



Memorial Sloan Kettering
Cancer Center



Does your patient complain of fatigue, breathlessness, leg swelling and neuropathy? Is it long-COVID, Lyme disease, chronic fatigue? Could this be *AL Amyloidosis*?

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Hematologist-Oncologist

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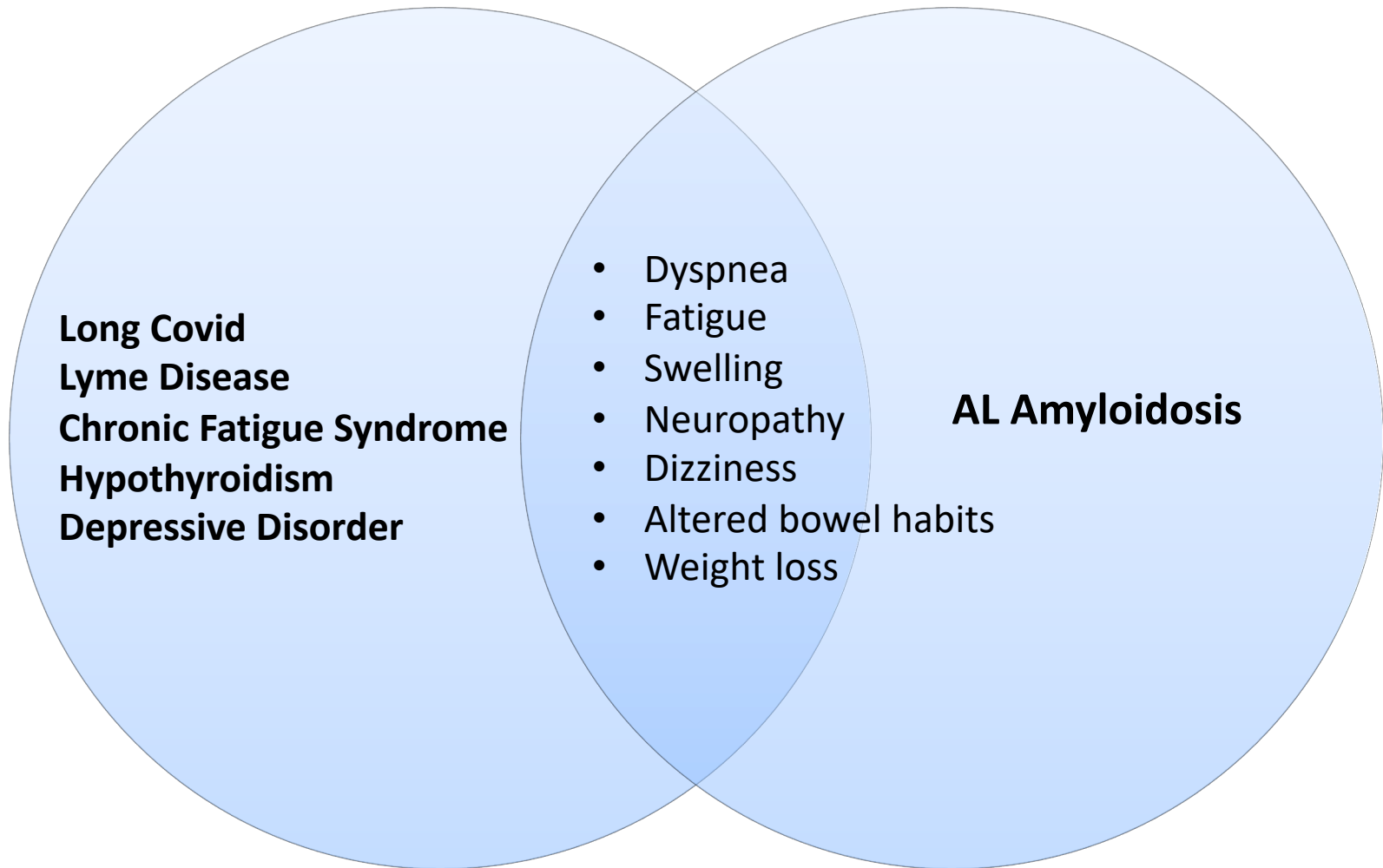
Cardio-Oncologist

Director, Cardiovascular Laboratories



Common signs and symptoms

Diagnostic overlap:



Objectives

- What is AL amyloidosis?
- What are the clues to the diagnosis, when to suspect?
- How does one diagnose it?
- Why is it important to make the diagnosis promptly?
- What is the current treatment approach and what are the goals of care?

Patient #1: RS

- 58F, came to medical attention with progressive myalgias and intermittent paresthesia (over years)
- Elevated ESR → Polymyalgia rheumatica
 - Tx steroids w some improvement
- Exertional chest pain.
 - ECG: NSR, low voltage QRS
 - ECHO: mild LVH (IVSd 1.3cm), LVEF 50-55%, moderate diastolic dysfunction
 - Exercise stress test: non-specific ectopy, no ischemia
- LE edema → Nephrosis
 - Renal biopsy: **lambda light chain amyloidosis** involving the glomeruli and blood vessels

2009 -
2011

Mid -
2011

March
2012

June
2012

RS came to MSK

July
2012

- CBC normal, Cr 0.8, **ALB 3.3**
 - Free kappa 0.42mg/dl, **free lambda 7.38mg/dl, k:l 0.06,**
 - SPEP neg, IFE neg
 - **BNP 269,** TROP neg
 - **24hr Urine TP: 5.1 g/24 hrs**
-
- Cardiac MRI: Diffuse late gadolinium enhancement suggestive of amyloid.
 - Bone marrow: 10% lambda restricted PCs, amorphous eosinophilic deposits + Congo red.

Lambda light chain amyloidosis
Mayo cardiac stage II
Renal stage II

2009

Symptoms onset

2012

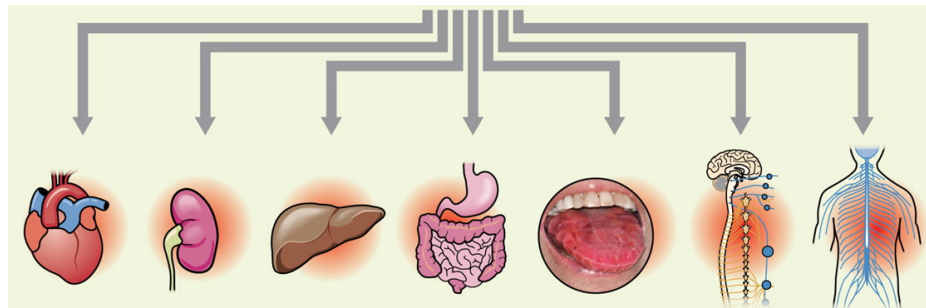
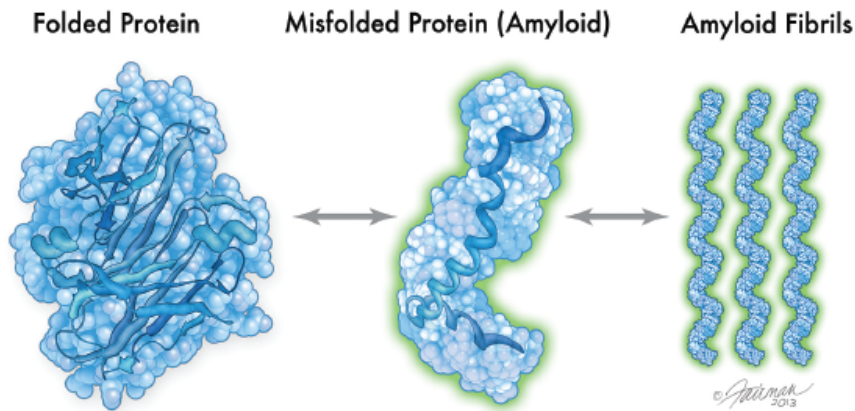
Diagnosis



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What is Amyloidosis?

- *Amylum* – starch (Latin)
- Protein misfolding disorder



Types of Amyloid:

Over 30 amyloidogenic proteins

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	A β 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.

Amyloid subtype classification

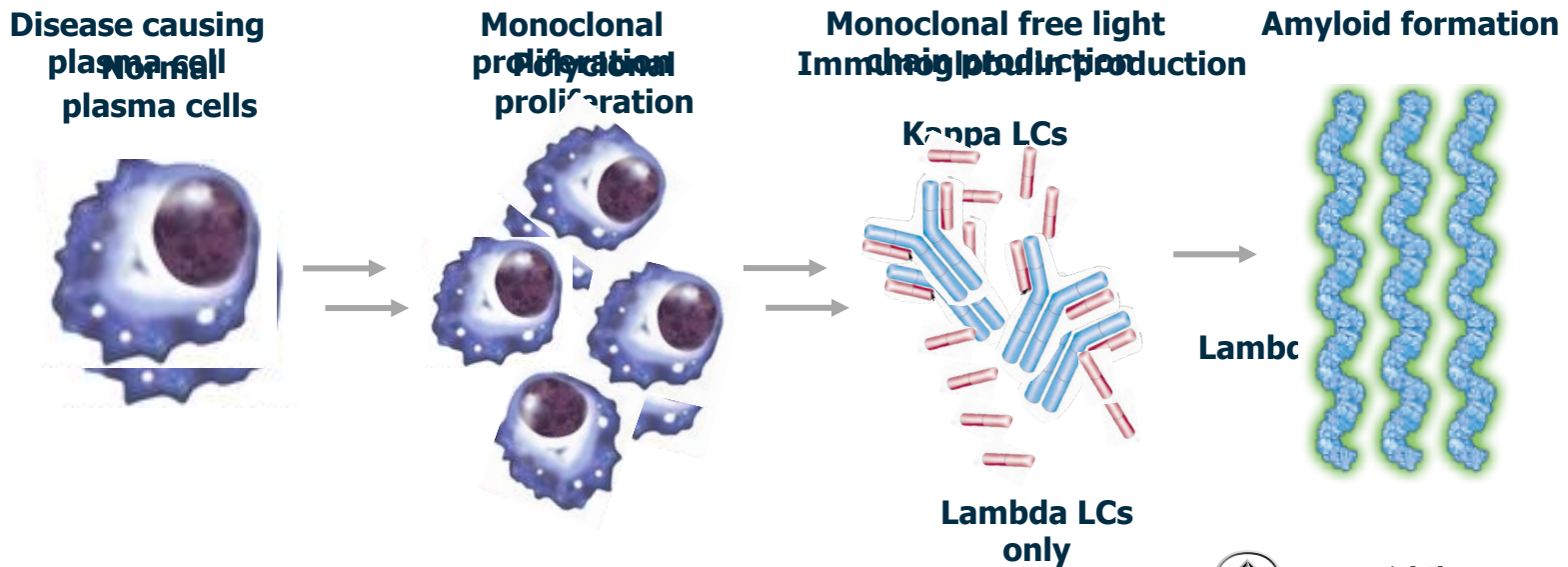
TYPE OF AMYLOIDOSIS	PRECURSOR PROTEIN	USUAL AGE AT ONSET	MAIN ORGANS INVOLVED	AVERAGE SURVIVAL TIME IN UNTREATED PATIENTS	SPECIFIC TREATMENT
AL or light chain (primary)	Abnormal immunoglobulin light chains	50+	All except central nervous system; heart involved in 50% of cases	Determined by extent of cardiac disease; varies from 3 mos - >10 yrs	Chemotherapy aimed at plasma cells
Familial ATTR	Mutant TTR	20-70+ (partially dependent on mutation)	Peripheral and autonomic neuropathy; heart	7 to 10 years for neuropathy	Liver transplantation; Agents to stabilize TTR (tafamidis) or suppress its production
Wild-type ATTR	Wild-type TTR	70+	Heart, soft tissue (carpal tunnel syndrome)	5 to 7 years	Agents to stabilize TTR (tafamidis) or suppress its production
AA (secondary)	Serum amyloid A (SAA), inflammatory protein	Teens upward	Liver, kidney; heart rarely	10+ years	Treatment of underlying inflammatory condition

Adapted from Falk and Hershberger. Chapter 77. Braunwald's 11th edition.

AL (light chain) Amyloidosis

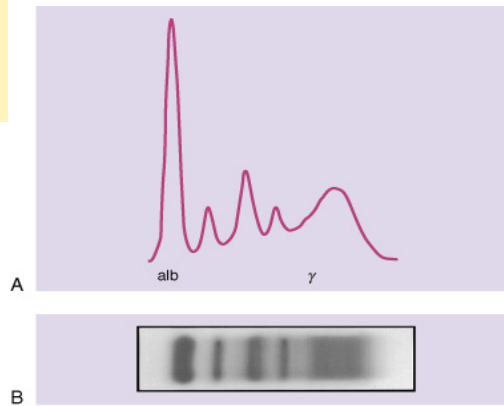
What causes it?

- Plasma cell disorder
 - Pathologic plasma cells arise in the bone marrow
- Disease causing protein: **Light chains (LC)**
 - Monoclonal – meaning the light chains are identical and can be traced back to a single, original diseased plasma cell

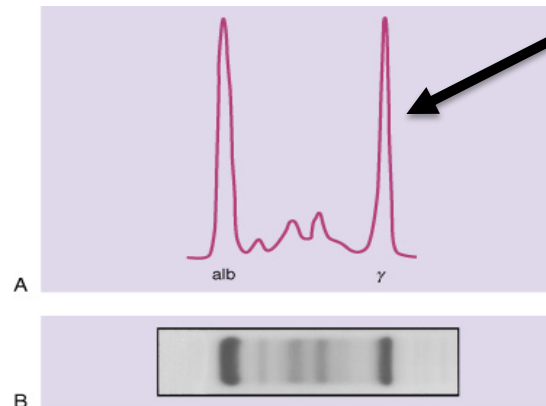


Monoclonal gammopathy evaluation

- Serum and urine protein electrophoresis (SPEP + UPEP)



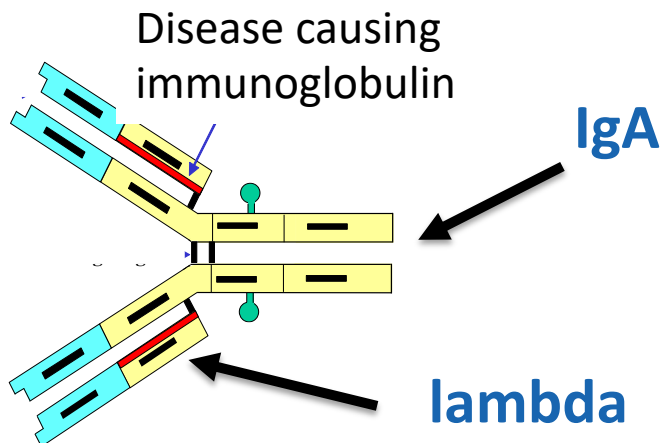
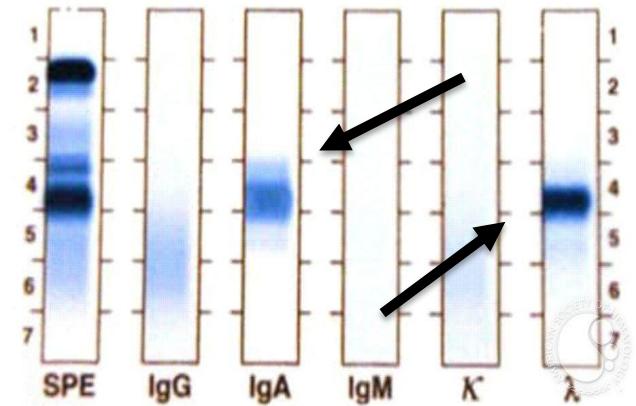
Normal SPEP



Abnormal SPEP

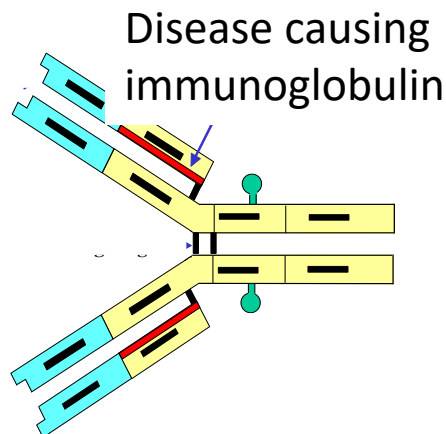
M spike

- Immunofixation

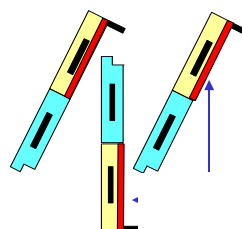


Monoclonal gammopathy evaluation

- Multiple myeloma
- AL Amyloidosis



**Intact immunoglobulin
Detected by SPEP**



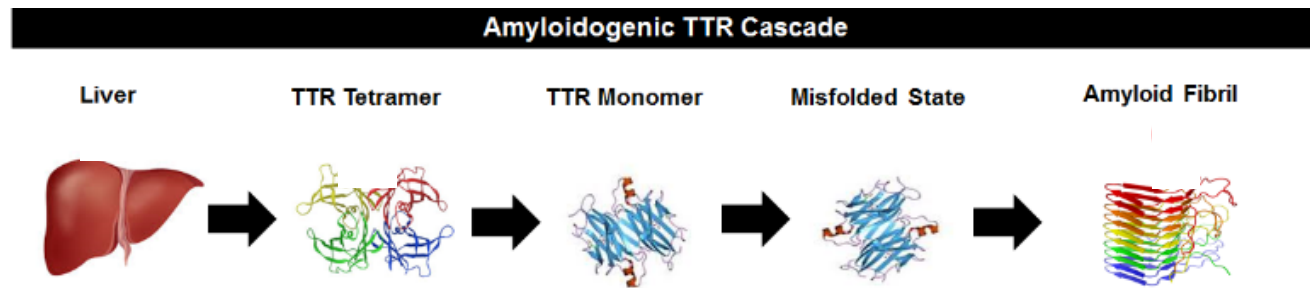
Freely circulating LCs

Serum free light chain assay:

Over-production of one light chain type (kappa or lambda) as measured by an elevated free light chain level and abnormal k:l ratio

ATTR Amyloidosis

Precursor Protein: Transthyretin



Castano, Mauer ACC 2015

TYPE OF AMYLOIDOSIS	PRECURSOR PROTEIN	USUAL AGE AT ONSET	MAIN ORGANS INVOLVED	AVERAGE SURVIVAL TIME IN UNTREATED PATIENTS
Wild-type ATTR	Wild-type TTR	70+	Heart, soft tissue (carpal tunnel syndrome)	5 to 7 years
Familial ATTR	Mutant TTR	20-70+ (partially dependent on mutation)	Peripheral and autonomic neuropathy; heart	7 to 10 years for neuropathy

Falk and Hershberger. Chapter 77. Braunwald's 11th edition

Important to distinguish AL from ATTR Amyloidosis

- **Monoclonal gammopathy of undetermined significance (MGUS)**
 - Occurs in 3% of the white population > 50 years
 - Incidence increases with age (~10% in patients 80 years or older)
- **ATTR**
 - True incidence and prevalence unknown
 - 80-89 year olds make up 50% of those diagnosed with wild-type ATTR
- **BU study:** Among 226 patients with biopsy-proven ATTR, including wild-type (N = 155) and hereditary (N = 71), MGUS was found in 39% and 49%, respectively

Different amyloidosis subtypes require different therapies

Patient #2: FR

- 52F, presenting with progressive cough, dyspnea and decreased effort tolerance over 1 year.
- Extensive work-up:
 - allergist, GI and ENT consultation. No definitive etiology found.
 - Stress test showing reduced exercise capacity; unremarkable otherwise
- Worsening symptoms with DOE after one block
- Syncope after getting out of the car and walking in the parking lot. Admitted to the hospital, work-up:
 - ECG: sinus rhythm with 1st degree AV block and low voltage
 - Echo: concentric LV hypertrophy. No wall motion abnormality
 - Stress test: chronotropic incompetence; drop in HR during exercise with near syncope
 - Cardiac MRI: circumferential delayed enhancement c/w an infiltrative cardiomyopathy

Early
2014

2014
-
2015

Mid/
late
2015

Patient #2 FR

Early
2016

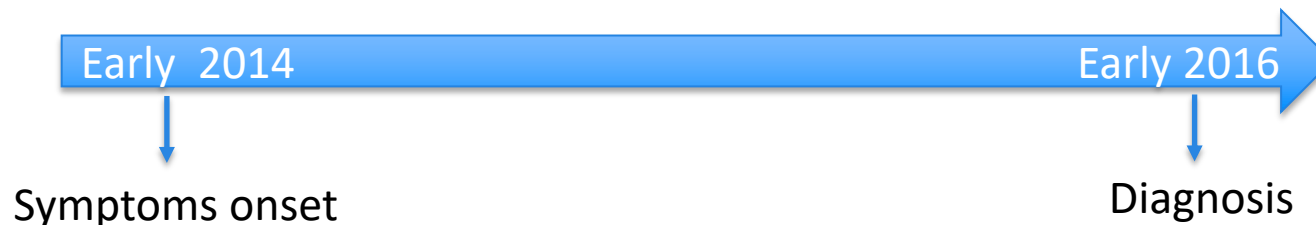
- Labs:

- Free lambda 9.93mg/dl, free kappa 1.39mg/dl, kappa/lambda ratio 0.14
- SPEP no monoclonal protein, serum + urine IFE + lambda light chain
- BNP 923; troponin negative; Cr. 1.1; albumin 4.3

- Tissue biopsy

- Bone marrow biopsy showed < 5% plasma cells, lambda light chain restricted; amyloid seen in a vessel wall
- Fat Pad biopsy negative for amyloid
- Endomyocardial biopsy showed congo red positive for amyloid deposition; AL subtype confirmed on mass spect

Lambda light chain amyloidosis with cardiac involvement
Mayo Stage II Disease

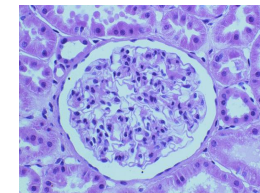
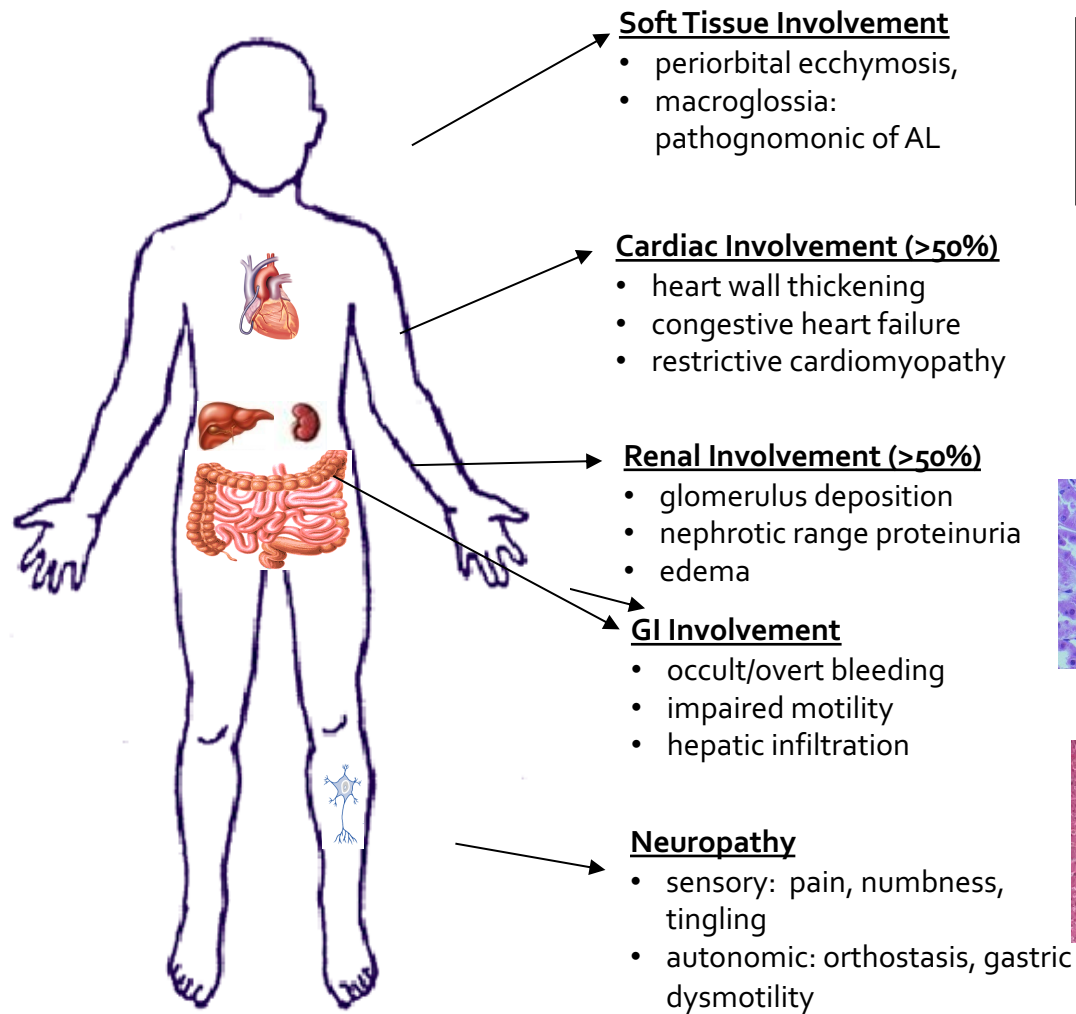




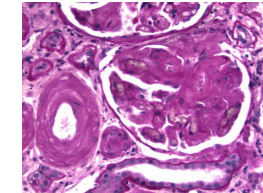
**What are the clues to the
diagnosis?**

When to suspect?

AL Amyloidosis: Multi-Organ System Involvement



Normal Kidney



Amyloid in glomerulus



Normal Liver



Amyloid in liver sinusoids

Clinical Presentation:

Common Signs/Symptoms

- Fatigue
- Dizziness/syncope
- Weight loss
- Paresthesias
- Edema
- Dyspnea
- Carpal tunnel syndrome
- Hoarseness
- Mucocutaneous lesions
- Hepatomegaly
- Cardiac dysrhythmias
- Alternating constipation and diarrhea
- Orthostasis
- Bleeding tendency
- Frothy urine

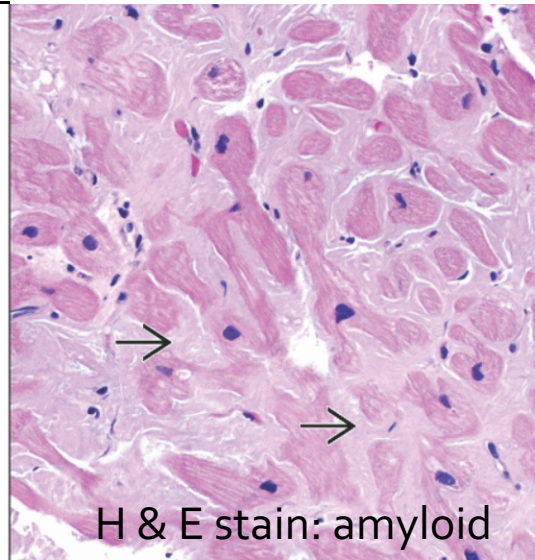
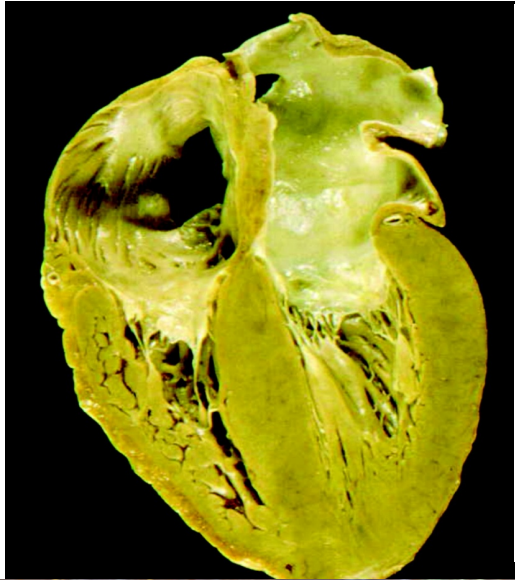
Diagnosis often delayed due to multisystemic presentations.

4 = average number of MDs seen before diagnosis

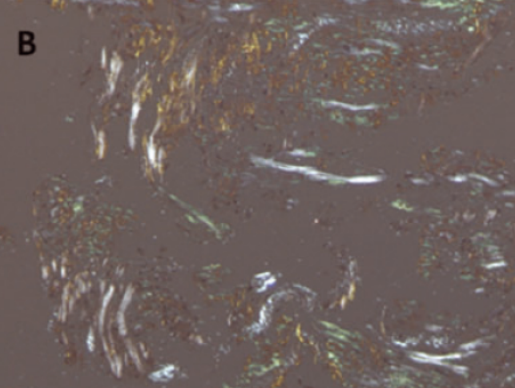
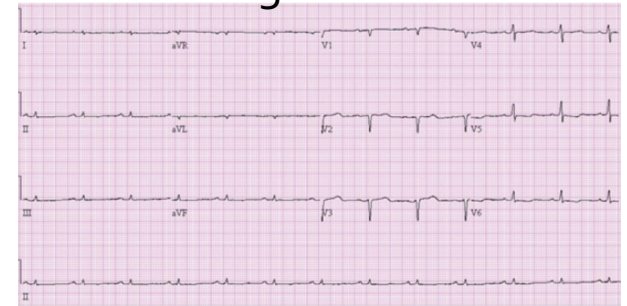
> 1/3 of patients are diagnosed >1 year after the onset of symptoms

**In a survey of 443 patients
220 cardiologists missed the diagnosis**

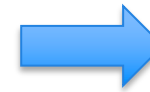
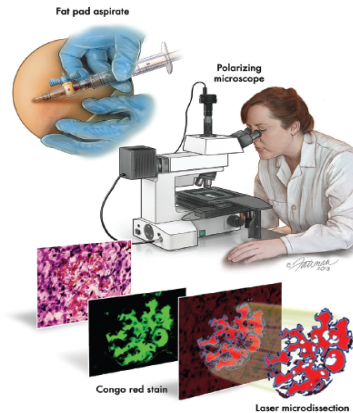
Cardiac Amyloidosis



low voltage on ECG



Congo red stain



Mass Spectroscopy:
AL vs. TTR

Cardiac Amyloidosis: Clinical Manifestations

- Heart failure
 - Restrictive cardiomyopathy with predominant right heart failure symptoms
- Angina
 - Amyloid infiltration of intramyocardial and microvessels
- Syncope
 - Exertional syncope due to low and fixed cardiac output
 - Postural hypotension due to autonomic neuropathy
 - Tachyarrhythmias
 - Atrial fibrillation/cardioembolic stroke
 - Ventricular arrhythmia
 - Bradyarrhythmia/AV block
- Sudden death
 - Asystole, PEA, ventricular arrhythmia

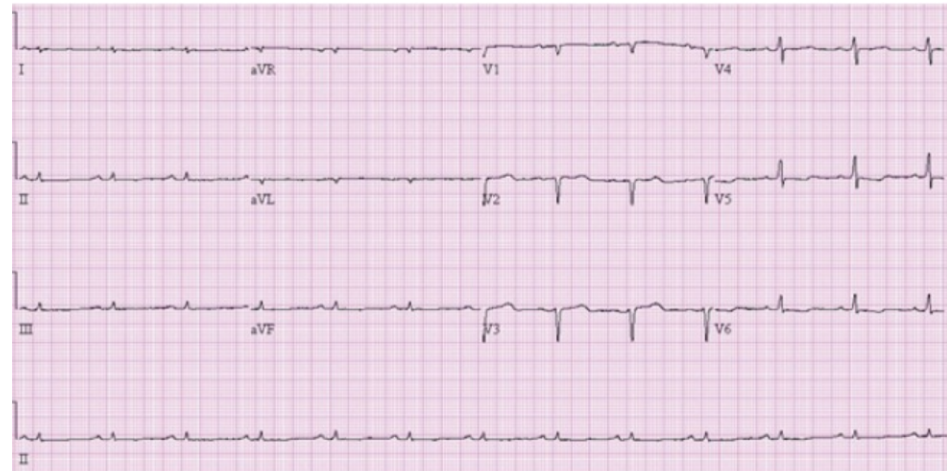
Cardiac Amyloidosis

When to Suspect: Clues to Diagnosis

ECG: Low voltage in the limb leads and pseudo-infarct pattern in the precordial leads

127 AL amyloid patients with biopsy proven cardiac involvement

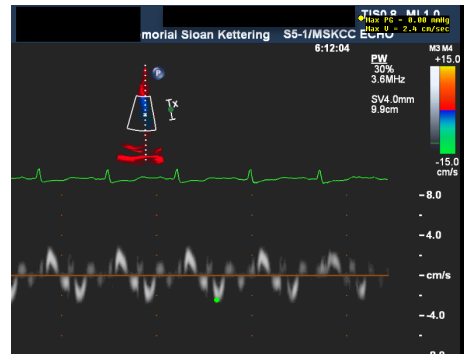
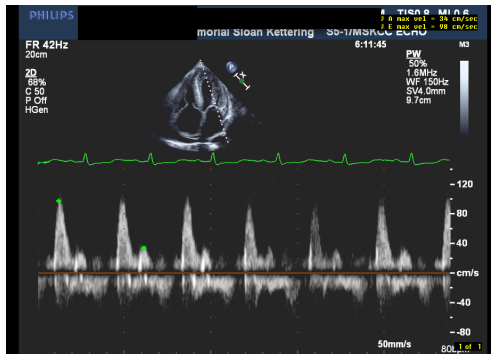
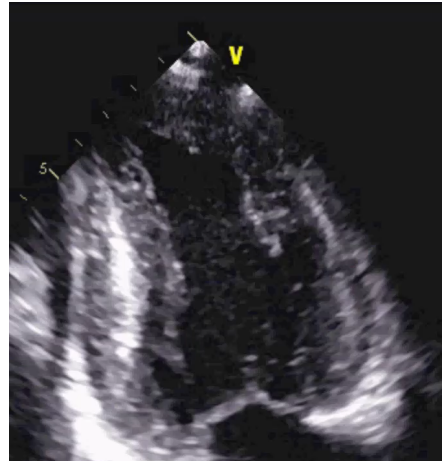
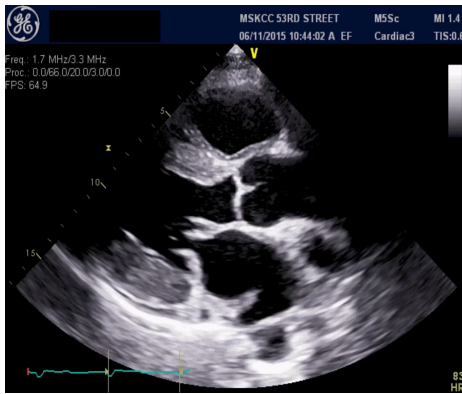
- Low voltage - 45%
- Pseudoinfarct – 47%
- Atrial fibrillation – 10%
- LVH - 7%



Murgah B, AJC 2005

Cardiac Amyloidosis

Clues to Diagnosis – When to Suspect Cardiomyopathy with unexplained “hypertrophy on echo”



E/A >2, DT <150 msec

Typical Features:

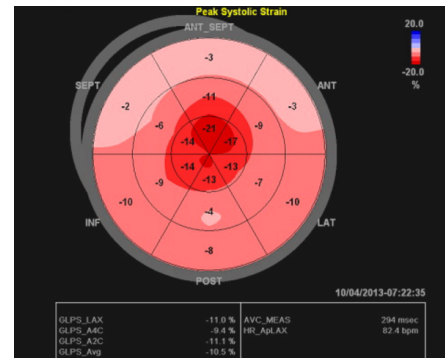
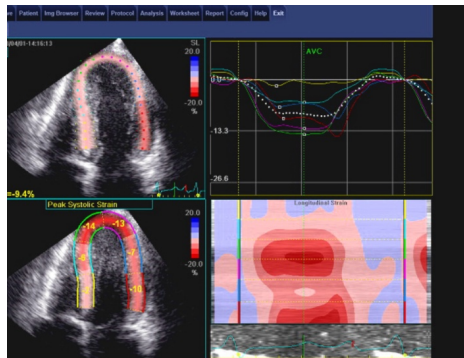
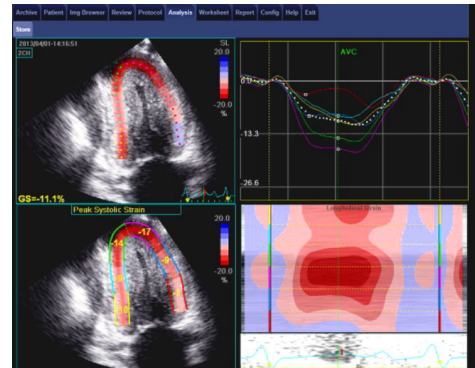
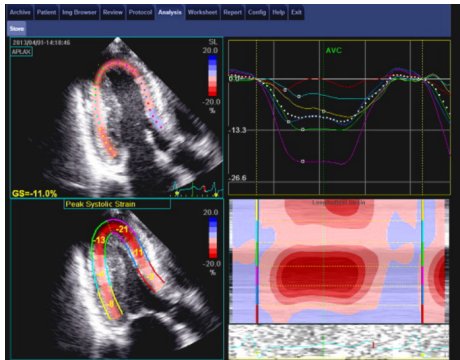
- Increased wall thicknesses with decreased LV end-diastolic volume
- Granular/sparkling appearance of the LV myocardium
- Typically preserved or mildly reduced LV EF
- Valve thickening and pericardial effusion
- Increased right and left atrial volumes; reduced atrial function
- RV thickening, reduced RV myocardial velocities
- Diastolic dysfunction from abnormal relaxation to restrictive LV filling pattern

Cardiac Amyloidosis

Clues to Diagnosis – When to Suspect

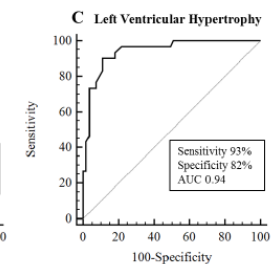
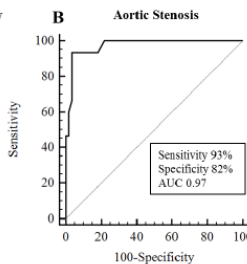
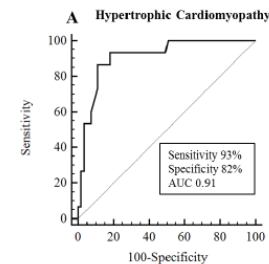
Global Longitudinal Strain

- Impaired GLS with normal LVEF; worse at the base and mid ventricular regions compared to the apex - “apical sparing” pattern
- May be useful for differentiating cardiac amyloidosis from other causes of thick heart pathology



Difference in Relative Regional Longitudinal Strain between Groups.

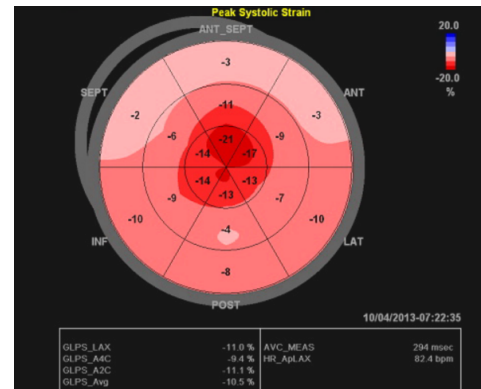
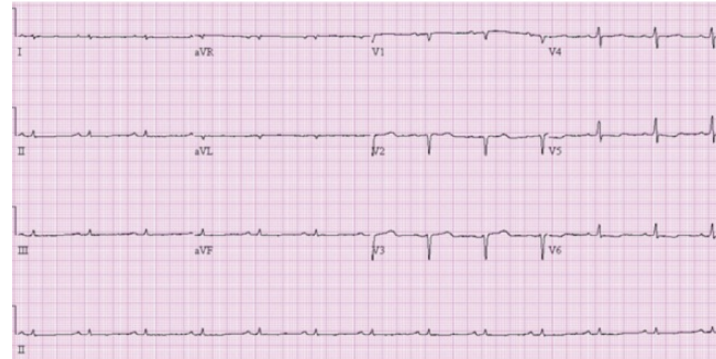
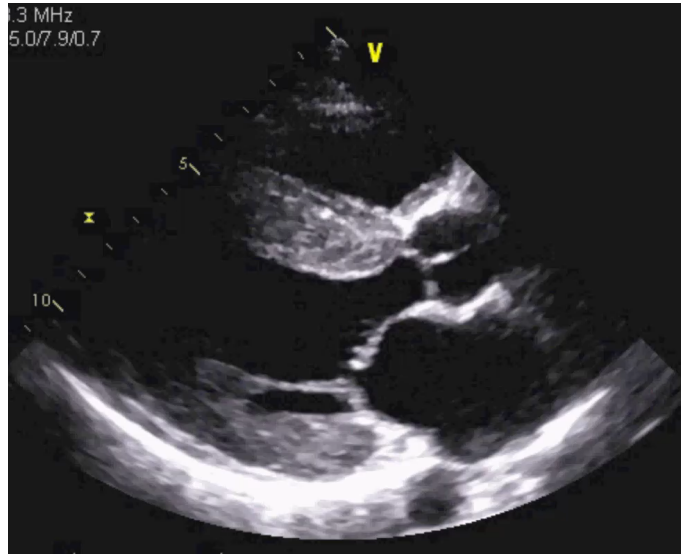
$$\text{Relative apical LS} = \frac{\text{Average apical LS}}{\text{Average basal LS} + \text{Average mid LS}} \geq 1$$



Phelan D. CV Imaging Heart 2012

Cardiac Amyloidosis: Clues to Diagnosis

Disconnect between 'LVH' + low voltage

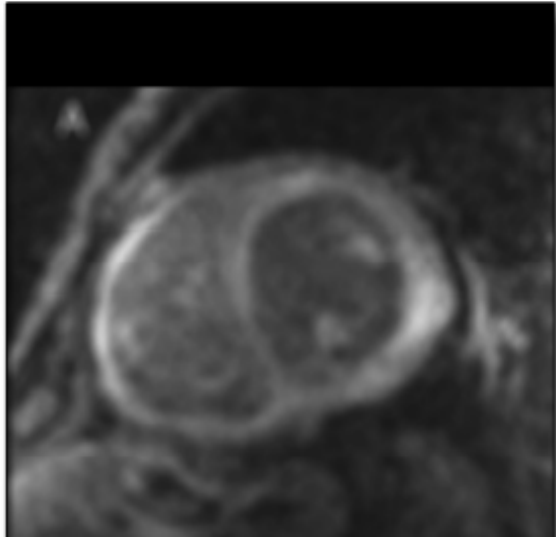


- Unexplained "hypertrophy" on echo
- Normal LVEF with low GLS, particularly with an apical sparing pattern

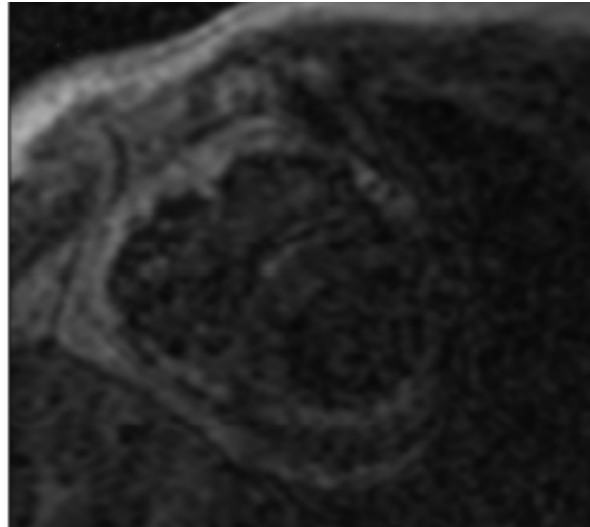
Diagnosis of Cardiac Amyloid by MRI

Pattern of Delayed Gadolinium Enhancement: Diffuse to Patchy

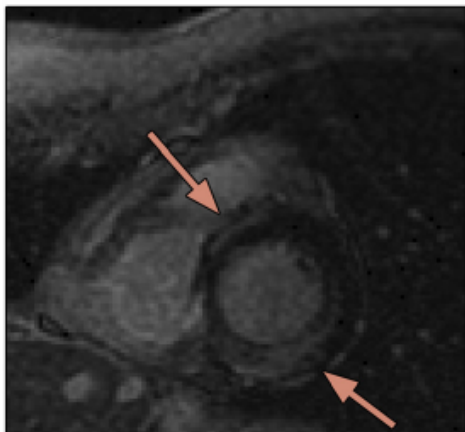
Diffuse Enhancement



Inability to null the myocardium



Focal Patchy

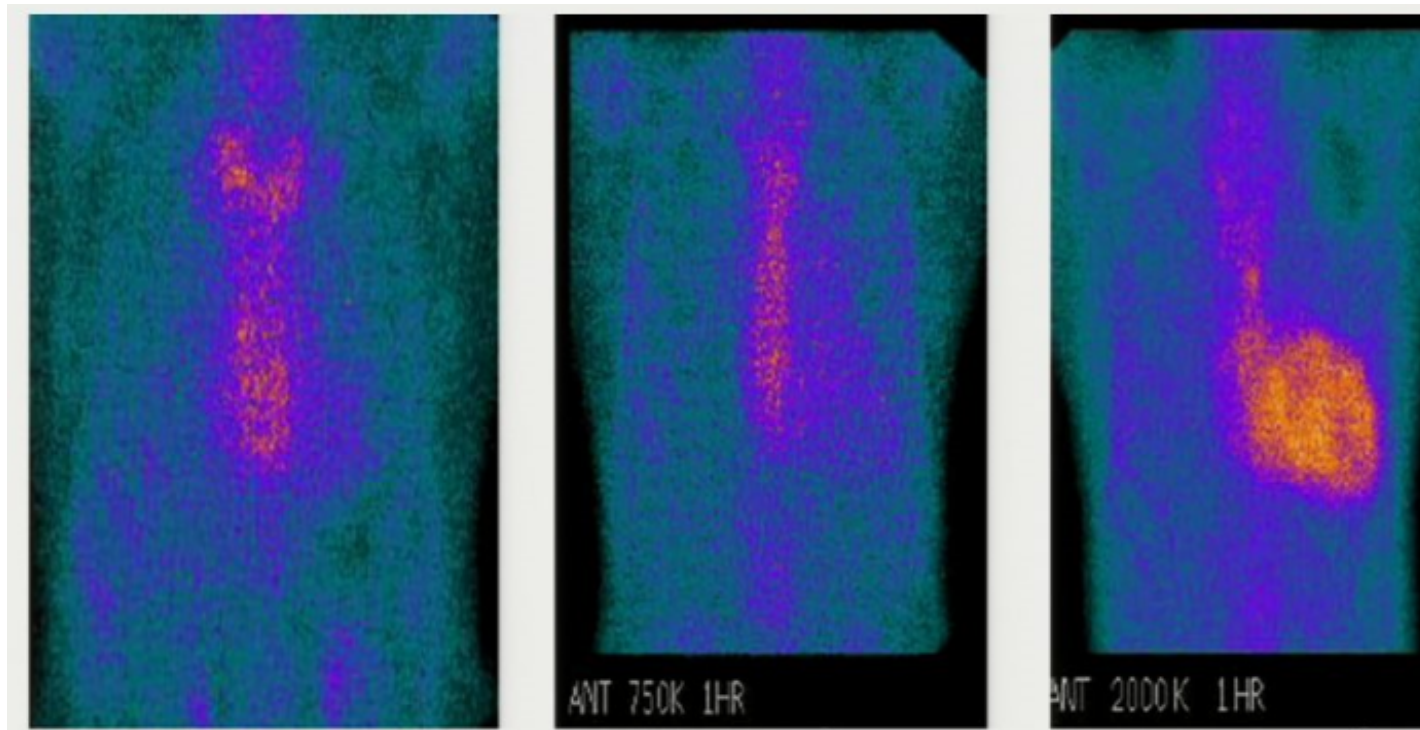


- ~ 90% sensitivity and specific
- PPV, NPV ~ 90-93%
- Negative scan does not exclude the diagnosis

Ruberg F, Berk J. Circulation 2012

Boynton, JACC CV Imaging 2016

Technetium Pyrophosphate Scan Diagnosis of TTR Amyloidosis



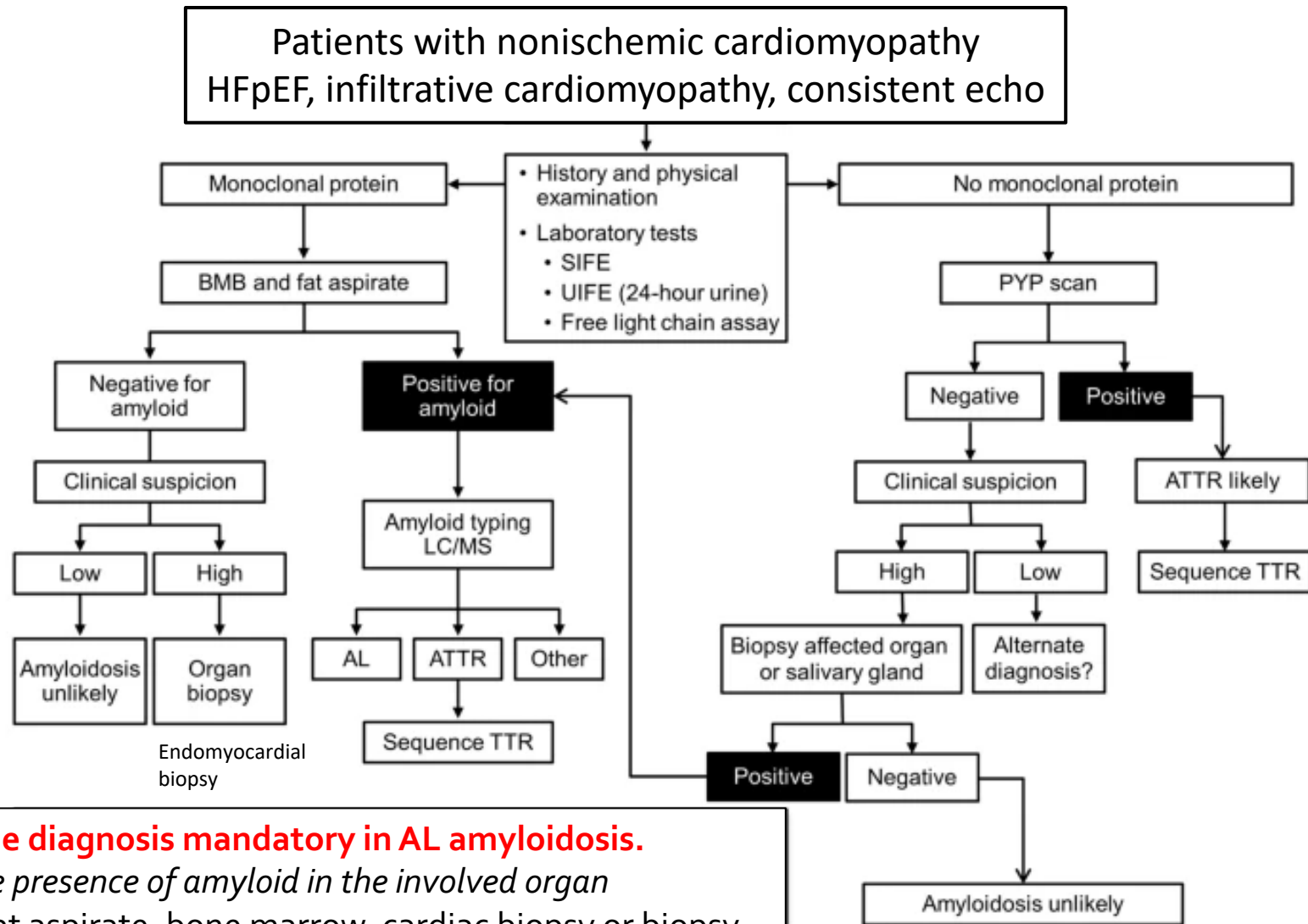
HFpEF

AL Cardiac Amyloid

ATTR Cardiac Amyloid

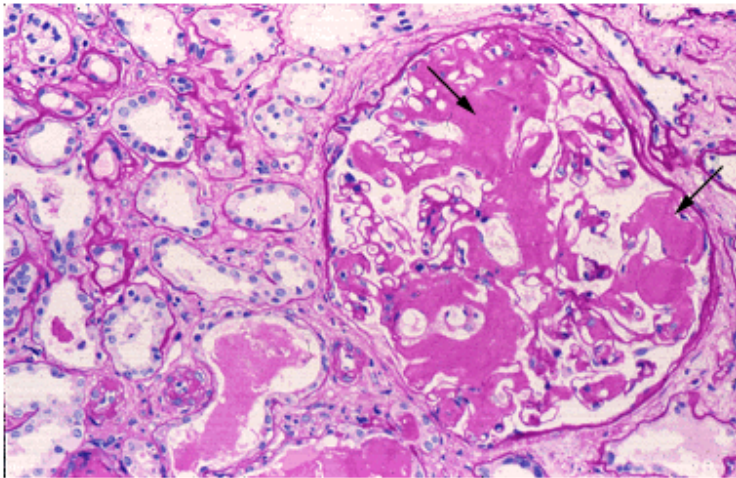
Bokhari et al, Circ Cardiovasc Imaging 2013

Diagnostic Algorithm



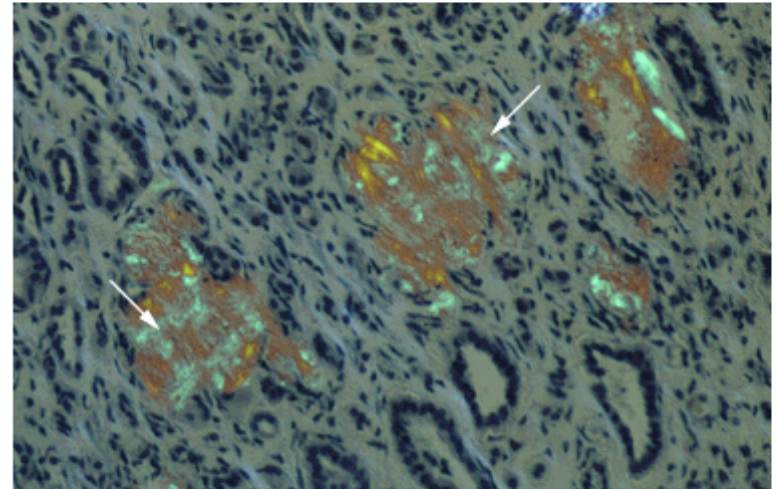
Renal Involvement in AL Amyloidosis: Pathologic Features

Light micrograph showing glomerular amyloidosis



- Nodular amorphous material extending from the mesangium into the capillary loops, narrowing or closing the capillary lumen
- Appearing pale, light pink on H/E stain

Congo red stain in amyloidosis



- Green birefringence of interstitial amyloid deposits, viewed under polarized light

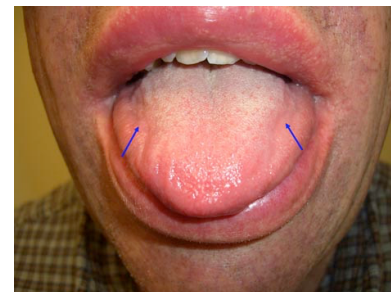
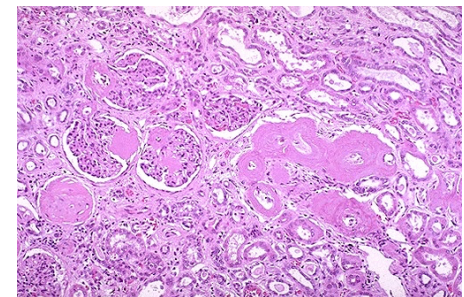
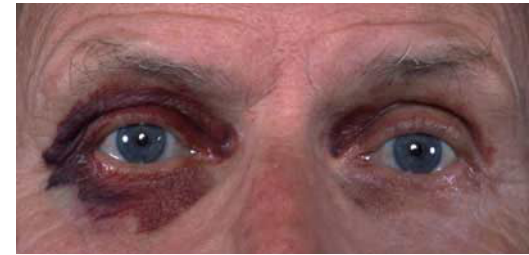
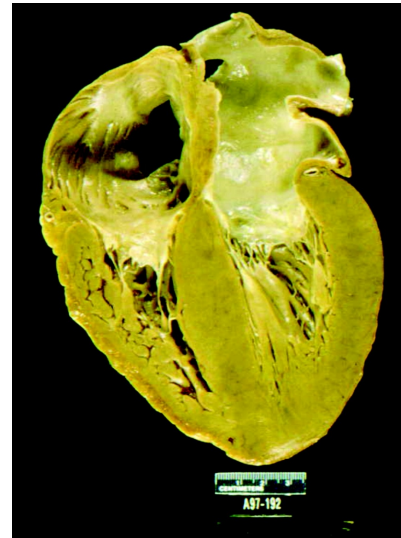
Renal Involvement in AL Amyloidosis

Clinical Manifestation

- Glomerular deposits
 - Proteinuria/nephrotic syndrome
 - ESRD in 20% of patients with nephrotic syndrome
- Vascular deposits
 - Leading to narrowing of the vascular lumen
 - Progressive chronic kidney disease w/ rise in Cr
- ESRD is associated with worse survival. Proteinuria >5 g/24 and eGFR <50 ml/min predict progression to dialysis best.

AL Amyloidosis: Multi-organ system involvement

- Cardiac: HFpEF, arrhythmias, hypotension, ✓
- Renal: proteinuria/nephrotic syndrome, renal failure ✓
- Neurologic: peripheral neuropathy, autonomic dysfunction
- GI: dysphagia, malabsorption, GI bleeding, liver dysfunction
- Soft tissue/ENT: macroglossia, periorbital purpura, carpal tunnel syndrome, nail changes.



Consider the diagnosis in pts presenting with HF associated with proteinuria and other systemic illnesses.

Patient #3: QD

- 49M, previously physically active, developed dyspnea; stopped going to the gym
- Hospitalized for asthma exacerbation + Pneumonia
 - Tx steroids, bronchodilators + diuresed
- Unable to ambulate 20 yards → cardiac evaluation
 - Nuclear stress test: LVEF 25%, no ischemia
 - Initiated on heart failure medications
- Pulmonary evaluation → optimize asthma regimen
 - Thoracentesis with 1L clear fluid drained
- Cardiology 2nd opinion
 - ECHO: severely increased LV wall thickness (IVSd 1.9cm), mild global hypokinesis, LVEF 47%. + diastolic dysfunction, GLS 6%.
 - ECG: NSR 91bpm, low voltage, poor R wave progression
 - Cardiac MRI: diffuse subendocardial LGE

July
2019

April
2020

August
2020

October
2020

Nov
2020

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

Dec
2020

- Bone marrow: 10% lambda light chain restricted PCs, No evidence of amyloidosis.
- Fat pad biopsy: negative
- Endomyocardial biopsy: **lambda light chain amyloidosis**

Jan
2021

Mayo (2004) cardiac stage IIIB
Lambda light chain amyloidosis

July 2019

Jan 2021

onset of symptoms

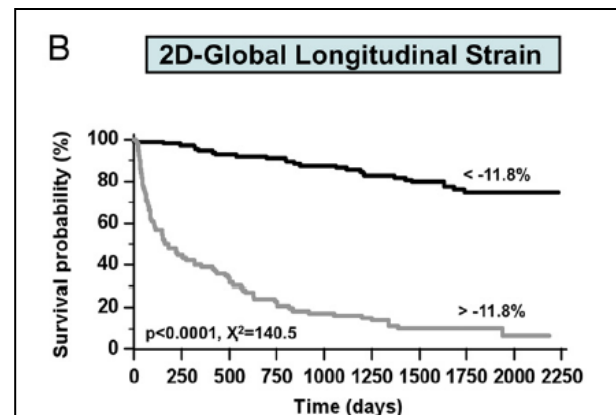
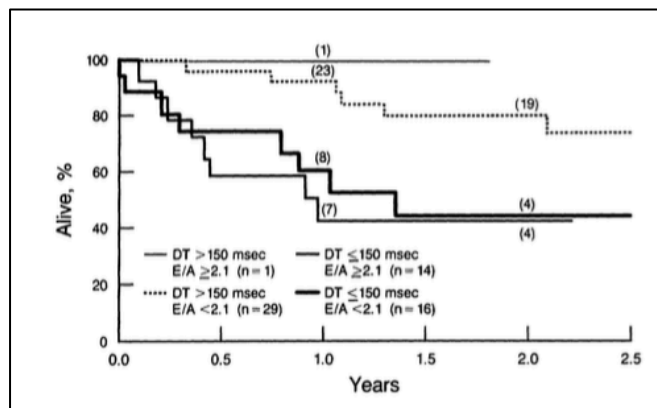
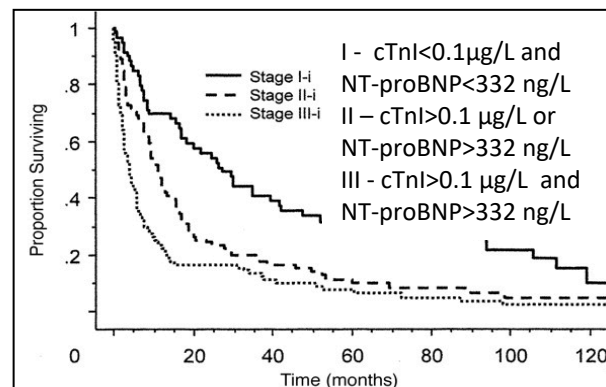
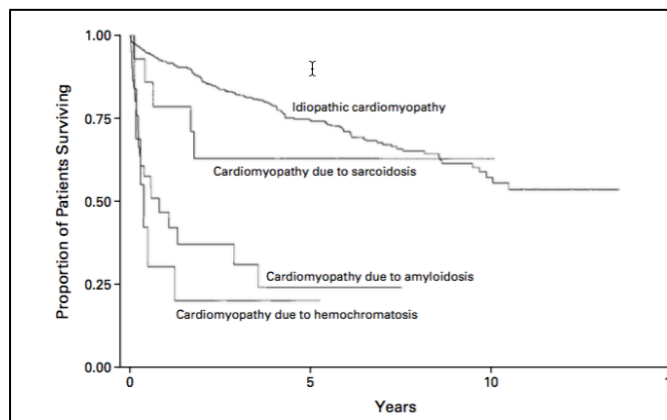
diagnosis



Prognosis and Staging of AL Amyloidosis

Predictor of Survival: Extent of Cardiac Involvement

Importance of Timely Diagnosis



Klein et al. Circulation 1991

Felker et al. NEJM 2000

Dispenzieri et al. JCO 2004

Buss et al, JACC 2016

Baseline Prognostic Staging Systems

Cardiac Biomarker Based: Tn and NT-proBNP/BNP

Models	Variables and cutoffs	Stages
Mayo2004	<ul style="list-style-type: none"> • NT-proBNP, 332 ng/L (or BNP, 81 ng/L) • cTnT, 0.035 ng/mL (or cTnI, 0.1 ng/mL) 	Stage I: both variables below the cutoffs Stage II: one variable above the cutoff Stage III: both variables above the cutoffs
Mayo2004 European	Mayo 2004 stage III is divided into two groups according to <ul style="list-style-type: none"> • NT-proBNP, 8500 ng/L (or BNP, 700 ng/L) 	Stage IIIa: Mayo2004 stage III and NT-proBNP (or BNP) below the cutoff Stage IIIb: Mayo2004 stage III and NT-proBNP (or BNP) above the cutoff
Mayo2012	<ul style="list-style-type: none"> • NT-proBNP, 1800 ng/L • cTnT, 0.025 ng/mL (or cTnI 0.1 ng/mL, or hs-cTnT 40 ng/L) • dFLC, 180 mg/L 	Stage I: all markers below the cutoffs Stage II: one marker above the cutoffs Stage III: two markers above the cutoffs Stage IV: all markers above the cutoffs

NT-proBNP, amino-terminal portion of pro-brain natriuretic peptide type B; BNP, natriuretic peptide type-B; cTnT, cardiac troponin T; cTnI, cardiac troponin I; hs-cTnT, high sensitivity cardiac troponin T; dFLC, difference between involved and uninvolved free light chain concentration.

Ability to Identify High Risk Patients

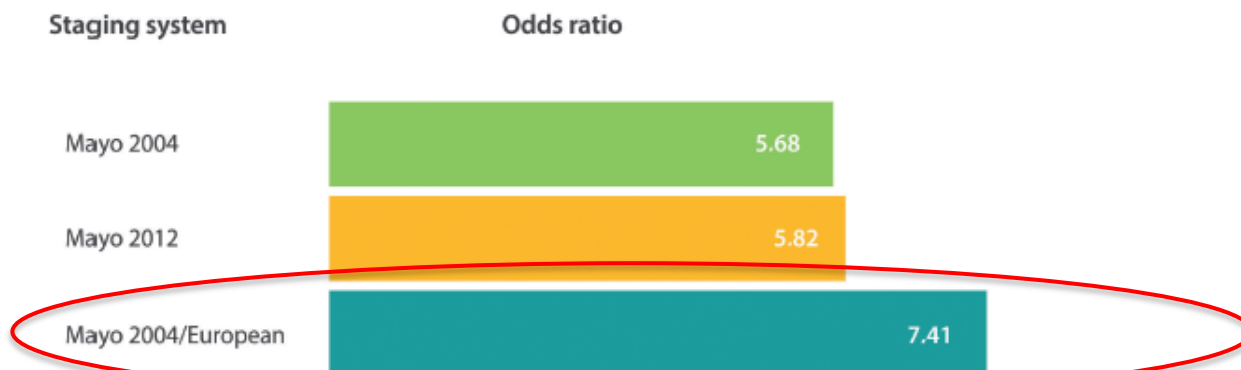
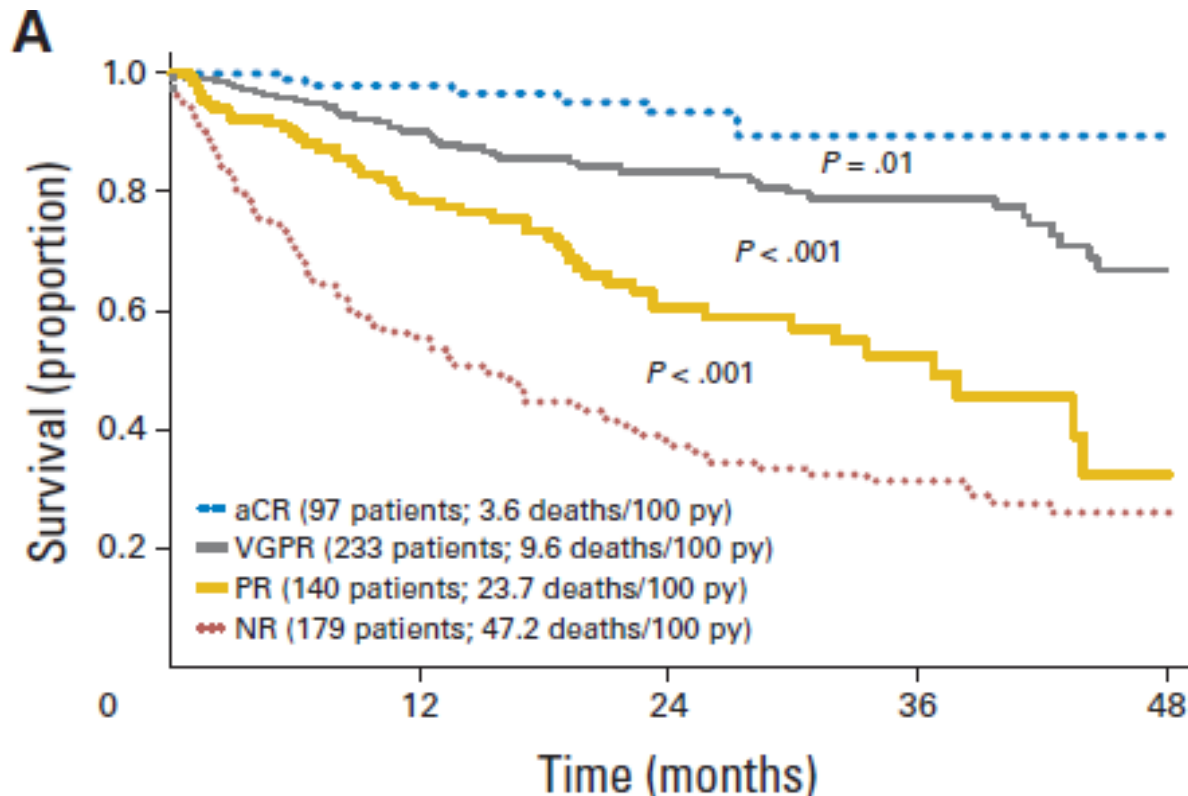


Figure 1. Odds ratio for very early death (within 6 months of diagnosis) of patients classified as being at highest risk by the three staging systems. Data from 1,065

Predictor of Survival: Hematologic Response to Treatment

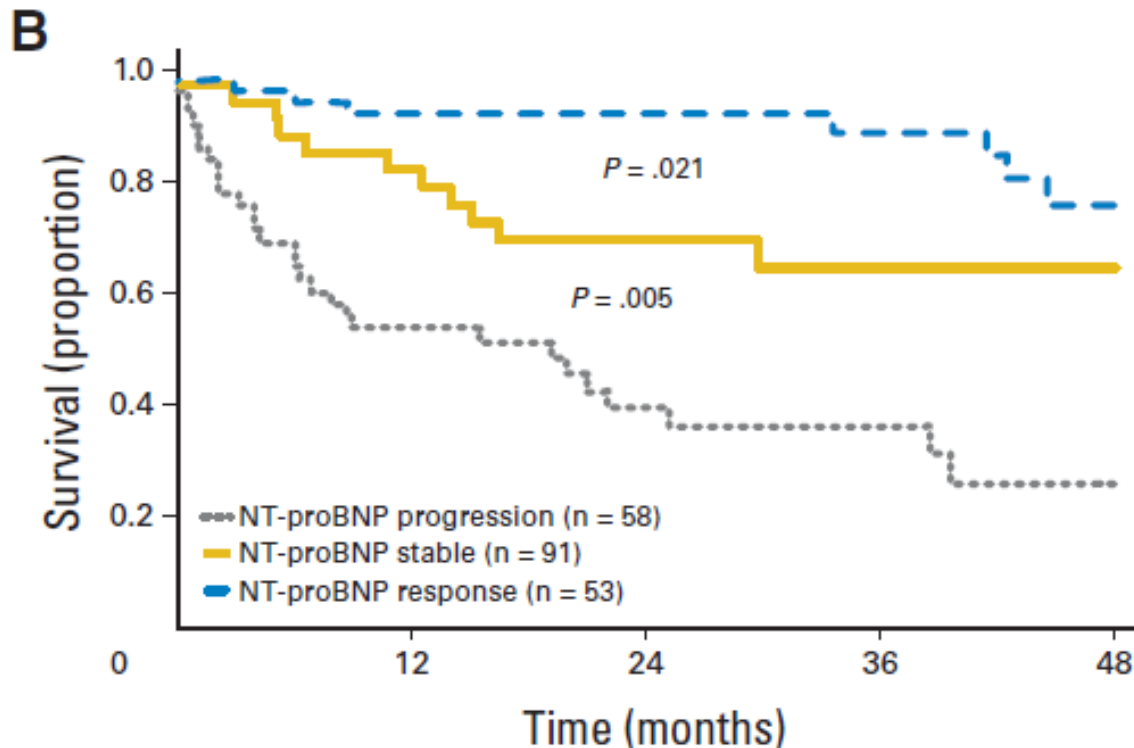


- Hematologic response based on the serum free light chain assay in blood:
CR (complete remission) = negative serum and urine, and normal FLC ratio; VGPR (very good partial response) = dFLC <40 mg/L; PR (partial response) = dFLC decrease >50%; NR = no response
- Hematologic response to therapy (VGPR and CR) is strongly associated with improved organ outcome**

Palladini et al, J Clin Oncol 2012

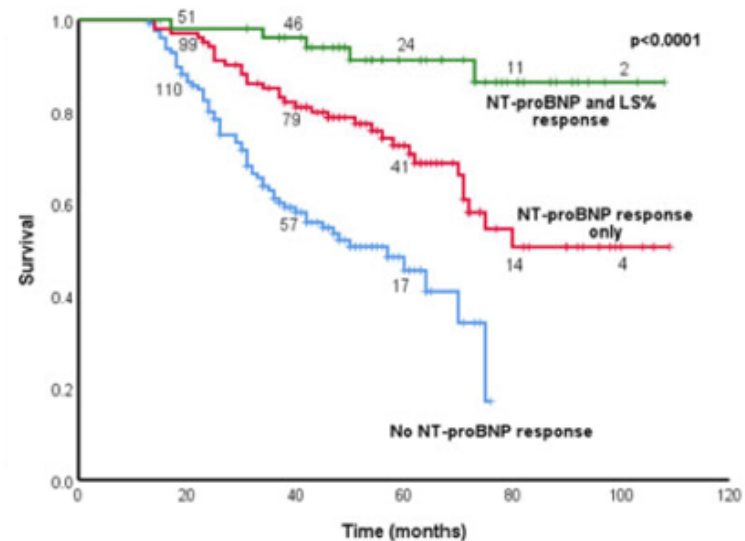
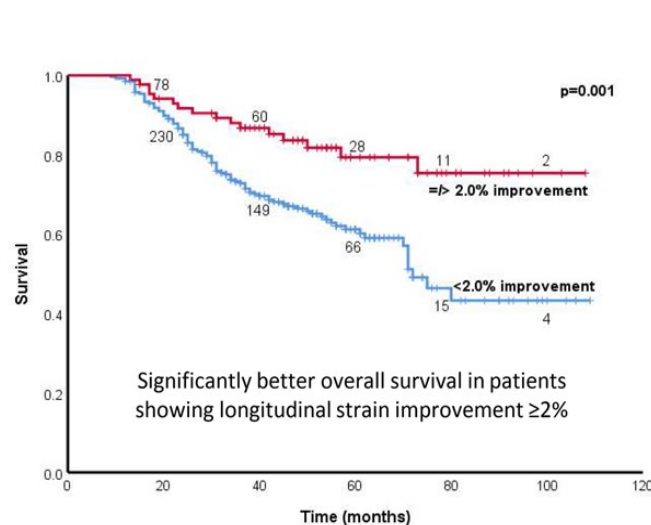
Predictor of Survival: Cardiac Response to Treatment

- NT-pro BNP Response: $>30\%$ and >300 ng/dl decrease
- BNP: $\geq 30\%$ and ≥ 50 pg/ml decrease



Predictor of Survival: Cardiac Response to Treatment

- Improvement in GLS is associated with better survival
- Pts with both NT-proBNP and GLS response showed best survival outcome



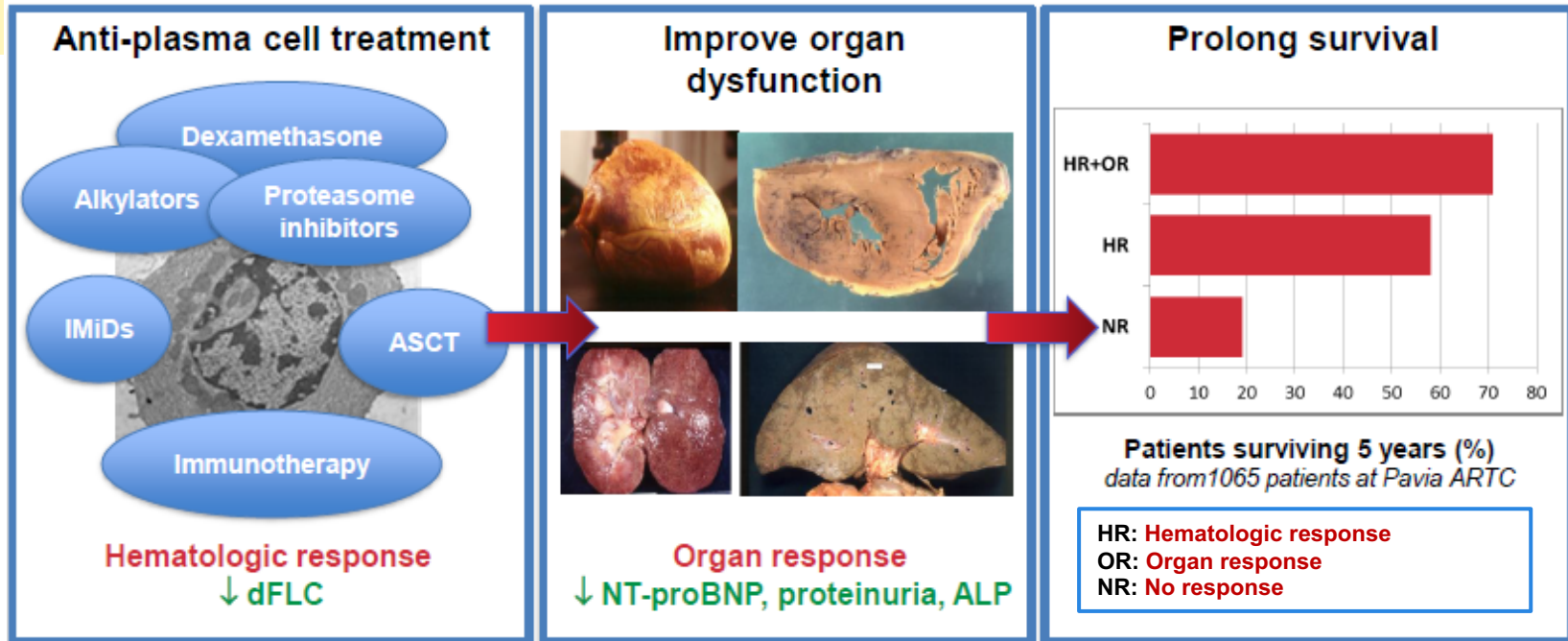
Cohen OC.et. Al Eur H J 2021



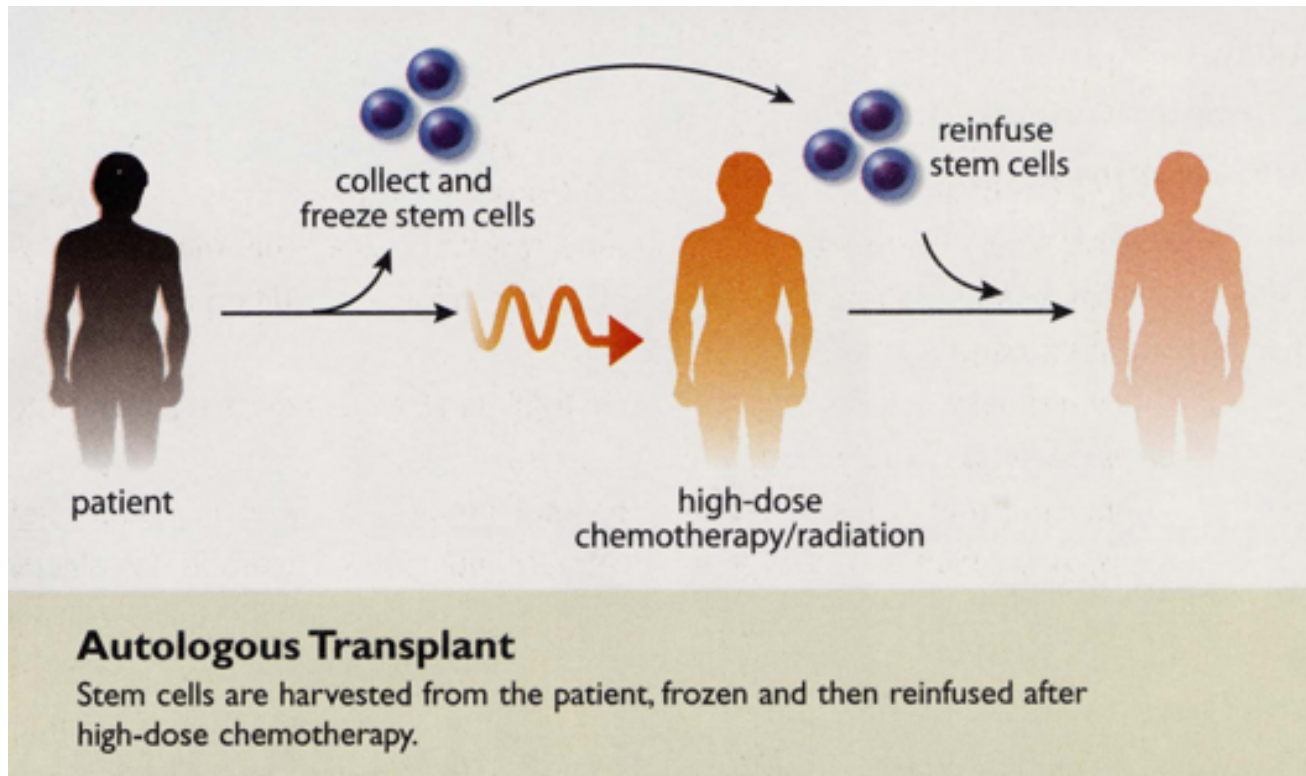
How is AL Amyloidosis treated?

What are the goals of therapy?

Targeting the plasma cell to improve organ function and prolong survival



High dose melphalan + autologous stem cell transplant for AL



AL Amyloidosis: Eligible for ASCT



Age (years)	≤ 60	> 60
No cardiac or renal compromise	MEL 200	MEL 140
With cardiac and/or renal compromise	MEL 140	MEL 100

3 month
staging

~
33%

CR

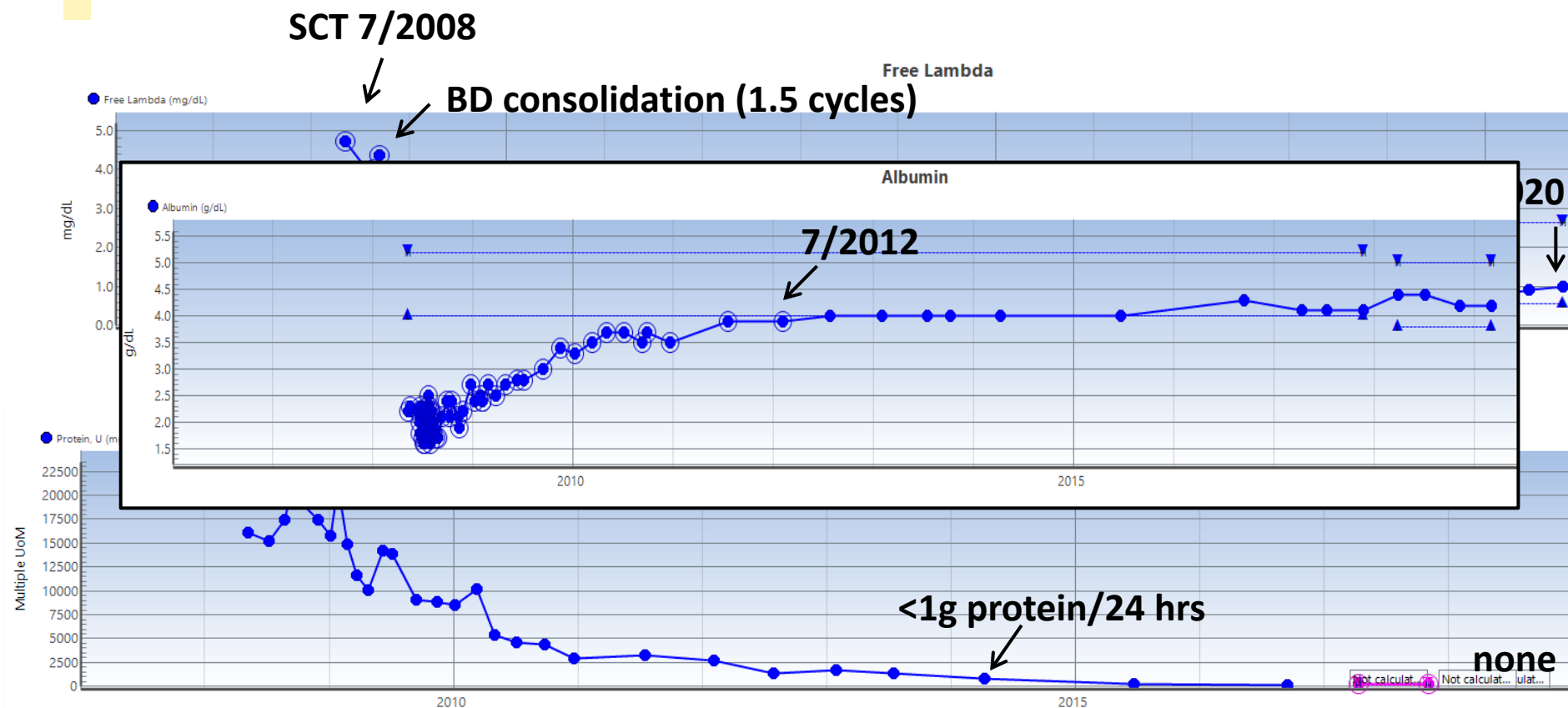
Observation

< CR

Consolidation

Bortezomib
↓
60% CR

Organ responses evolve over time



Bortezomib-based therapy studied in variety of settings

- **Bortezomib, cyclophosphamide & dexamethasone (VCd)**

- Stem cell sparing, preferred in renal compromise
- Retrospective series (N= 230), heme ORR 60%, CR 23%
- Organ response suboptimal/delayed, poor outcome in t(11;14)

Venner et al. *Blood* 2012.
Mikhael et al. *Blood* 2012.
Palladini et al. *Blood* 2015.

- **Bortezomib, melphalan & dexamethasone (BMDex)**

- Prospective RCT BMDex (N=53) vs Mdex (N=56), BMDex ORR 81%, CR 23%
- Prolonged PFS and OS, 50% reduction in mortality
- Overcome poor outcome in t(11;14)

Kastritis et al. *JCO* 2020.

- **Bortezomib-based induction prior to high dose melphalan**

- Lower relapse and improved PFS vs no induction

Cornell et al. *JCO* 2020.

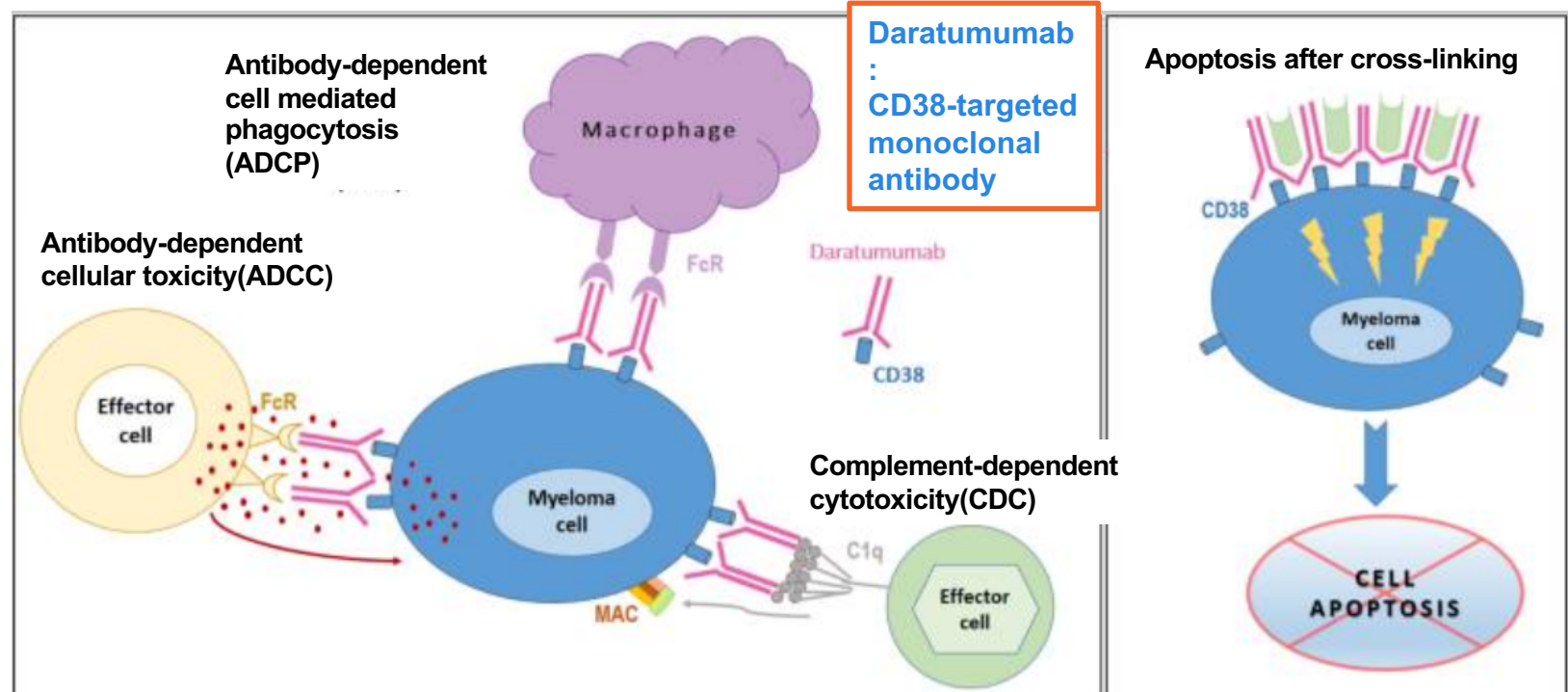
- **Attenuated bortezomib or low dose combinations**

- High risk patients (stage IIIb, NYHA class III or IV)

Jaccard et al.
Hematologica 2014.

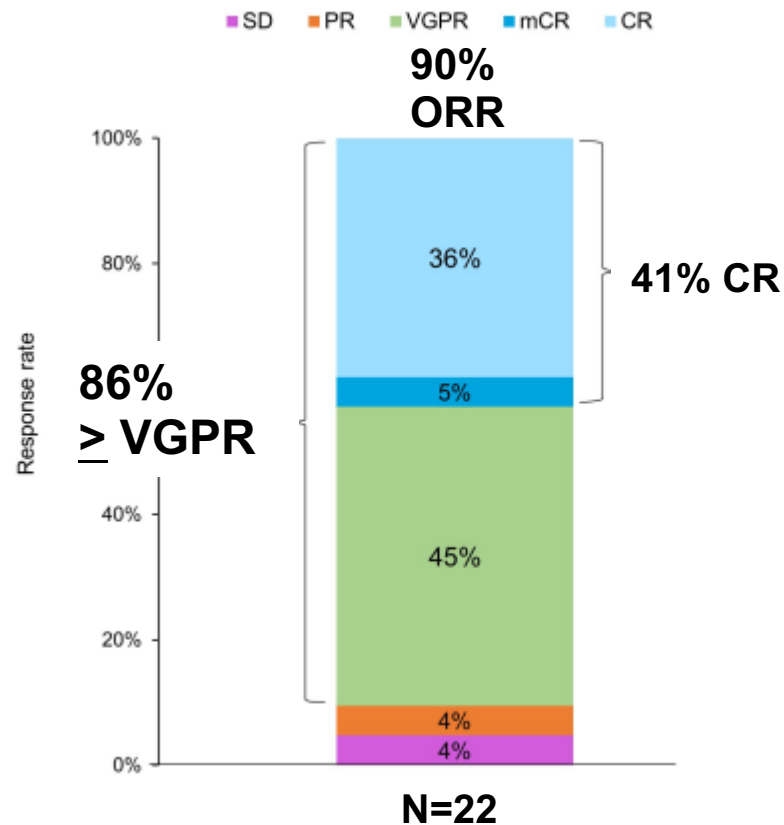
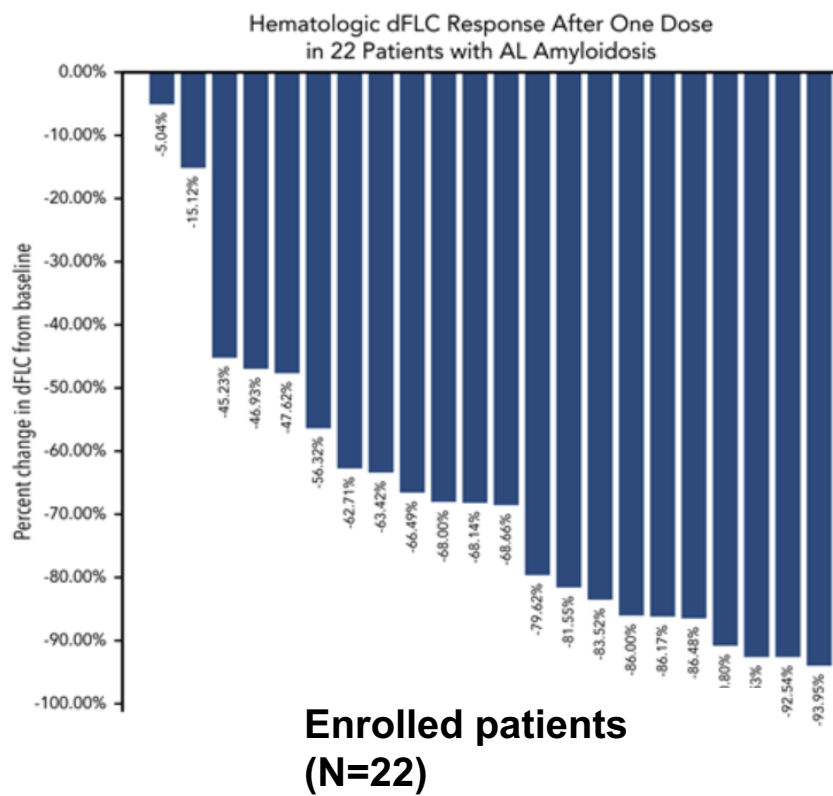
Bortezomib-based induction = standard of care

Daratumumab approved as plasma cell directed therapy for multiple myeloma in 2015

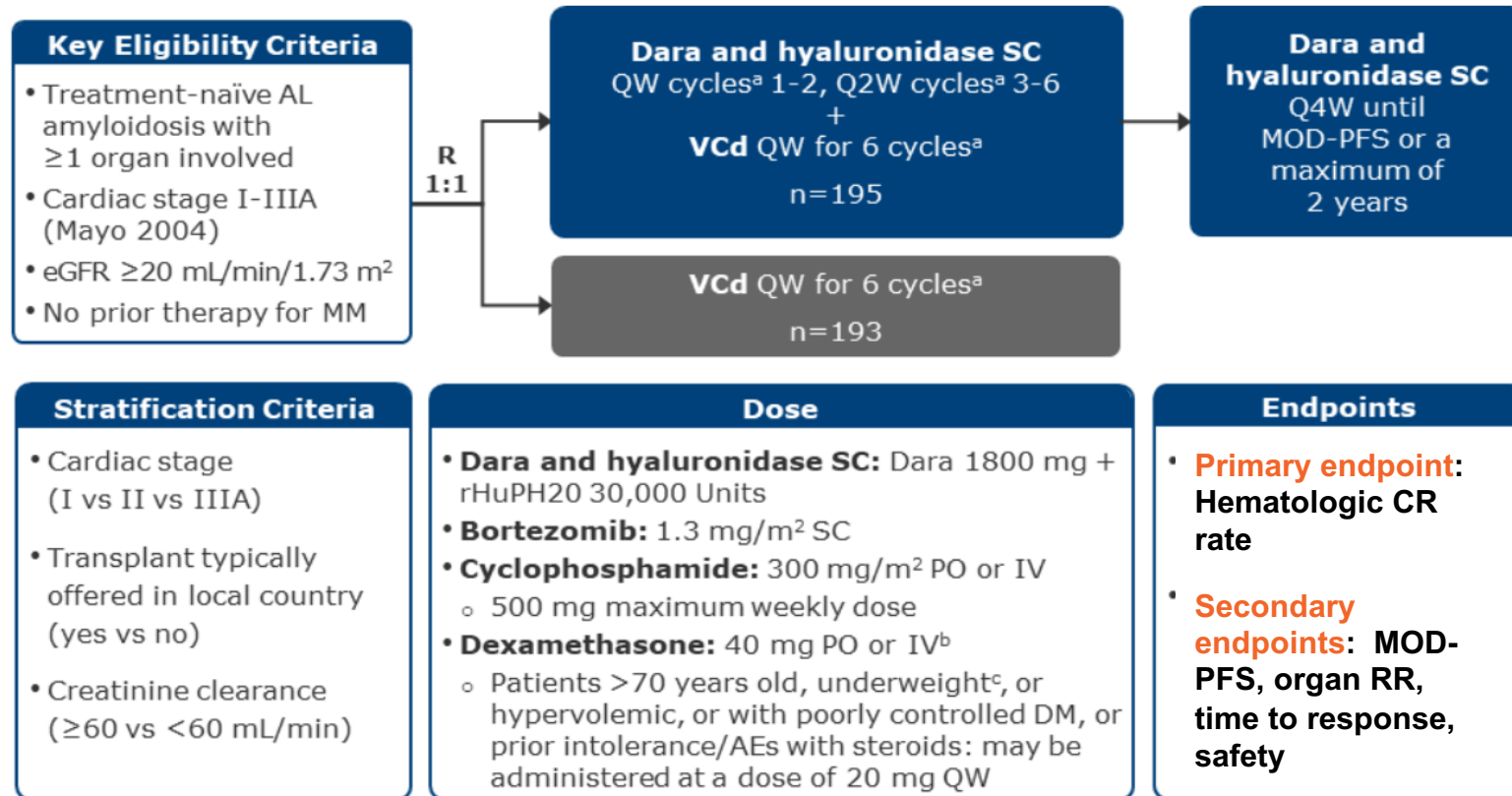


Phase II study of daratumumab in relapsed AL

Hematologic response after *one dose* of daratumumab



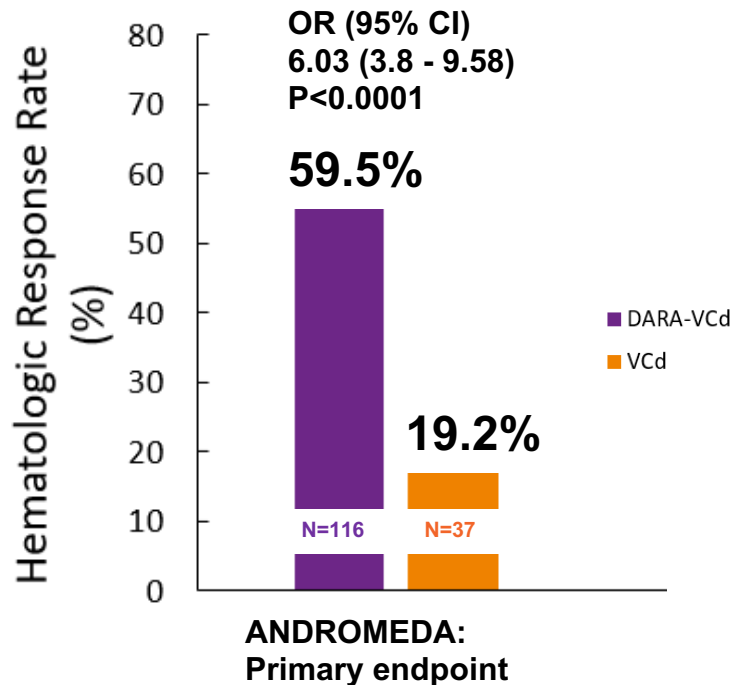
ANDROMEDA trial: VCd vs VCd + Daratumumab in newly diagnosed patients with Primary AL Amyloidosis



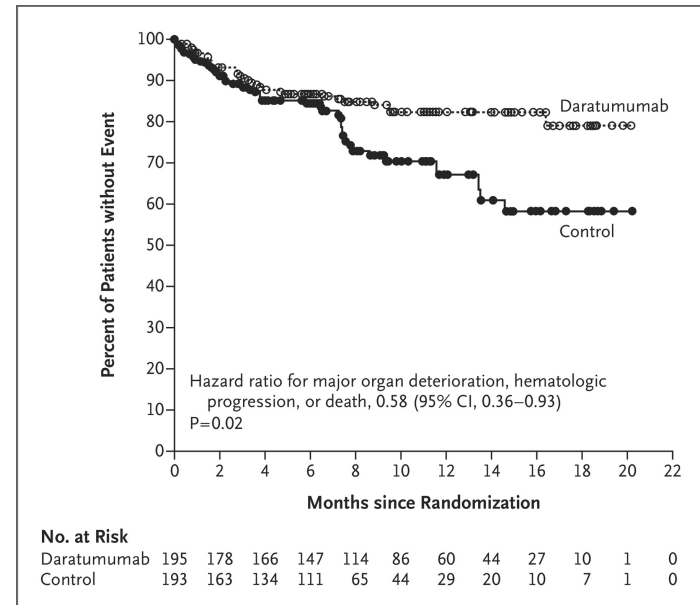
ANDROMEDA trial:

Primary and secondary endpoints

Hematologic CR rate



*Major organ deterioration (MOD)-PFS



*MOD-PFS defined by: death, cardiac deterioration, ESRD, hematologic progression



FDA Approves First and Only Treatment for AL Amyloidosis

DARZALEX FASPRO[®]
(daratumumab and hyaluronidase-
fihj) Becomes the First FDA-
Approved Treatment for Patients
with Newly Diagnosed Light Chain
(AL) Amyloidosis

January 15, 2021

Choice of upfront therapy – since 2021

- **CyBorD + Daratumumab**

Stem cell sparing, preferred in patients with renal compromise,
favorable outcome in patients with t(11;14)

- **High risk patients** (stage IIIb, NYHA class III or IV) – **single agent daratumumab** with intensive supportive care

- **Upfront AHCT**

< 10% PCs, ≤ 2 organ involvement, Mayo stage I/II cardiac disease

Key Points (1)

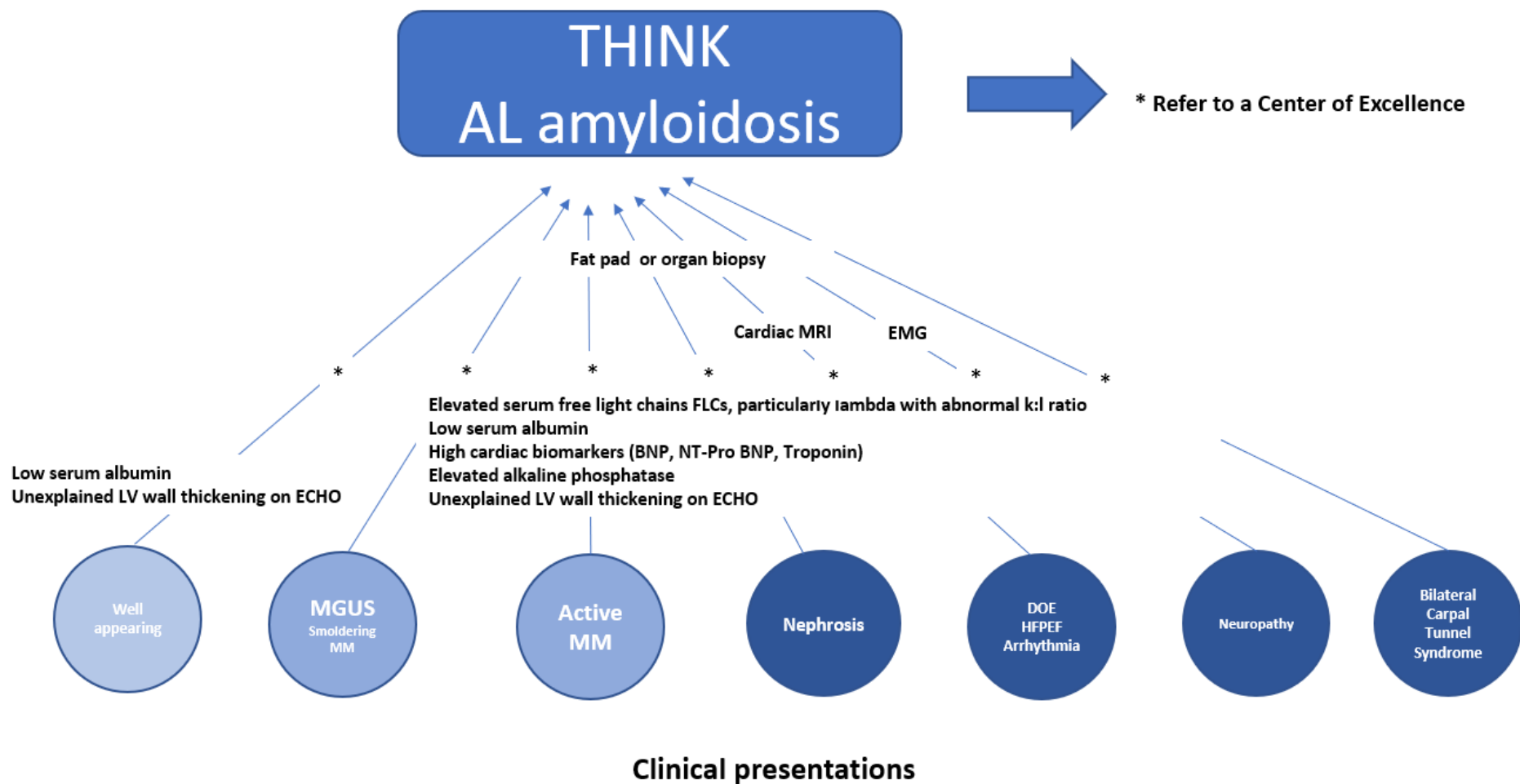
- What is amyloidosis?
 - AL (light chain) amyloidosis, a plasma cell disorder producing monoclonal light chains that misfold, aggregate and deposit in tissues; leads to dysfunction of organs, often multi-systemic
 - ATTR (transthyretin) amyloidosis, arising from precursor protein produced in the liver, transthyretin; primarily involves heart and nervous system
- Diagnosis - clues and when to suspect?
 - Often elusive; presents with multisystemic signs/symptoms
 - Unexplained LV hypertrophy on echo, with low voltage on ECG, should raise suspicion for cardiac amyloidosis.
 - Diagnosis of AL amyloidosis:
 - elevated serum free light chains, clonal BM plasma cells, tissue biopsy positive for amyloidosis; mass spect showing lambda/kappa subtype

Key Points (2)

- **Prognosis**
 - Extent of cardiac involvement = strongest determinant of survival
 - Cardiac biomarker (NT proBNP + troponin) staging predicts survival in newly diagnosed patients
 - Renal biomarkers (proteinuria + GFR) predict risk of progression to hemodialysis
- **Treatment goals**
 - Elimination of clonal plasma cells, reduction of circulating light chains + organ improvement
 - Hematologic complete remission (CR) is associated with organ improvement and better survival
 - Cardiac response defined by >30% and >300 ng/L decrease if baseline NT-proBNP \geq 650 ng/L

**Timely diagnosis + treatment
critical to prevent irreversible organ damage**

Conceptual Model to Facilitate Early Diagnosis of AL Amyloidosis



QUESTIONS ?



Thank You!

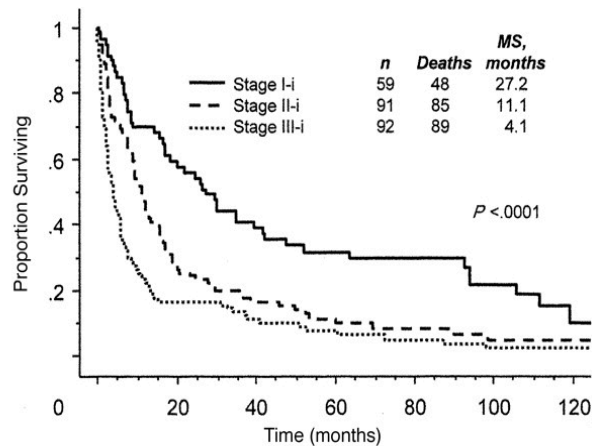
Laboratory findings suggestive of AL amyloidosis

- Abnormal serum free light chain assay
- Screen for organ involvement
 - Cardiac: BNP, NT-ProBNP, Troponin
 - Renal: serum ALB, 24hr urine total protein
 - Liver: alkaline phosphatase
 - Coagulopathy: factor X

Prognostic Staging Systems

Cardiac Biomarker Based: Troponin and NT-proBNP

Mayo Staging System



Stage I

- cTnI < 0.1 µg/L and NT-proBNP < 332 ng/L

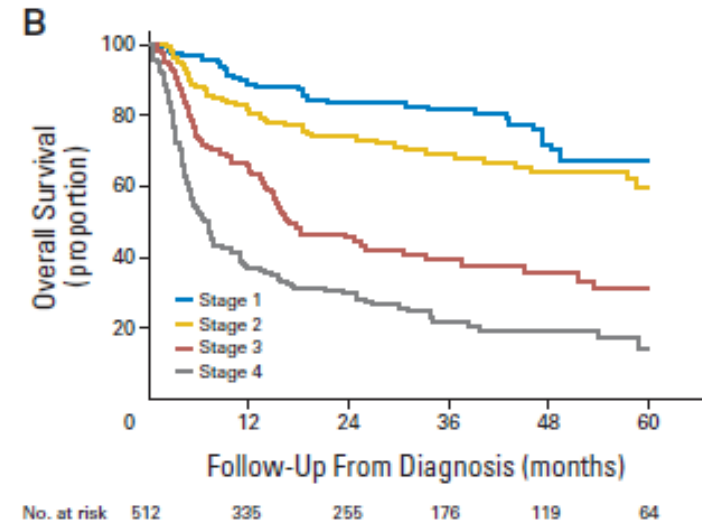
Stage II

- cTnI > 0.1 µg/L or NT-proBNP > 332 ng/L

Stage III

- cTnI > 0.1 µg/L and NT-proBNP > 332 ng/L

Revised Mayo Staging System



3 prognostic variables (cTnT ≥ 0.025 ng/mL, NT-proBNP ≥ 1,800 pg/ml or BNP > 400, FLC-diff ≥ 18 mg/dL)

Stage I - score 0

Stage II – score 1

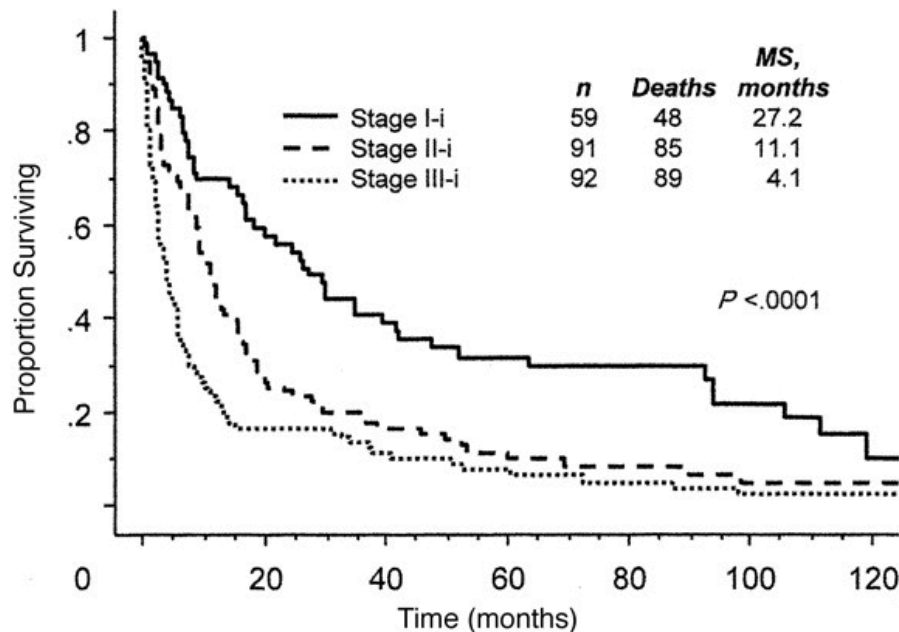
Stage III – score 2

Stage IV – score 3

Serum Cardiac Biomarker Based Staging System: Troponin and NT-proBNP

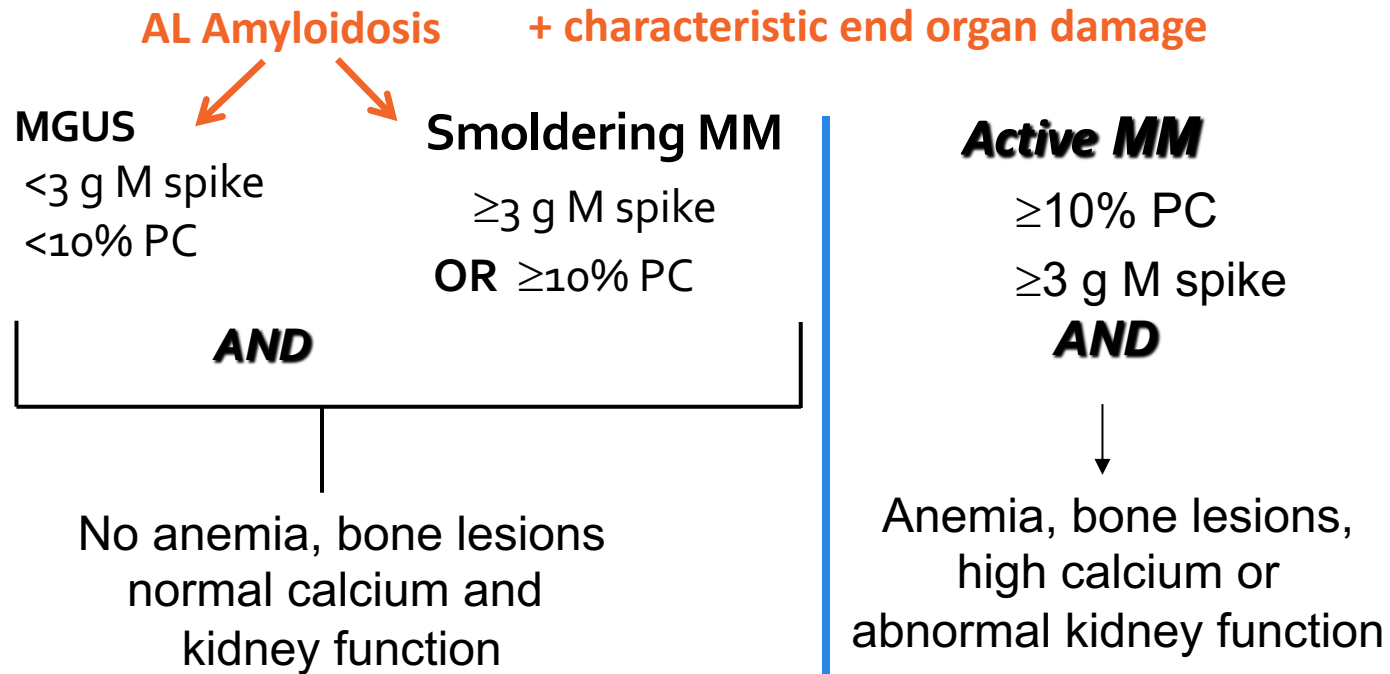
- Sensitive markers for the presence of cardiac amyloidosis
- Strongly prognostic in AL amyloidosis

Mayo Staging System



Stage I - cTnI < 0.1 µg/L and NT-proBNP < 332 ng/L
Stage II - cTnI > 0.1 µg/L or NT-proBNP > 332 ng/L
Stage III - cTnI > 0.1 µg/L and NT-proBNP > 332 ng/L

Plasma cell dyscrasias



* BM PCs > 60%, >1 focal lesion MRI, sFLC ratio>100

Munshi N. IMWG 2011.

*Rajkumar V. Lancet 2014.