Cardiac Amyloidosis: early diagnosis and novel treatments

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Saint Luke's
MID AMERICA HEART INSTITUTE

Disclosures

- Pfizer – grant support, speaker, and consultant
- Alnylam – consultant

Objectives

- Review epidemiology and workup of cardiac amyloidosis
- Systemic manifestations
- Common misconceptions
- Examine novel treatment strategies in ATTR amyloidosis

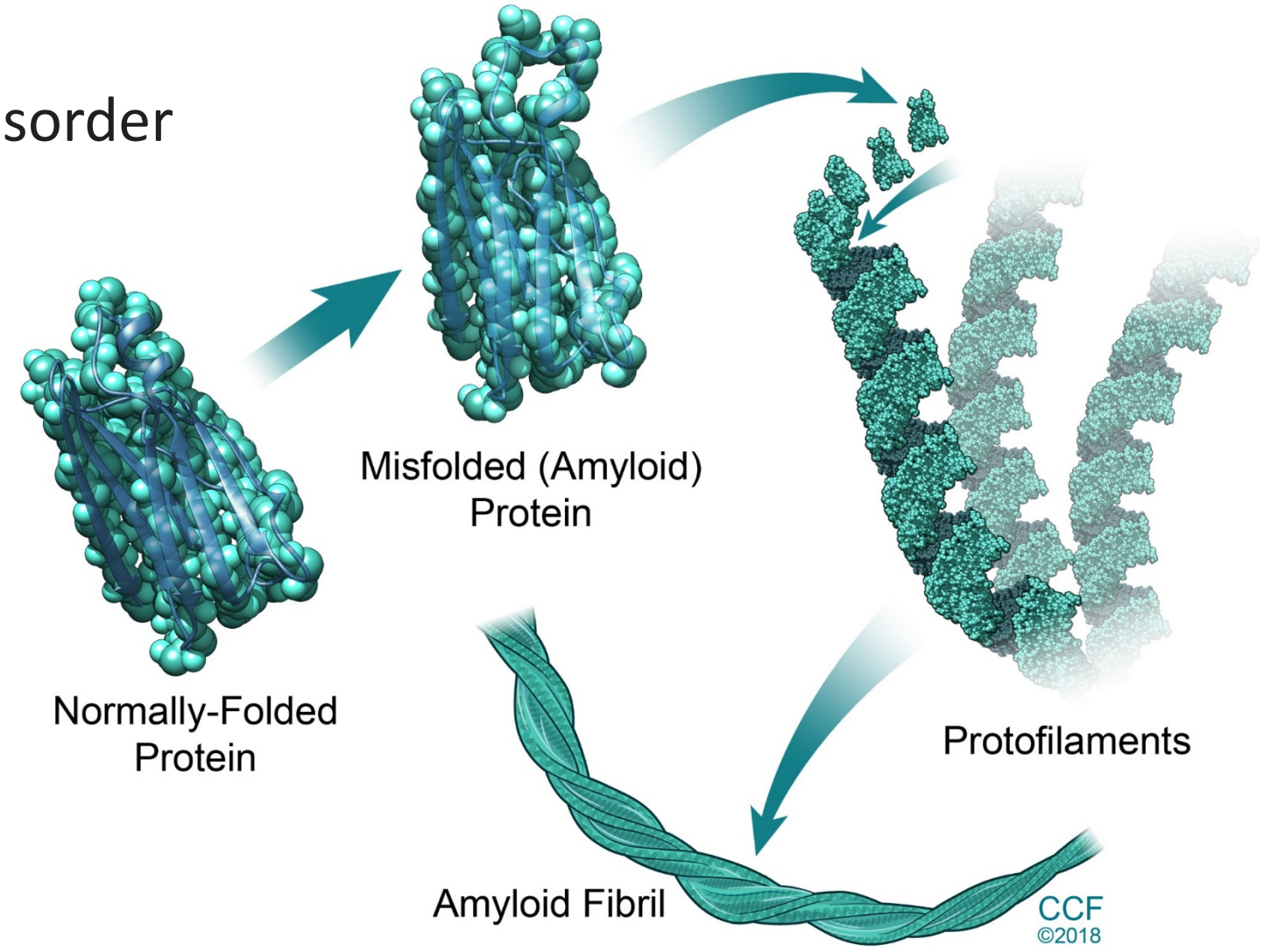
Case

- 70 year old white male
- Symptoms of leg swelling and dyspnea with recent HF admission

2D ECHO MEASUREMENTS					
LV Diastolic Diameter Base LX	5.1 cm	3.6-5.4	LVPW Diastolic Thickness	1.4 cm	0.6-1.1
LV Systolic Diameter Base LX	4.3 cm	2.3-4.0	LVOT Diameter	2.1 cm	
LA Systolic Diameter LX	5.6 cm	2.3-3.8	Aorta at Sinuses Diameter	3.4 cm	2.1-3.5
IVS Diastolic Thickness	1.5 cm	0.6-1.1	Ascending Aorta Diameter	4.2 cm	2.1-3.4
AORTIC VALVE **DOPPLER**					
AV Peak Velocity	104 cm/s		LVOT AV Vel Ratio	0.71	
AV Peak Gradient	4.3 mmHg				
TRICUSPID VALVE **DOPPLER**					
RV Systolic Pressure	32.7 mmHg				

What is amyloidosis?

- Protein misfolding disorder

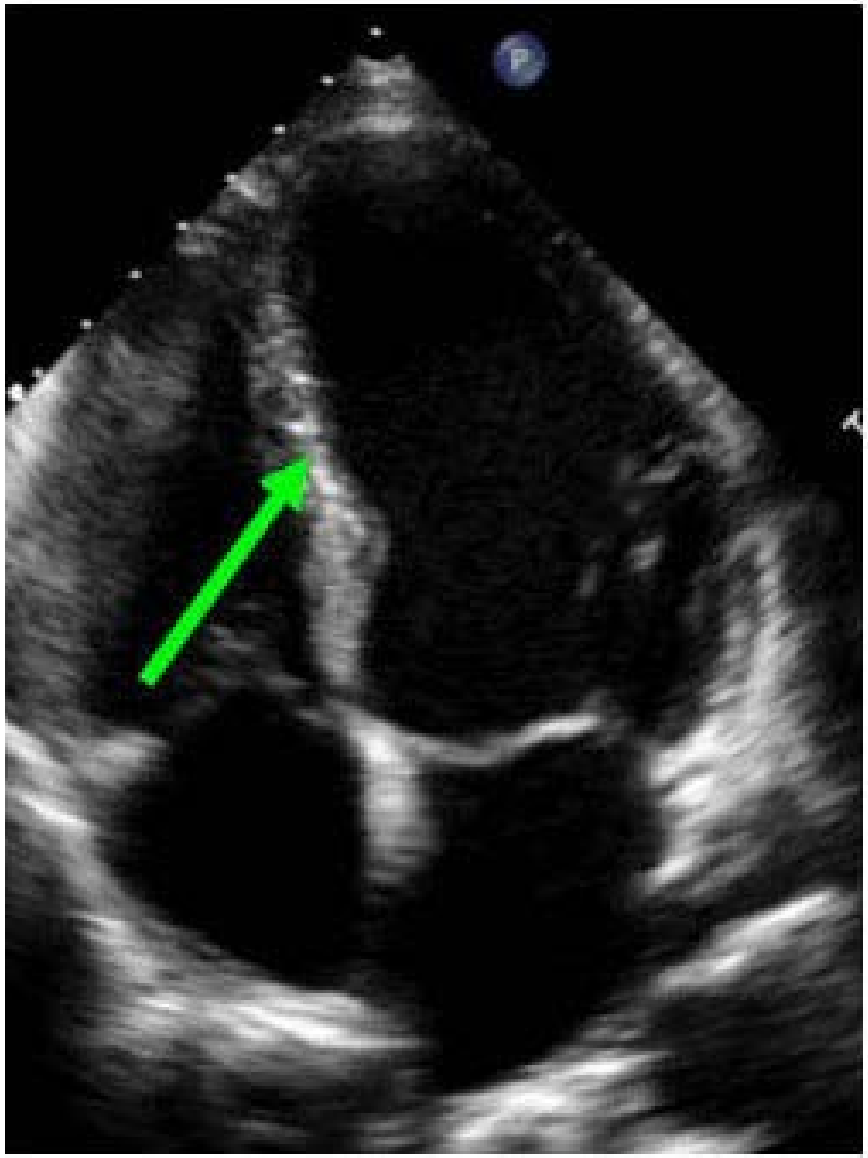


Over 30 Amyloidogenic Proteins

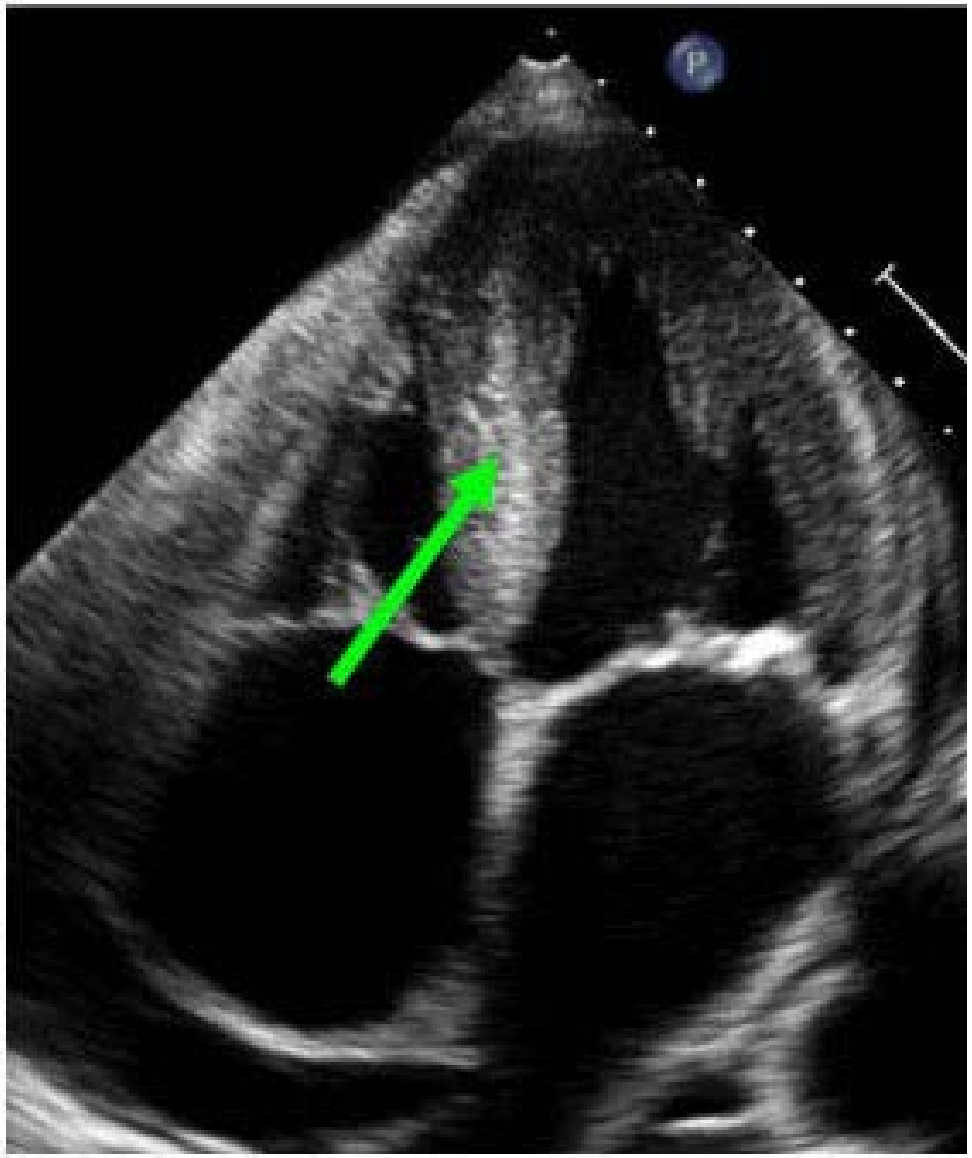
Table 1 Main protein types causing amyloidosis with the emphasis on cardiovascular system involvement

Amyloid protein	Precursor	Distribution	Syndrome
AL	**Immunoglobulin light chain**	Systemic/localised	Primary/myeloma associated
AH	**Immunoglobulin heavy chain**	Systemic/localised	Primary/myeloma associated
AA	**Serum amyloid A**	Systemic	Secondary
Aβ_2 Microglobulin	**β_2 Microglobulin**	Systemic	Secondary
ATTR	**Transthyretin**	Systemic	Senile systemic/familial
AANF	**Atrial natriuretic factor**	Localised	Atrial isolated
AApoA-I	**Apolipoprotein A-I**	Localised/systemic	Aortic/familial
AApoA-II	Apolipoprotein A-II	Systemic	Familial
Amed	**Lactadherin**	Localised	Aortic
Agel	Gelsolin	Systemic	Familial
Alys	Lysozyme	Systemic	Familial
Afib	Fibrinogen α chain	Systemic	Familial
Acys	Cystatin C	Systemic	Familial
Aβ	Aβ Protein precursor	Localised	Alzheimer's disease, aging
AprP	Prion protein	Localised	Spongiform encephalopathies
Abri	ABri protein precursor	Localised	Familial dementia
Acal	(Pro)calcitonin	Localised	Thyroid tumours derived from C cells
AIAPP	Islet amyloid polypeptide	Localised	Langerhans islets, insulinomas
Apro	Prolactin	Localised	Prolactinomas, pituitary in elderly
Ains	Insulin	Localised	Iatrogenic
Aker	Kerato-epithelin	Localised	Familial, cornea
Alac	Lactoferrin	Localised	Familial, cornea

Proteins involved in the cardiovascular system are in bold.

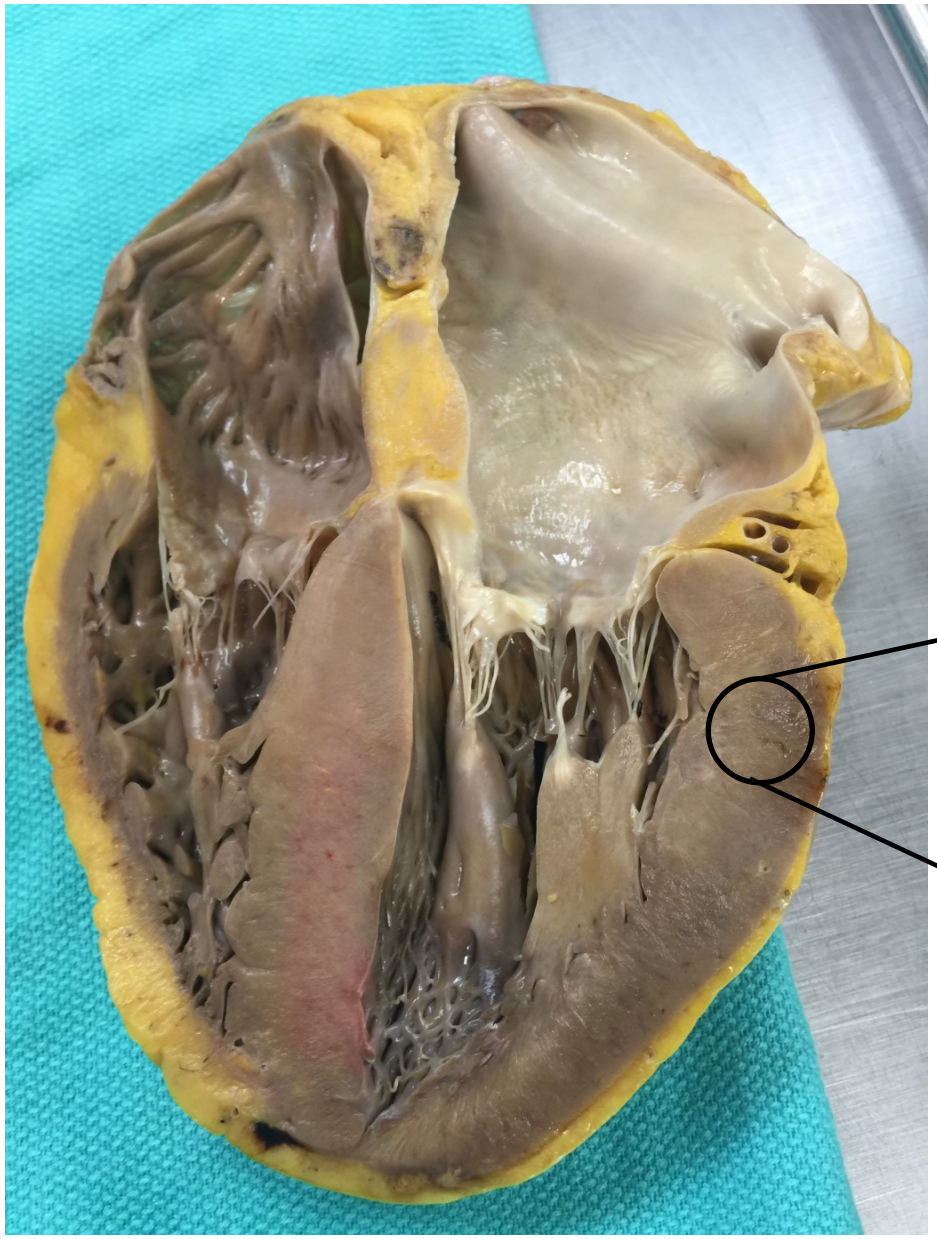


Normal Patient

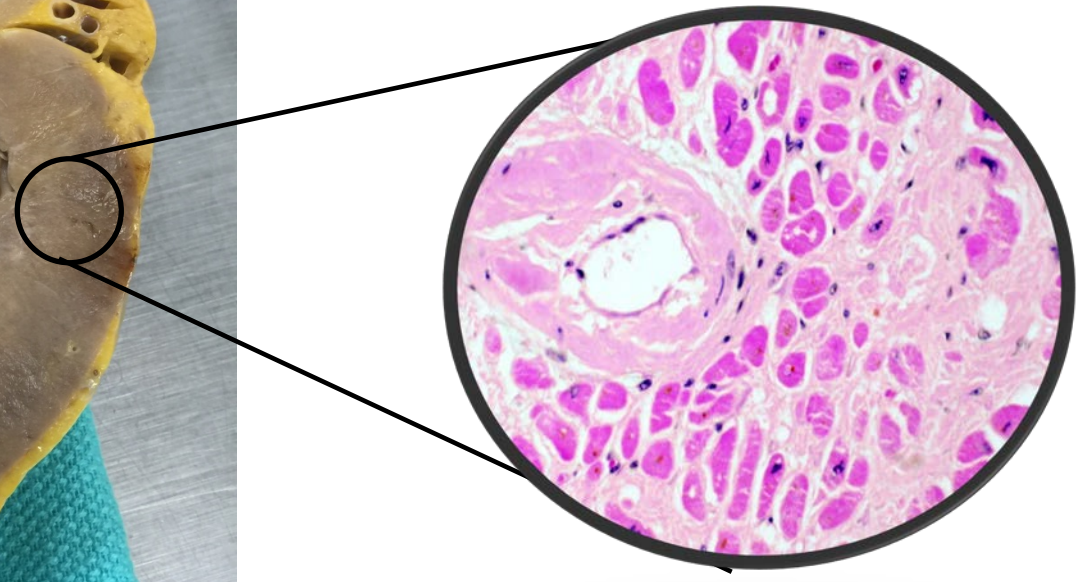


Patient with Amyloid Deposits in Heart

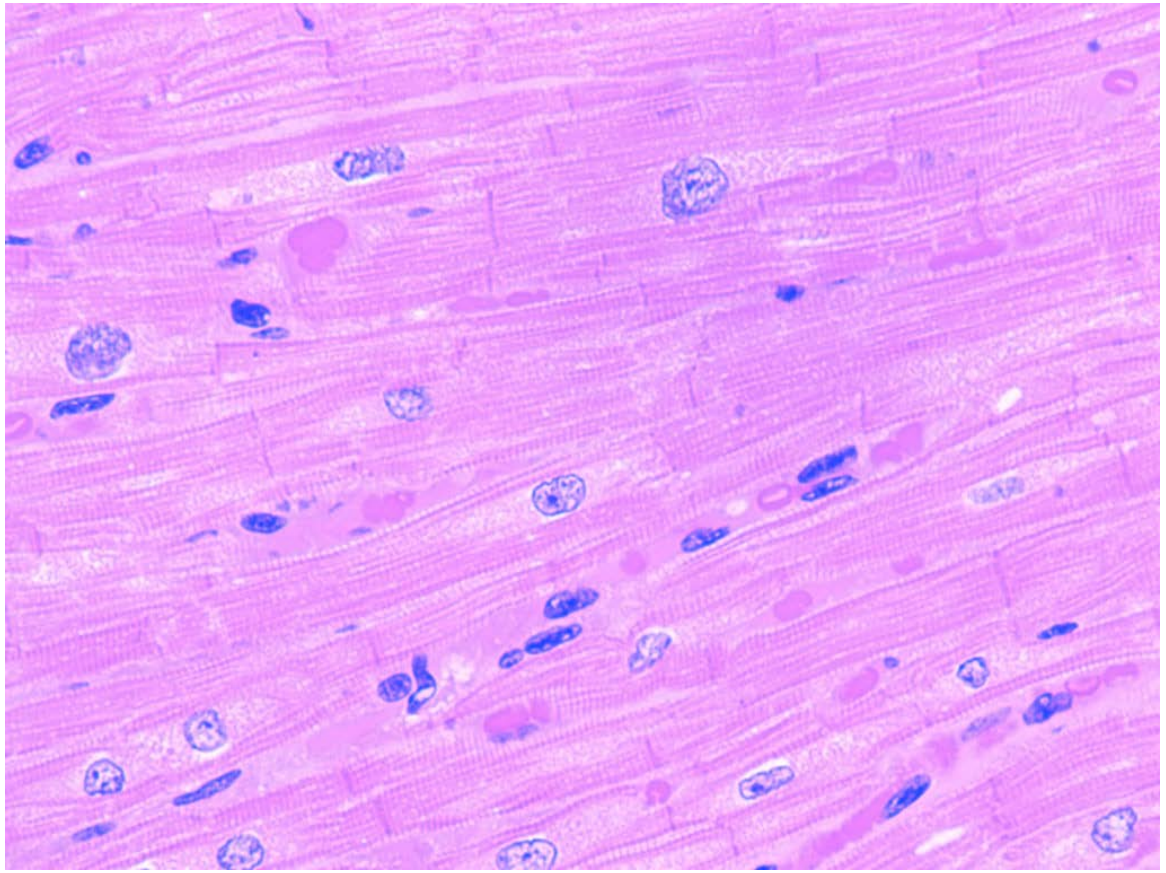
Pathology: Diffuse involvement



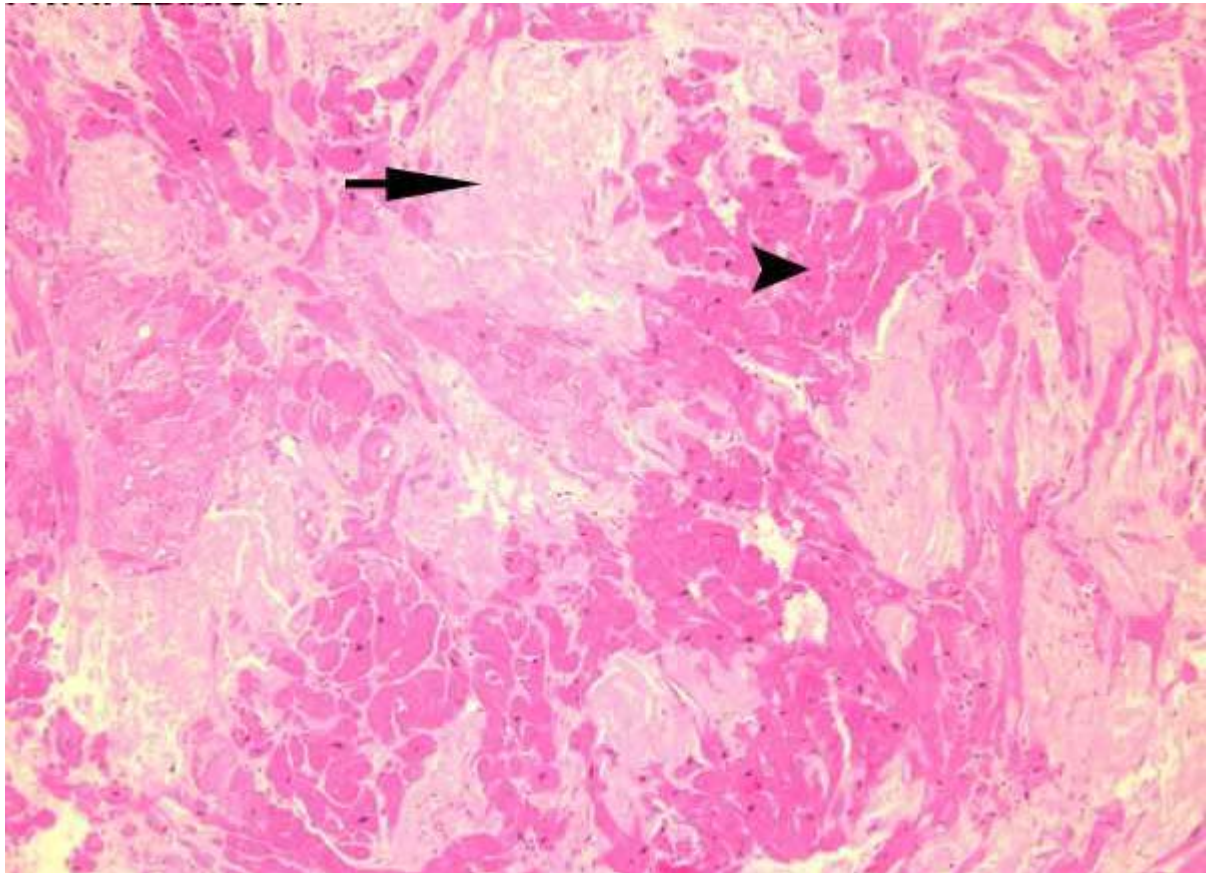
- Increase in LV mass without dilatation
- Atrial infiltration impairing atrial contraction
- Conduction system / valves
- Microvascular ischemia



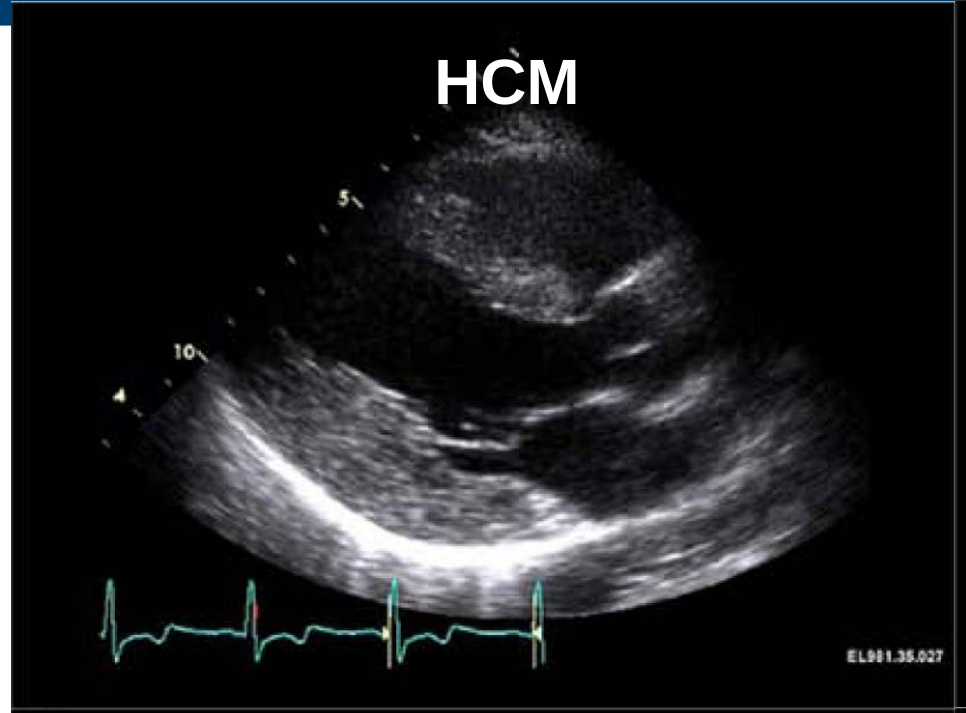
Normal heart



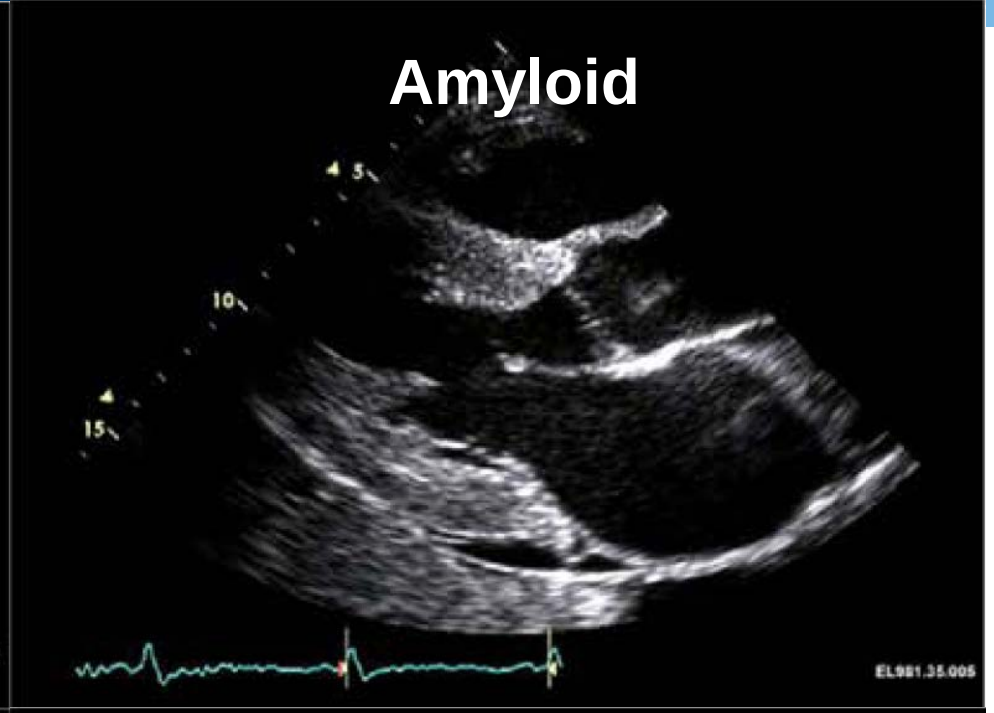
Cardiac amyloid



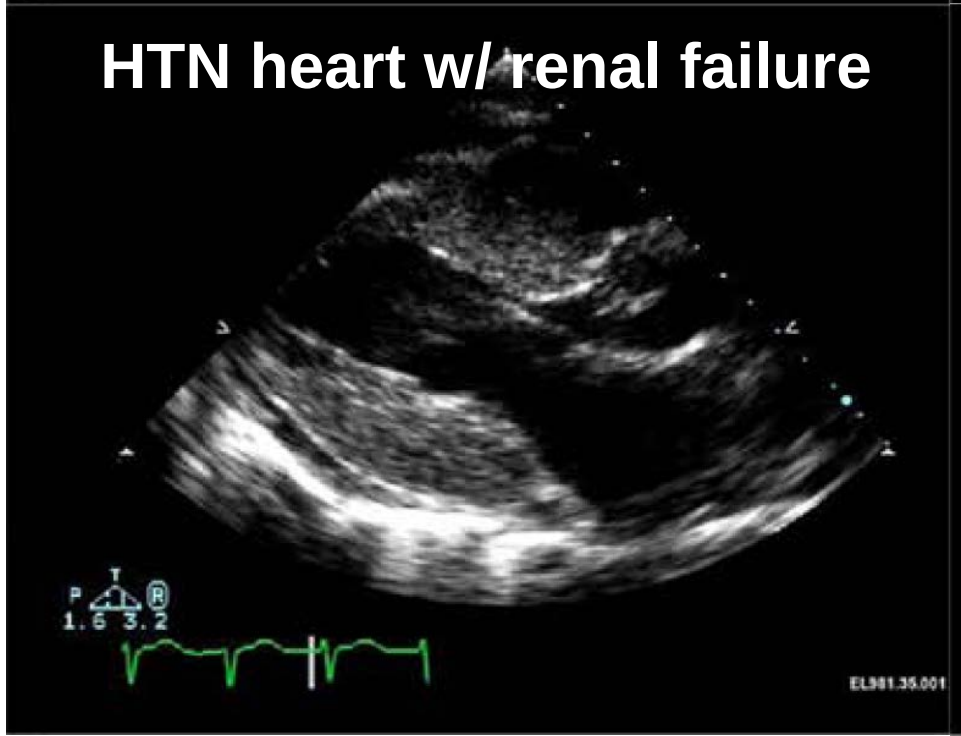
HCM



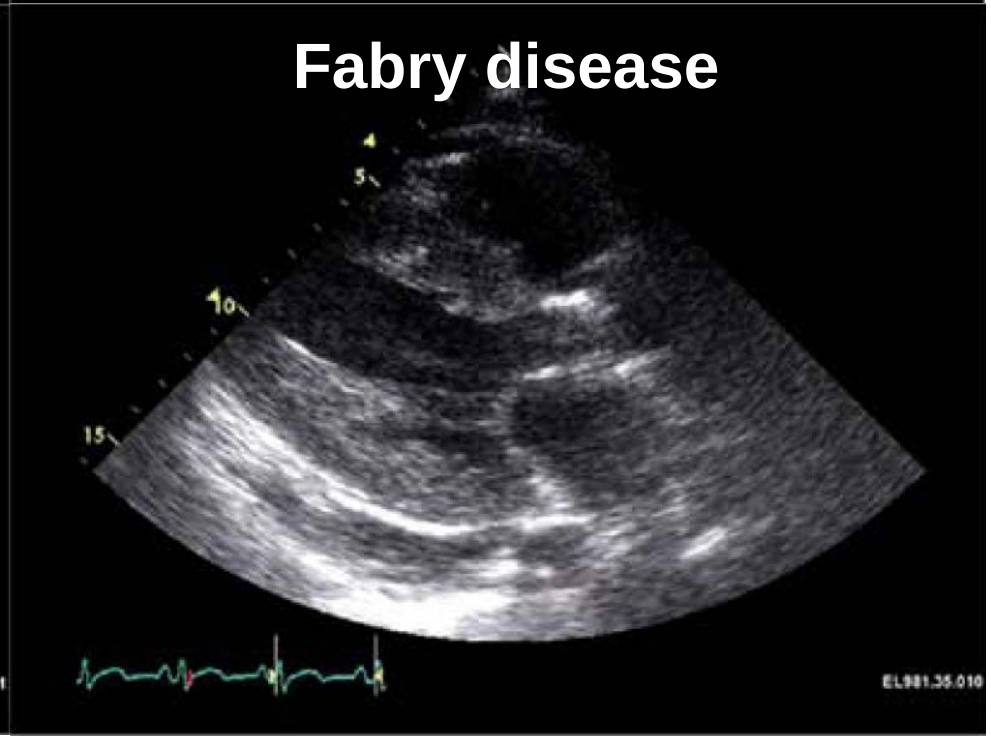
Amyloid



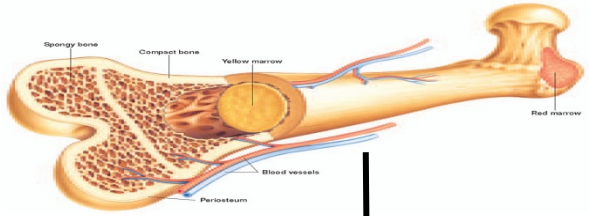
HTN heart w/ renal failure



Fabry disease



2 Main Types of Systemic Amyloidosis

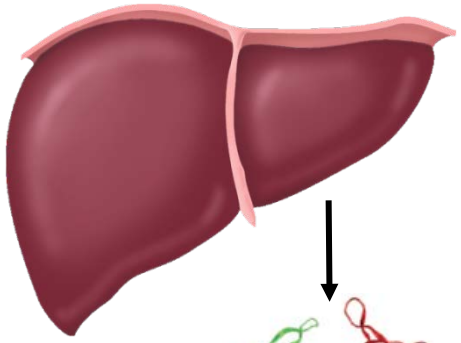


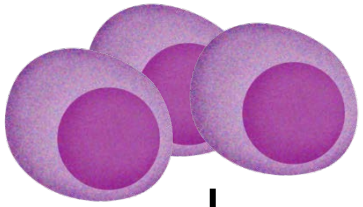
AL

Light chain amyloidosis

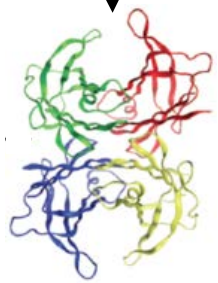
ATTR

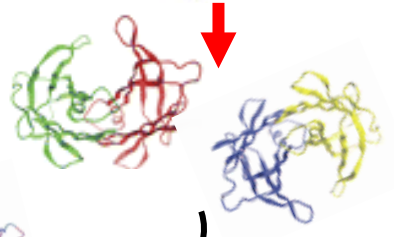
Transthyretin amyloidosis

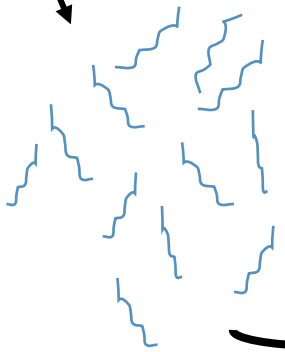


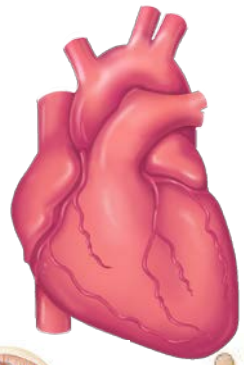


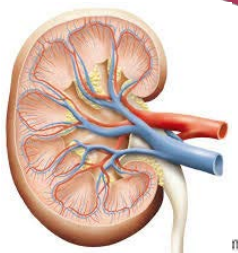
Wild type
or
Mutant

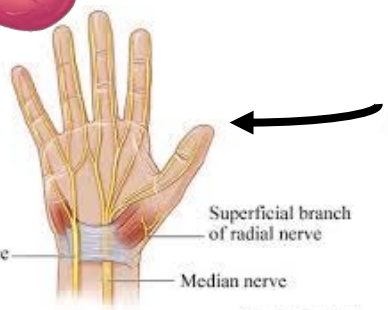


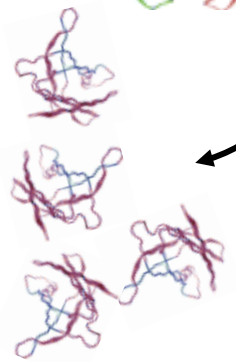






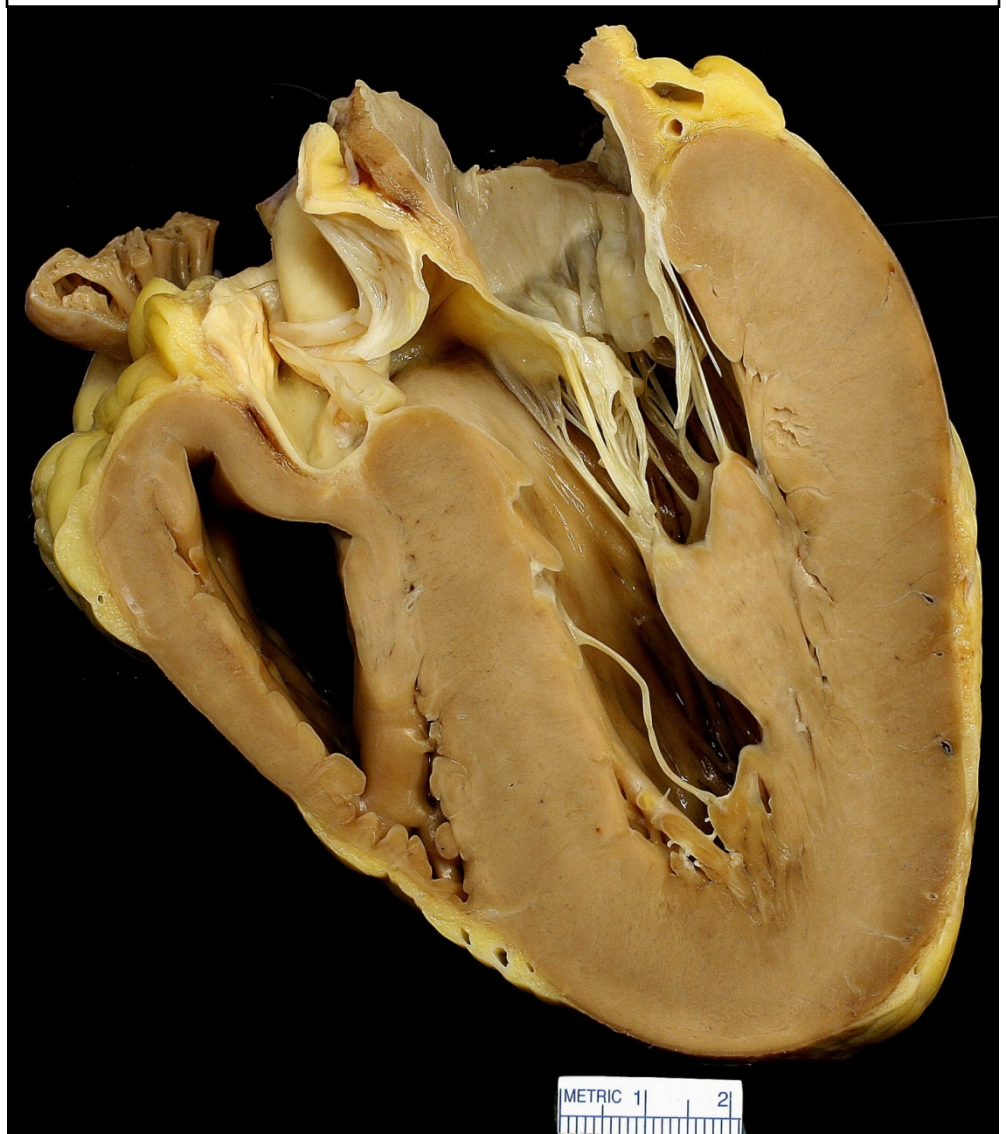
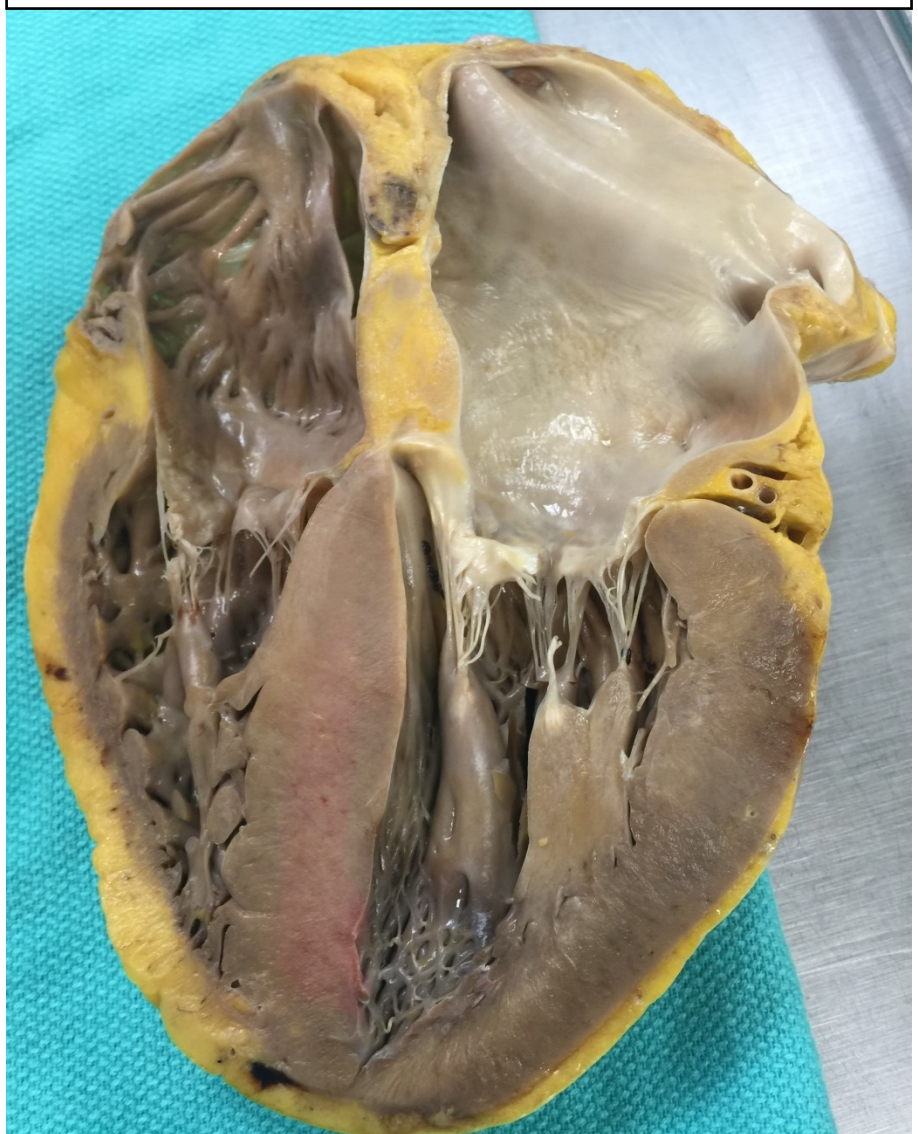






AA < 5%
Isolated atrial (ANF)
Apolipoprotein A1
Other hereditary

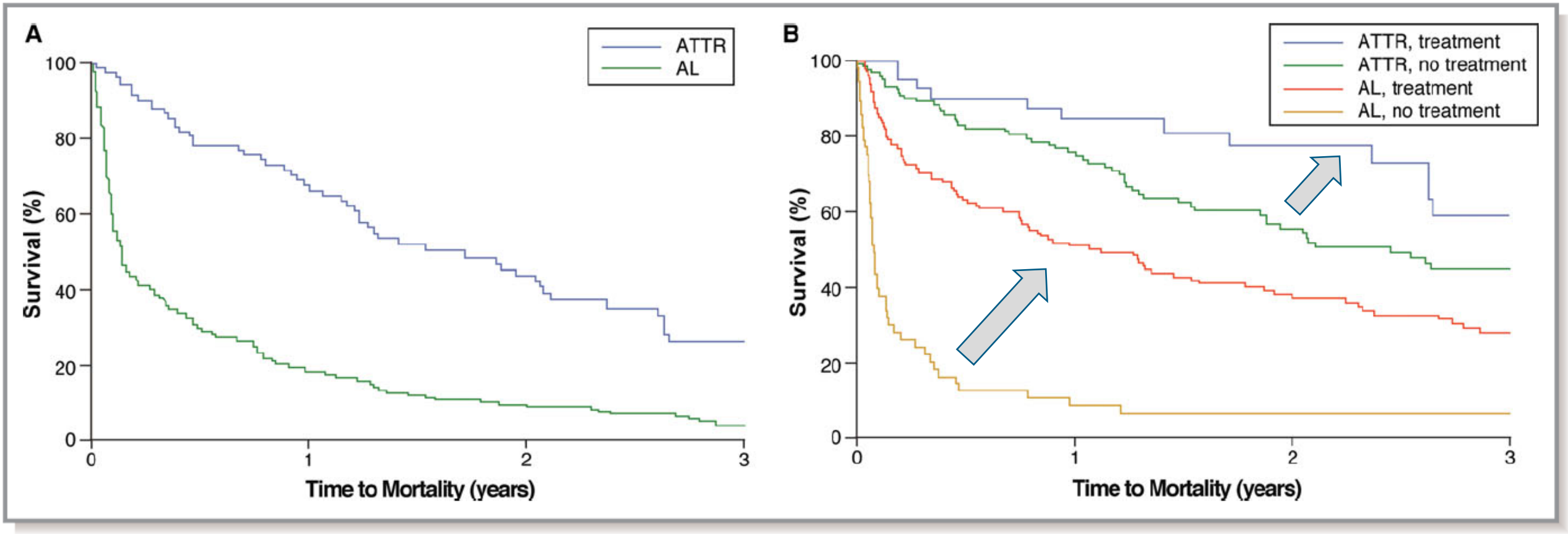
Which type of amyloidosis is this?

AL Amyloidosis	ATTR Amyloidosis
	

Why do you need to tell the amyloid subtype?

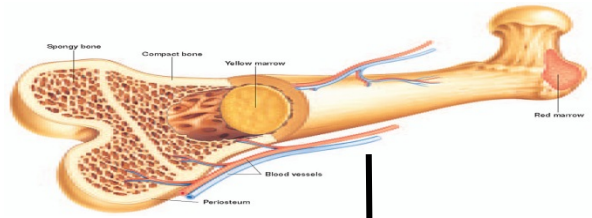
Different treatments
Different prognosis
Genetic component

Prognosis and treatment in amyloidosis



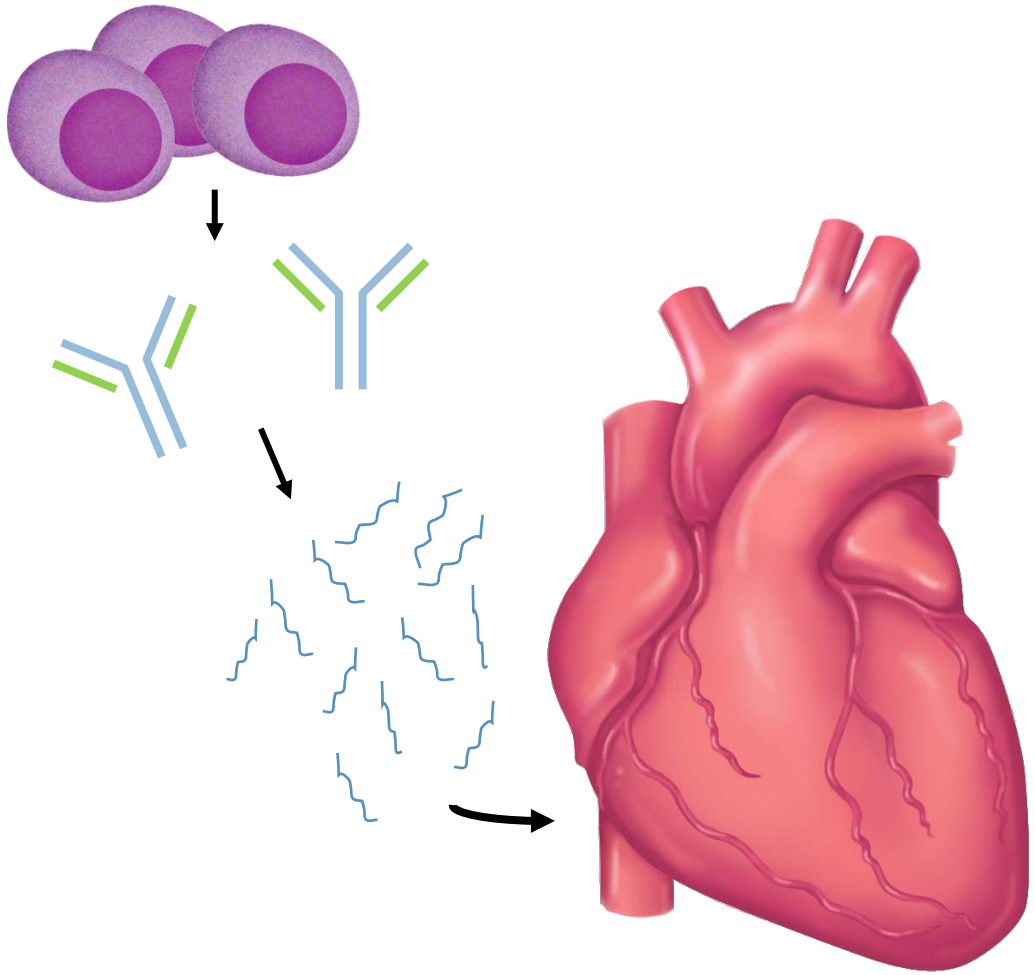
J Am Heart Assoc. 2016 Subtype-Specific Prognosis in Cardiac Amyloidosis *Sperry et al*

2 Types of Amyloid that Affect the Heart

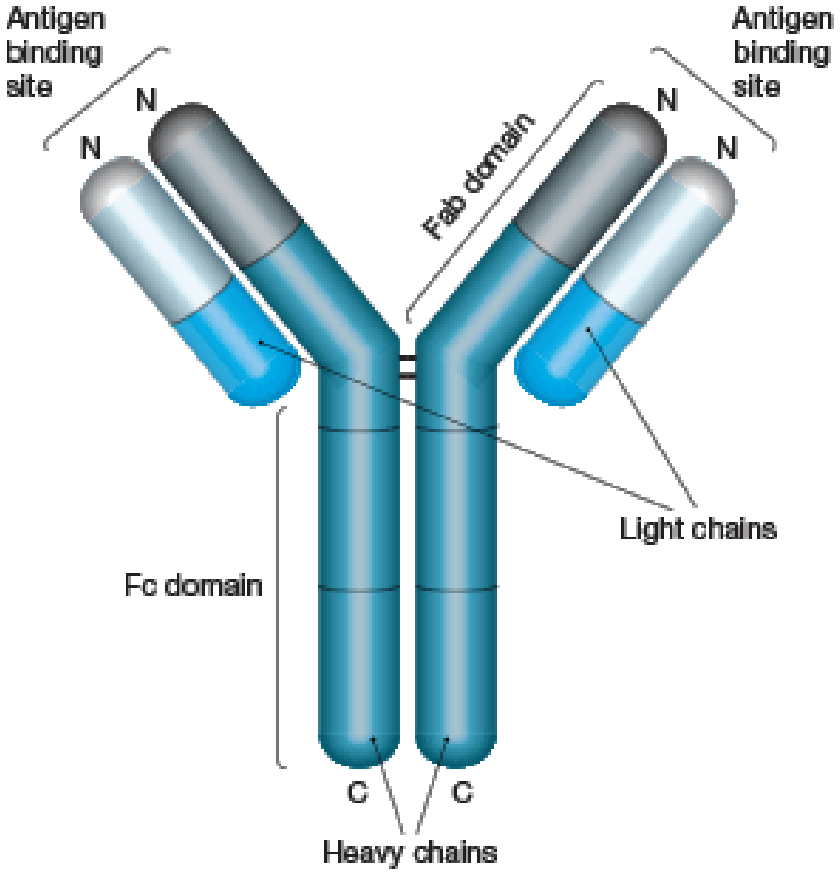


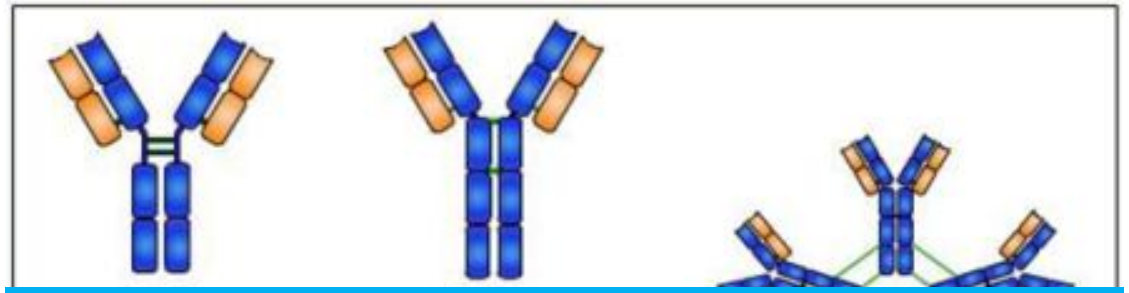
AL

Light chain amyloidosis



Immunoglobulins i.e. antibodies



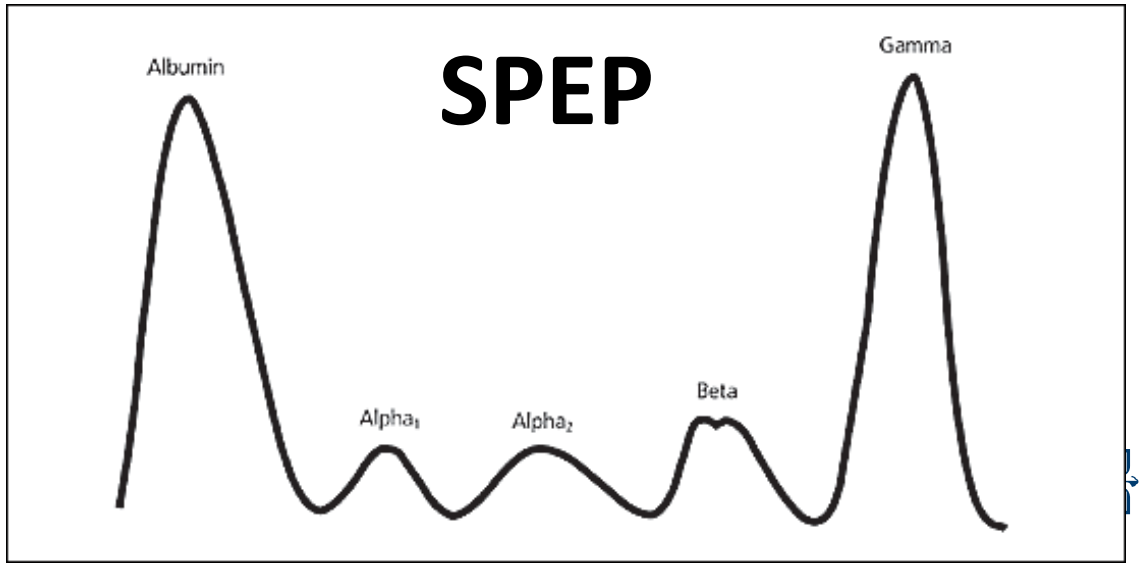


Free kappa+lambda light chains

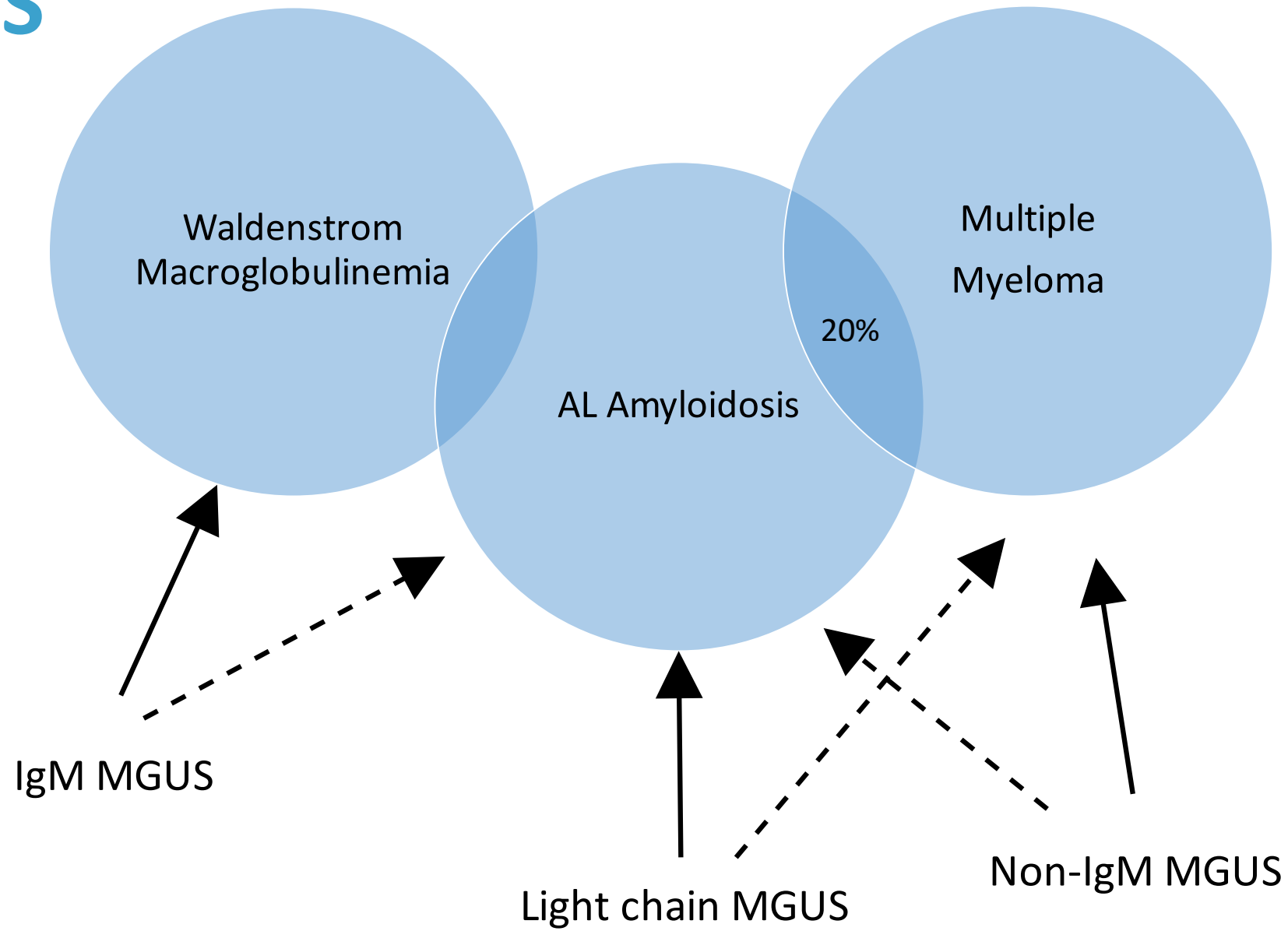
Serum immunofixation

Urine immunofixation

~~**SPEP/UPEP**~~



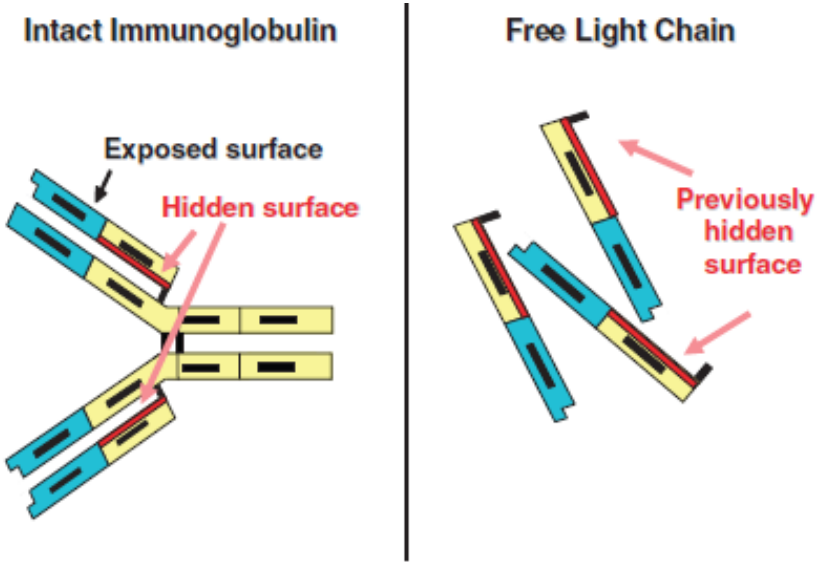
MGUS

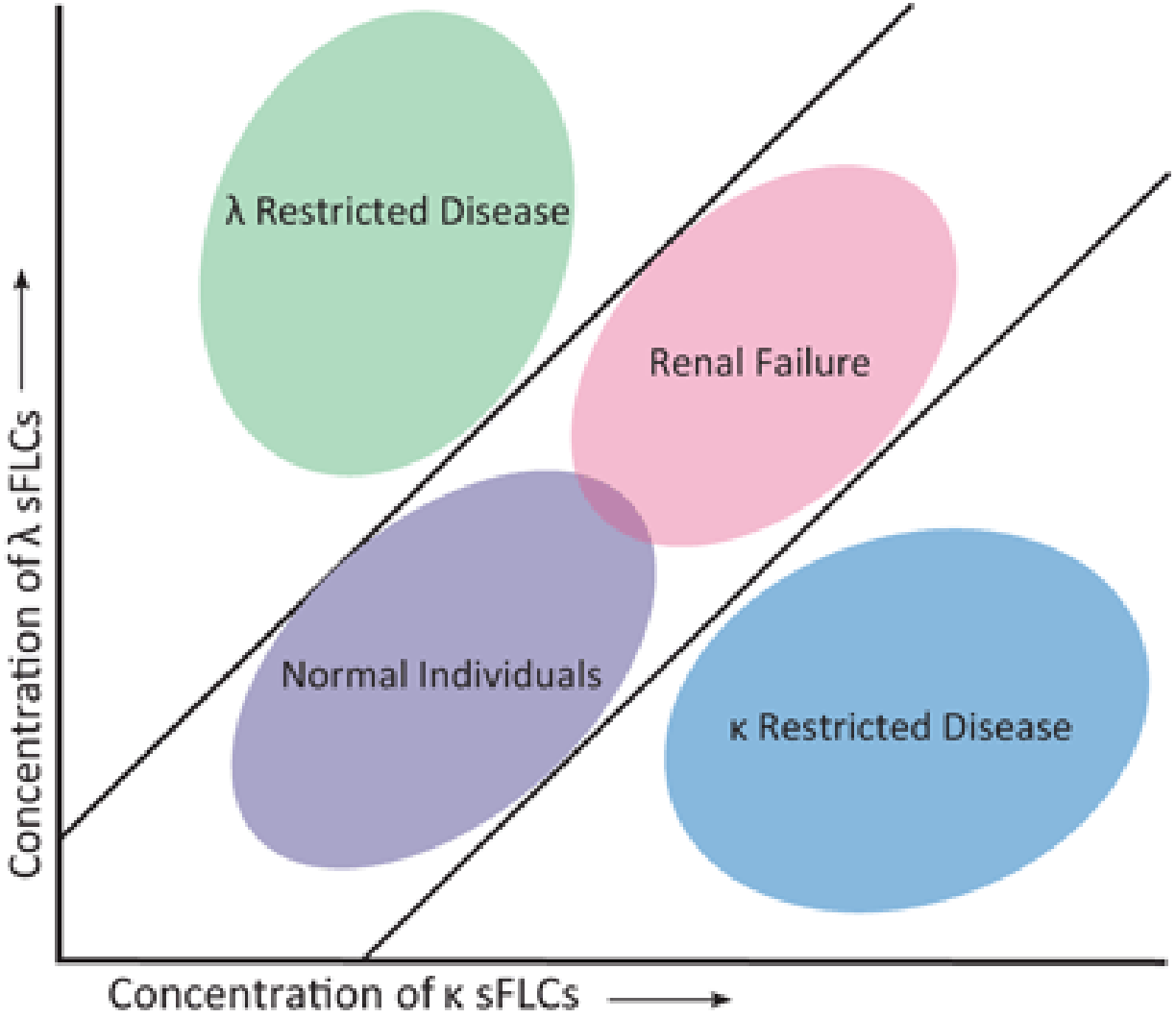

Waldenstrom Macroglobulinemia
AL Amyloidosis
Multiple Myeloma
20%
IgM MGUS
Light chain MGUS
Non-IgM MGUS

Serum Free-Light Chain Assay
- Useful for Diagnosis, Prognosis, Respons

Kappa Free, Serum	3.30 - 19.40 mg/L	34.3 (H)
Lambda Free, Serum	5.7 - 26.3 mg/L	475.0 (H)
K/L Ratio, Serum	0.26 - 1.65	0.07 (L)

Principle





Free kappa+lambda light chains serum

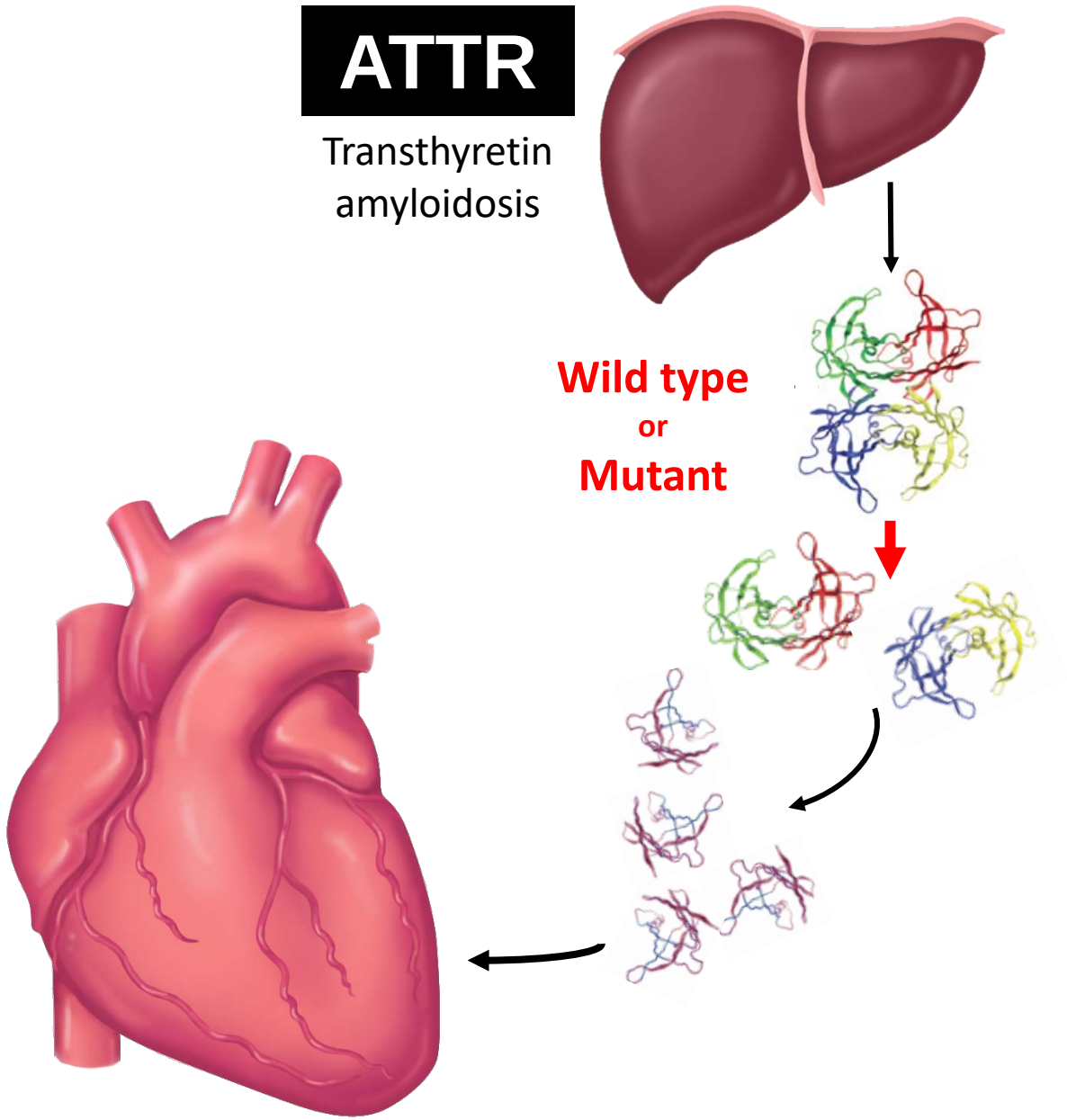
Serum immunofixation

Urine immunofixation

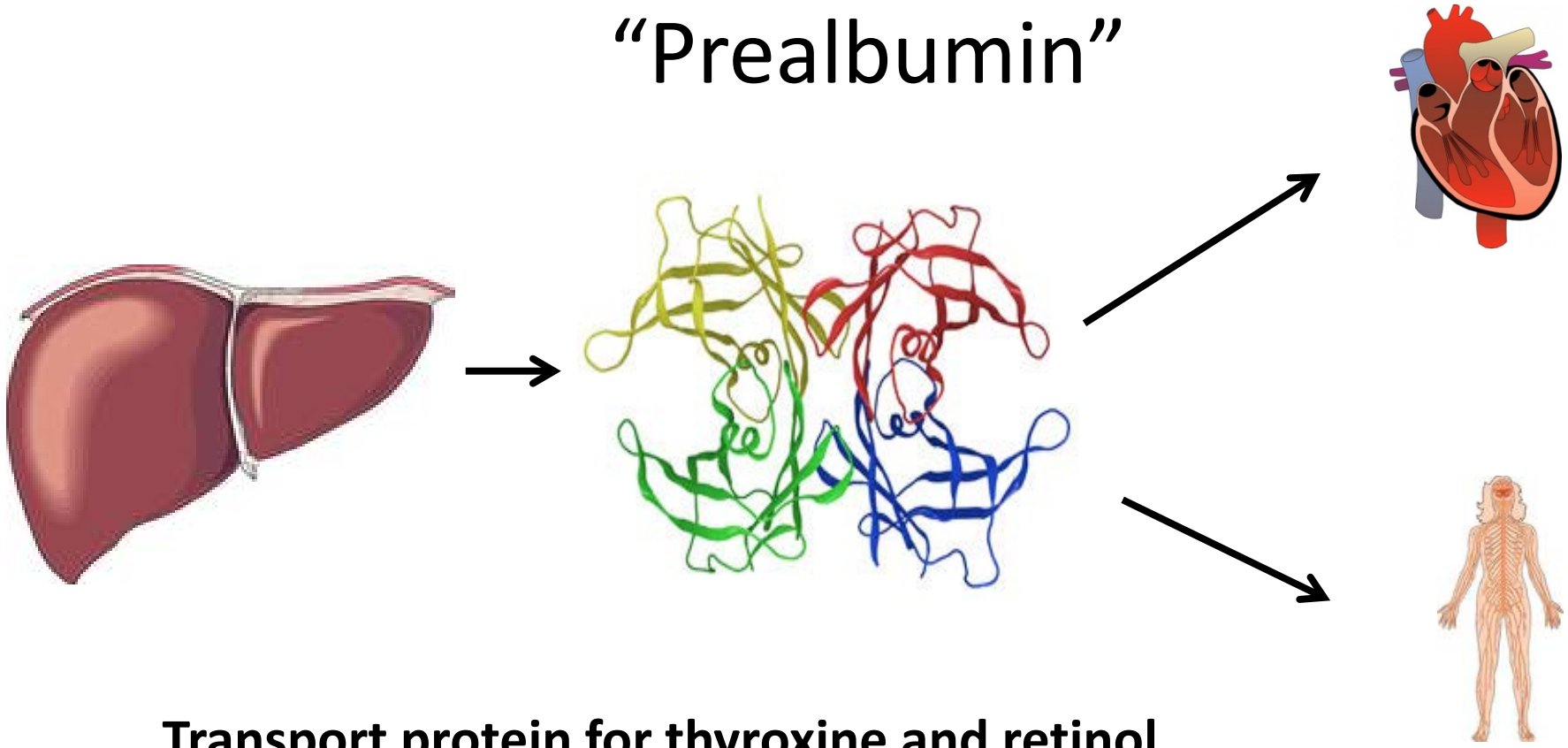
99%

~~**CPEP/UPEP**~~

2 Types of Amyloid that Affect the Heart



Transthyretin (TTR)
"Prealbumin"



Transport protein for thyroxine and retinol

Homotetramer: 4 identical monomers 127 amino acids each

> 100 mutations described: single amino acid substitutions

ATTRwt = amyloid transthyretin wild type

"Wild type transthyretin amyloidosis"
~~"Senile systemic amyloidosis" (SSA)~~
~~"Senile cardiac amyloidosis"~~
Median age 73
Bilateral carpal tunnel / spinal stenosis common
Median survival about 4 years

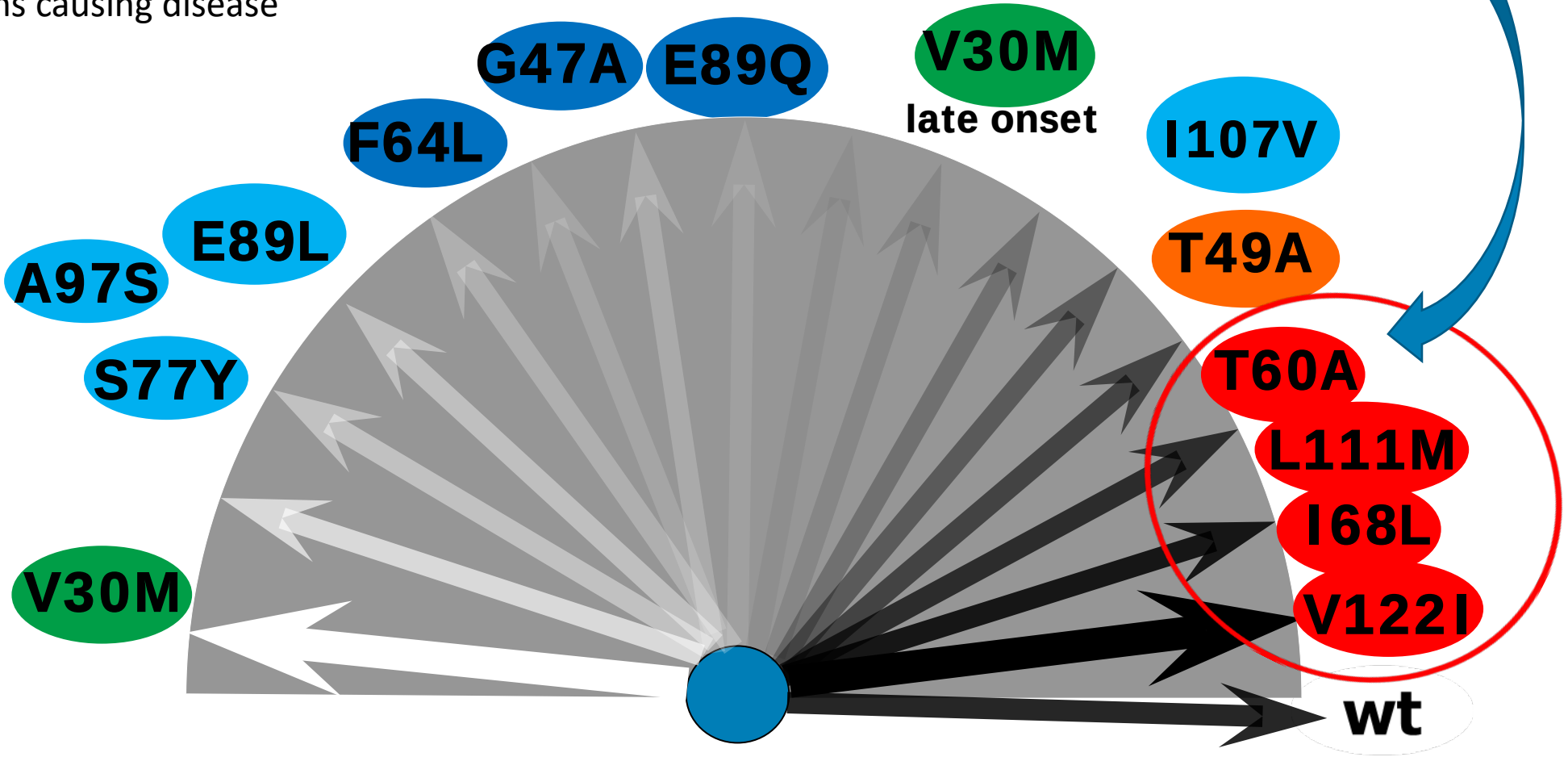
ATTRm = amyloid transthyretin mutant

"Hereditary transthyretin amyloidosis"
"Familial amyloid cardiomyopathy (FAC)
"Familial amyloid polyneuropathy (FAP)
Age of onset different depending upon mutation
Most common mutation V122I seen in 3.5% AA*
Median survival for V122I mutation 2.5 years

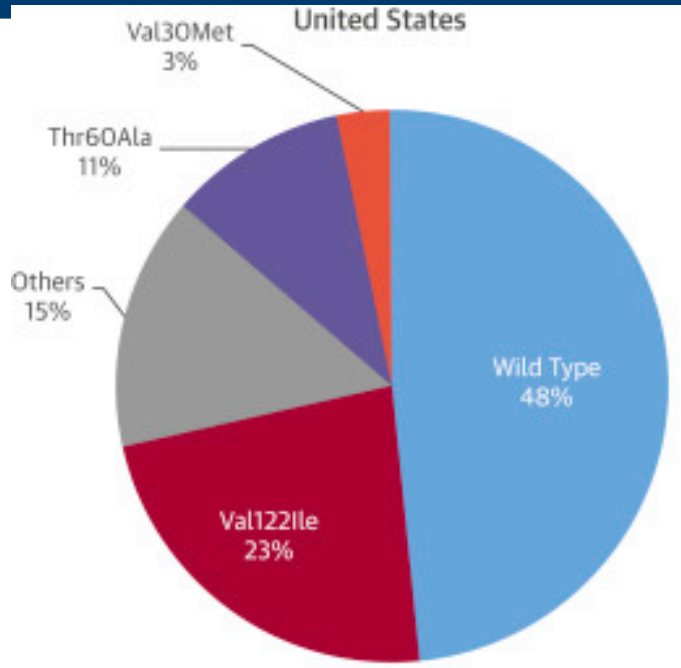
*Quarta, NEJM 2015

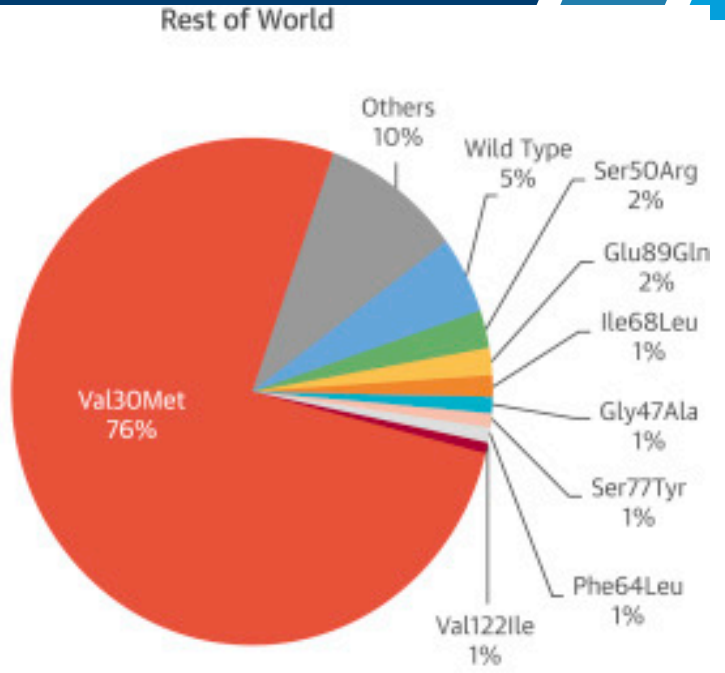
Familial Amyloid Cardiomyopathy = FAC

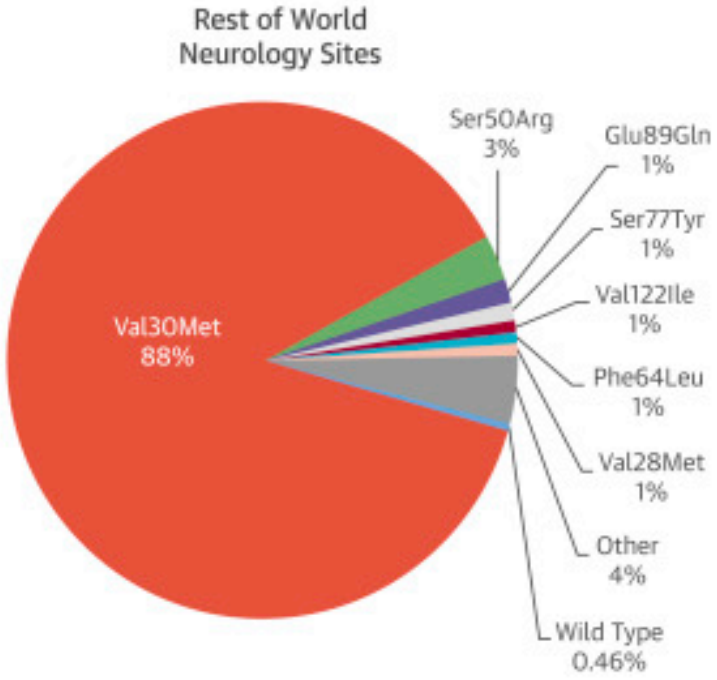
112+ mutations causing disease

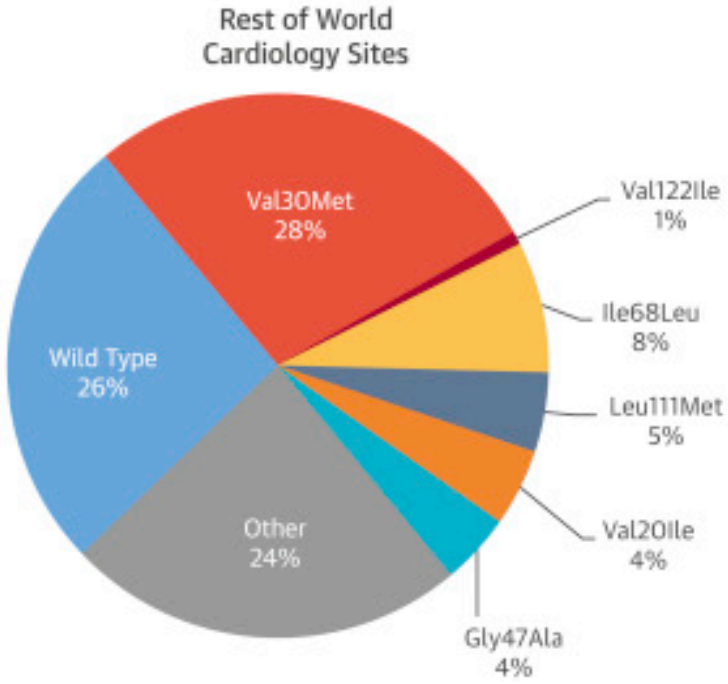


“Neurologic” **Phenotype** “Cardiac”


United States
Val30Met
3%
Thr60Ala
11%
Others
15%
Wild Type
48%
Val122Ile
23%


Rest of World
Others
10%
Wild Type
5%
Ser50Arg
2%
Glu89Gln
2%
Ile68Leu
1%
Gly47Ala
1%
Ser77Tyr
1%
Phe64Leu
1%
Val122Ile
1%
Val30Met
76%


Rest of World
Neurology Sites
Ser50Arg
3%
Glu89Gln
1%
Ser77Tyr
1%
Val122Ile
1%
Phe64Leu
1%
Val28Met
1%
Other
4%
Wild Type
0.46%
Val30Met
88%


Rest of World
Cardiology Sites
Val30Met
28%
Val122Ile
1%
Ile68Leu
8%
Leu111Met
5%
Val20Ile
4%
Gly47Ala
4%
Other
24%
Wild Type
26%

Variable	AL (n=191)	ATTR (n=169)	*P* Value
Age, y	64.7±11.0	75.3±8.9	<0.001
Male	116 (61)	136 (81)	<0.001
White	157 (82)	112 (66)	<0.001
Body surface area, m^2	1.92±0.26	2.00±0.24	0.005
Hypertension	90 (47)	108 (64)	0.002
Hyperlipidemia	80 (44)	98 (58)	0.006
Diabetes mellitus	47 (25)	48 (28)	0.472
Smoking	92 (48)	93 (55)	0.197
Atrial fibrillation	65 (34)	93 (55)	<0.001
Anemia	80 (44)	80 (47)	0.525
CAD requiring PCI or CABG	33 (17)	42 (25)	0.091
NYHA class ≥3	122 (64)	104 (61)	0.743
eGFR, mL/min per 1.73 m^2	65.4±26.4	59.9±23.4	0.039
β-Blocker	73 (38)	97 (57)	<0.001
ACEI/ARB	61 (32)	74 (44)	0.022
Antihypertensive	118 (62)	126 (75)	0.013
Diuretic	158 (83)	139 (82)	1.000
Amyloid-specific treatment	135 (71)	44 (26)	<0.001

AL

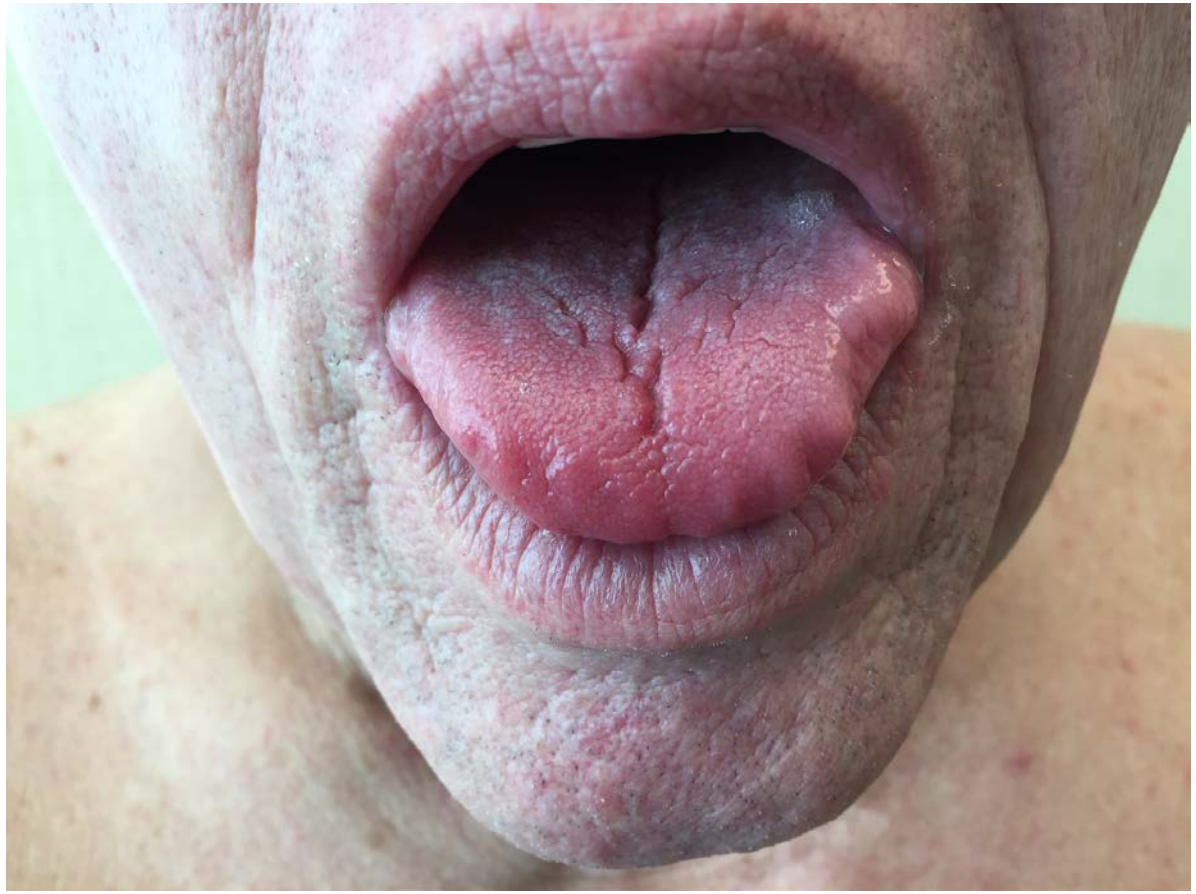
- Age 40s-70s
- Men = women
- Proteinuria
- Macroglossia, periorbital purpura, petechiae
- Carpal tunnel syndrome
- Orthostatic hypotension!
- GI involvement (diarrhea)

ATTR

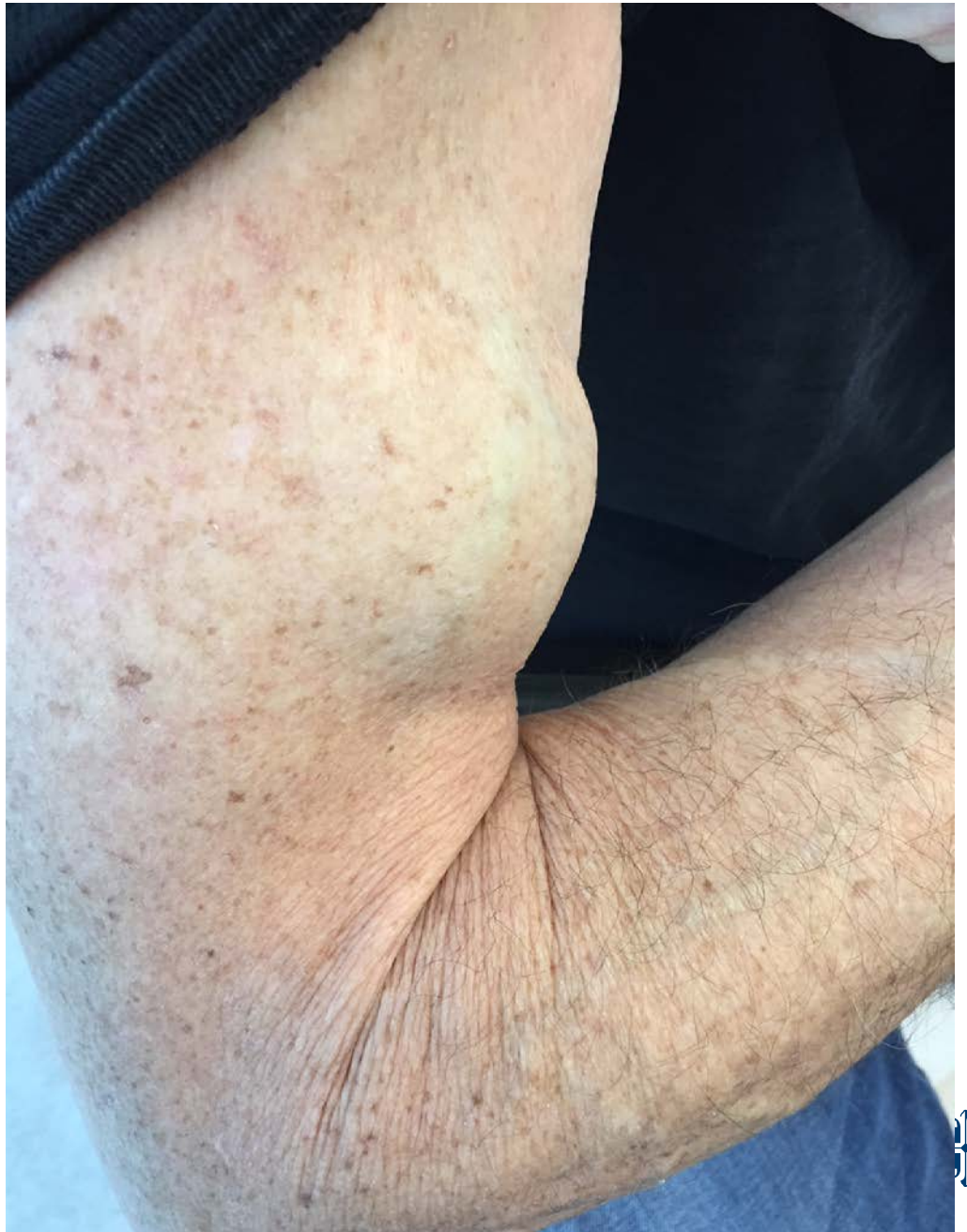
- Age 60s-80s
- Men > women
- African Americans (V122I mutation)
- HFpEF
- Low-flow low-gradient AS
- Bilateral carpal tunnel syndrome
- Spinal stenosis
- Peripheral neuropathy (in some variants)

Subtype-Specific Prognosis in Cardiac Amyloidosis *Sperry et al*

AL Amyloidosis



ATTR Amyloidosis



Non cardiac manifestations

- Polyneuropathy
  - Small fiber neuropathy most common
  - Carpal tunnel syndrome
- Autonomic neuropathy
  - Hypotension, orthostatic hypotension
  - GI motility issues
- Tendon/ligament issues
  - Carpal tunnel syndrome
  - Biceps tendon rupture
  - Trigger finger
  - Spinal stenosis

Tenosynovial and Cardiac Amyloidosis in Patients Undergoing Carpal Tunnel Release

Brett W. Sperry, MD,[a,b] Bryan A. Reyes, MD,[c] Asad Ikram, MBBS,[a] Joseph P. Donnelly, MD,[a]
Dermot Phelan, MD, PhD,[a] Wael A. Jaber, MD,[a] David Shapiro, MD,[c] Peter J. Evans, MD, PhD,[c] Steven Maschke, MD,[c]
Scott E. Kilpatrick, MD,[d] Carmela D. Tan, MD,[d] E. Rene Rodriguez, MD,[d] Cecilia Monteiro, MD,[e]
W.H. Wilson Tang, MD,[a] Jeffery W. Kelly, PhD,[e] William H. Seitz, Jr, MD,[c] Mazen Hanna, MD[a]

- 98 patients
- 12% of men ≥ 50 and women ≥ 60 years old with bilateral carpal tunnel syndrome undergoing carpal tunnel release had amyloid deposits in the wrist
- 2 had previously unknown cardiac involvement
- 1 had previously unknown hATTR neuropathy (Leu58His)
- 1 had Ala81Thr mutation without cardiac or neuropathic involvement

Tenosynovial and Cardiac Amyloidosis in Patients Undergoing Carpal Tunnel Release

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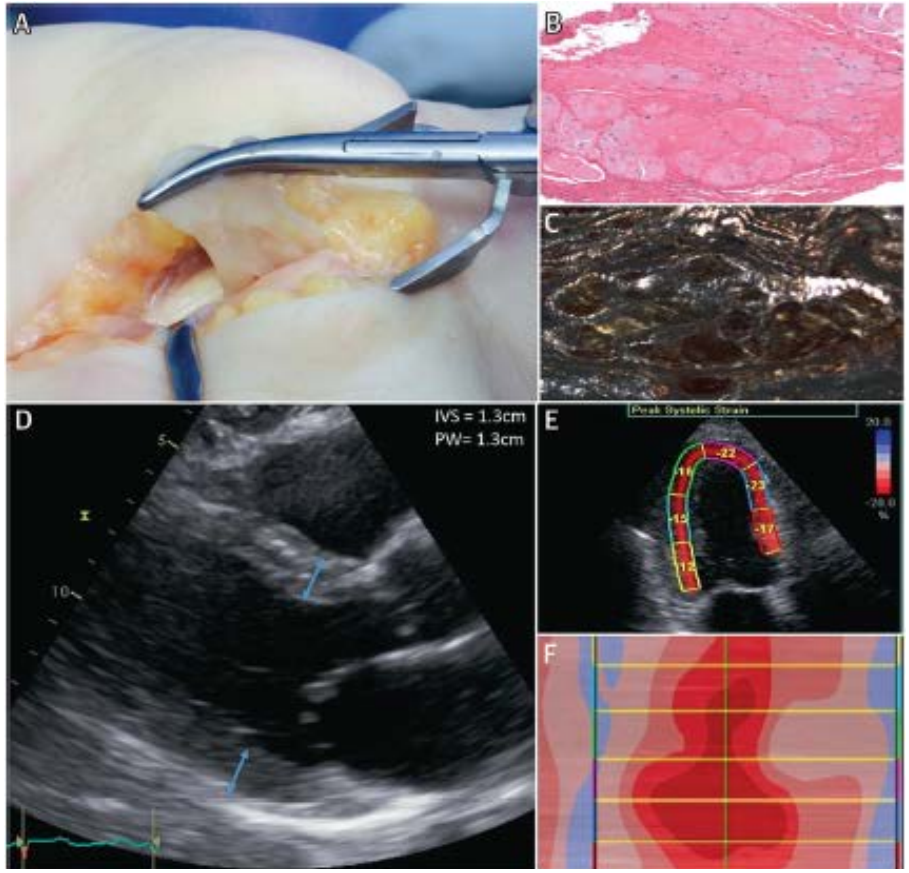
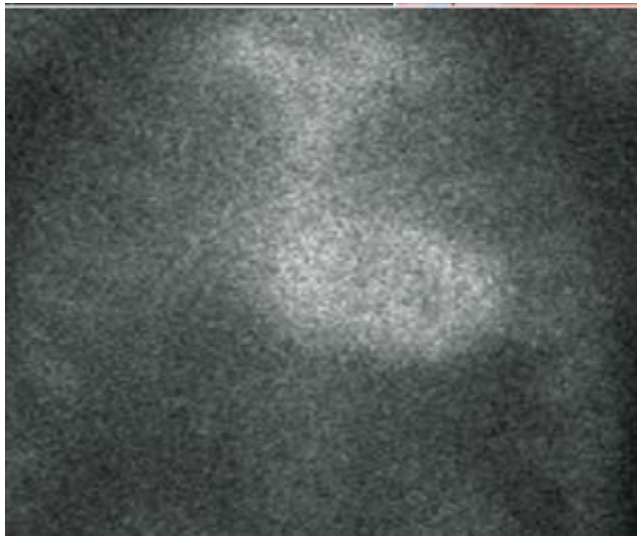
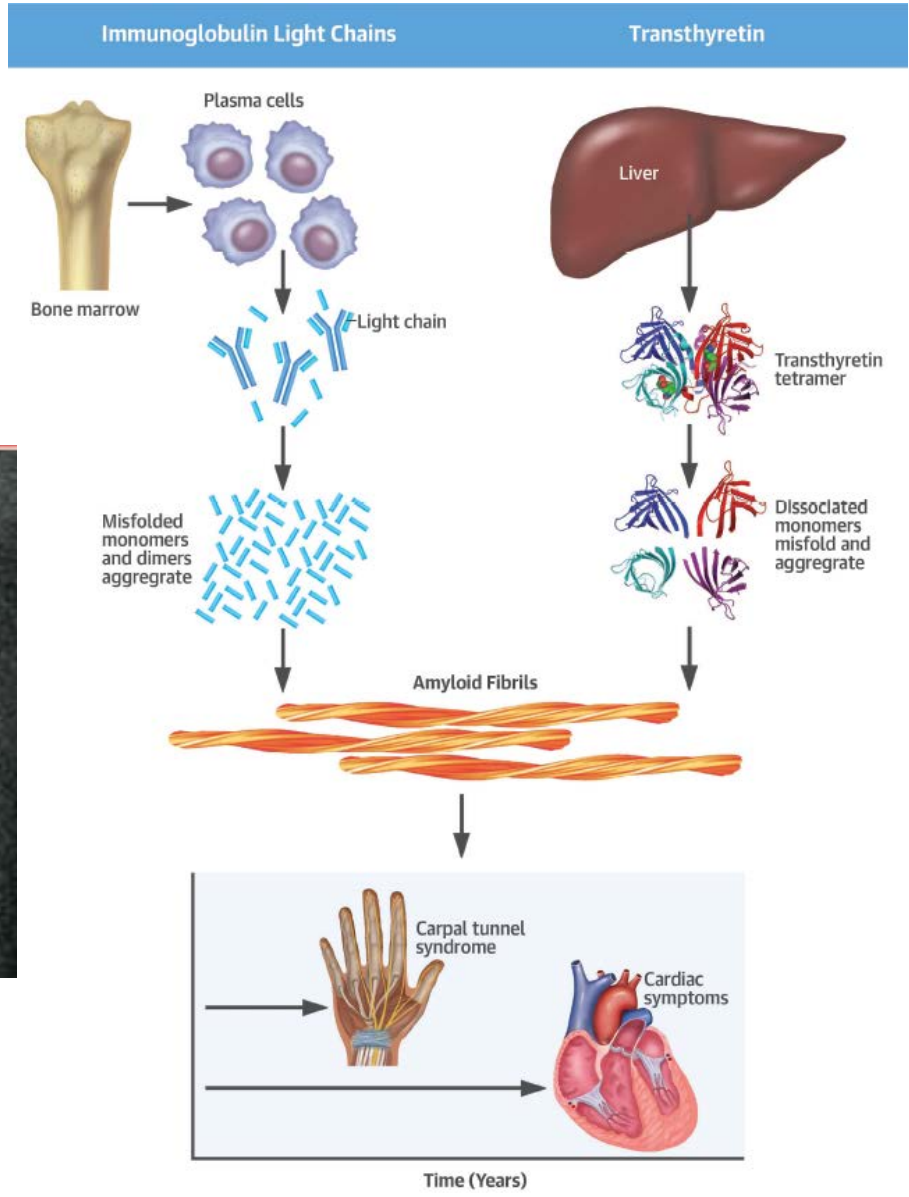
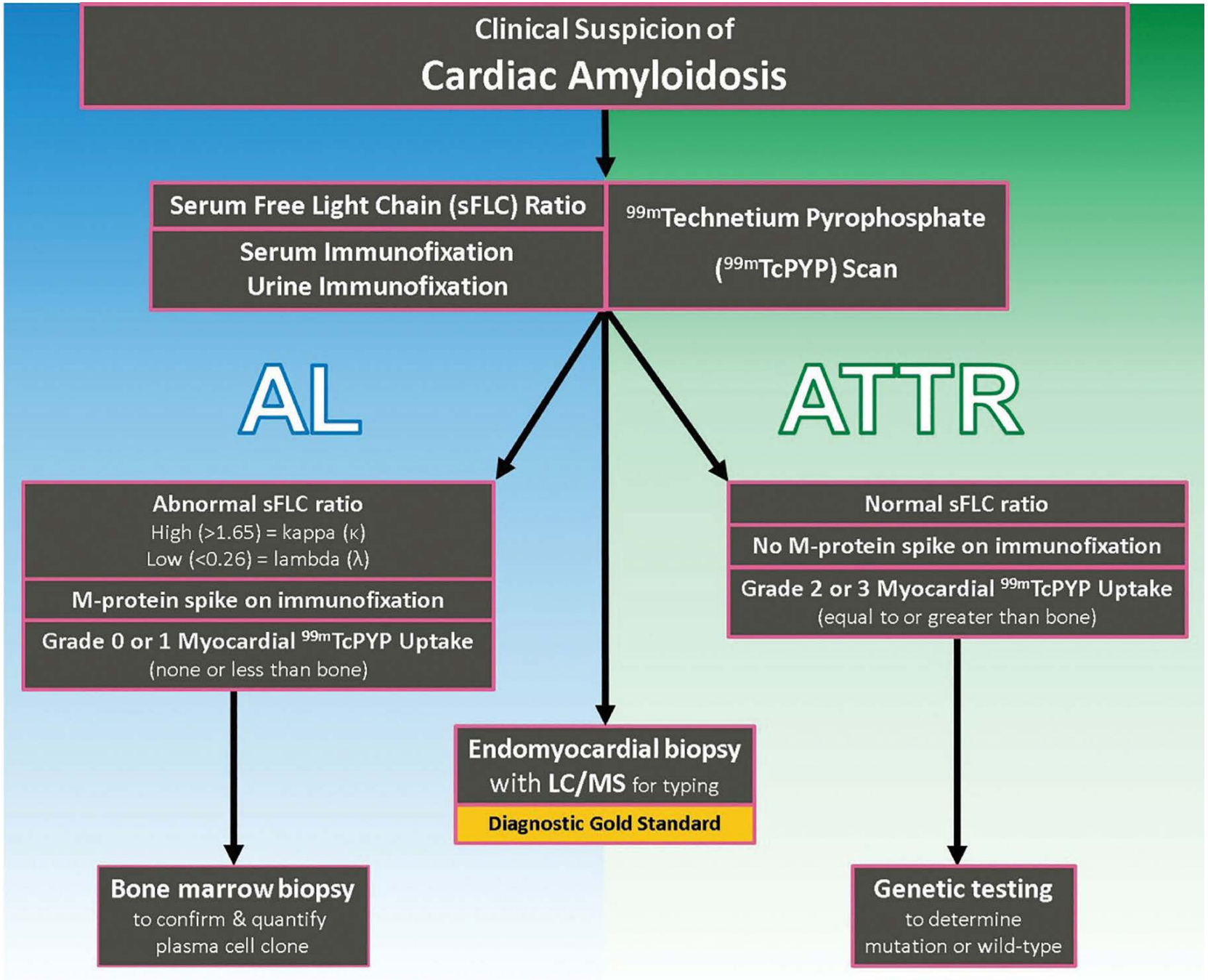






Non cardiac manifestations

- Renal
  - Proteinuria
  - Nephrotic syndrome
- Gastrointestinal
  - Liver infiltration
  - Autonomic GI neuropathy
  - Direct GI mucosal infiltration



LC/MS = liquid chromatography/mass spectrometry

Donnelly,
CCJM 2017

Red Flags for Cardiac Amyloidosis

Echocardiography:
- Low voltage on ECG and thickening of the septum/posterior wall > 1.2 cm
- Thickening of right ventricle free wall, valves

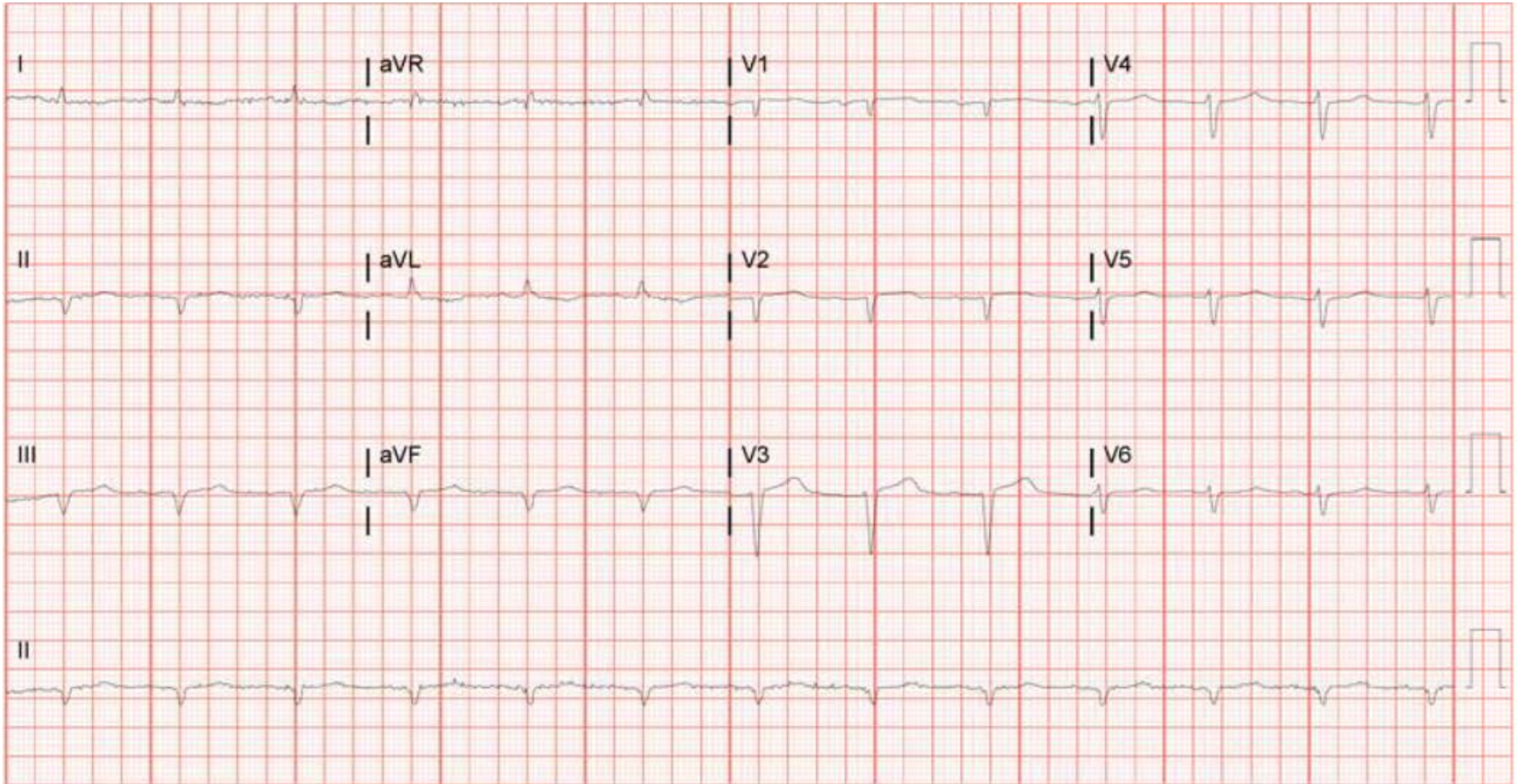
Intolerance to beta-blockers or ACE inhibitors

Low normal blood pressure in patents with a previous history of hypertension

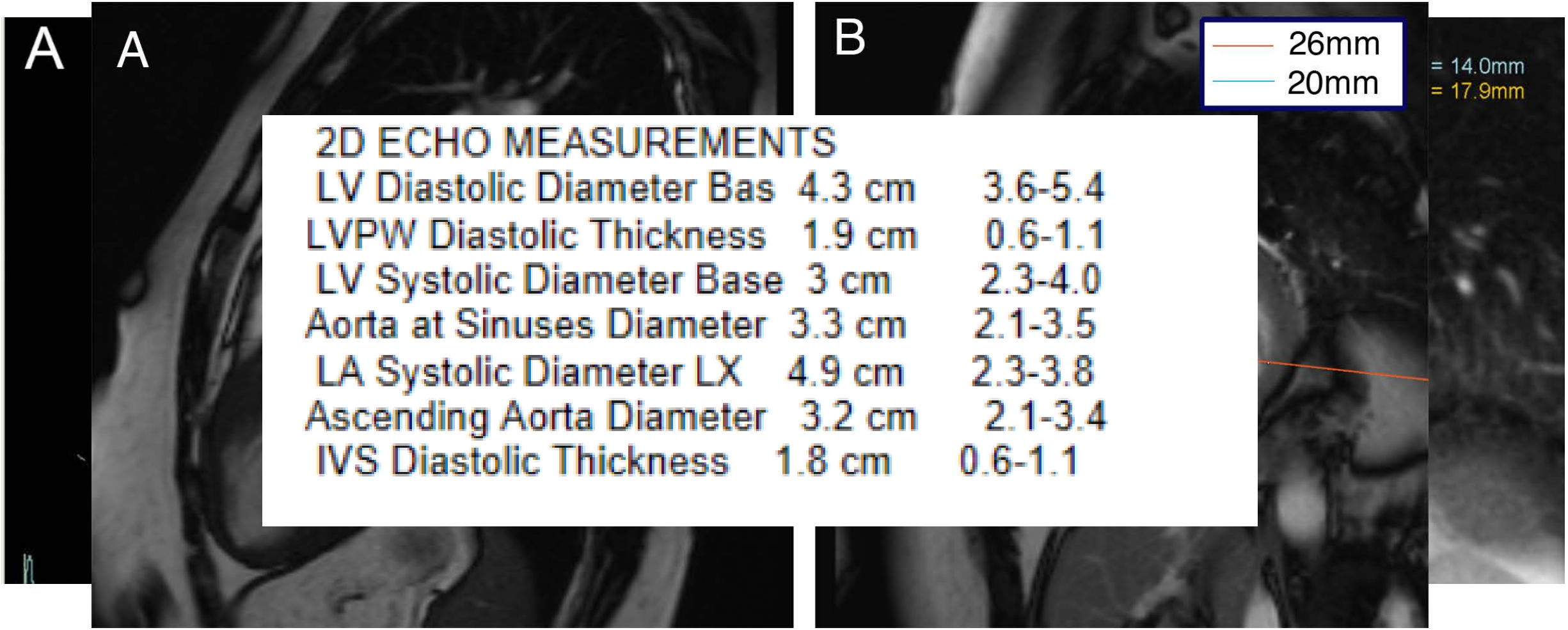
History of bilateral carpal tunnel syndrome, often requiring surgery

AL	ATTR
HFpEF + nephrotic syndrome	White male age ≥ 60 with HFpEF + history of carpal tunnel syndrome and/or spinal stenosis
Macroglossia and/or periorbital purpura	African American age ≥ 60 with HFpEF without a history of hypertension
Orthostatic hypotension	New diagnosis of hypertrophic cardiomyopathy in an elderly patient
Peripheral neuropathy	New diagnosis of low flow, low gradient aortic stenosis in an elderly patient
MGUS	Family history of ATTRm amyloidosis

Pseudoinfarct pattern, Low voltage *

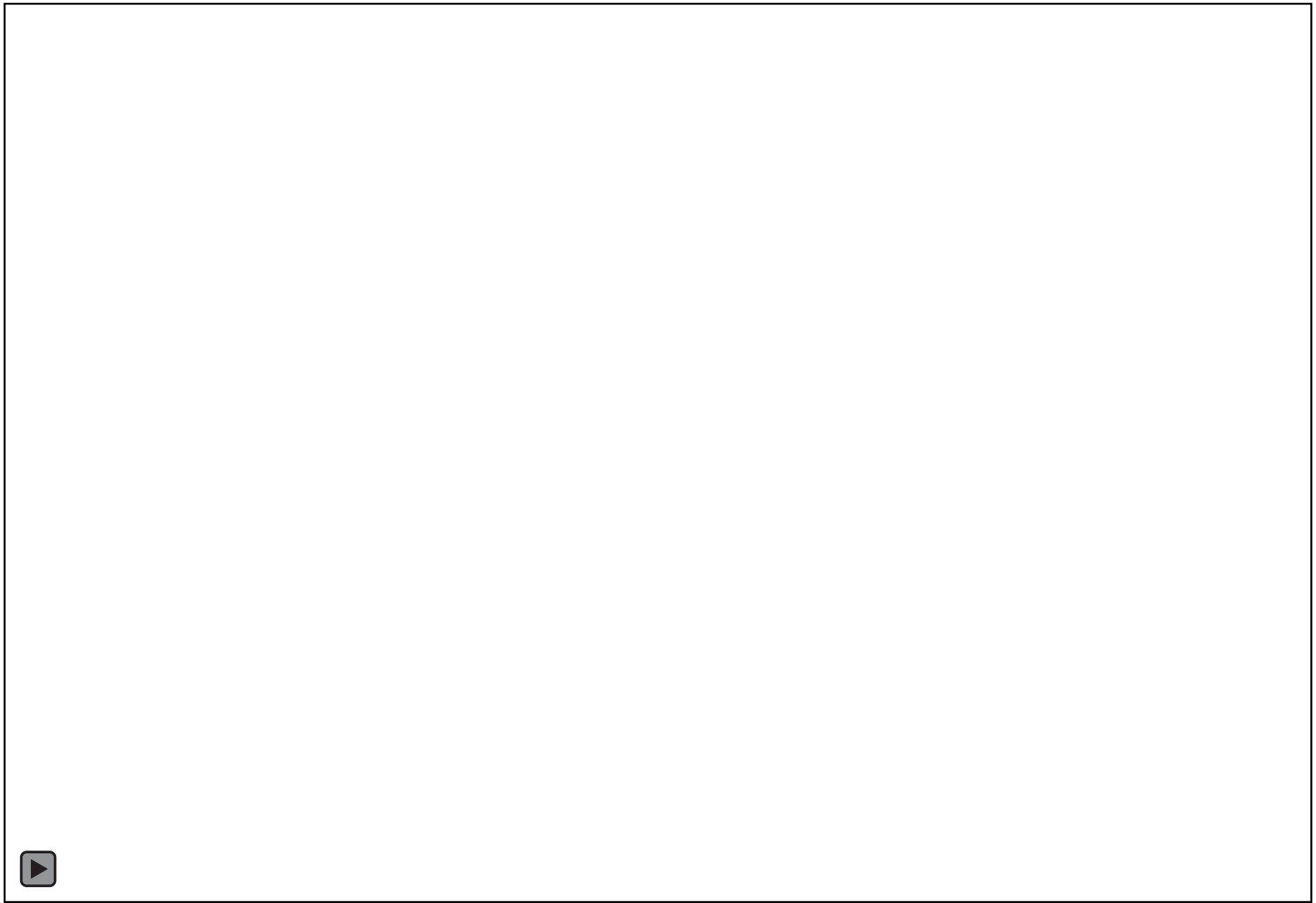


Echo – wall thickness

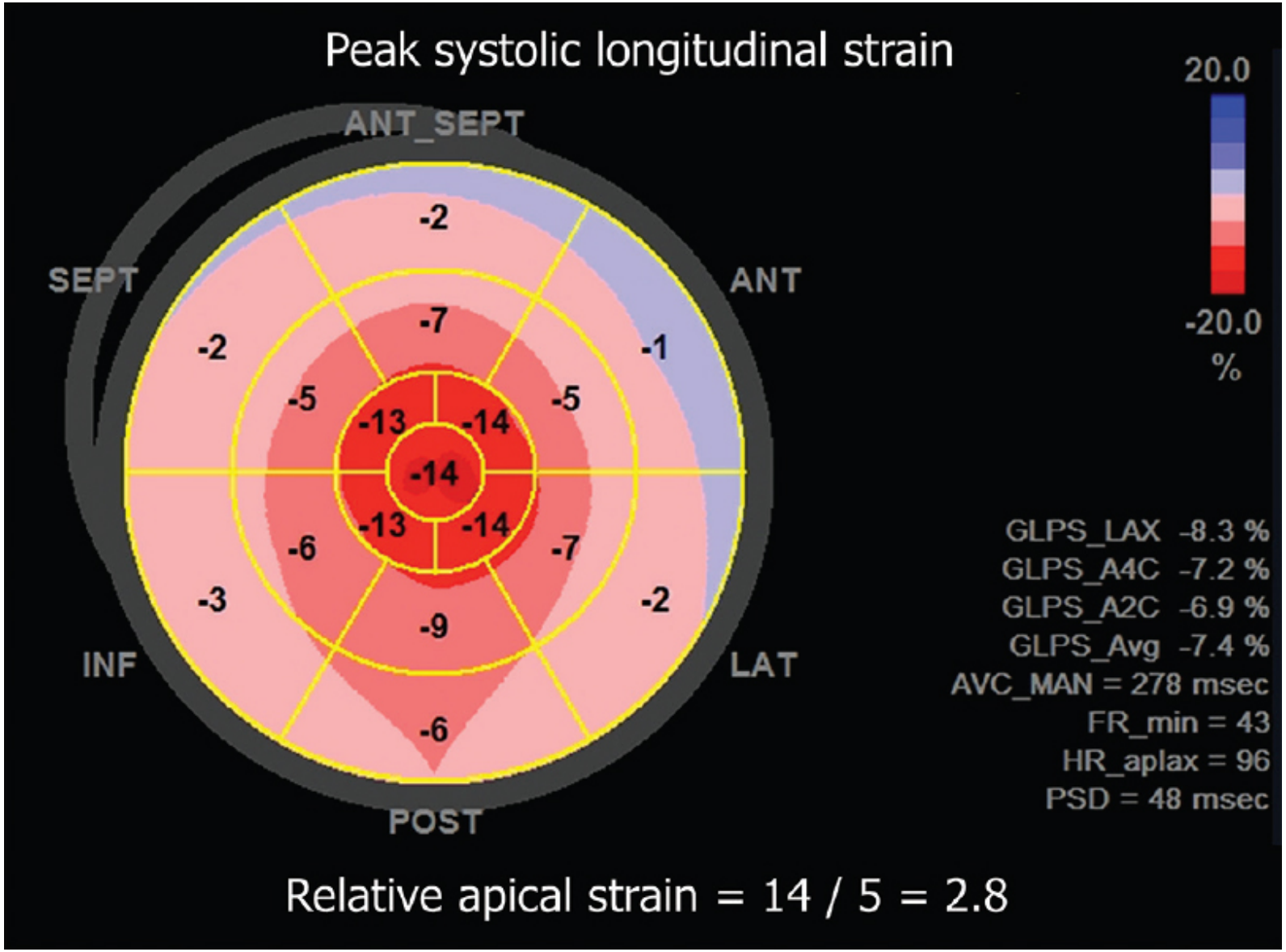


Phelan, Sperry et al. AJC 2012

Echo

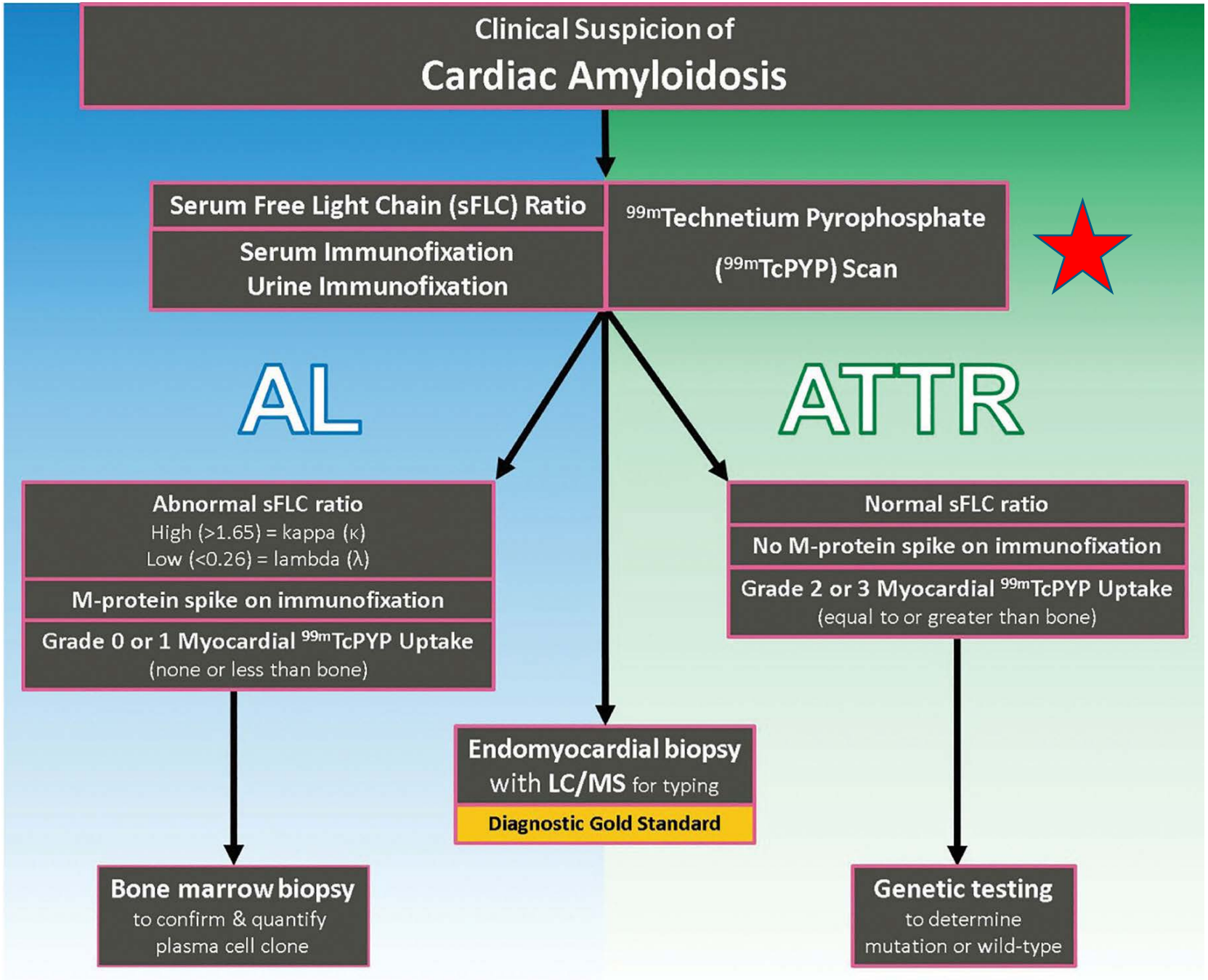


Apical Sparing Pattern: “Relative strain”



$$\frac{\text{Apical}}{\text{Basal + mid}} > 1.0$$

Phelan et al. Heart 2012
Sperry et al. Heart 2016



LC/MS = liquid chromatography/mass spectrometry

Donnelly,
CCJM 2017

ASNC

ASNC
PRACTICE POINTS

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

OVERVIEW

The purpose of this document is to identify the critical

diagnosis is confirmed by endomyocardial biopsy and typing of amyloid fibrils as needed.

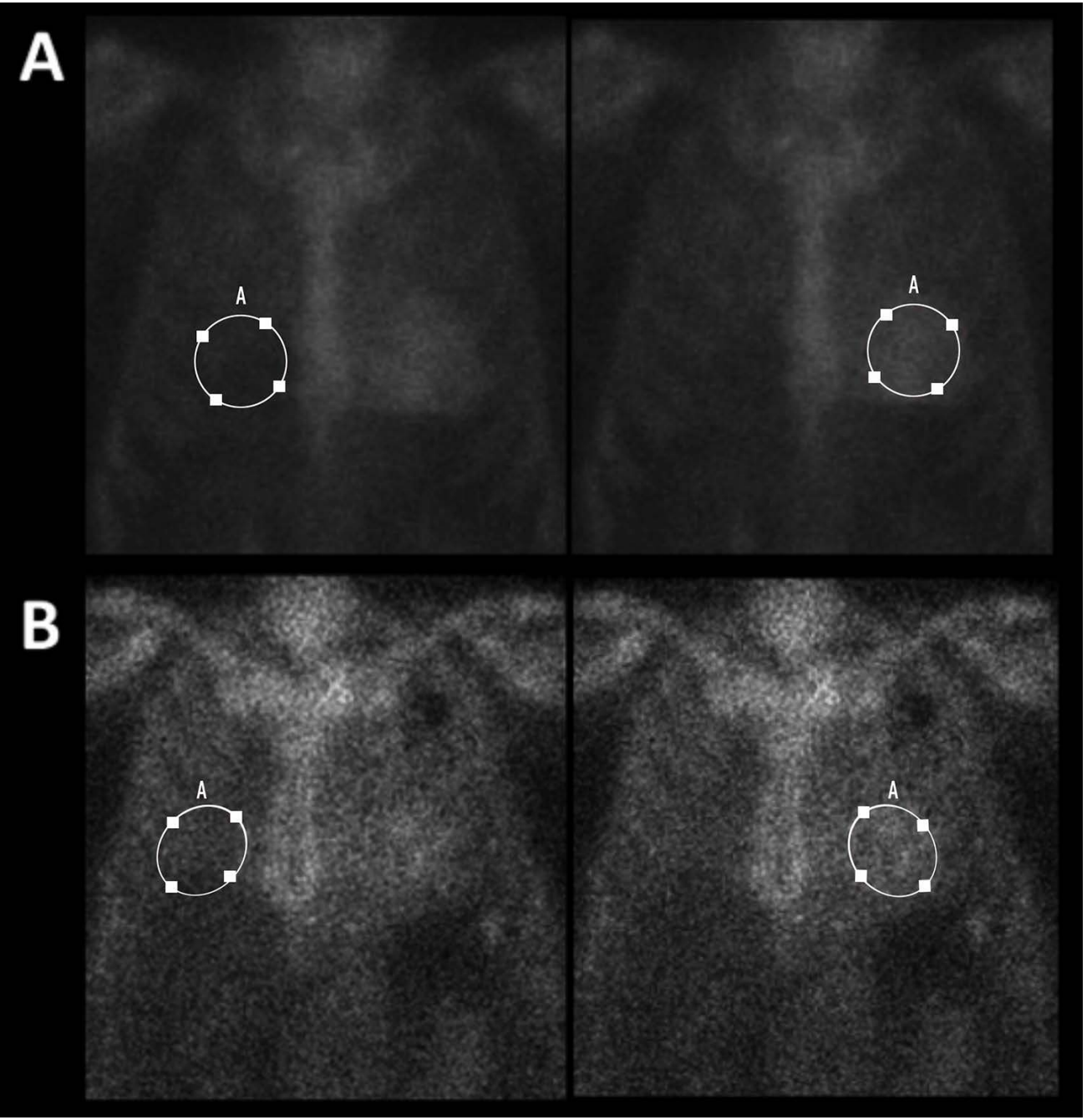
"**Bone Scintigraphy** enables the diagnosis of ATTR to be made reliably without the need for histology in patients who do not have a monoclonal gammopathy."

EXPERT CONSENSUS RECOMMENDATIONS

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

EXPERT CONSENSUS RECOMMENDATIONS

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



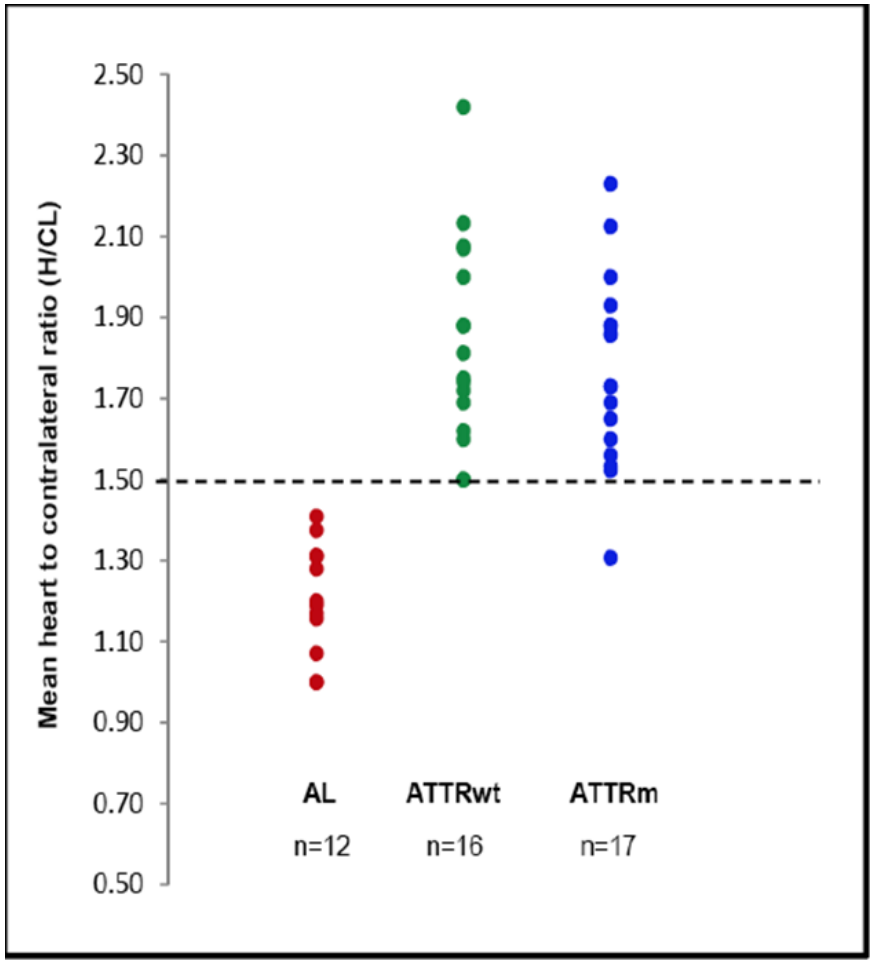
Perugini score

0 – absent uptake - NEGATIVE

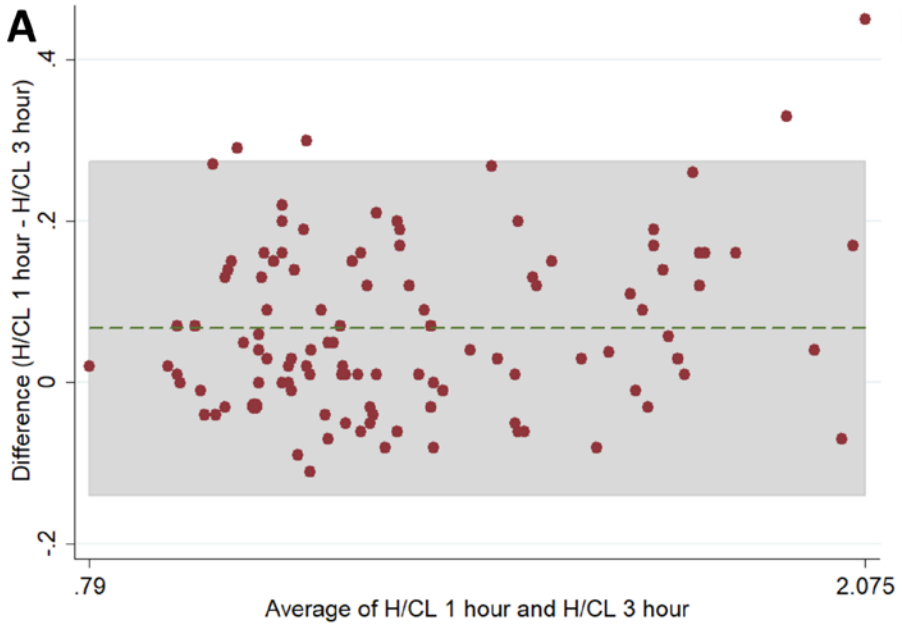
1 – less than rib – INDETERMINATE

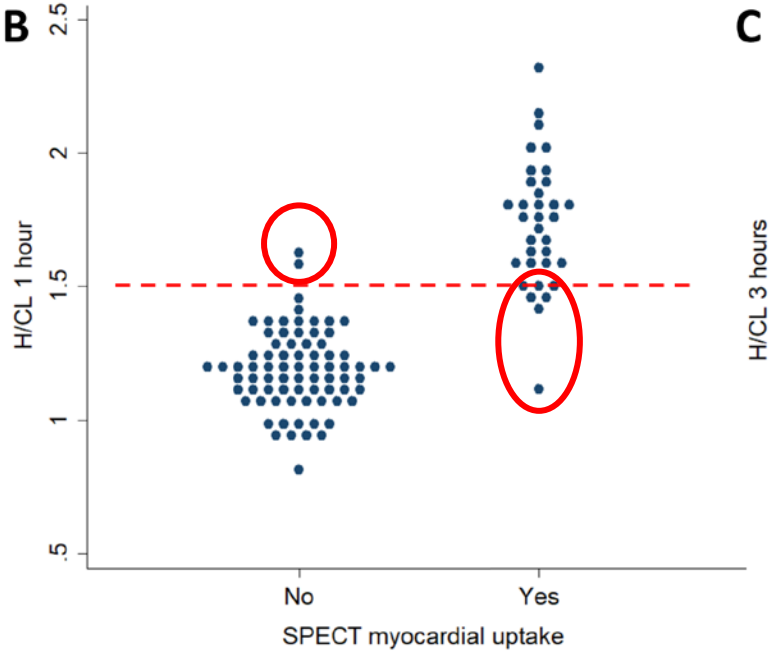
2 – equal to rib – LIKELY POSITIVE

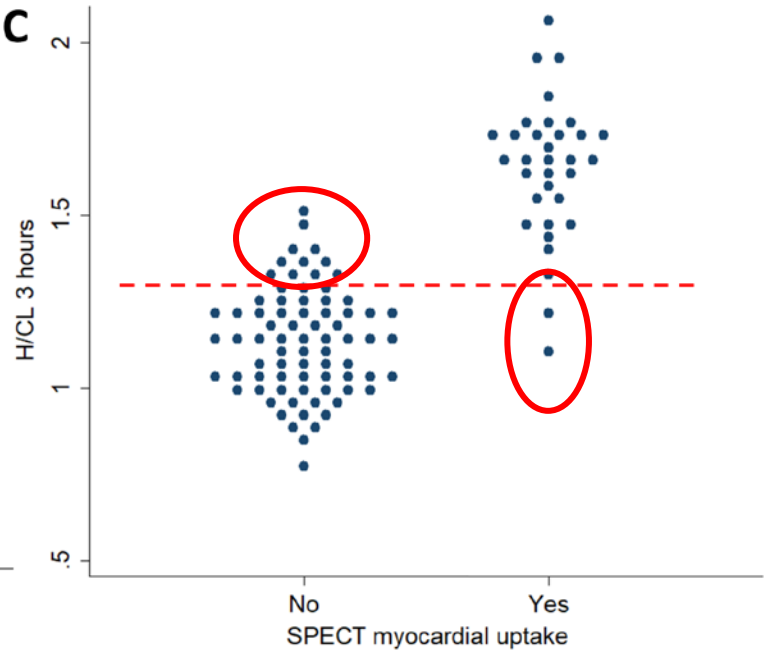
3 – greater than rib – POSITIVE

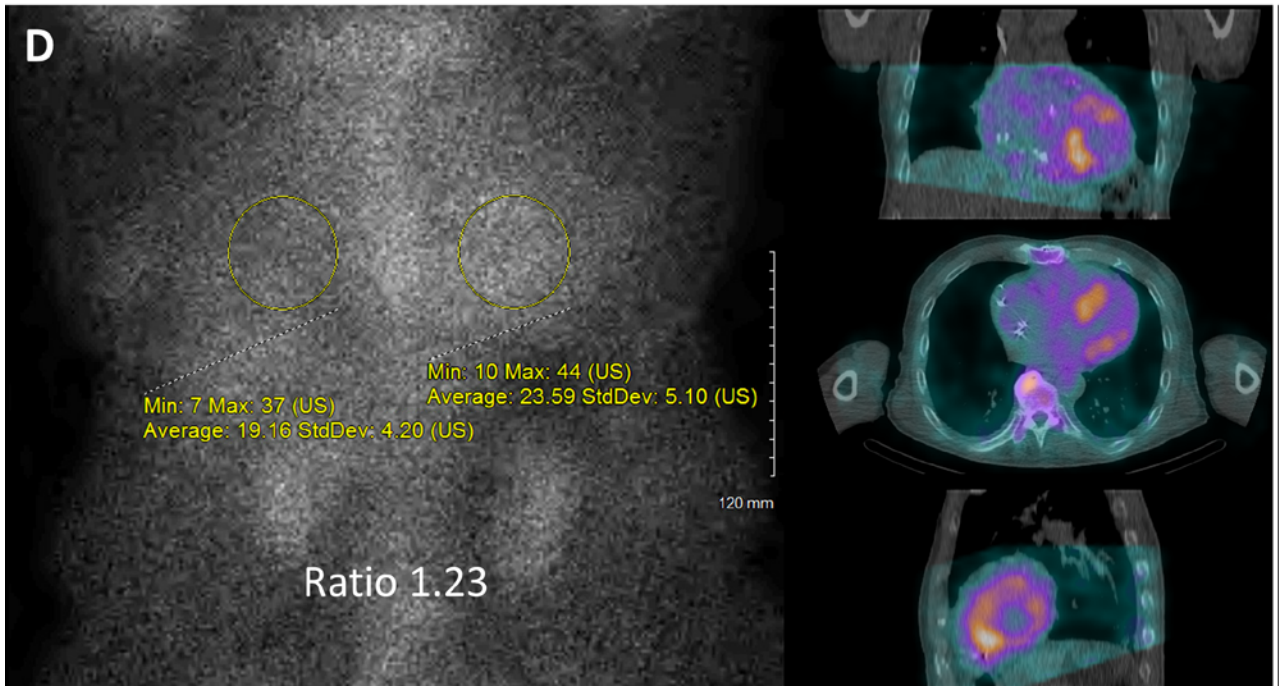


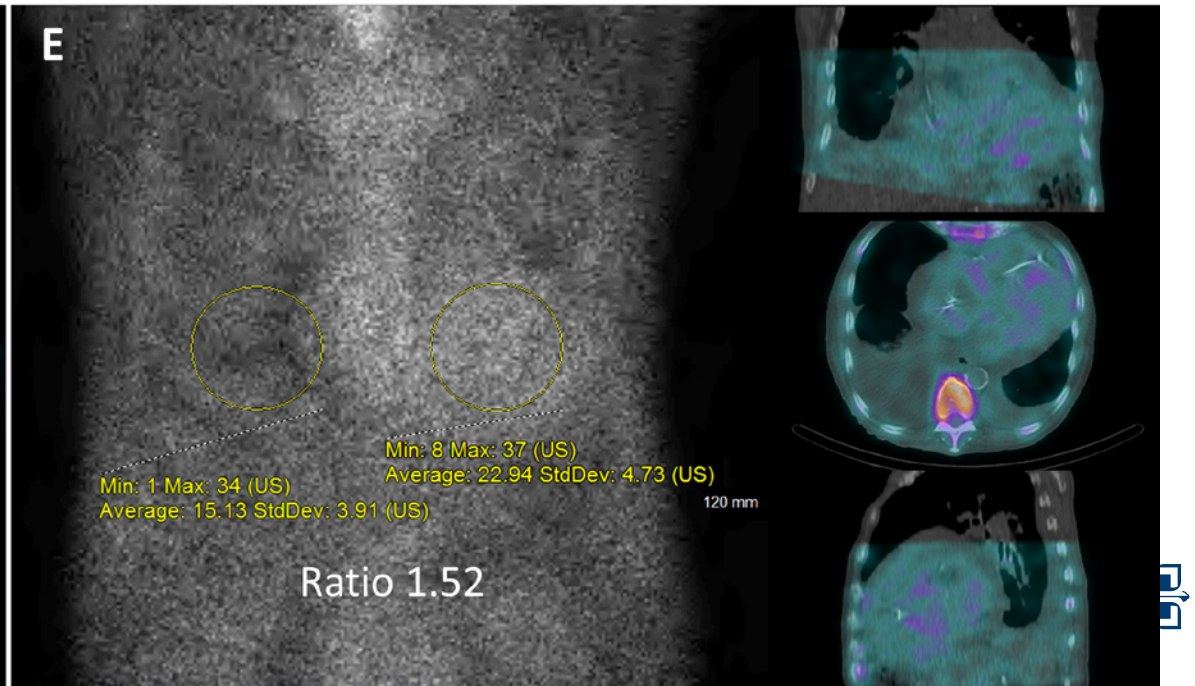
Sperry et al, JNC 2020

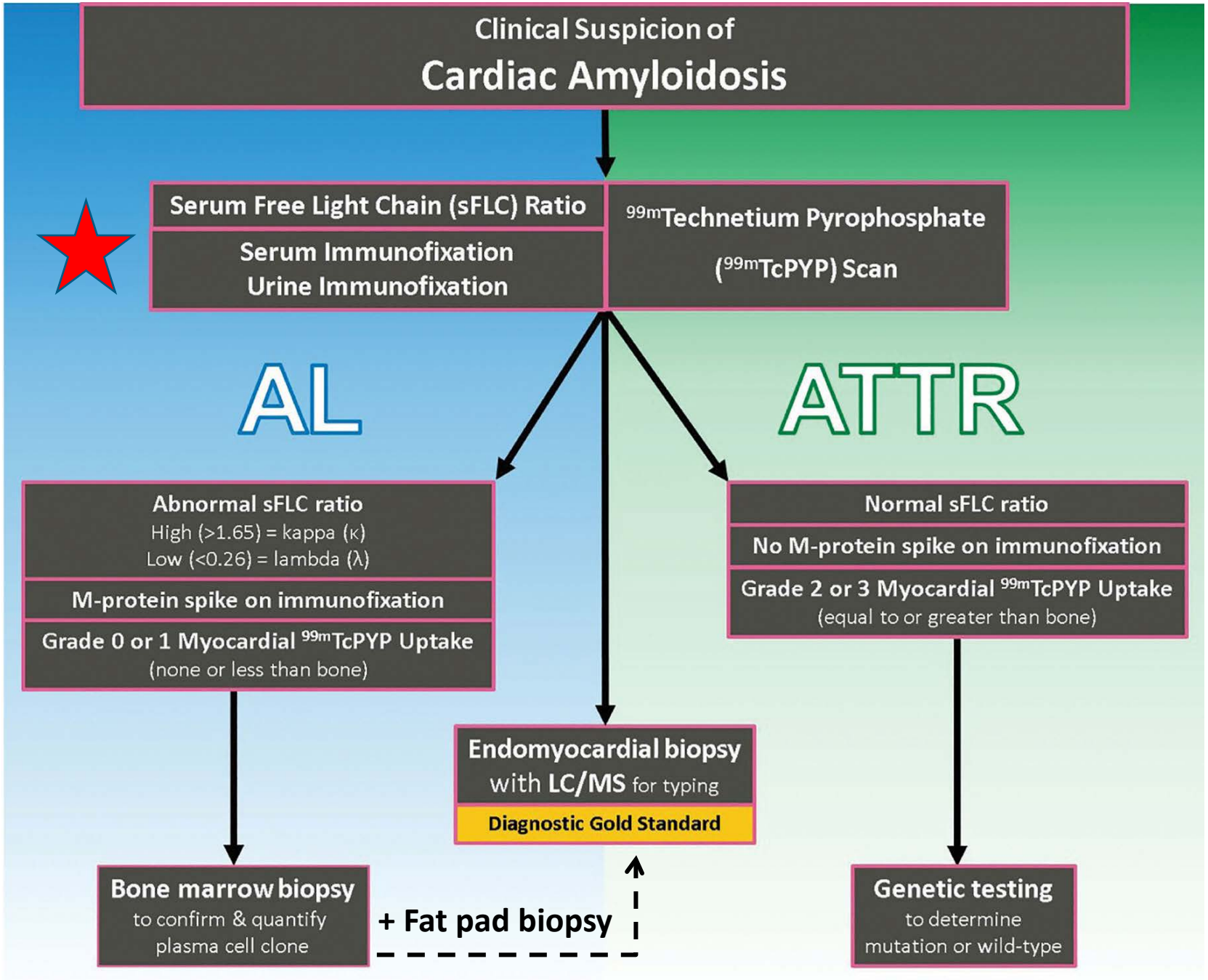












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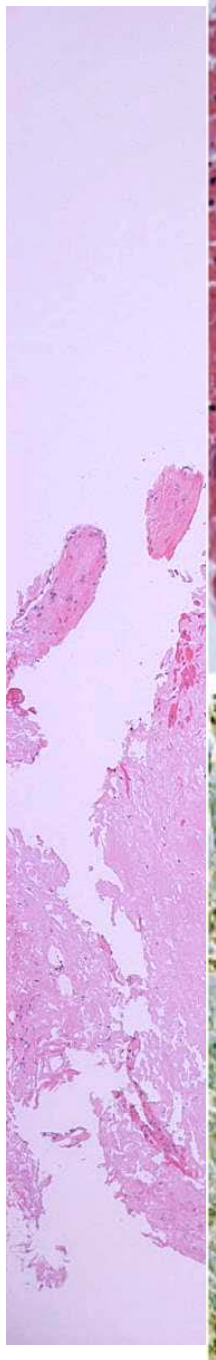
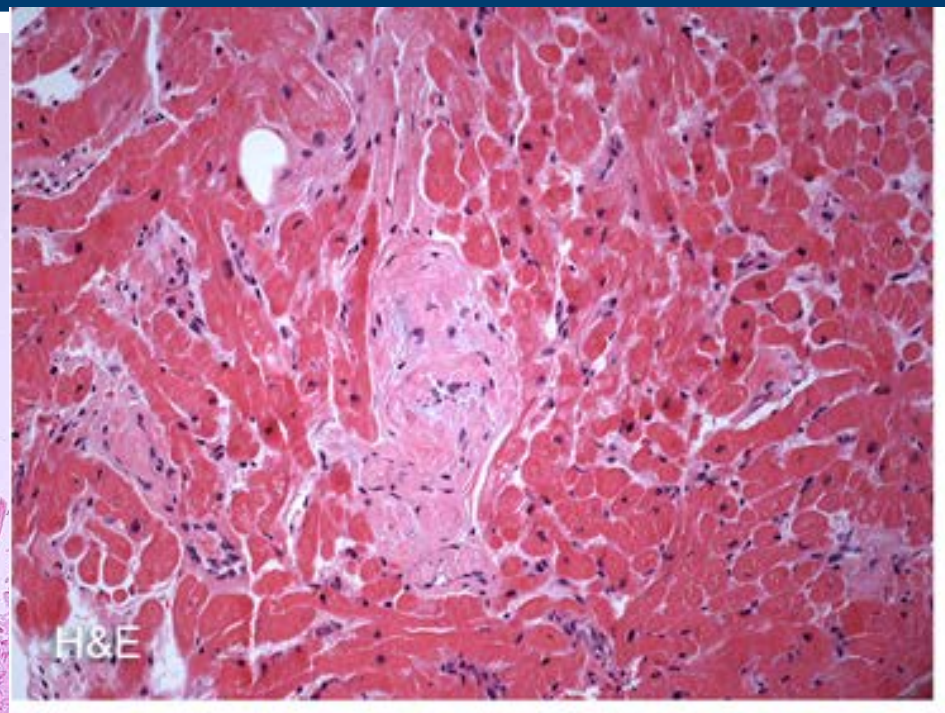
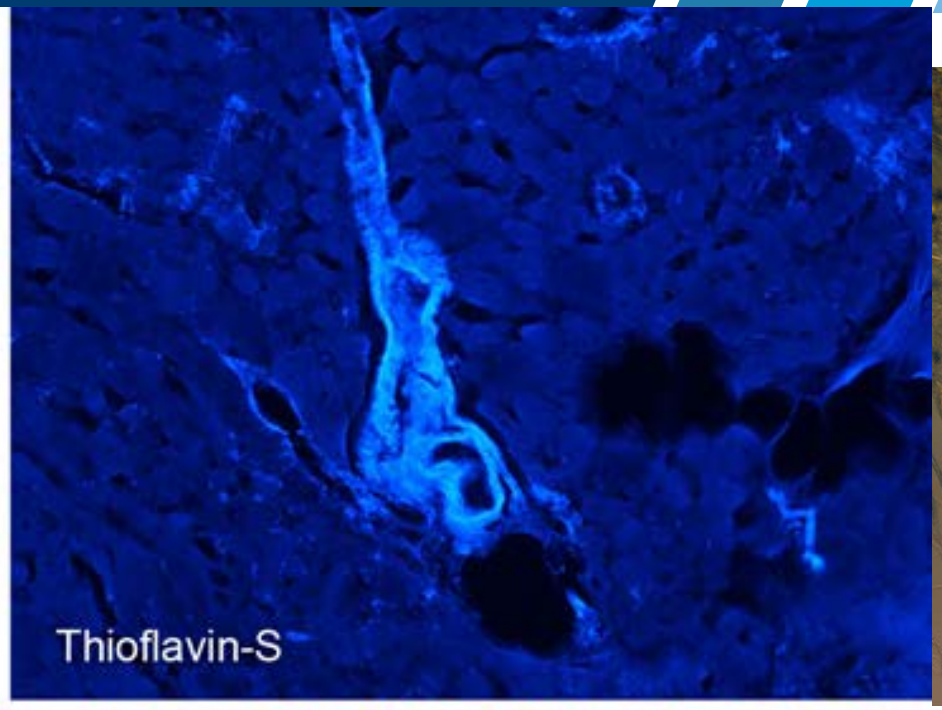
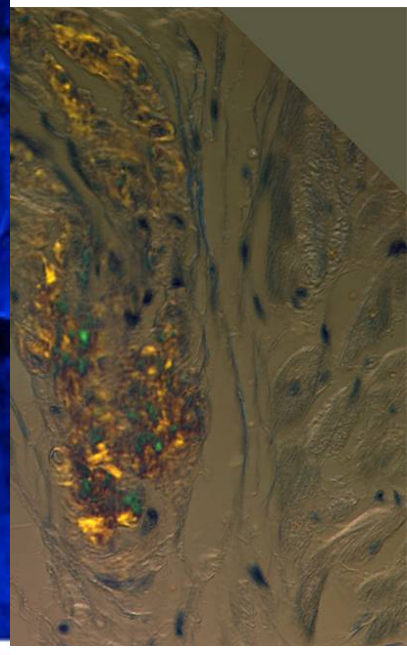
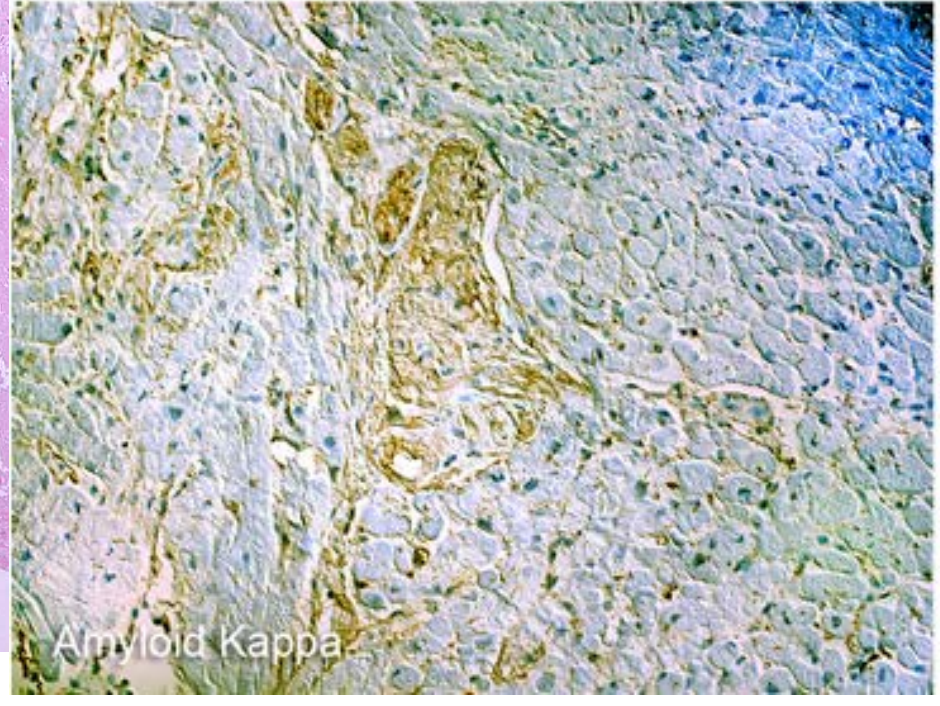
Donnelly,
CCJM 2017

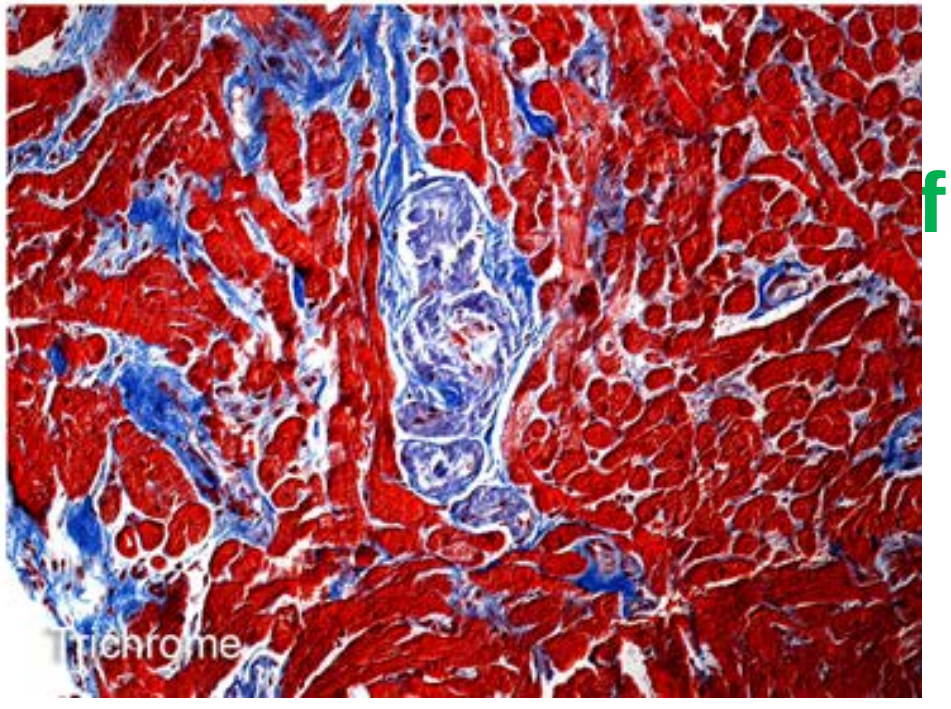












fringence

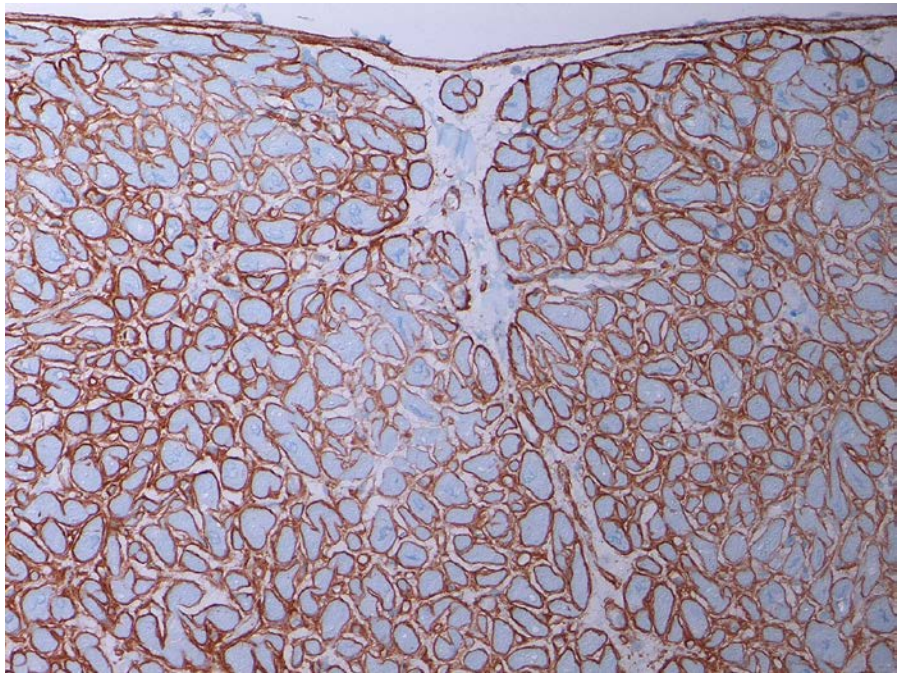
MUST SUBTYPE THE AMYLOID!!

Congo Red only tells you if it is amyloid

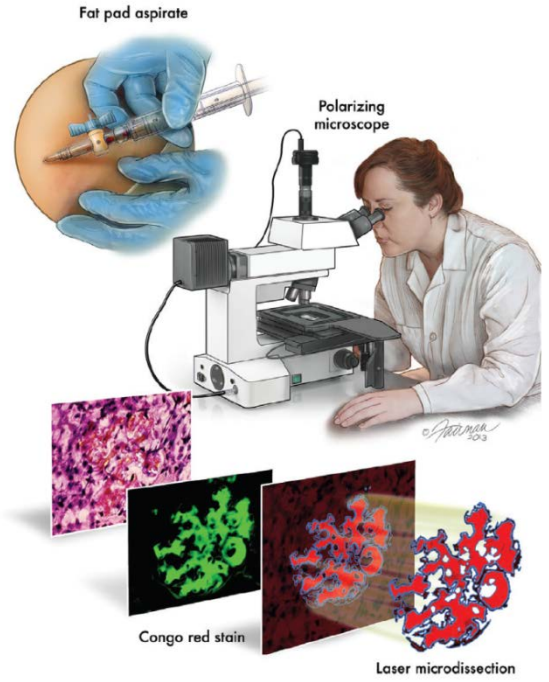
(What type, AL? TTR?, other?)

- Prognosis
- Treatment

Immunofluorescence



Mass Spectrometry



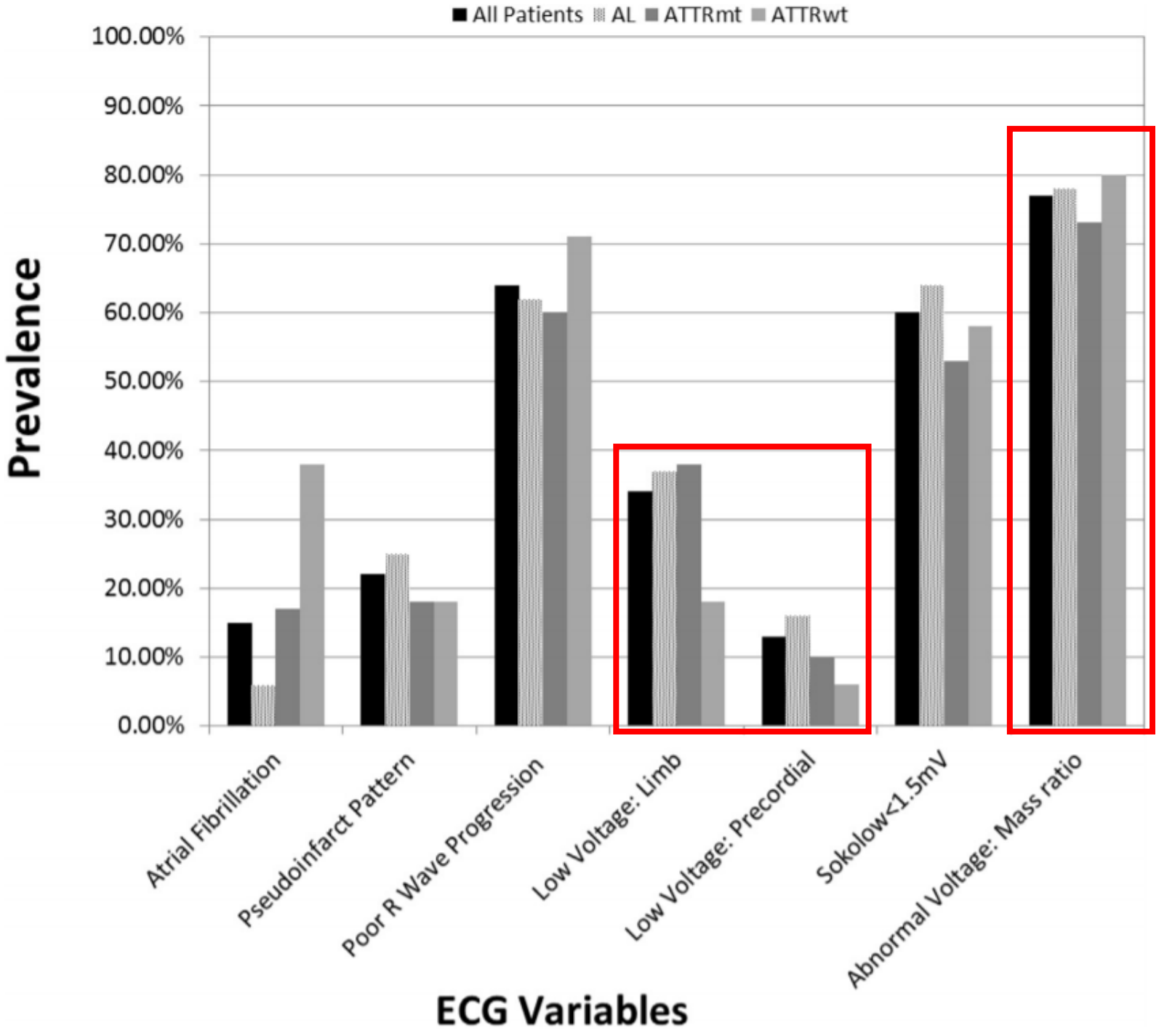
Common misconceptions

- **Rare**
  - **13% of patients admitted with HFpEF and septal thickness >12mm**
  - **16% of patients undergoing TAVR (22% of men undergoing TAVR)**
  - **30% of patients with LFLG AS with EF <50%**
  - **12% of men ≥ 50 and women ≥ 60 years old with bilateral carpal tunnel syndrome undergoing carpal tunnel release**

EHJ (2015) 36, 2585-2594
Castano et al EHJ 2017
Treibel et al Circ Imaging 2016
Sperry et al JACC 2018

Common misconceptions

- **Rare**
  - Under-appreciated and under-recognized cause of HFpEF
- **Low voltage on ECG is a good screening test**



Cyrille, Maurer et al. AJC 2014

Common misconceptions

- **Rare**
  - Under-appreciated and under-recognized cause of HFpEF
- **Low voltage on ECG is a good screening test**
  - Many patients with amyloidosis do not meet low voltage criteria
- **Fat pad biopsy has high sensitivity**

Diagnostic sensitivity of fat pad fine needle aspiration in different cardiac amyloidoses

Amyloid type	*n*	Number positive by Congo red staining	Diagnostic sensitivity (CI)
Systemic AL amyloidosis	216	181	84% (78–88%)
ATTRm	113	51	45% (36–54%)
Val122Ile	69	23	33%
Thr60Ala	21	14	67%
ATTRwt	271	42	15% (11–20%)

Common misconceptions

- **Rare**
  - Under-appreciated and under-recognized cause of HFpEF
- **Low voltage on ECG is a good screening test**
  - Many patients with amyloidosis do not meet low voltage criteria
- **Fat pad biopsy has high sensitivity**
  - 85% for AL, but only 15% for wild type ATTR
- **SPEP is sufficient to exclude AL amyloidosis**
  - Usually NORMAL
- **Cardiac amyloidosis is the great masquerader**
- **Need an invasive and risky endomyocardial biopsy for diagnosis**
  - Not for ATTR. For AL, will need some tissue diagnosis → non cardiac options = bone marrow, fat pad, skin lesion, kidney

Common misconceptions

- **Everyone dies so it is not worth diagnosing**

Treatments

- AL amyloidosis

AL Therapeutic Regimens

The New England Journal of Medicine

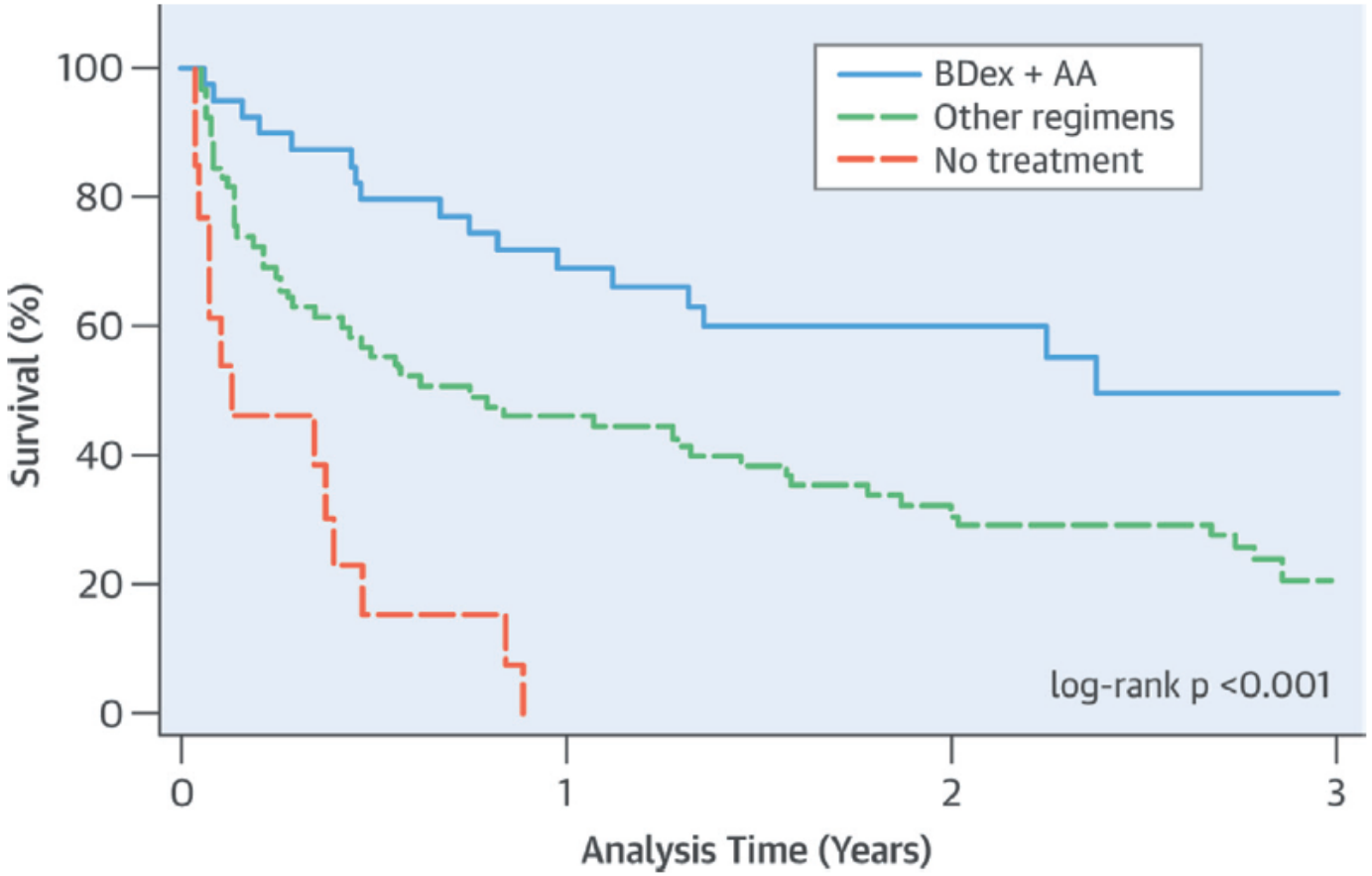
A TRIAL OF THREE REGIMENS FOR PRIMARY AMYLOIDOSIS: COLCHICINE ALONE, MELPHALAN AND PREDNISONE, AND MELPHALAN, PREDNISONE, AND COLCHICINE

Robert A. Kyle, M.D., Morie A. Gertz, M.D., Philip R. Greipp, M.D., Thomas E. Witzig, M.D., John A. Lust, M.D., Ph.D., Martha Q. Lacy, M.D., and Terry M. Therneau, Ph.D.

AL Amyloidosis Therapeutic Options

Decreased light chain production					Fibril destabilizers
Steroids	**Proteasome Inhibitors**	**Immunomodulatory Drugs (IMiDs)**	**Alkylating Agents**	**Other**	**Novel Agents**
Prednisone	Bortezomib (Velcade)	Lenalidomide (Revlimid)	Melphalan (oral) (Alkeran)	Daratumumab (Darzalex)	CAEL-101 (11-1F4)
Dex	Carfilzomib (Kyprolis)	Thalidomide (Thalomid)	Melphalan (IV) (Transplant)	Isatuximab (SAR650984)	Dezamizumab (GSK[illegible]8852) (anti-SAP mAB)
	Ixazomib (Ninlaro)	Pomalidomide (Pomalyst)	Cyclophosphamide (Cytoxan)	Venetoclax (Venclexta)	NP[illegible]001
	Marizomib		Bendamustine (Treanda)		Doxycycline / TUDCA
	Oprozomib				EGCG (Green tea extract)
					Curcumin (Turmeric)

CENTRAL ILLUSTRATION Chemotherapy in AL Amyloidosis With Heart Failure: Kaplan-Meier Survival Estimates



Sperry, B.W. et al. J Am Coll Cardiol. 2016;67(25):2941-8.

Kaplan-Meier curve representing the association between treatment regimen and all-cause mortality. There was a significant association between treatment regimen and survival ($p < 0.001$), with the lowest mortality seen in the bortezomib, dexamethasone, and alkylating agent (BDex+AA) cohort.

Treatments

- AL cardiac amyloidosis
  - Bortezomib + cyclophosphamide + dexamethasone (CyBorD)
  - Daratumumab
  - CyBorD + daratumumab
  - High dose melphalan + ASCT → considered in patients with less cardiac involvement
- ATTR cardiac amyloidosis

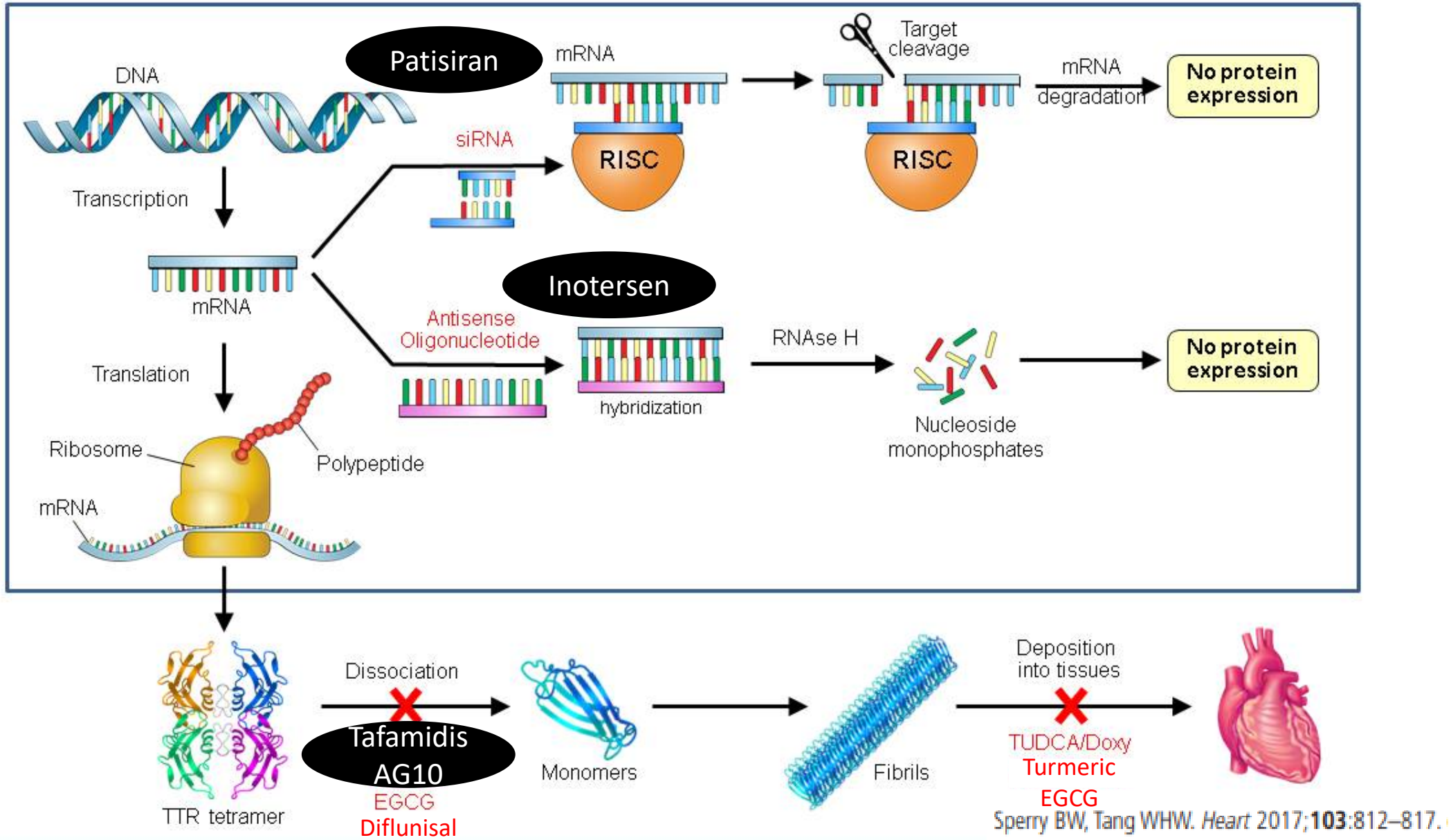


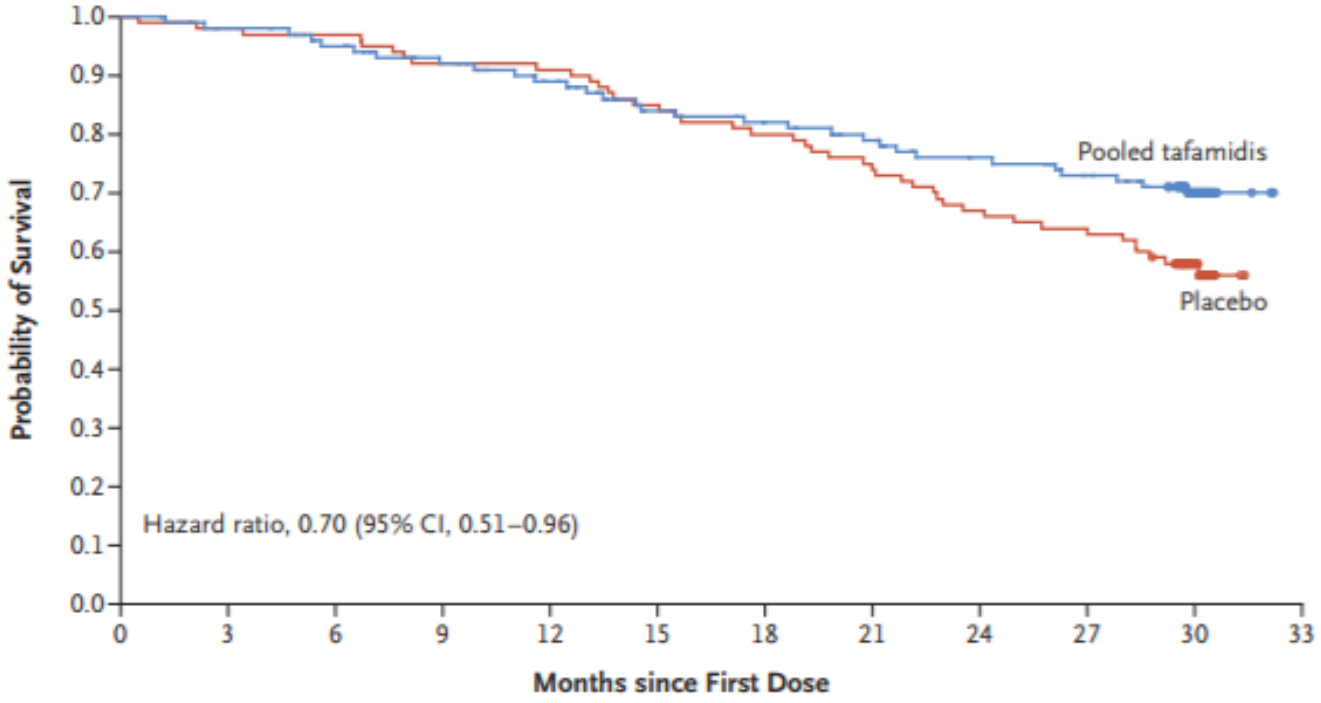
Figure 2: Transthyretin protein production and drug mechanisms of action

The TTR gene is transcribed into mRNA and translated into a protein. The protein folds into monomers which are aggregated into a tetramer. Translation of TTR mRNA can be blocked by using either a small interfering RNA (siRNA) or an antisense oligonucleotide. siRNA is a synthetic double-stranded RNA which uses the RNA-induced silencing complex (RISC) to cleave TTR mRNA. Anti-sense oligonucleotides are short complementary DNA sequences which hybridize with the mRNA which is recognized and cleaved by an RNase. Tafamidis, diflunisal or EGCG work on the folded TTR protein by stabilizing the tetramer and preventing dissociation into monomers which can form fibrils. TUDCA/Doxycycline and anti-SAP antibodies act by allowing re-uptake of deposited fibrils and also preventing some fibril deposition.

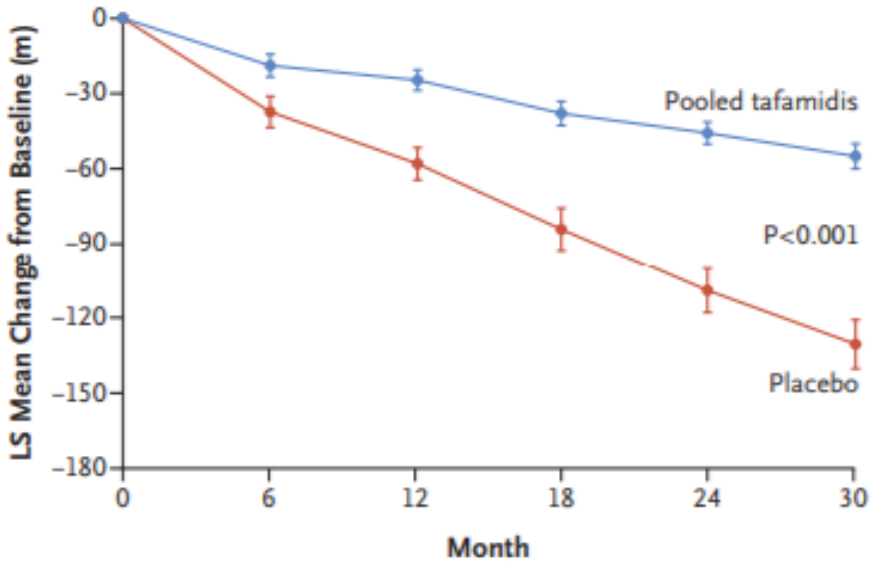
ORIGINAL ARTICLE

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*

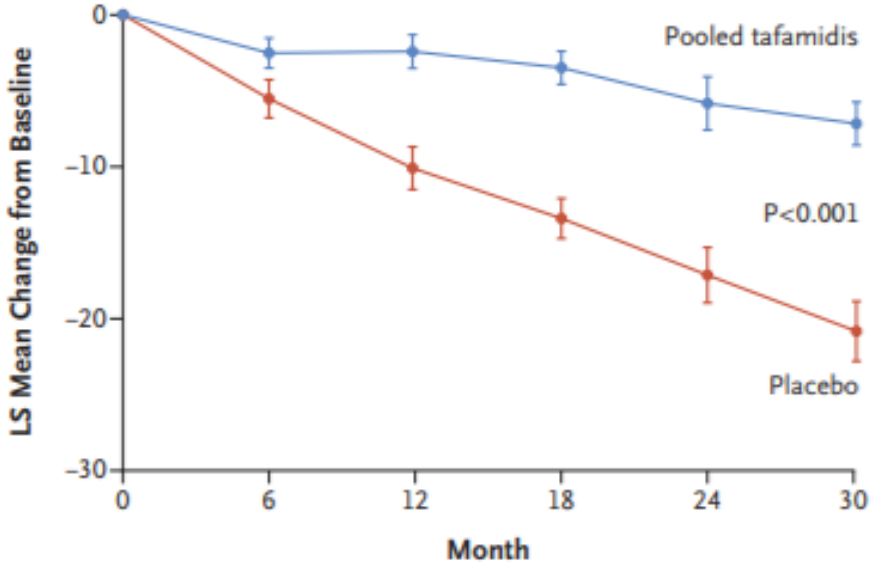


A Change from Baseline in 6-Minute Walk Test



No. of Patients						
Tafamidis	264	233	216	193	163	155
Placebo	177	147	136	111	85	70

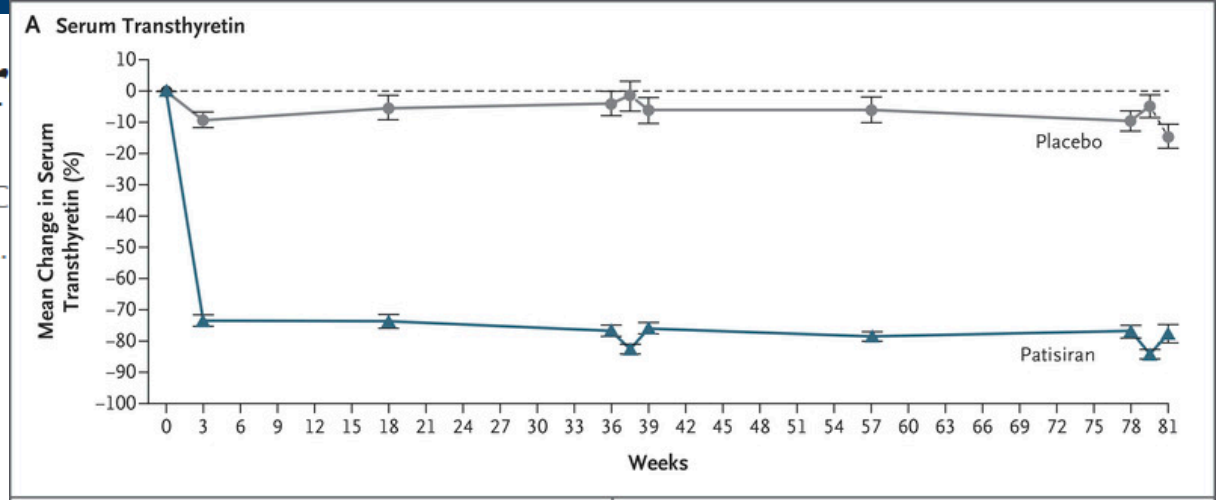
B Change from Baseline in KCCQ-OS

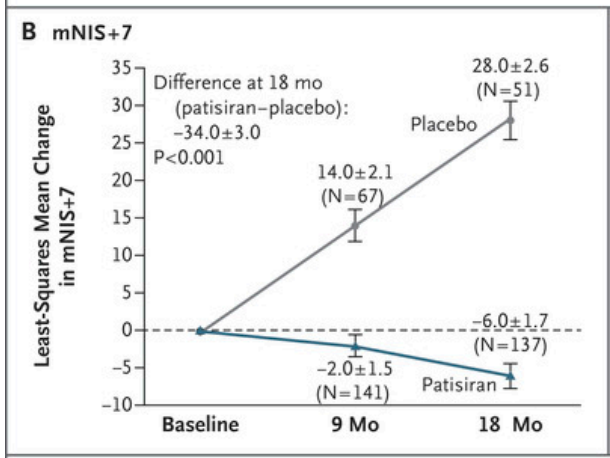


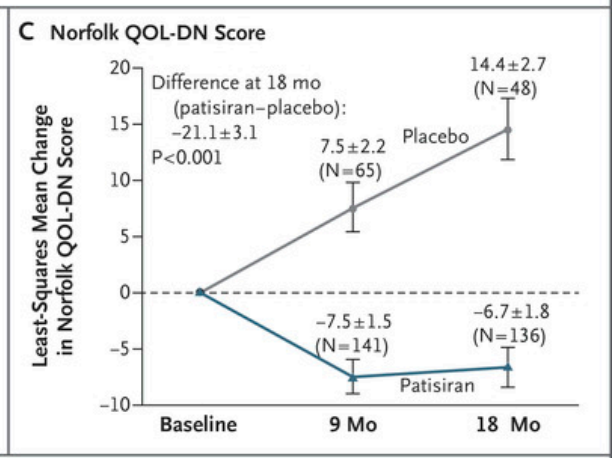
Patisiran, an RNAi Therapeutic, for Her

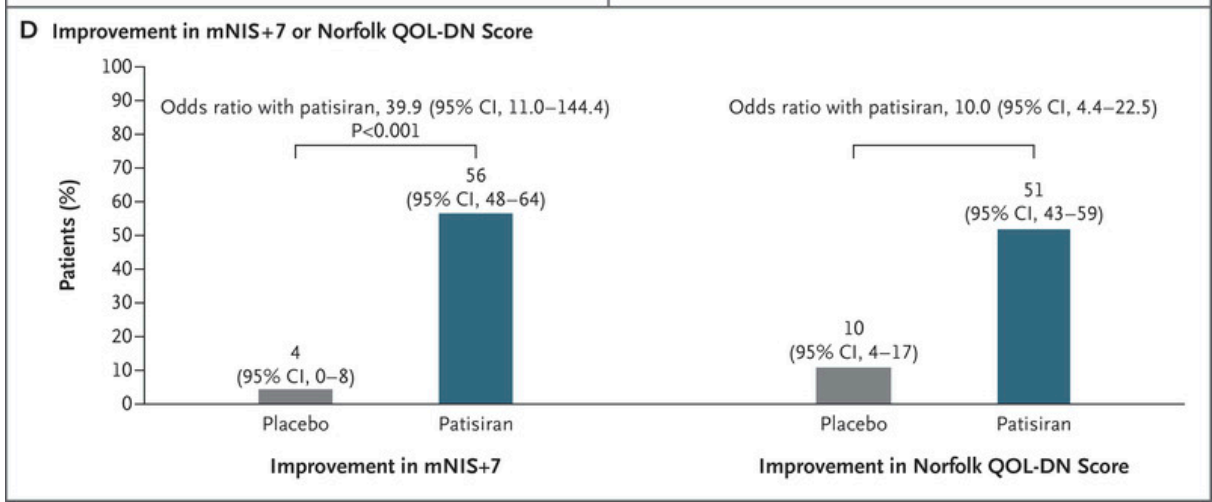
David Adams, M.D., Ph.D., Alejandra Gonzalez-Duarte, M.D., William D. O'Riordan, M.D., C
Tournev, M.D., Hartmut H. Schmidt, M.D., Teresa Coelho, M.D., John L.

- IV infusion q3 weeks
- 225 patients → 18 month follow up
- Results: difference in mNIS+7 (34 points) and Norfolk QOL-DN (21 points)
- Side effects: infusion reactions in 20% of patients (10% in placebo)





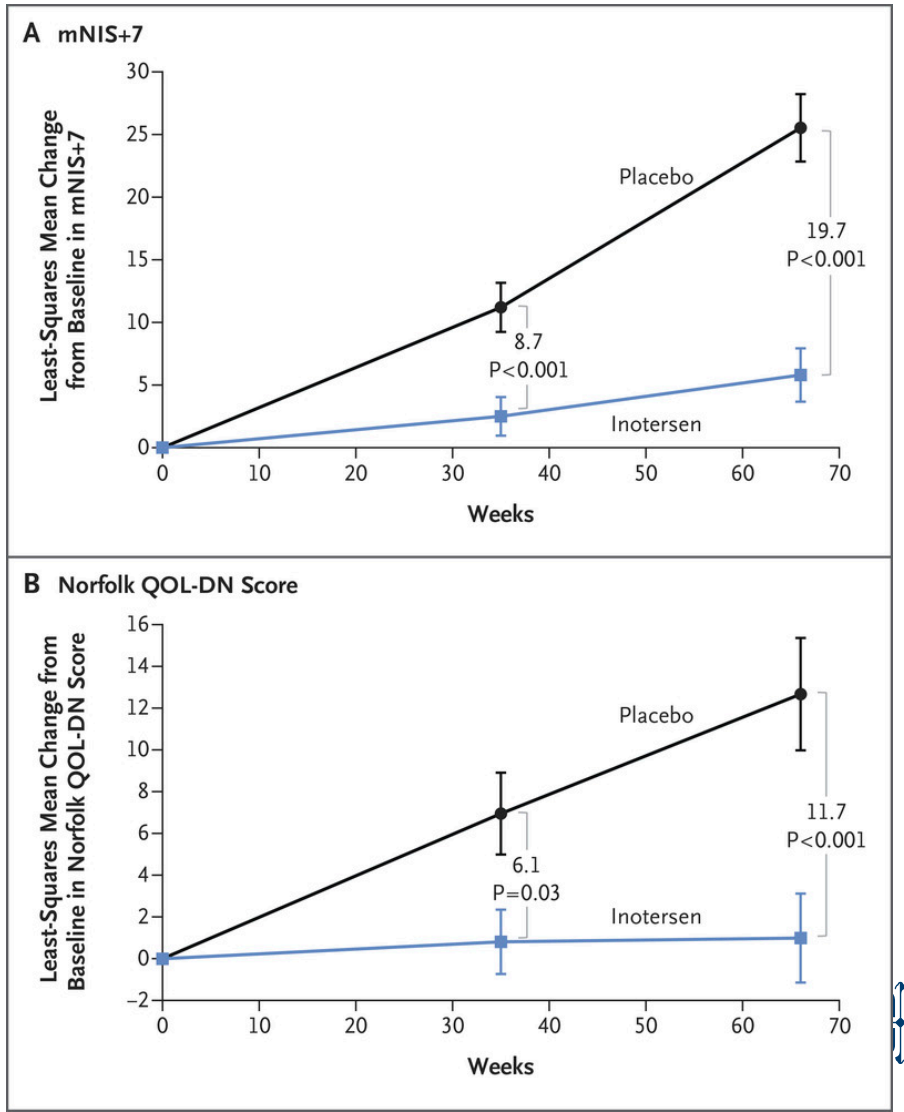




Inotersen Treatment for Patients with Hereditary Transthyretin Amyloidosis

Merrill D. Benson, M.D., Márcia Waddington-Cruz, M.D., Ph.D., John L. Berk, M.D., Michael Polydefkis, M.D., M.H.S., Peter J. Dyck, M.D., Annabel K. Wang, M.D., Violaine Planté-Bordeneuve, M.D., Fabio A. Barroso, M.D., Giampaolo Merlini, M.D., Laura Obici, M.D., Morton Scheinberg, M.D., Thomas H. Brannagan, III, M.D., et al.

- Placebo controlled RCT
- 172 patients
- 15 month follow up
- hATTR with polyneuropathy
- Weekly SQ inotersen
- Results: improved mNIS+7 (19.7 points) and Norfolk QOL-DN (11.7) neuropathy scores
- Side effects: 5 deaths in inotersen group, none in placebo.
  - Glomerulonephritis (3%) and thrombocytopenia (3%)



Treatments

- **AL cardiac amyloidosis**
  - Bortezomib + cyclophosphamide + dexamethasone (CyBorD)
  - Daratumumab
  - CyBorD + Daratumumab
  - High dose melphalan + ASCT → considered in patients with less cardiac involvement
  - Doxycycline, turmeric/curcumin
  - Advanced therapies

- **ATTR cardiac amyloidosis**
  - Green tea extract (EGCG 600-800mg/day), doxycycline/TUDCA, turmeric (curcumin)
  - Patisiran (IV infusion) or Inotersen (SQ injection) for hATTR neuropathy
  - Tafamidis (oral) for wtATTR and hATTR cardiomyopathy
  - Clinical trials
  - Advanced therapies

Research and Development

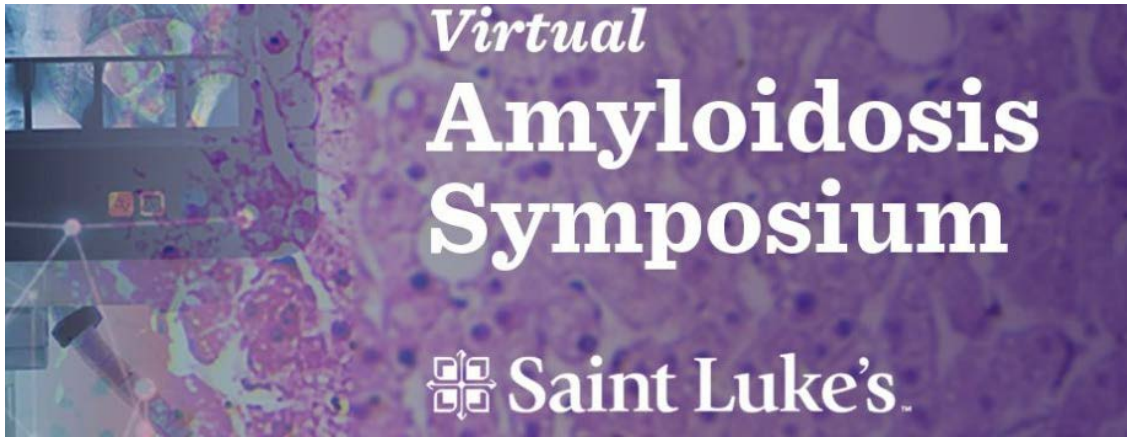
- AG10 (TTR stabilizer)
- Patisiran in cardiomyopathy
- Vutrisiran in cardiomyopathy
- Akcea-TTR-LRx (newer version of inotersen)

Summary

- High clinical suspicion for amyloidosis in the right situation
- Look for red flags
- Initial workup:
  - Serum studies for AL → free light chains kappa/lambda, serum IFE, urine IFE
  - CV myocardial PYP imaging (ie technetium pyrophosphate) for ATTR
- Don’t miss AL amyloidosis! Cardiac / hematologic emergency
- Novel treatment options

Saint Luke's MAHI Amyloidosis Program

- www.saintlukeskc.org/amyloidosis
- amyloid@saintlukeskc.org



THANK YOU