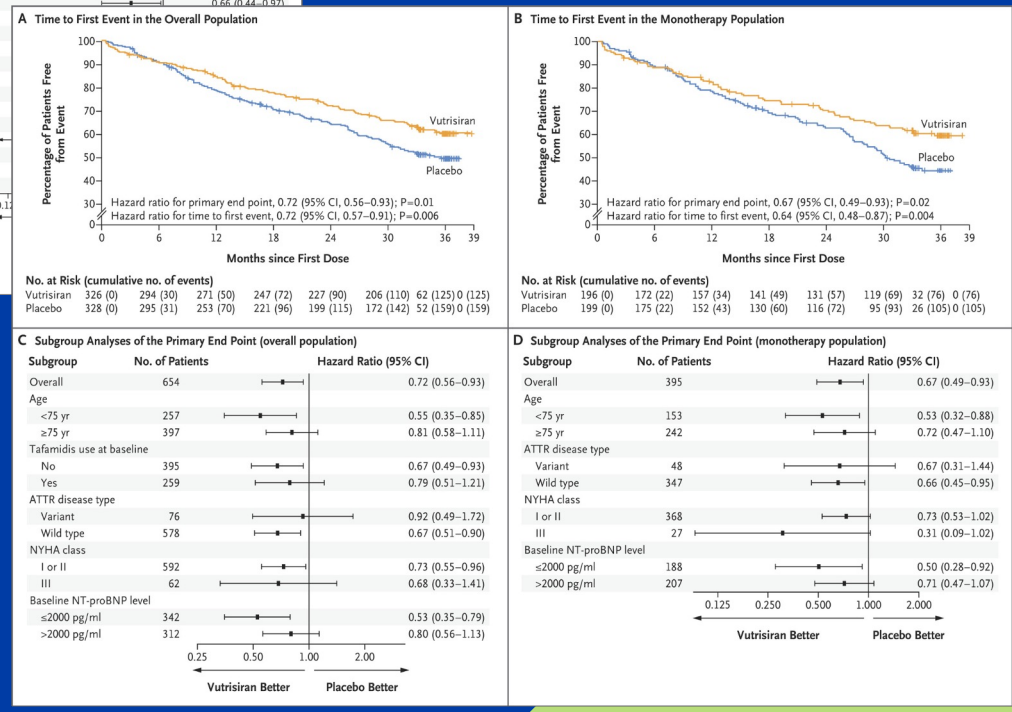
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Vutrisiran in Patients with Transthyretin Amyloidosis with Cardiomyopathy

M. Fontana, J.L. Berk, J.D. Gillmore, R.M. Witteles, M. Grogan, B. Drachman, T. Damy, P. Garcia-Pavia, J. Taubel, S.D. Solomon, F.H. Sheikh, N. Tahara, J. González-Costello, K. Tsujita, C. Morbach, Z. Pozsonyi, M.C. Petrie, D. Delgado, P. Van der Meer, A. Jabbour, A. Bondue, D. Kim, O. Azevedo, S. Hvitfeldt Poulsen, A. Yilmaz, E.A. Jankowska, V. Algalarrondo, A. Slugg, P.P. Garg, K.L. Boyle, E. Yureneva, N. Silliman, L. Yang, J. Chen, S.A. Eraly, J. Vest, and M.S. Maurer, for the HELIOS-B Trial Investigators*

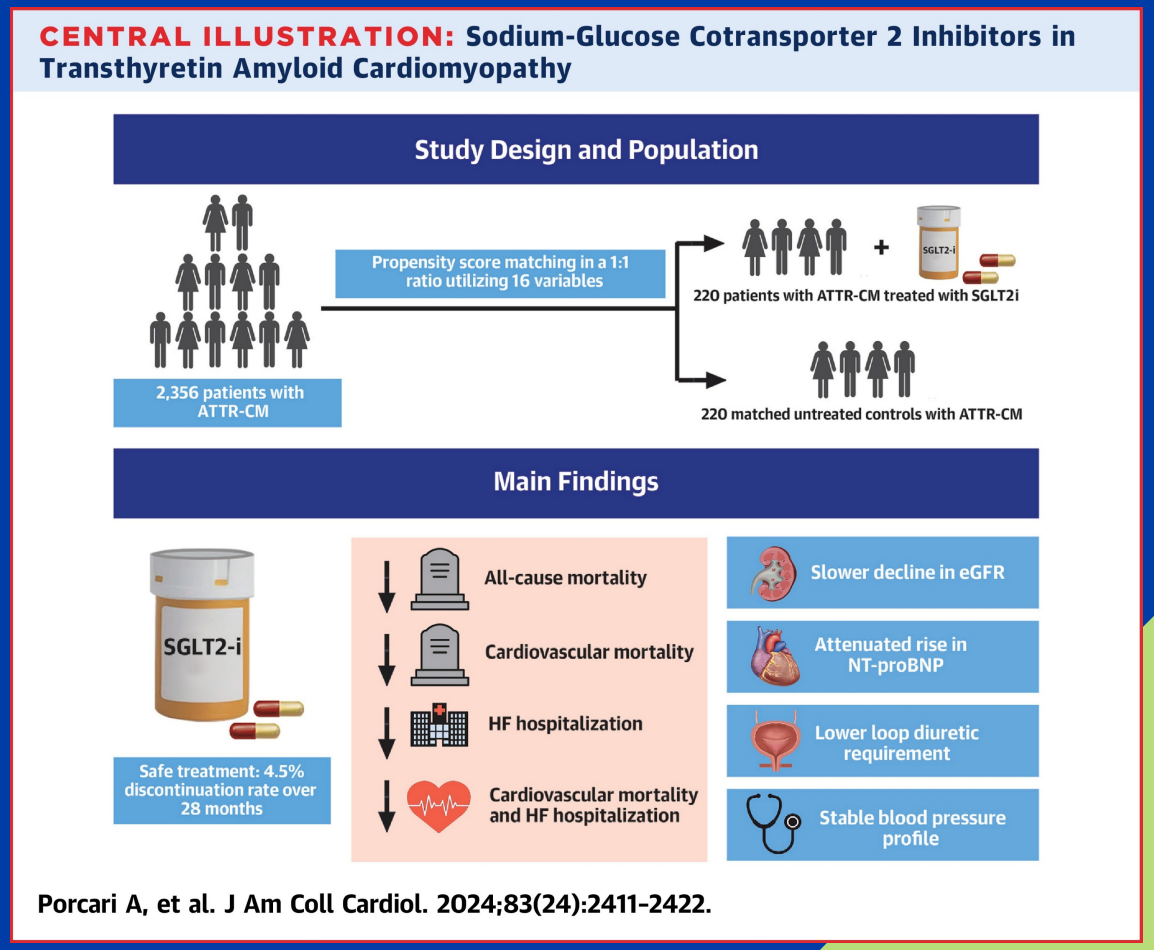




- Multi-center, double blind, phase three placebo- controlled trial
- 654 patients
- Randomized 1:1 to receive vutrisiran 25 mg vs placebo
- 40% patients already taking tafamidis and additional 12% were started on tafamidis during the study period
- 36 months
- Primary endpoint: composite of death from any cause and recurrent cardiovascular events

MANAGEMENT : HEART FAILURE MANAGEMENT

- If HFrEF: limited evidence for traditional GDMT
- Loop diuretics for decongestion
- Often BB not well tolerated in advanced disease -> this is due to fixed stroke volume, though this is generally in later stage amyloid
    - Often diagnosed earlier these days
- In AL CCBs bind to amyloid fibrils and can lead to HB
- Observational studies with potential benefit for SGLT2i and MRA



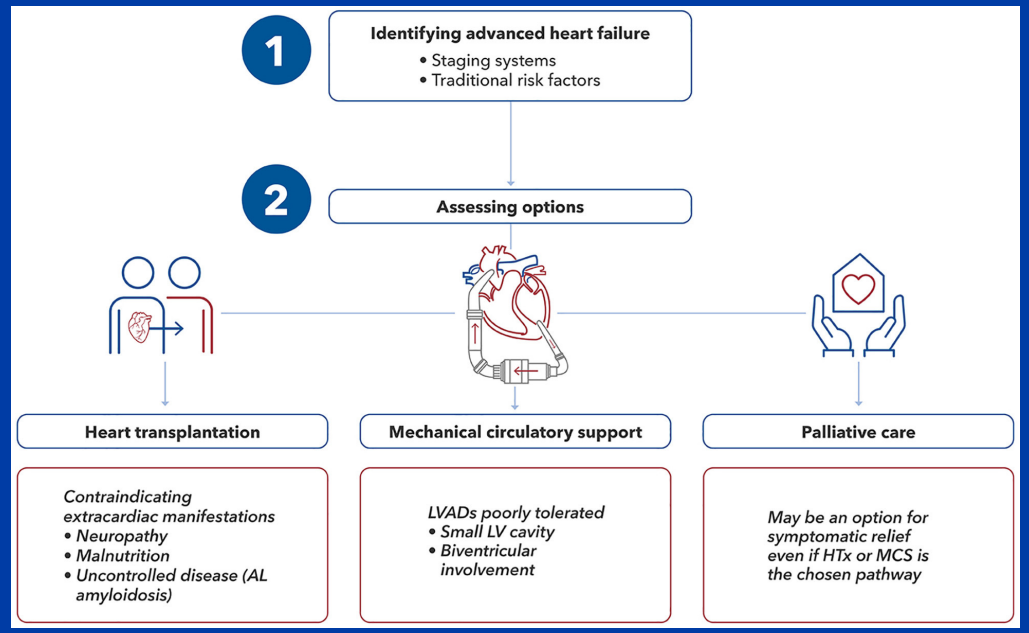
Ioannou A, Massa P, Patel RK, Razvi Y, Porcari A, Rauf MU, Jiang A, Cabras G, Filisetti S, Bolhuis RE, Bandera F, Venneri L, Martinez-Naharro A, Law S, Kotecha T, Virsinskaite R, Knight DS, Emdin M, Petrie A, Lachmann H, Wechelakar A, Petrie M, Hughes A, Freemantle N, Hawkins PN, Whelan C, McMurray JJV, Gillmore JD, Fontana M. Conventional heart failure therapy in cardiac ATTR amyloidosis. Eur Heart J. 2023 Aug 14;44(31):2893-2907. doi: 10.1093/eurheartj/ehad347. Erratum in: Eur Heart J. 2024 Apr 7;45(14):1251. doi: 10.1093/eurheartj/ehae140. PMID: 37216684; PMCID: PMC10424879.

MANAGEMENT : ARRHYTHMIA MANAGEMENT

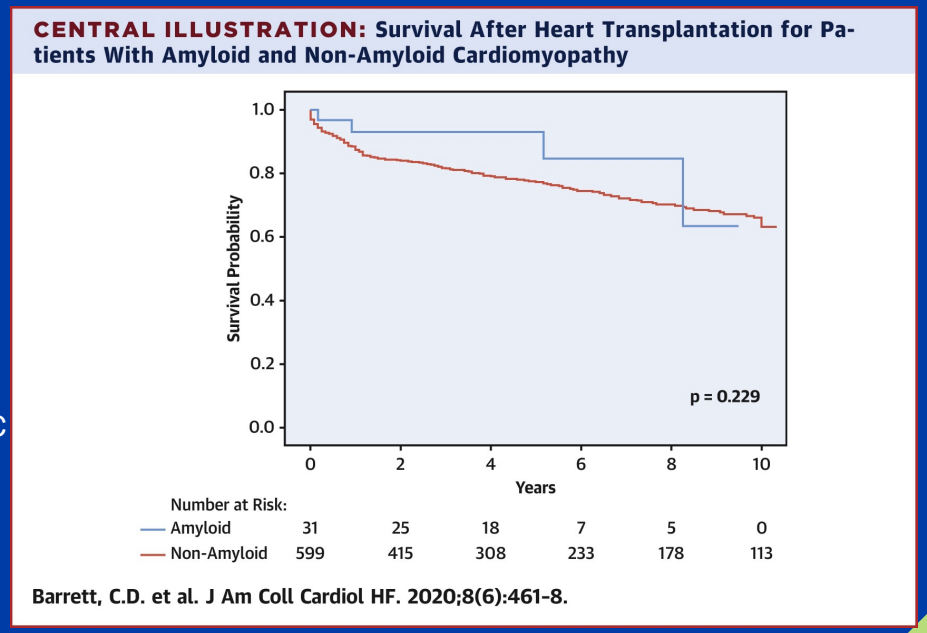
- Atrial Fibrillation
  - Anticoagulation regardless of CHA2DS2-VASc
  - Often do not tolerate AF well
  - No evidence for rhythm vs rate control

- Conduction system disease
  - Monitoring recommended at least with EKG
  - IIb recommendation for ICD in patients with amyloid CM and NSVT on monitoring
    - No recommendation for primary prevention
  - CRT may be helpful in PPM-dependent patients given pre-existing myocardial dysfunction

MANAGEMENT : ADVANCED THERAPIES



In carefully selected patients with cardiac amyloidosis, heart transplantation can be an effective therapeutic option with outcomes like those transplanted for other causes of heart failure.



Barrett CD, Alexander KM, Zhao H, Haddad F, Cheng P, Liao R, Wheeler MT, Liedtke M, Schrier S, Arai S, Weisshaar D, Witteles RM. Outcomes in Patients With Cardiac Amyloidosis Undergoing Heart Transplantation. JACC Heart Fail. 2020 Jun;8(6):461-468. doi: 10.1016/j.jchf.2019.12.013. Epub 2020 May 6. PMID: 32387068.
Writing Committee; Kittleson MM, Ruberg FL, Ambardekar AV, Brannagan TH, Cheng RK, Clarke JO, Dember LM, Frantz JG, Hershberger RE, Maurer MS, Nativi-Nicolau J, Sanchorawala V, Sheikh FH. 2023 ACC Expert Consensus Decision Pathway on Comprehensive Multidisciplinary Care for the Patient With Cardiac Amyloidosis: A Report of the American College of Cardiology Solution Set Oversight Committee. J Am Coll Cardiol. 2023 Mar 21;81(11):1076-1126. doi: 10.1016/j.jacc.2022.11.022. Epub 2023 Jan 23. Erratum in: J Am Coll Cardiol. 2023 Mar 21;81(11):1135. doi: 10.1016/j.jacc.2023.02.013. PMID: 36697326.

THE ROAD AHEAD: EMERGING THERAPIES

Clinical Trials available at Northwell for ATTR-CA

- TRITON-CM : Phase 3 - Evaluate the efficacy of ***nucresiran*** compared to placebo on reducing all-cause mortality and cardiovascular events, on additional assessments of cardiovascular events and/or death, and on patient-reported health status and health-related quality of life. ACTIVELY ENROLLING.

- CLEOPATTRA: Phase 3 - Evaluate whether treatment with ***coramitug*** can help reduce the risk of heart-related death and illness in participants with ATTR-CM. EXPECTED START 05/2026.

- MAESTTRO: Non-interventional, Prospective, Multi-country Study Collecting Real-world Data on the Characteristics, Treatment Patterns, and Outcomes of Patients With Transthyretin (ATTR) Amyloidosis. ACTIVELY ENROLLING.

CONCLUSIONS

It is NOT rare

- 16.8% of patients with **HFpEF** have ATTR
- 16% of patients undergoing **TAVR** for severe AS have ATTR
- 11.7% of patients referred for **TEER** for severe MR were noted to have concomitant cardiac amyloidosis
- 9% of patients initially labelled as **HCM** had cardiac amyloidosis

Recognize clinical clues

- Orthopedic: carpal tunnel, lumbar stenosis, tendon rupture
- Cardiac: Increased LV wall thickness, apical sparing on strain, low voltage on EKG
- Neurological: Polyneuropathy, autonomic dysfunction

Essential to rule out AL

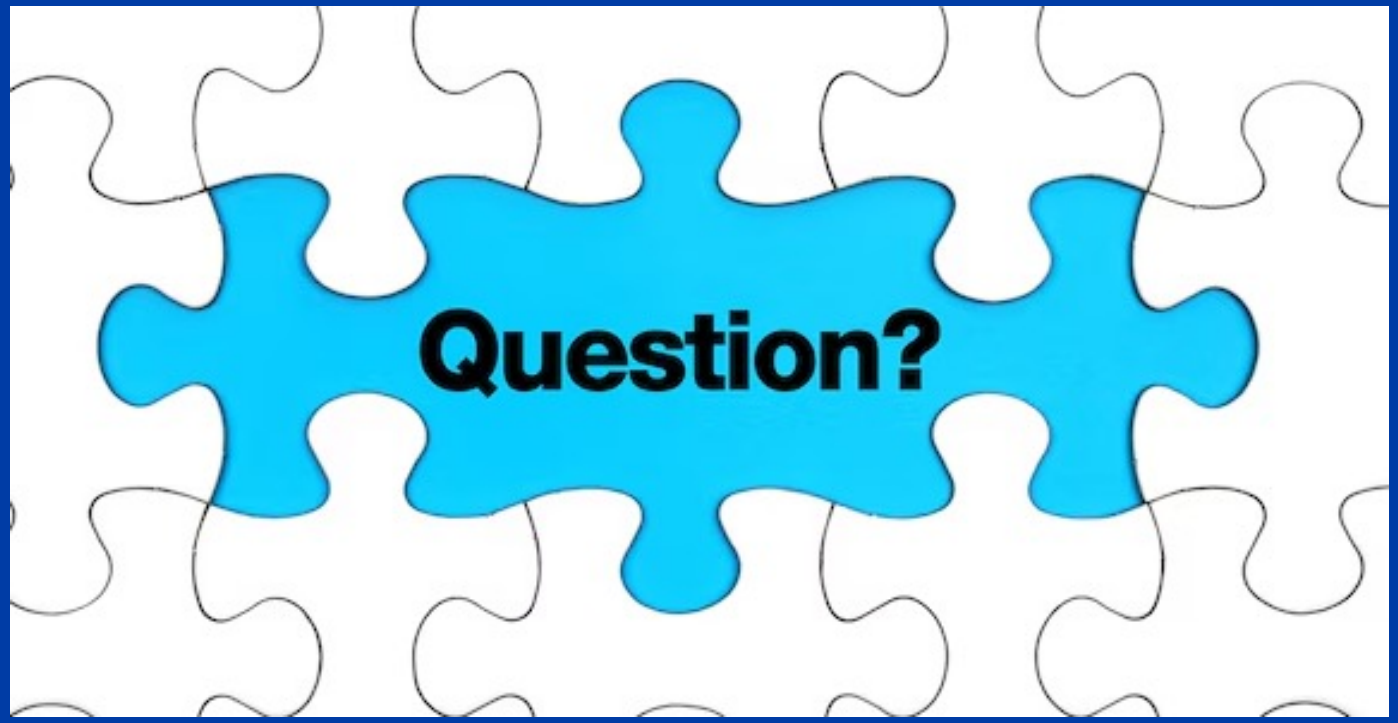
- Requires IFE of urine and serum, serum free light chain assay
- Negative AL testing has high NPV for AL
- Negative AL & PYP + → non-invasive diagnosis of ATTR

Early diagnosis

- Screen high-risk patients
- Use multi-modality imaging (Echo w / strain, Nuclear scan, Cardiac MRI)
- Approved treatments for ATTR-CM: Stabilizer (tafamidis, acoramidis), Silencer (Vutrisiran)
- Clinical trials: Silencer (Eplonterson), Degraders (Coramitug), Gene therapy (CRISPR-CAs9)

“From nothing we can do to a treatable disease”

WE ARE TRULY CRACKING THE CODE



REFER EARLY!

Contact information:

For referrals, please call at (516) 562-1462

Email: duppal@northwell.edu

THANK YOU

Northwell[SM]
Cardiovascular Institute