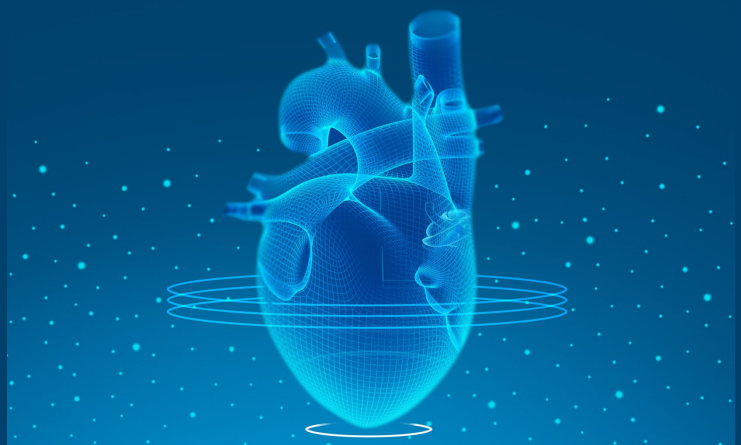
Minneapolis Heart Institute Foundation

GRAND ROUNDS



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Cardiac Amyloidosis:
From Heart Failure to Heart Success

Siu-Hin Wan, MD, FACC, FAHA, FHFSA
Director of Heart Failure, United Hospital
Allina Health Minneapolis Heart Institute

Allina Health
MINNEAPOLIS HEART INSTITUTE

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Disclosures

- No disclosures

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Objectives

- 1. Describe the pathophysiology of cardiac amyloidosis
- 2. Summarize the diagnostic workup and imaging features of cardiac amyloidosis
- 3. Determine prognosis and treatment for cardiac amyloidosis

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Case

- 50 year old African American man
- Worsening exertional dyspnea for 2 months, PAF, carpal tunnel, no Fam Hx
- Exam: JVD, bibasilar crackles, and 2+ pitting bilateral lower extremity edema
- EKG: low voltage limb leads
- Echo: LVEF 55%, grade 2 DD, concentric hypertrophy, thick valves and thick RV free wall, strain with apical sparing
- cMRI: diffuse subendocardial late gad enhancement
- SPEP/UPEP, free light chains, immunofixation: normal kappa/lambda ratio, no monoclonal protein spike, elevated NTproBNP and troponin
- PYP: 3+ visual score
- Genetics: Val122Ile ATTRm

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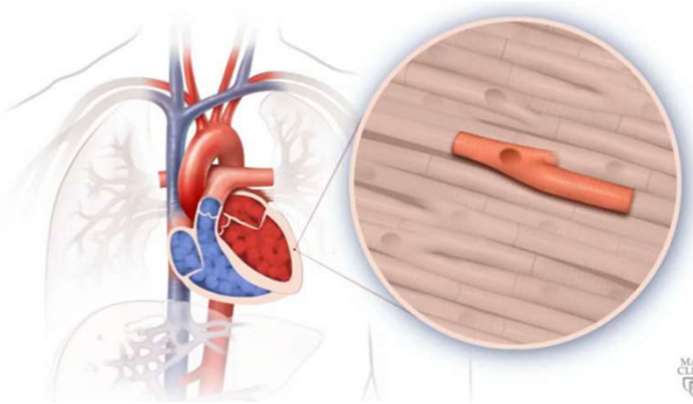
Amyloidosis and the Heart

Definition

- Amyloidosis
  - Extracellular deposition of serum protein fibrils
  - Beta-pleated sheets
  - Deposits in a variety of organs
    - Cardiac
    - Kidney
    - Liver
    - Nervous system



Courtesy: Dr. Martha Grogan

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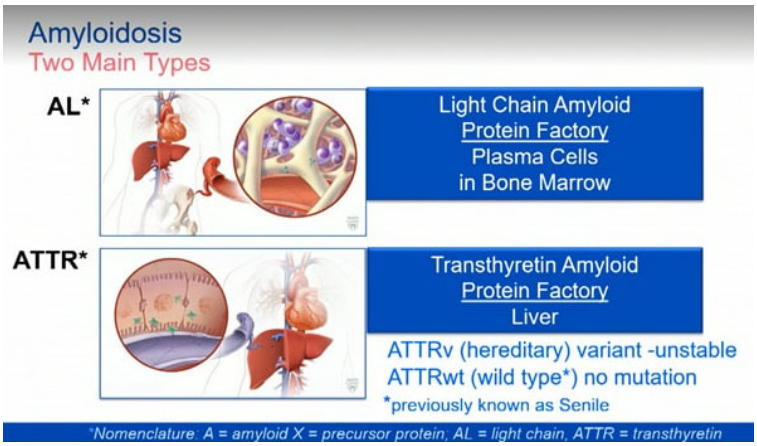
Amyloidosis and the Heart

Cardiac Amyloidosis

- Types of Cardiac Amyloidosis
  - Light chain (AL)
  - Transthyretin (ATTR)
    - Hereditary (ATTRh/m/v)
    - Wild type (ATTRwt)

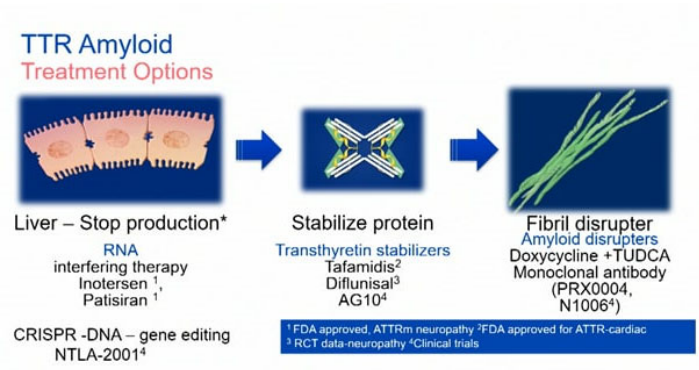


Courtesy: Dr. Martha Grogan

Amyloidosis and the Heart

TTR amyloid

- Transthyretin
  - Produced in liver
  - Transports thyroid hormone
- TTR Amyloid
  - Liver produces TTR, but then breaks apart and monomers form misfolded amyloid and deposit in end organs



Courtesy: Dr. Martha Grogan

Amyloidosis and the Heart

Epidemiology

- Age of onset
  - AL
    - Age >= 40 years
  - ATTR
    - Age >= 70 years
- Cardiac symptoms
  - Dyspnea
  - Lower extremity edema
  - Hepatic congestion
  - Syncope

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Amyloidosis and the Heart

Complications

- Heart failure with preserved ejection fraction
- Arrhythmias
  - Bradycardia and sinus node dysfunction
  - AV block
  - Ventricular arrhythmias
- Thromboembolism
- Aortic stenosis

Cavalcante, J; Schelbert, E; et al. Cardiac amyloidosis is prevalent in older patients with aortic stenosis and carries worse prognosis. Journal of Cardiovascular Magnetic Resonance. 19, 1, 5 Dec 2016, 98.

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Amyloidosis and the Heart

Extra cardiac involvement

AL amyloidosis

- Kidney
  - Proteinuria, nephrotic syndrome
- Peripheral neuropathy
- Carpal tunnel syndrome
- Gastrointestinal
  - GI bleeding
- Macroglossia
- Periorbital purpura

Wan, SH; Gertz, MA; Grogan, M. Periorbital Purpura, Macroglossia, Vessel Fragility, and Restrictive Cardiomyopathy: A Case of Amyloid Heart Disease. Presented at: Asia Pacific Congenital & Structural Heart Intervention Symposium. Hong Kong, China, September 23-25, 2016.

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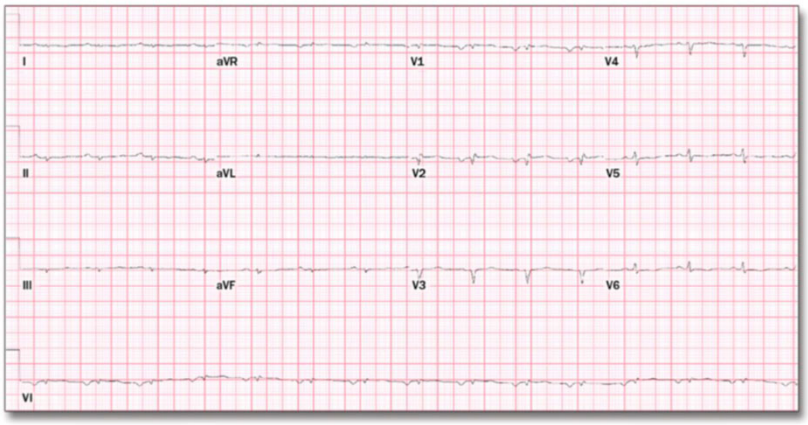
Amyloidosis and the Heart

Diagnosis

EKG

Low Voltage



Courtesy: American College of Cardiology

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Heart Failure and Cardiomyopathies

Cardiac Amyloidosis

Restrictive Cardiomyopathies

- Primary
  - Idiopathic
- Secondary
  - Infiltrative cardiomyopathies
    - Amyloidosis
    - Sarcoidosis
  - Hemochromatosis
  - Storage diseases (eg Fabry)
  - Cancer
  - Radiation

Courtesy: American College of Cardiology

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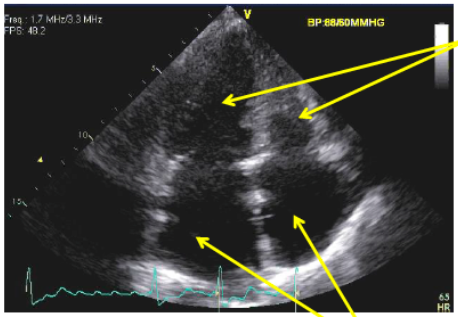
Echocardiography

Features of Restrictive Cardiomyopathies

Echocardiographic features of RCM



Normal RV/LV EF and volumes

Increased LV wall thickness seen infiltrative processes

Bi-atrial enlargement
LA volume index (>50 mL/m^2)

Vaitkus PT, et al. Am Heart J 1991;122:1431–41.

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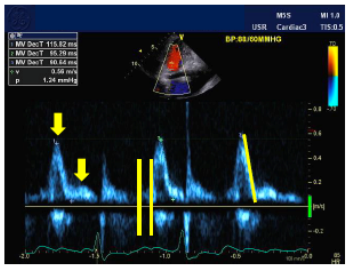
Echocardiography

Features of Restrictive Cardiomyopathies

Predominant early diastolic filling

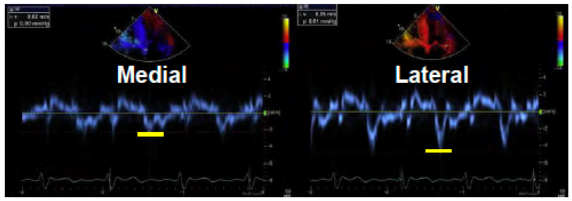
Decreased atrial filling



Decel. time (< 150 msec)

IVRT (< 50 msec)

Decreased septal and lateral e'



E/e' ratio >14

Nagueh SF, et al. *J Am Soc Echocardiogr* 2016;29:277-314. Ha JW, et al. *Am J Cardiol* 2004;94:316–

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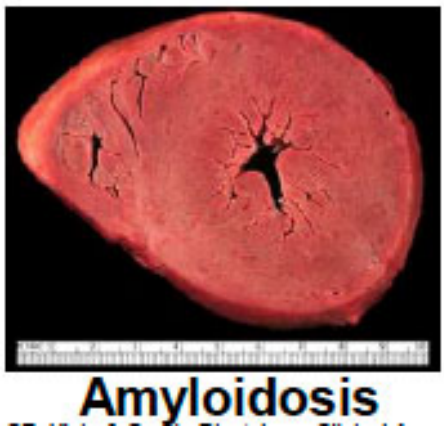
Echocardiography

Features of Cardiac Amyloidosis

Echocardiographic findings

- Biventricular thickening
  - >12mm for LV wall
- Myocardium speckling appearance
- Dilated atria
- Interatrial septal thickening
- Valvular thickening
- Right sided heart failure
  - Dilated IVC
- Pericardial effusion



Courtesy: American College of Cardiology
Dr. Samuel Unzek

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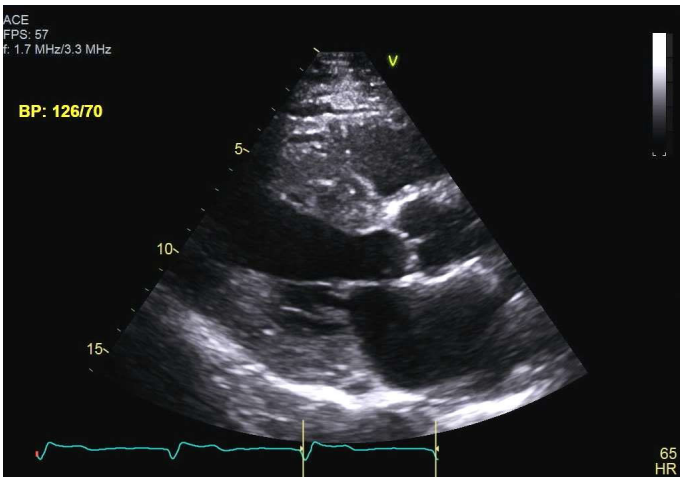
Echocardiography

Features of Cardiac Amyloidosis



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Courtesy: Dr. Martha Grogan

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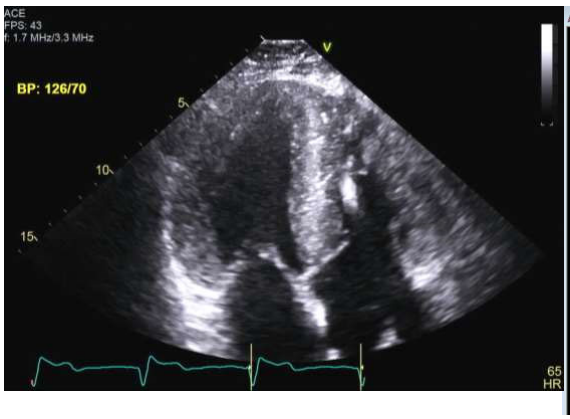
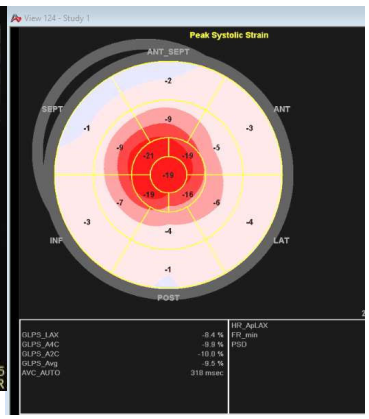
Echocardiography

Features of Cardiac Amyloidosis





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Courtesy: Dr. Martha Grogan

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Labs

Cardiac Amyloidosis

Elevated levels

- Troponin
- BNP or NTproBNP

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Screening for Cardiac Amyloidosis

European Society of Cardiology

Left Ventricular Wall Thickness ≥ 12 mm

+ ≥1 of

- Heart failure in ≥ 65 years
- Aortic stenosis in ≥ 65 years
- Hypotension or normotensive if previously hypertensive
- Sensory involvement, autonomic dysfunction
- Peripheral polyneuropathy
- Proteinuria
- Skin bruising
- Bilateral carpal tunnel syndrome
- Ruptured biceps tendon
- Subendocardial/transmural LGE or increased ECV
- Reduced longitudinal strain with apical sparing
- Decreased QRS voltage to mass ratio
- Pseudo Q waves on ECG
- AV conduction disease
- Possible family history

Garcia-Pavia, P; et al. Diagnosis and treatment of cardiac amyloidosis: a position statement of the ESC Working Group on Myocardial and Pericardial Diseases. EHJ, 42, 16, 21 Apr 2021.

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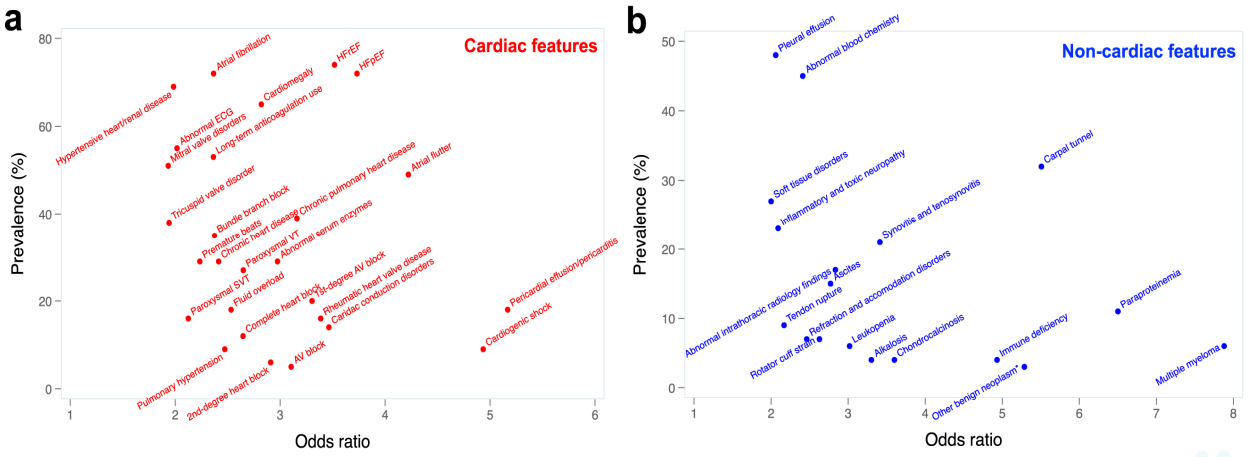
Odds ratio and Prevalence

ATTR Cardiomyopathy



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Shah, SJ; et al. A machine learning model for identifying patients at risk for wild-type transthyretin amyloid cardiomyopathy. Nature Communications, 12, 2725 (2021).

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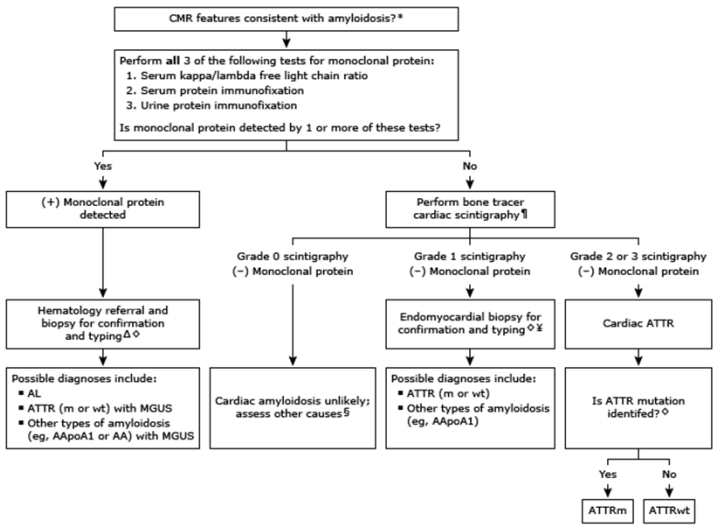
Diagnosis

Cardiac Amyloidosis



Cardiac MRI

- Late gadolinium enhancement
- Parametric T1 mapping
- Increased extracellular volume fraction

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Courtesy: UpToDate

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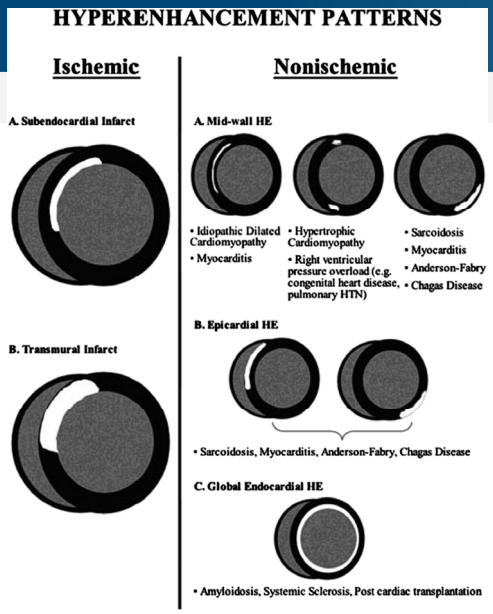
Diagnosis

Cardiac Amyloidosis



Edelman et al. *Clinical Magnetic Resonance Imaging.* NY: 2005. 23

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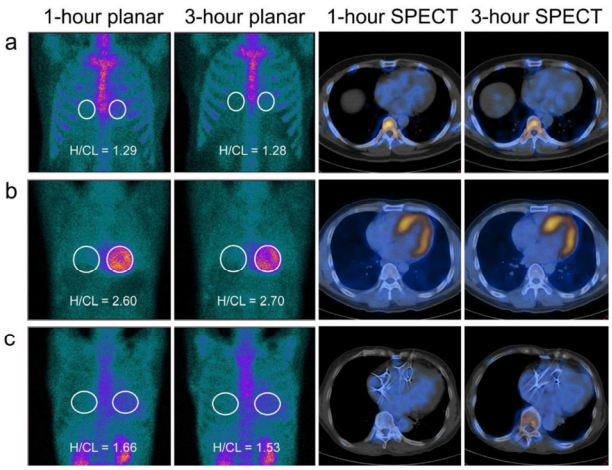
Diagnosis

Cardiac Amyloidosis



PYP scan

H/CL ratio ≥1.5 on a 1-h image

H/CL ratio ≥1.3 on a 3-h image

American College of Cardiology 24

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Prognosis

Cardiac Amyloidosis

prognostic information in cardiac amyloidosis

Anatomic	Doppler	Strain
LV wall thickness	Restrictive filling	Peak LS of the basal anteroseptal seg ≥ -7.5%
Ejection fraction	Myocardial performance index	Mean LV basal strain
Right ventricular size and function	Abnormal ejection time >240 ms	Reduced global longitudinal strain
Increased left atrial size	Short deceleration time (≤150 msec) + E/A ratio of >2.	Abnormal right ventricular strain <17%
Rapid progression of increased LV wall thickness	Stroke volume index	Apical LS >-14.5%
	TAPSE <16	RRSR ≥ 1.19
	Low MAPSE	LSR_{dias} < 0.85 S^{-1}

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Courtesy: Dr. Samuel Unzek

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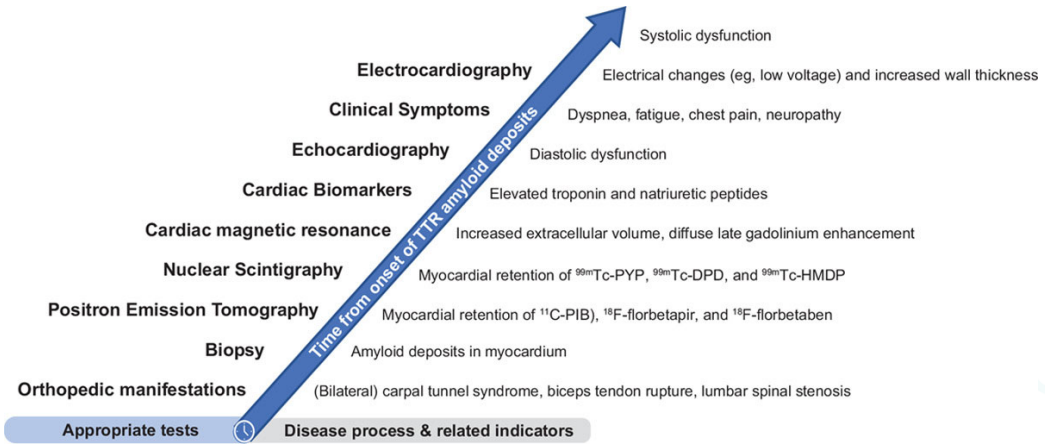
Amyloidosis and the Heart

Diagnosis (TTR cardiac amyloidosis)



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Maurer, MS, et al. Expert Consensus Recommendations for the Suspicion and Diagnosis of Transthyretin Cardiac Amyloidosis. Circulation Heart Failure, 2019; 12:e0060775.

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Prognosis

Cardiac Amyloidosis

- ATTRwt
  - Median survival 3-5 years
- ATTRh
  - Median survival 4-5 years
- AL
  - Median survival 6 months
  - Improves to 5-6 years with treatment

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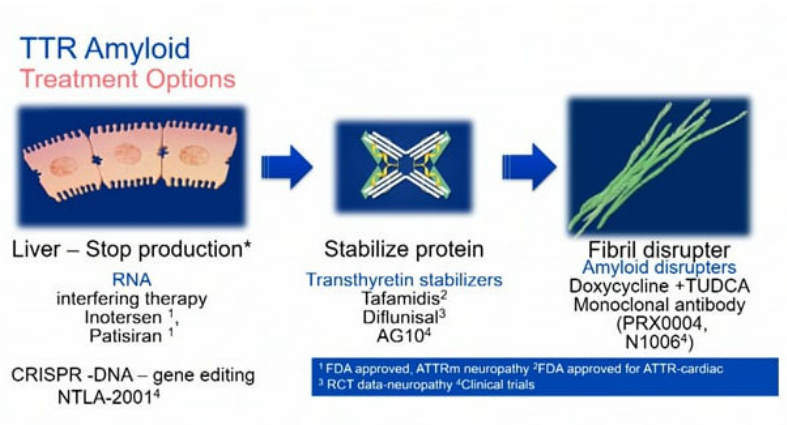
Treatment

Cardiac Amyloidosis



Courtesy: Dr. Martha Grogan

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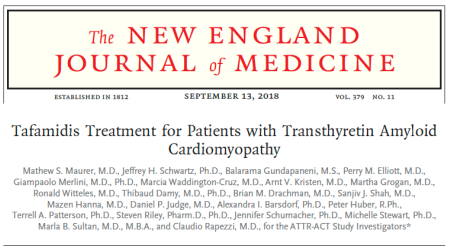
Tafamidis

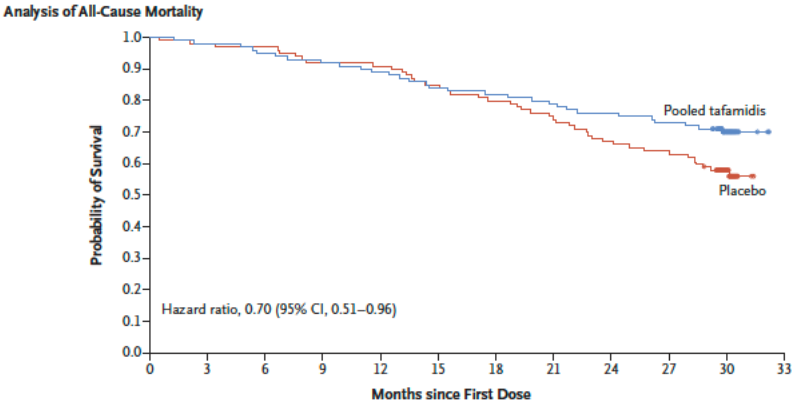
Cardiac Amyloidosis


The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 13, 2018 VOL. 379 NO. 11

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., Mazen Hanna, M.D., Daniel P. Judge, M.D., Alexandra I. Barsdorf, Ph.D., Peter Huber, R.Ph., Terrell A. Patterson, Ph.D., Steven Riley, Pharm.D., Ph.D., Jennifer Schumacher, Ph.D., Michelle Stewart, Ph.D., Marla B. Sultan, M.D., M.B.A., and Claudio Rapezzi, M.D., for the ATTR-ACT Study Investigators*



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Treatment

Cardiac Amyloidosis

- Heart failure with preserved ejection fraction
  - Spironolactone
  - Avoid beta blockers (heart rate dependent)
  - Avoid ACEI/ARB (orthostatic hypotension)
- Arrhythmias
  - Atrial fibrillation
  - Unclear if ICD beneficial
- Thromboembolism
- Aortic stenosis
- Heart and Liver Transplantation
  - ATTRm
- Neuropathy in hTTR
  - Patisiran, Vutrisiran, Inotersen, Eplontersen
- AL: chemotherapy (CyBorD), stem cell transplant

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Case

- 50 year old African American man
- Worsening exertional dyspnea for 2 months, PAF, carpal tunnel, no FamHx
- Exam: JVD, bibasilar crackles, and 2+ pitting bilateral lower extremity edema
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Objectives

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- 2. Summarize the diagnostic workup and imaging features of cardiac amyloidosis
- 3. Determine prognosis and treatment for cardiac amyloidosis

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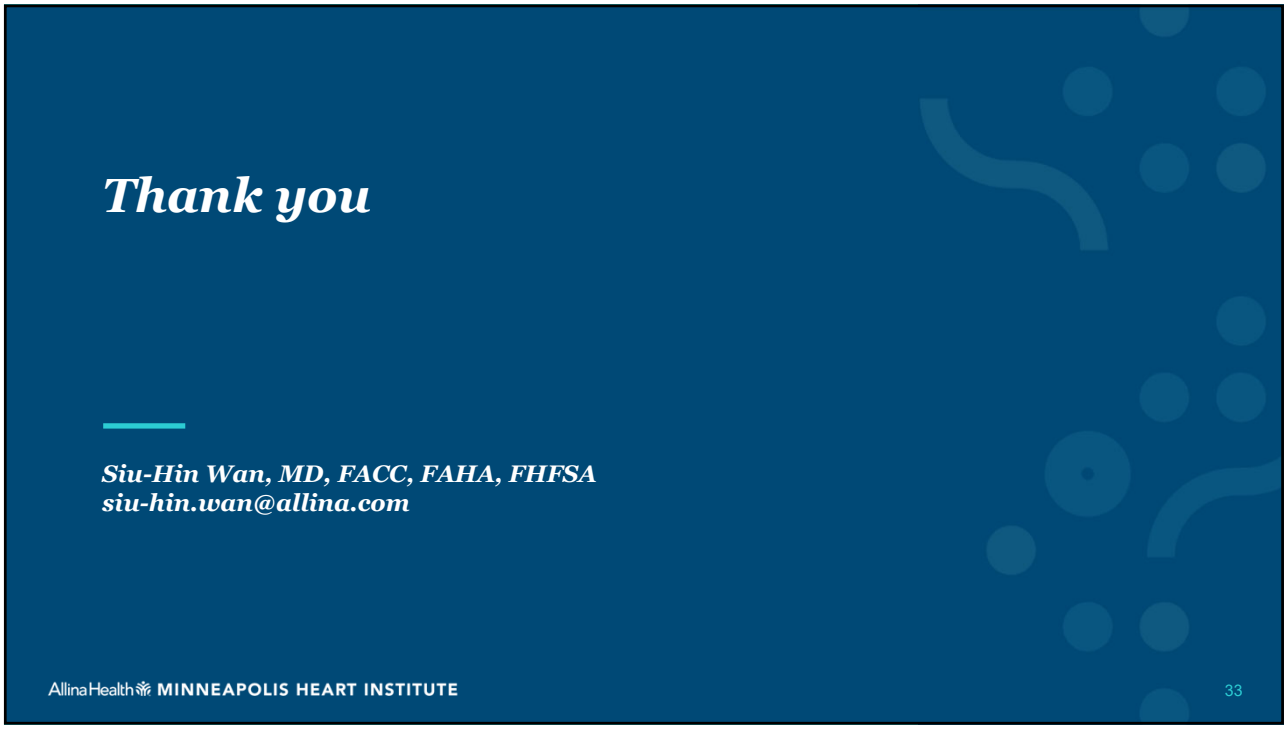
Thank you
Siu-Hin Wan, MD, FACC, FAHA, FHFSA
siu-hin.wan@allina.com
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