

Cardiac Amyloidosis As a Reason for
Heart Failure Exacerbation Among Older Adults:
The Impact of its Increasing Diagnosis in PALTC

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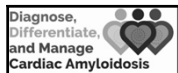
Past President, American Society Nuclear Cardiology

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Disclosures

- Pfizer: Speaker, Consultant
- Alnylam : Consultant, Speaker
- BridgeBio: Consultant
- Ionis: Grant reviewer
- Astellas: Speaker (inactive)

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Learning Objectives

- Understand that amyloidosis has a broad range of clinical manifestations that makes recognition difficult
- Identify which cardiac patients have signs or symptoms consistent with cardiac amyloidosis
- Learn indications for non-invasive testing for cardiac amyloid and how to interpret results
- Understand the value of early diagnosis on treatment options and prognosis

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Q1. Which inherited TTR gene variant is present in 3-4 of AfroAmericans is the most common in the US

- 1. Thr(60)Ala (T60A)
- 2 Val MET 30(V30M)
- 3. Val122Ile (V122)
- 4. Ile68Leu (I68L)

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Q2 Other than Endomyocardial Biopsy, Which of the Following Tests can be considered Diagnostic of wATTR

- CMR with increased ECV and Increased thickness
- Grade 3 PYP scan with negative clonal testing
- Grade 2 Pyp scan with elevated ntBNP and hs Troponin
- ECHO showing increased left ventricular thickness and abnormal longitudinal strain

5

Q3.

* 3. You suspect cardiac amyloidosis based on heart failure and history of bilateral carpal tunnel syndrome. Echocardiogram shows classic findings with left ventricular wall thickening and abnormal longitudinal strain with an apical sparing pattern. Serum free light chain assay was abnormal with elevated Kappa light chains, normal lambda light chains and a highly abnormal Kappa to lambda ratio. The patient's renal function was normal. The next best test to perform is:

- 1) Cardiac Magnetic Resonance-CMR
- 2) Endomyocardial biopsy
- 3) 99mTC-PYP imaging
- 4) TTR genetic test
- 5) No further testing needed

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Q4. A 77yoman with HFpEF has an echo suspicious for cardiac amyloidosis. He has a history of bilateral carpal tunnel surgery. Which test of the following would you order?

- 1) Tc- PYP scan , SPEP, UIEP
- 2) Serum light chains and serum and urine immunoelectrophoresis
- 3) CMR
- 5) Tc-99m PYP scan with serum and urine electrophoresis

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A Sad Story

- 76 yo Afro-Caribbean male with history of pacemaker 5 yrs prior. NO hx DM, HTN, CAD
- Saw Cardiologist two months prior. "Everything was good."
- Stress test negative
- ECHO EF 48% , Bi-atrial enlargement
Moderate concentric LVH

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WW

- Presented to ER abdominal pain, 20 pound weight loss , SOB, inability to walk
- Long history of numbness in hands and toes.
- Attributed to cervical and lumbar radiculopathy
- Progressive decrease in ability to walk

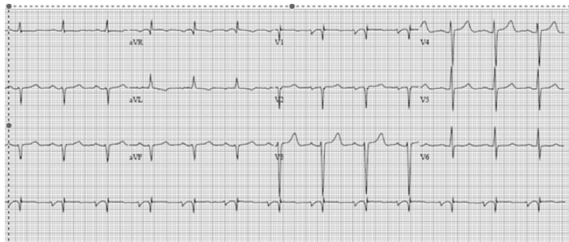
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WW – Data BAsE

- BUN/CR =28/1.2
- Nt-BNP 3200
- Tn 0.66
- EF 38%

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ECG



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ECHO



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Clinical Impression

- Heart failure – chronic diastolic
- Profound weakness and ambulatory limitation -refer to Neurology
- Weight loss , cachexia – refer to GI
- No testing to evaluate etiology of cardiac disease

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Neurology

- HX of C-spine fusion
- Bilateral arm weakness
- Atrophy of hand muscles
- Carpal tunnel
- Spine CT order , PT
- No other diagnostic test
- No explanation why he could not walk

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Gastroenterology

- Mild weight loss possibly due to systolic heart failure
- Suggest nutritional support – ENSURE
- No workup or testing

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Neurosurgery Consult

- Bilateral neuroforaminal spinal stenosis
- Not a candidate for surgery due to EF 38%

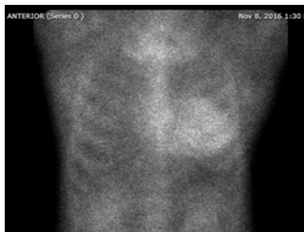
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Returned to ER Six Weeks Later

- Weaker , SOB, unable to swallow , unable to walk without use of walker
- ECG = new Afib
- ECHO= EF 20%
- Imaging for Amyloid
- Genetic testing

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PYP Planar



Cardiac Uptake
greater than
contralateral bone

Genetic Testing=
Val122I Mutation

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Transferred to Subacute Rehab

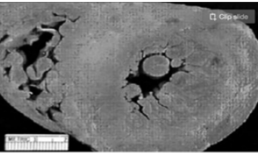
- Returned to ER after two weeks – fluid overload and weak
- Hospitalized x 10 days
- Transferred to nursing home
- Died in hospice 6 weeks later

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Summary

- Chronic Diastolic Heart Failure- Progression to systolic
- Paroxysmal Atrial Fibrillation
- Abnormal ECG- Low voltage
- Abnormal ECHO - LVH, Bi-atrial enlargement
- Peripheral Neuropathy
- Edema
- GI Symptoms –
- Bilateral CTS, spinal stenosis
- Weight loss and Cachexia

=



• Amyloidosis

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A Long Story with a Good Ending

A

Henry Masur

"A person living with HIV has a similar life expectancy to an HIV-negative person – providing they are diagnosed in good time, have good access to medical care, and are able to adhere to their HIV treatment."

— Initial

Hain, M.D., Gary Worr

Article

35 References 790 Citing Articles



DOI: 10.1056/NEJM198112103052402

05/4331-3438

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Clinician Understanding of Amyloid CCF Pilot Study

Results

	Not Confident	Somewhat Confident	Moderately Confident	Very Confident
How confident are you in diagnosing AFib-CM?	52 (88.5)	59 (101.6)	9 (15.5)	8 (13.5)
How confident are you in differentiating the types of AFib-CM?	68 (77.6)	8 (9.3)	6 (8.6)	6 (8.6)
How confident are you in identifying the clinical presentations of AFib-CM (such as HFpEF)?	40 (68.6)	25 (39.5)	10 (17.0)	10 (17.0)
How confident are you in identifying the 10 signs and symptoms of AFib-CM (such as further assessed)?	40 (68.6)	25 (39.5)	10 (17.0)	10 (17.0)
How confident are you in identifying the 10 signs and symptoms of AFib-CM (such as early assessed)?	52 (88.5)	25 (39.5)	10 (17.0)	10 (17.0)
How confident are you in identifying the 10 signs and symptoms of AFib-CM (such as central venous catheter)?	47 (80.3)	20 (32.7)	12 (20.3)	10 (17.0)
How confident are you with nuclear scintigraphy?	56 (94.8)	22 (35.0)	4 (6.5)	6 (8.6)
How confident are you with endomyocardial biopsy?	57 (94.8)	18 (28.2)	10 (17.0)	5 (7.5)
How confident are you with genetic testing to determine if AFib-CM is hereditary?	58 (97.6)	15 (23.0)	8 (13.0)	6 (8.6)
How confident are you in differentiating between light chain amyloidosis (AL) and AFib-CM?	57 (94.8)	18 (28.2)	12 (20.3)	7 (10.5)

Wolinsky, D and Sarkar, A. Submitted for Publication

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Epidemiology of HF

Diamond J .Curr Treat Options Cardio Med. (2022) 24:199.

- 6,000,000 Americans have Heart failure
- More than 1,000,000 hospitalizations per year
- 25% return in 30 days
- 50% return in 6 mo
- 700,000- new cases per year
Half of them HFpEF
- HOSPITALIZATION IS A SENTINAL EVENT
- Recurrent hospitalizations are associated with increased mortality

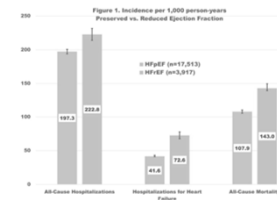
Huusko ESC Heart Failure 2020; 7: 2406-2417

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HFpEF

Prevalence & Epidemiology of HFpEF		
HFpEF Incidence	HFpEF Prevalence	HFpEF Clinical Outcomes
~ 27 cases per 10,000 person-years ~ 1.0% (1% of population) Lifetime risk 1 in 10 at age 65 years	~ 1.0% (1% of population) ~ 10% (10% of population) ~ 30% (30% of population)	> 5 year mortality 75-95% (GFR) (GFR) (GFR) > 30-day all-cause readmission rate 25%
Secular trends	1 incidence over time	1 prevalence over time
Sex differences	HFpEF incidence rising relative to HFpEF	HFpEF prevalence rising relative to HFpEF
HFpEF vs HFpEF	HFpEF incidence rising relative to HFpEF	HFpEF prevalence rising relative to HFpEF

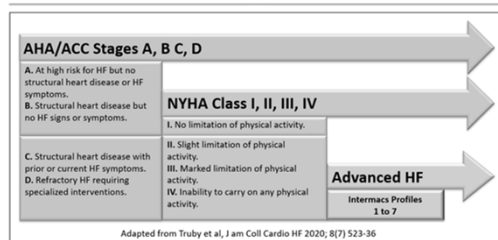
(Borlaug B. Am Coll Cardiol 2023;81:1810-1834)



Nichols et al. Eur Heart J 42 Suppl 1, 2021.

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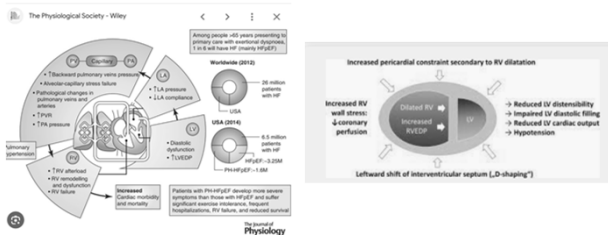
Classification of Heart Failure



Roger V. Circulation Research. 2021;128:1421–1434.

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HFpEF is Both “Forward” and “Backwards” Failure



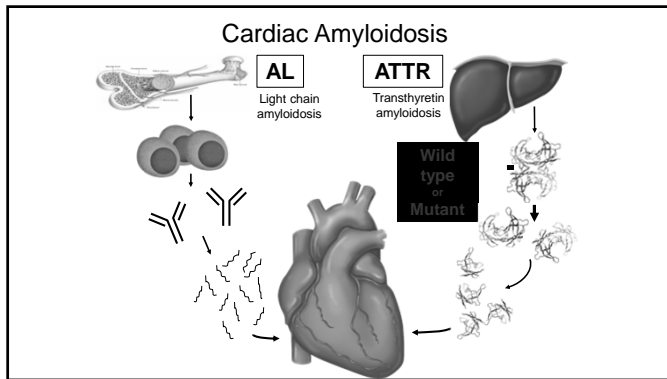
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What is amyloid?

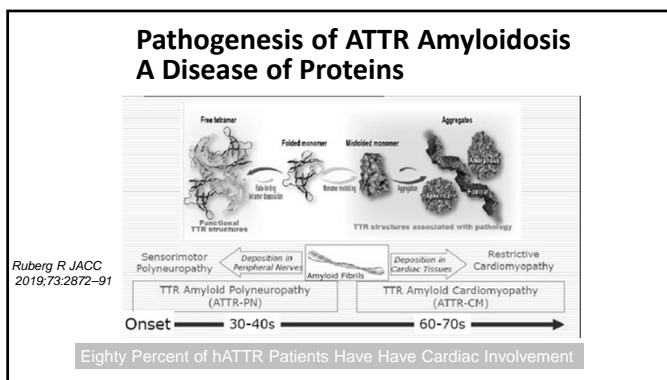
- Amyloid is a protein folding disorder leading to the deposition of insoluble amyloid fibrils in the heart and other tissues
- Amyloid is a systemic disease
- Name derived from Latin amyllum (starch)
- Histological diagnosis - aggregates of β -sheets that stain with Congo Red (green birefringence)

R. Virchow, 1854

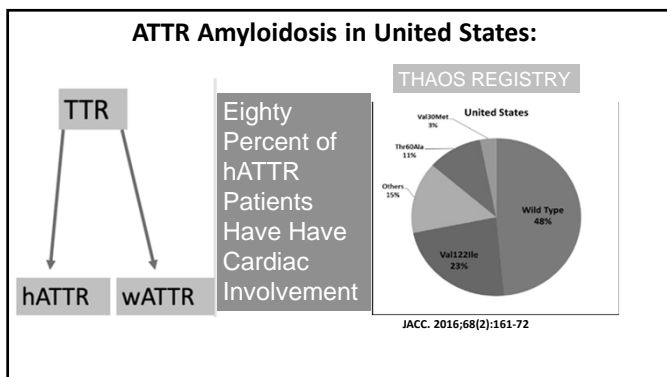
Ruberg, *Circulation* 2012



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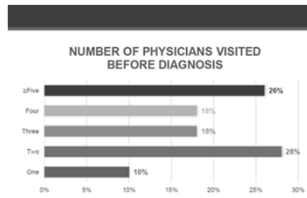
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Delayed Diagnosis of CA

- Time from Initial Sx → Dx is unacceptably high
 - AL-CA: 2 years, ~1/3 visited >5 physicians before Dx
 - ATTR-CA: there was a 3-year (median) delay in diagnosis (ATTR) amyloidosis.



Bishop, Emily E. (2018) Amyloid, DOI: [10.1080/13506129.2018.1498782](https://doi.org/10.1080/13506129.2018.1498782)
Maurer Circulation q2017;135:1357-1377.

Lousada et al., Adv Ther, 2015)

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Prevalence wATTR

Wild-type transthyretin amyloidosis as a cause of heart failure with preserved ejection fraction 
Esther González-López, María Gallardo Delgado, Gonzalo Guzzo-Moreno,
F. Javier de Haro del Moral, María Cobo-Ramos, Carolina Robles, Belén Borrás,
Clara Salas, Enrique Lara-Pérez, Luis Alonso-Pulgar... Show more
European Heart Journal, Volume 36, Issue 36, 7 October 2015, Pages 2585-2594,
<https://doi.org/10.1093/eurheartj/ehv338>
Published: 29 July 2015 Article history

Conclusion

ATTRwt is an underdiagnosed disease that accounts for a significant number (13%) of HFpEF cases. The effect of emerging TTR-modifying drugs should be evaluated in these patients.

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We Cannot Afford Not to Look for and Treat ATTR-CA

Heart Failure With Preserved Ejection Fraction Time for a Reset

Katherine A. A. Clark, MD, MBA¹, Eric J. Velazquez, MD²

¹ Author Affiliations

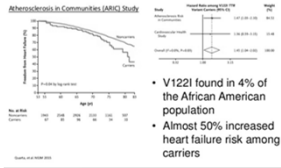
JAMA. 2020;324(15):1506-1508. doi:10.1001/jama.2020.15566

Of the estimated 5 million patients in the US diagnosed with heart failure (HF), approximately 50% have HF with preserved ejection fraction (HFpEF),^{1,2} and its prevalence is increasing by about 1% annually relative to that of heart failure with reduced ejection fraction (HFrEF).³ The mortality associated with HF is substantial, and HF was estimated to account for more than 80 000 deaths annually in the US as of 2017.⁴ In addition, because HF is projected to account for an estimated \$69.8 billion in annual health care spending by 2030, HFpEF represents an important public health issue that will increase as the population ages, with a concurrent increasing prevalence of associated risk factors, including hypertension, obesity, and diabetes.⁴

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V122I Mutation

Va1122ile mutation



Jacobson et al. NEJM 1997
Buxbaum et al. JACC 2006
Jacobson et al. Am J Cardiol 2011
Quarta et al. NEJM 2015

- General Profile
 - Age > 65 yrs
 - Heart failure symptoms
 - Severe symmetric "LV hypertrophy", Normal or mildly depressed LV ejection fraction
 - Normal or near normal QRS voltages
 - No or minimal neurologic impairment
 - Carpal tunnel syndrome (typically 8-10 years before heart failure symptoms)
 - Low penetrance but increased risk of incident heart failure

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Underdiagnosis

AMYLOIDOSIS IS LIKELY UNDER-DETECTED



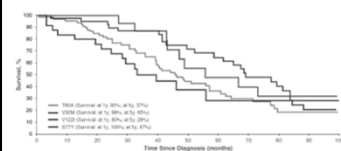
- Why do States with Highest Black Populations Have the Lowest Death Rates Due to Amyloid?
- Failure to Evaluate-Diagnose

Alexander KM JAMA Cardiol. 2018;8654-870

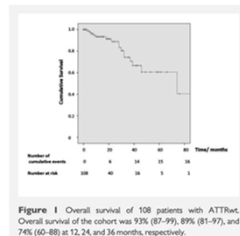
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Prognosis of ATTR CM- Historical

hATTR amyloidosis can lead to premature death in 4.7 years*



HEREDITARY



European Heart Journal (2017) 38, 1895-1904

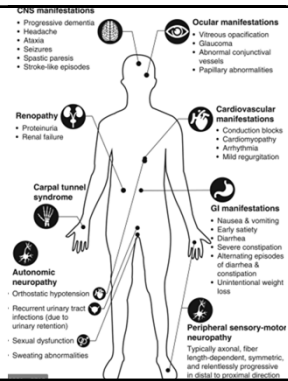
WILD TYPE

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Myriad of Symptoms in ATTR Amyloid

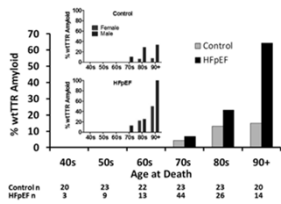
Stop, Look, Listen, then
Test
Remove Your
Preconceived Notions

Wiley OnLine Library



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HFpEF and ATTR

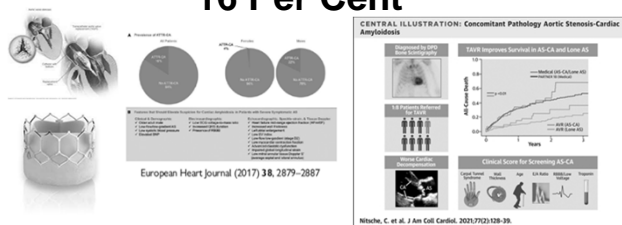


r Tanskanen, *Ann Med*, 2008; Cornwell, *Am J Med*, 1983; Mohammed, *JACC HF*, 2014

Mohammed *JACC Heart Fail* 113-22

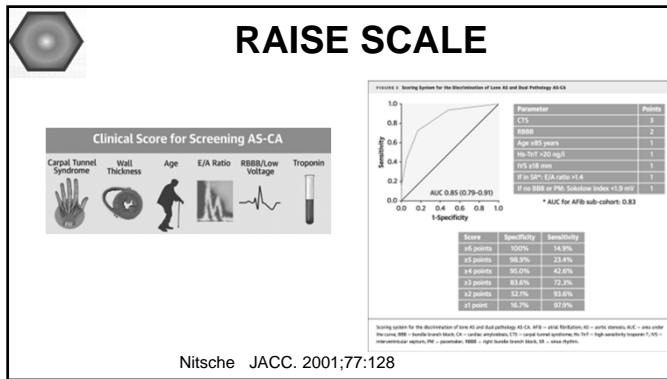
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Aortic Stenosis and ATTR 16 Per Cent



Nitsche, *J Am Coll Cardiol* 2021

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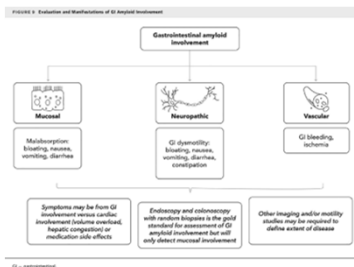
Orthopedic Abnormalities

- 10% of pts with bilateral carpal tunnel syndrome have ATTR
- 50% of ATTR patients have Bilateral CTS
- Up to 1/3 of patients undergoing spinal stenosis stain positive for amyloid
- Trigger finger
- Multiple joint replacement
- History rotator cuff surgery

Nativi-Nicolai, J. Heart Failure Reviews (2022) 27:785–793 Nicolai.

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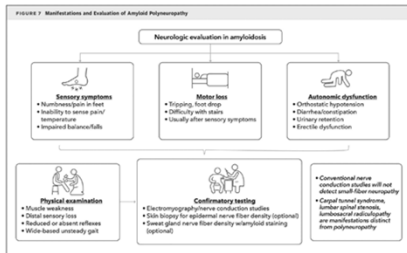
GI Manifestations ATTR



Kittleson et al
-2022-— 2023 ACC Expert Consensus Decision Pathway on Cardiac Amyloidosis

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Neurologic Manifestation of Amyloid



Kittleson et al 2022:— 2023 ACC Expert Consensus Decision Pathway on Cardiac Amyloidosis

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Most Common Confounding Diagnoses

- Hypertensive heart disease
- Hypertrophic Cardiomyopathy -40 % of LV increased thickening in A TTR-CM may be asymmetric.
- Five percent of HOCUM patients may also have cATTR
- Infiltrative Cardiomyopathy
- Aortic Stenosis – 14% patients presenting for TAVR also have ATTR -CM

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What is the “typical” ECG pattern cardiac Amyloid

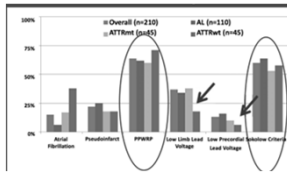
Low voltage limb leads.
Poor R wave progression



Figure 1. ECG of a patient with cardiac AL amyloidosis showing small QRS voltages (defined as ≤ 6 mm height), predominantly in the limb leads and pseudoinfarction pattern in the anterior leads.

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Commonest ECG Findings



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

Kittleson M. Circulation. 2020;142:e7-e22

- Low Voltage present in 40%
- Associated with advanced disease
- Lack of low voltage should not dissuade amyloid workup in appropriate patient

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Clues to Cardiac Amyloid – LVEF

- HFpEF- But usually mildly reduced LVEF .
- Typical EF 45-50%.
- HFrEF 30-45% does not preclude consideration of amyloid
- Severe LV dysfunction EF 10-25% unusual in absence of severe disease
- Increase LV thickness on ECHO without LVH on ECG

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Electrophysiologic Findings

- Refractory atrial fibrillation- multiple cardioversions and ablations
- RBBB with first degree A-V block or LAHB
- Intolerance to RV pacing
- Clinical deterioration in setting of rhythm management

Rappezzi C. Circulation. 2009;120:1203-1212

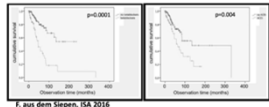
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Clinical-hemodynamics- Low Output

Low- normal BP in
setting of prior
hypertension

Intolerance

ACE/ARB and Beta Blockers in TTR Amyloid



F. von dem Stepen, ISa 2016

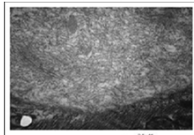
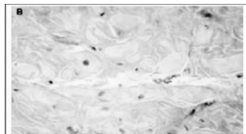
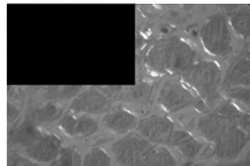
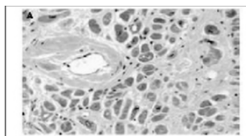


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Diagnostic Workup

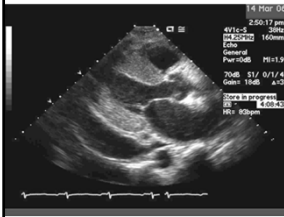
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“Gold Standard”-Endomyocardial Biopsy



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Cardiac Amyloidosis - Echo Suspicion

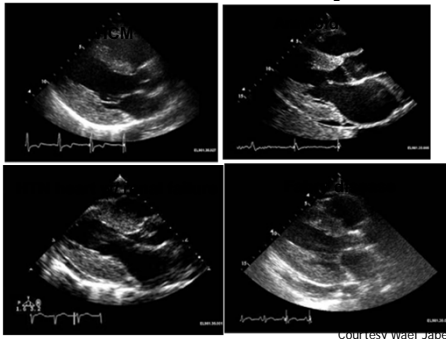


Echo Findings:

- Biventricular ↑ wall thickness
- "Granular sparkling pattern"
- ↑ RA and LA size / dyfn / stasis
- Mechanically silent Atria
- Thickened valves / atrial septum
- Pericardial effusion
- Pulmonary HTN
- Low stroke volume
- Abnormal diastolic function

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Which of these are Amyloid



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What is Strain?

= tissue deformation as a function of applied force

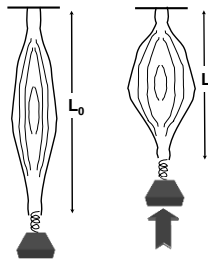
= relative change of length of an object (e.g. myocardial fiber)

L_0 = initial length

L = compressed length

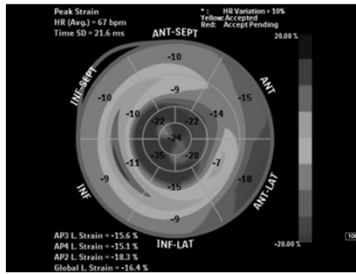
Strain = $(L - L_0)/L_0$

Strain Rate = rate of change



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Apical Sparing



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ECHO

- Suggestive not diagnostic or pathognomic
- Not all patients with typical echo findings have amyloid
- Not all patients with amyloid have all the echo findings
- CANNOT PRESCRIBE THERAPY BASED ON ECHO ALONE
- SUGGESTIVE ECHOES NEED FOLLOWUP

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Fat Pad Aspirate Poor Test for ATTR

- Sensitivity for AL amyloid of 70 % at best
- Positive in < 50 % of subjects with TTR cardiac amyloid



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Potential Utility of CMR in Cardiac Amyloidosis

1. Increase suspicion of presence of disease
2. Diffuse late enhancement that can either be subendocardial or transmural, that does not follow coronary distribution,
3. poor myocardial signal nulling on PSIR LGE sequence
4. Marked increase in extracellular volume (>40%) or native (non-contrast) T1
5. Confers prognostic value
 - Transmural or high ECV, worst prognosis
 - Absence of LGE, best prognosis
6. Serial imaging for response to therapy

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ASNC CARDIAC AMYLOIDOSIS PRACTICE POINTS

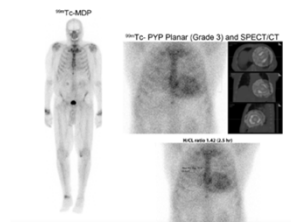
^{99m}Tc-Technetium-
Pyrophosphate Imaging
for Transthyretin
Cardiac Amyloidosis

<https://www.asnc.org/Files/Practice%20Resources/Practice%20Points/ASNC%20Amyloid%20Practice%20Points%20FINALfeb26.pdf>

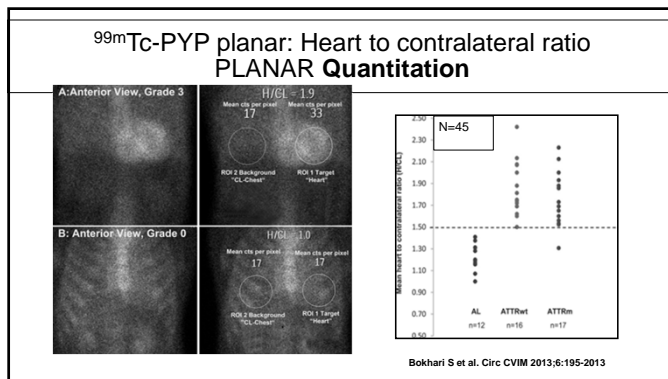
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Tc-PYP Scan

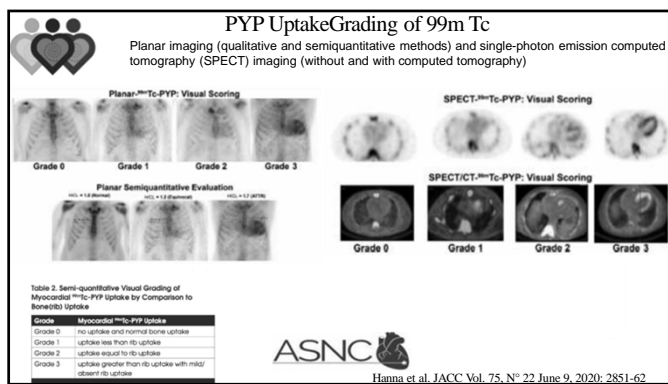
- PYP is calcium avid
- Bone imaging agent
- 1970's used to diagnose acute myocardial infarction
- Mechanism for binding to amyloid tissue unclear



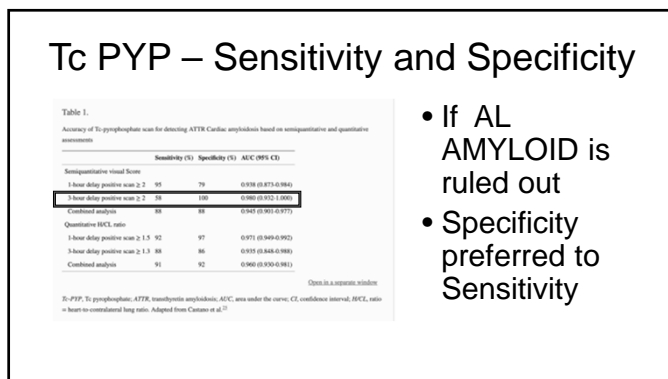
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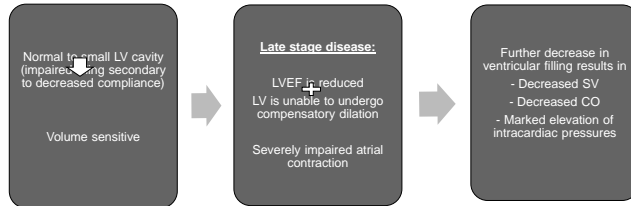
Clonal Testing for AL Amyloid

Test	What Does it Detect?	Most Sensitive Test For	Normal Range
SPEP	Clonal immunoglobulin and/or clonal light chain	Confirming clonal immunoglobulin production	No M spike present
UPEP	Clonal immunoglobulin and/or clonal light chain	Confirming clonal light chain production	No M spike present
Serum Free Light Chain Assay	Ratio of serum kappa lambda light chains	Detecting low level clonal light chain production, clarity assumed if ratio is far from 1:1	Kappa lambda ratio < 0.26-1.65

Assay	Kappa	Lambda	κ/λ Ratio	Result Range*
Freelite	0.33-1.94	0.57-2.63	0.26-1.65	0.37-3.1
mg/dL	3.3-19.40	5.7-26.30		
Siemens N-Latex	0.82-2.89	0.91-3.26	0.53-1.51	Not applicable
mg/dL	8.24-28.9	9.10-32.6		

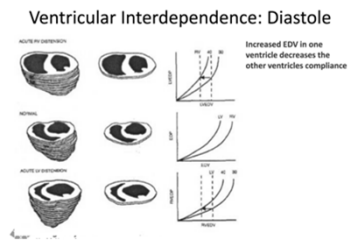
*Proposed extended range of κ/λ ratio using the freelite assay in patients with renal dysfunction, from The Binding Site, Inc. This correction is not applicable to Siemens N-Latex κ/λ assay. Ratios may be reported as κ/λ or λ/κ. A ratio of 1.0 is a ratio of 1:1. A ratio of 0.5 is a ratio of 1:2. A ratio of 2.0 is a ratio of 2:1. A ratio of 0.25 is a ratio of 1:4. A ratio of 4.0 is a ratio of 4:1. A ratio of 0.125 is a ratio of 1:8. A ratio of 8.0 is a ratio of 8:1. A ratio of 0.0625 is a ratio of 1:16. A ratio of 16.0 is a ratio of 16:1. A ratio of 0.03125 is a ratio of 1:32. A ratio of 32.0 is a ratio of 32:1. A ratio of 0.015625 is a ratio of 1:64. A ratio of 64.0 is a ratio of 64:1. A ratio of 0.0078125 is a ratio of 1:128. A ratio of 128.0 is a ratio of 128:1. A ratio of 0.00390625 is a ratio of 1:256. A ratio of 256.0 is a ratio of 256:1. A ratio of 0.001953125 is a ratio of 1:512. A ratio of 512.0 is a ratio of 512:1. A ratio of 0.0009765625 is a ratio of 1:1024. 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PATHOPHYSIOLOGY: Amyloid is not only a disease of abnormal cardiac filling, but also a disease of diminished cardiac output



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Ventricular Interdependence



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Diuretics

- Diuretic - Use Torsemide, Bumetanide, They have better intestinal absorption
- PRN metolazone- do not delay- start with 3-5 lb weight gain
- Spironolactone + loop diuretic is generally well tolerated
- Adjust diuretics based on clinical status
- IV diuretics: Use with close monitoring as it may result in progressive azotemia and hypotension

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Management

- Avoid ACE, ARB, ARNI:
 - Safety and efficacy is uncertain (no clinical trials)
 - May provoke profound hypotension in AL amyloidosis (possibly by exposing a subclinical autonomic neuropathy)
 - Better tolerated in TTR amyloid (wild type)
- Avoid digoxin:
 - Amyloid fibrils bind to it and this interaction may increase risk for digitalis toxicity
- ARNI
 - No concrete data

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Management

- Avoid ACE, ARB, ARNI
 - C
 - b
 - n
- Avoid digoxin
 - M
 - a

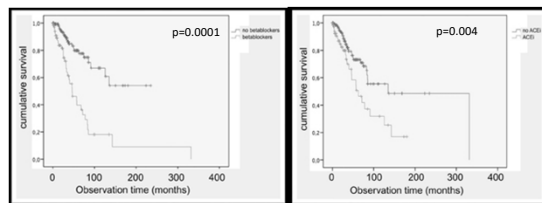


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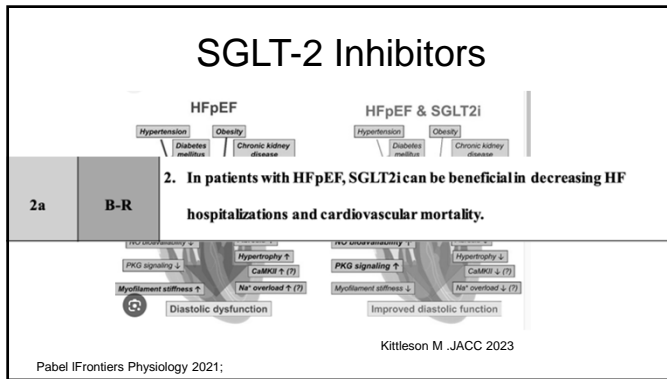
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ACE/ARB and Beta Blockers in Cardiac Amyloid

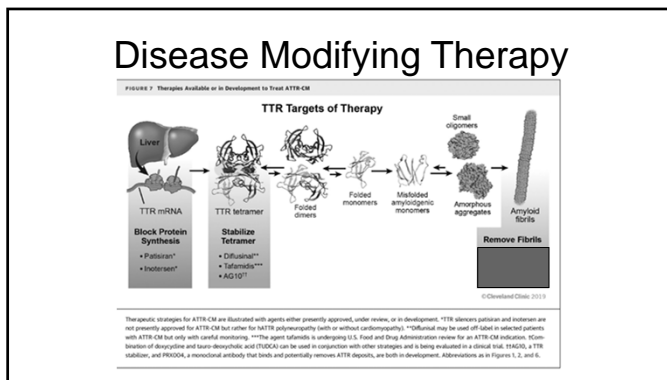


F. aus dem Siepen, ISA 2016

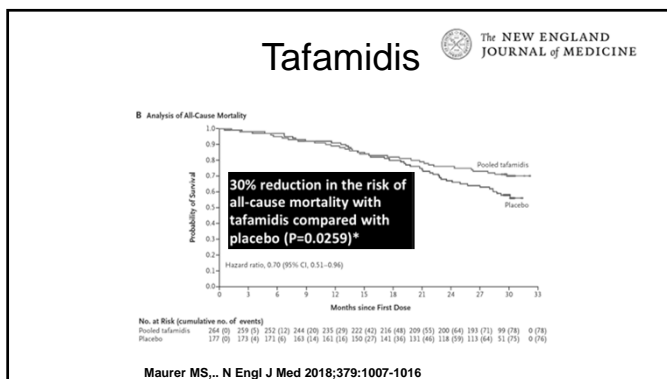
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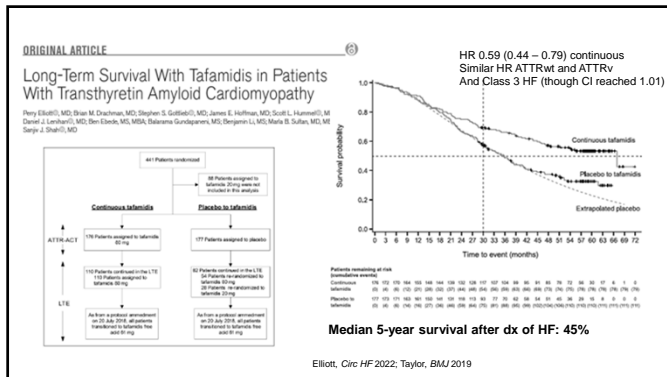
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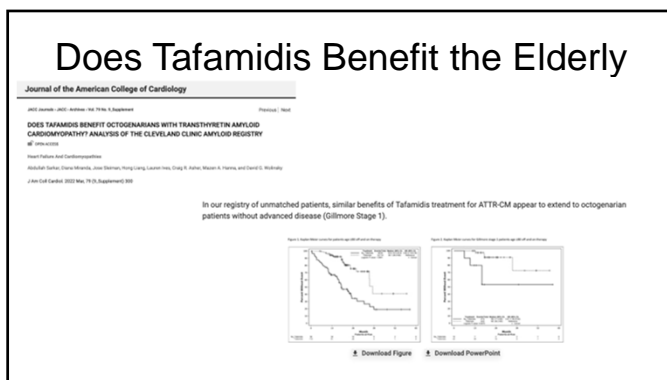
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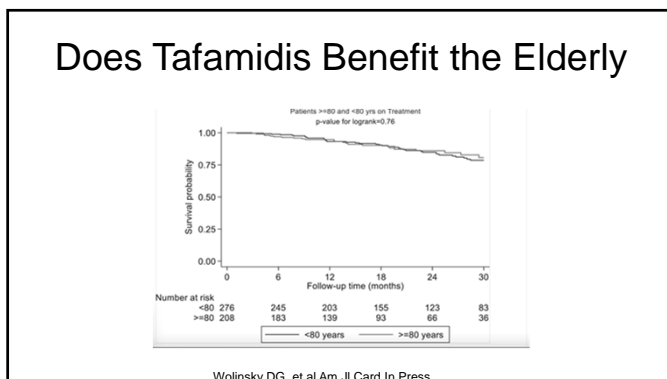
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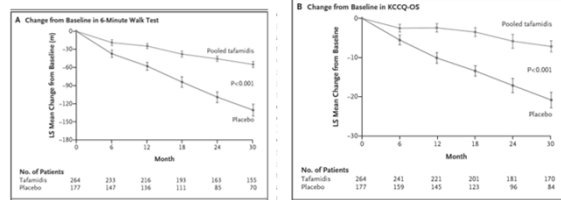


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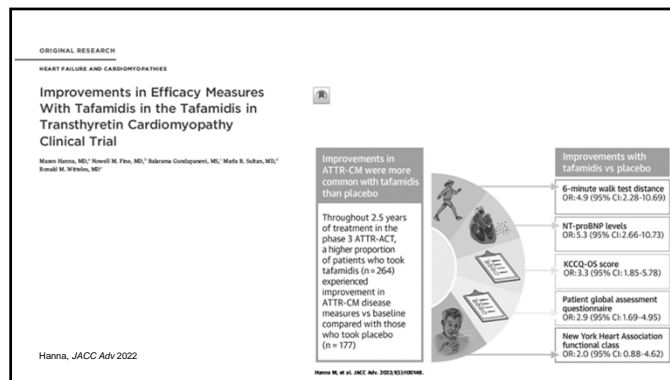
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Tafamidis – Reduces Rate of Clinical Deterioration

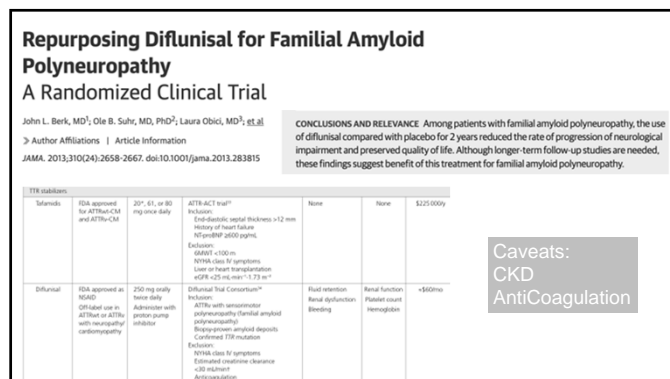


Maurer MS, N Engl J Med 2018;379:1007-1016

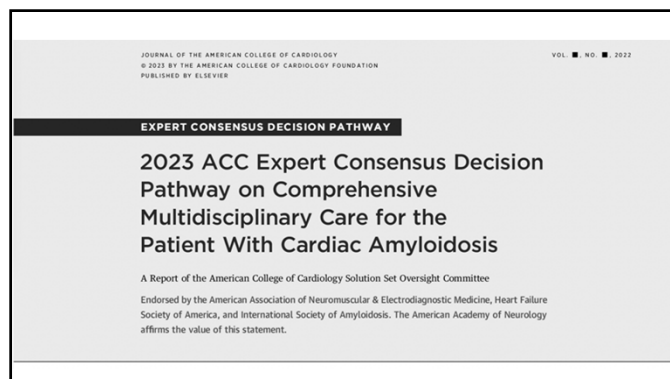
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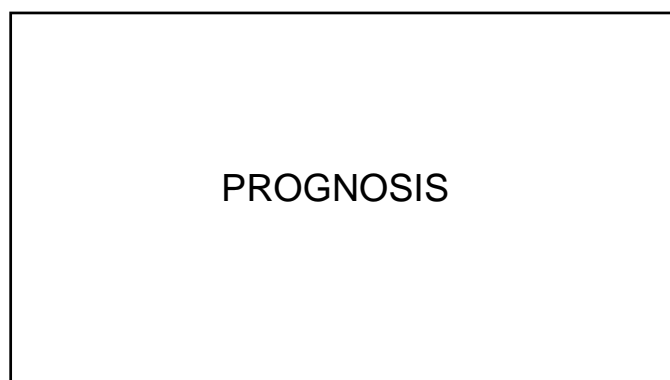
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Staging Systems ATTR Mayo and Gilmour (NAC)

Table 1 Clinical staging systems for transthyretin amyloid cardiomyopathy

Grogan et al., 2016 (Mayo) ¹ ATTRwt		Gilmour et al., 2018 (NAC) ¹⁴ ATTRwt and ATTRwt		Cheng et al., 2020 (Columbia) ¹⁵ ATTRwt and ATTRwt	
Staging parameters: Troponin T >0.05 ng/mL NT-proBNP >3000 pg/mL		Staging parameters: eGFR <45 mL/min NT-proBNP >3000 pg/mL		Scoring parameters: Mayo or NAC score (0 to 2 points) Daily dose of furosemide or equivalent: 0 mg/kg (0 points), >0–0.5 mg/kg (1 point), >0.5–1 mg/kg (2 points), and >1 mg/kg (3 points) NYHA class I–IV (1 to 4 points)	
Stage	Median survival	Stage	Median survival	Score	Mean survival
Stage I (0 parameters)	66 months	Stage I (0 parameters)	69.2 months	Score 1–3	78 months
Stage II (1 parameter)	40 months	Stage II (1 parameter)	46.7 months	Score 4–6	48 months (Mayo) 45.6 months (NAC)
Stage III (2 parameters)	20 months	Stage III (2 parameters)	24.1 months	Score 7–9	26.4 months (Mayo) 22.8 months (NAC)

ATTRwt, variant transthyretin amyloid cardiomyopathy; ATTRwt, wild-type transthyretin amyloid cardiomyopathy; eGFR, estimated glomerular filtration rate; HF, heart failure; NAC, UK National Amyloidosis Centre; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association.

Garcia-Pavia European Journal of Heart Failure (2021)23, 895–905

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Organ dysfunction due to Amyloid infiltration

- Shrinking heart: 100%
- Heart failure, NYCT, chest pain: 100%
- Stomach and digestive tract disease: 90%
- Lowest serum albumin: 90%
- Cardiomegaly: 90%
- Diagnosed cardiomyopathy: 100%
- Neurologic impairment: 90%

Phenotype and Types of Frailty Domains and Status

Domain	Frailty Status
Depression (GDS-15): 100% and 100%	Frailty: 100%
Depression (PHQ-9): 100%	Frailty: 100%
Depression (GDS-15): 100%	Frailty: 100%
Depression (PHQ-9): 100%	Frailty: 100%
Depression (GDS-15): 100%	Frailty: 100%
Depression (PHQ-9): 100%	Frailty: 100%
Depression (GDS-15): 100%	Frailty: 100%
Depression (PHQ-9): 100%	Frailty: 100%
Depression (GDS-15): 100%	Frailty: 100%
Depression (PHQ-9): 100%	Frailty: 100%

33-50 % of Patients with ATTR Demonstrate Frailty

Legend:
 Frail (Red)
 Non-Frail (Green)

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2023 ACC Expert Consensus Decision Pathway on Comprehensive Multidisciplinary Care for the Patient With Cardiac Amyloidosis

PCP: Searching for ATTR

EXPERT CONSENSUS DECISION PATHWAY

CENTRAL ILLUSTRATION Screening for ATTR-CM

Patient populations deemed at risk of ATTR-CM

Heart failure OR presence of "red flag" signs/symptoms	OR	Male >65 years
AND Increased wall thickness >14 mm	OR	Female >70 years

Wittes, R.M. et al. / J Am Coll Cardiol HF. 2019;7(5):309-36.

Patient populations deemed at risk of ATTR-CM to the extent that warrant screening, ATTR-CM = transthyretin amyloid cardiomyopathy.

FIGURE 2 Clinical Manifestations of Cardiac Amyloidosis*

Cardiac	Multisystemic	Neurologic	Autonomic Dysfunction
Heart failure	Cardiac tamponade	Peripheral neuropathy in hands and feet	Orthostatic hypotension/ intolerance to blood pressure medications
Atrial fibrillation	Back pain/radiating spinal stenosis	Weakness, numbness, tingling, and pain	Chronic diarrhea, constipation/weight loss
Bradycardia	Fluid overload	Shoulder, knee and hip pain or surgery	Exercise intolerance
Bradyarrhythmias/conduction system disease	Legg-Strauss	Weakness, difficulty walking and falls	Respiratory dysfunction

Kittleson et al
-2022—2023 ACC Expert Consensus Decision Pathway on Cardiac Amyloidosis

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Clinical characteristics of wild-type trypsinogen cardiac amyloidosis: disproving myths


Editor: González-Lera^{1,2}, Cristina Engdahl³, Fernando Domínguez⁴, Cristina González-Quiroga⁵, Joana de Almeida-Pereira⁶, Agneta Riklund⁷, Clara Balle⁸, Maria Gálvez⁹, Plaza-Cabrera¹⁰, *Rosendo Lera¹¹, Rosendo Lera-Pérez¹², Carmen Pato¹³, Luis Alonso-Agudo¹⁴, Claudio Serrano¹⁵ and Pablo Ramirez-Pardo¹⁶

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Cardiology : Spectrum of Amyloid


ATTRwt's clinical spectrum

↓



Mode of presentation:

- HF (57.5%)
- AF (30.4%)
- Stroke
- HCM or RCM (13.9%)
- Degenerative AS
- Incidental (11.7%)



Age, gender and ethnicity

- Median age at onset (IQR)
- Female (45%)
- 100% of patients were white (n=10)

ECG






- AF (30.4%)
- Left bundle branch block (20.2%)
- Normal (29.2%)
- Prolonged QTc (10.2%)
- Prolonged QT (10.2%)

Echocardiography

- Hypertrophic CM (57.5%)
- Dilated CM (13.9%)
- Normal (11.7%)
- Restrictive CM (16.9%)

Survival

- Median survival at onset (IQR)
- 12, 24 and 36 months: 85, 50 and 24% respectively

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Q1. Which inherited TTR gene variant is present in 3-4 of AfroAmericans is the most common in the US

- 1. Thr(60)Ala (T60A)
- 2 Val MET 30(V30M)
- 3. Val122Ile (V122)
- 4. Ile68Leu (I68L)

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Cardiac Amyloid

- If you don't think of looking for it , you won't find it



But if you find it You can help

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Q1. Which inherited TTR gene variant is present in 3-4 of Afro-Americans is the most common in the US

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Q2 Other than Endomyocardial Biopsy, Which of the Following Tests can be considered Diagnostic of wATTR

- CMR with increased ECV and Increased thickness
- Grade 3 PYP scan with negative clonal testing
- Grade 2 PYP scan with elevated ntBNP and hs Troponin
- ECHO showing increased left ventricular thickness and abnormal longitudinal strain

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Q3.

* 3. You suspect cardiac amyloidosis based on heart failure and history of bilateral carpal tunnel syndrome. Echocardiogram shows classic findings with left ventricular wall thickening and abnormal longitudinal strain with an apical sparing pattern. Serum free light chain assay was abnormal with elevated Kappa light chains, normal lambda light chains and a highly abnormal Kappa to lambda ratio. The patient's renal function was normal. The next best test to perform is:

- 1) Cardiac Magnetic Resonance-CMR
- 2) Endomyocardial biopsy
- 3) 99mTC-PYP imaging
- 4) TTR genetic test
- 5) No further testing needed

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Q3.

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Q4. A 77yo man with HFpEF has an echo suspicious for cardiac amyloidosis. He has a history of bilateral carpal tunnel surgery. Which test of the following would you order?

- 1) Tc- PYP scan , SPEP, UIEP
- 2) Serum light chains and serum and urine immunoelectrophoresis
- 3) CMR
- 5) Tc-99m PYP scan with serum and urine electrophoresis

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Q4. A 77yo man with HFpEF has an echo suspicious for cardiac amyloidosis. He has a history of bilateral carpal tunnel surgery. Which test of the following would you order?

- 1) Tc- PYP scan , SPEP, UIEP
- 2) Serum light chains and serum and urine immunoelectrophoresis
- 3) CMR
- 5) Tc-99m PYP scan with serum and urine immunoelectrophoresis

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SUMMARY

- Amyloidosis is a multisystem disorder caused by the deposition of abnormal proteins in myocardial tissue and other organs
- Cardiac Amyloidosis (ATTR-CM) is an underrecognized cause of heart failure in the elderly population
- ATTR-CM can be identified by invasive techniques in most patients
- AL amyloidosis must be ruled out before the diagnosis of ATTR-CM is made
- Disease modifying therapy is available to stabilize what was once felt to be a terminal disease

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