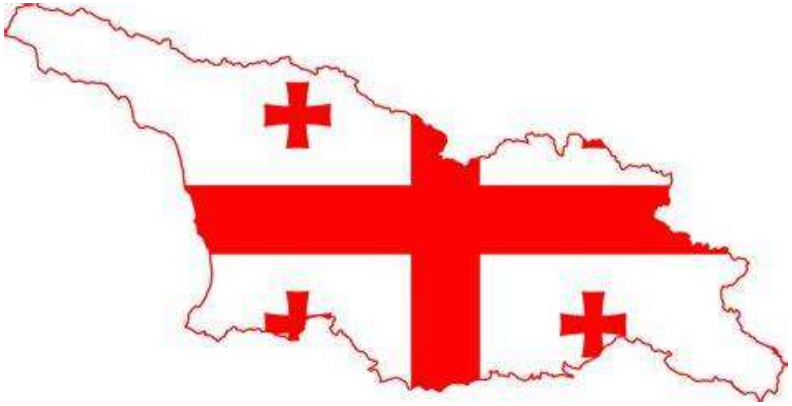


საქართველო

FATAL DISEASE

Nino Chaghiashvili MD, PHD, FESC Tbilisi, Georgia

2024

Medical History

65y.o ♀

Complaints:

- ✓ Progressive worsening dyspnea
- ✓ Easy fatigability for the last several months
- ✓ Dizziness
- ✓ Voice hoarseness,
- ✓ Numbness on her limbs
- ✓ Pain in hands
- ✓ Easy bruising
- ✓ Foaming urine
- ✓ Weight lost 10 kg last 6 months

Past Medical History :

2013 SVT Ablation
HCV diagnosed – not treated
2015 Atrial Fibrilation diagnosed

DRUGS:

Bisoprolol2.5 mg
Furosemide 40 mg
Aspirin 100mg
No anticoagulants

Physical examination findings

Vitals:

HR 60’

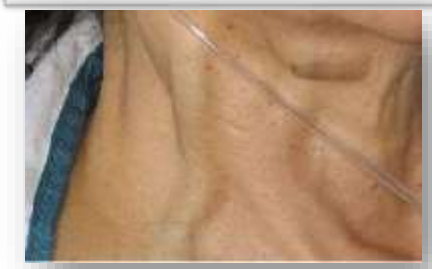
BP — **95/55mmHg**

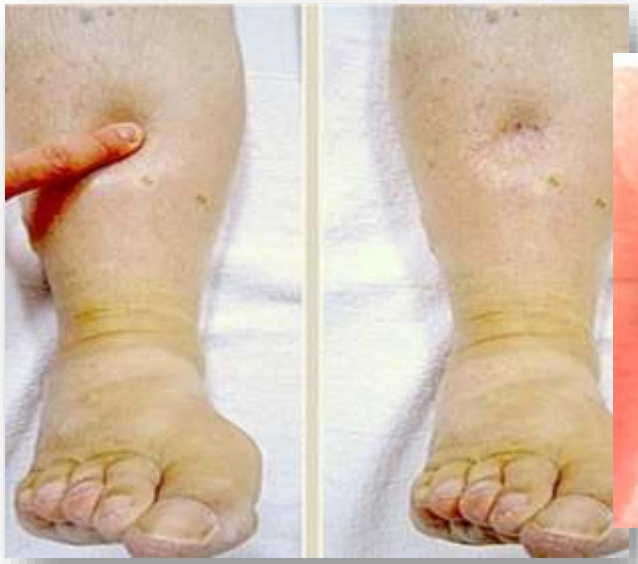
| **75/52 mmHg**

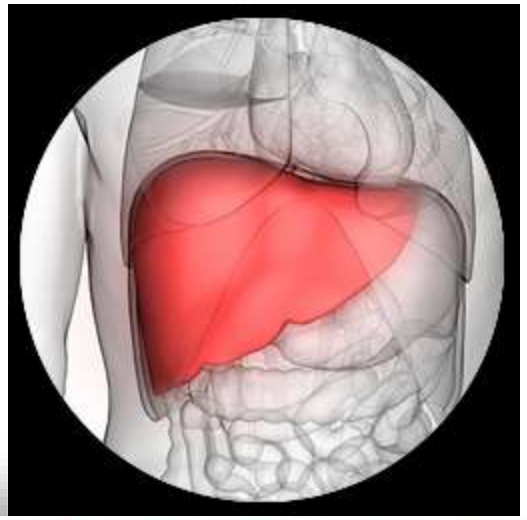
→ postural hypotention

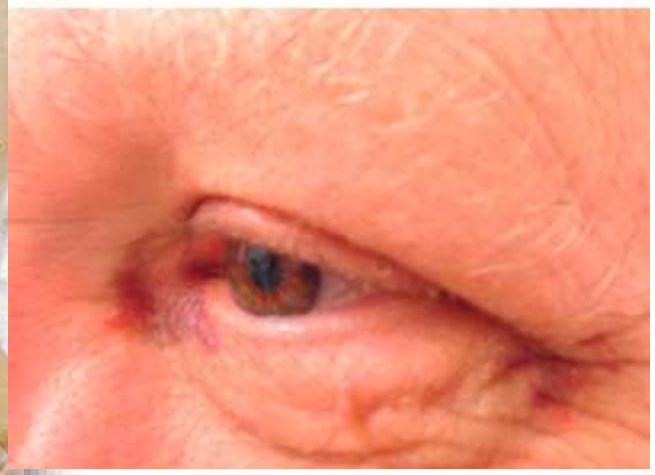
Sat 88%

RR 30’

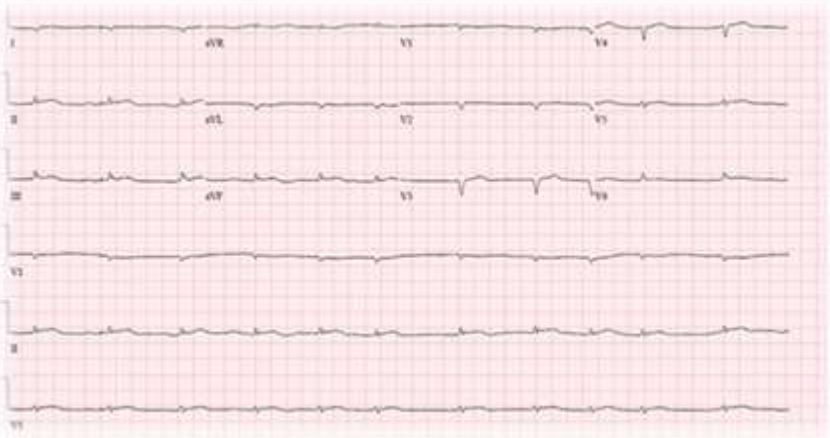




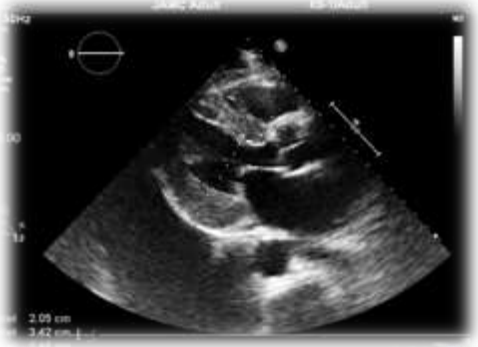


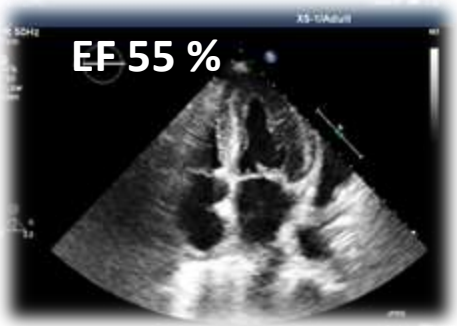


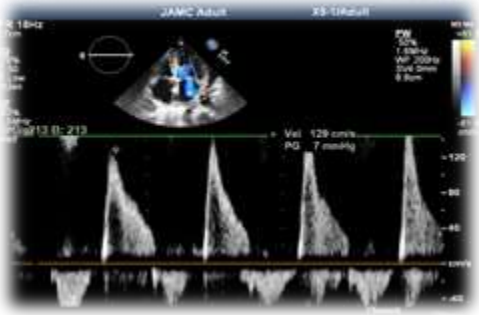
INVESTIGATIONS

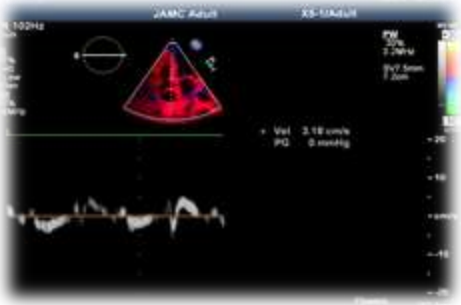


Electrocardiogram

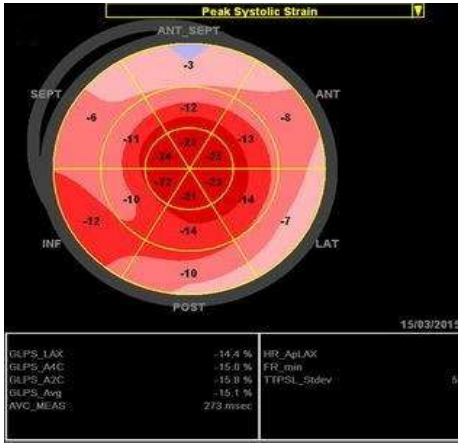








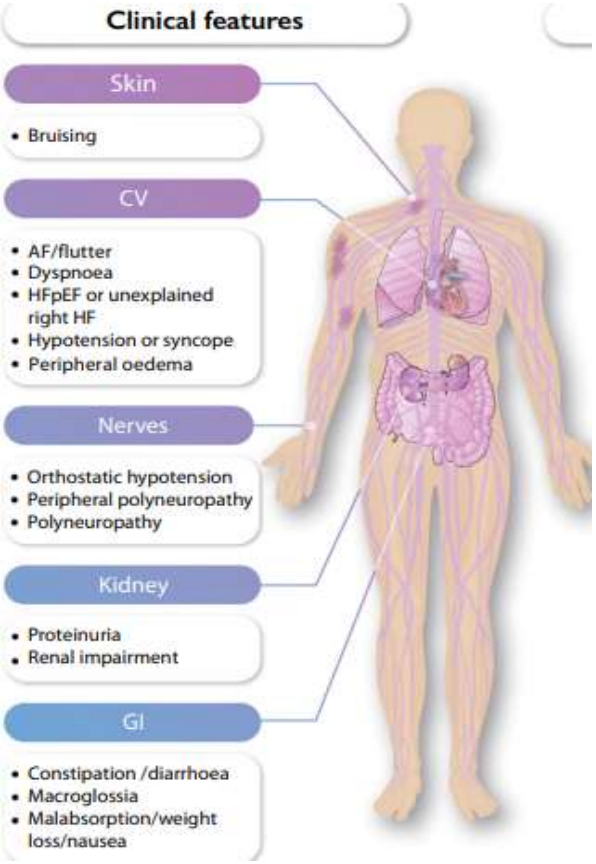
TTE



Speckle Tracking Strain Imaging : GLS -15.1% ↓

Coronarography shows normal coronary arteries

LABS: CBC: WBC 6,2 10^9 /l , RBC 4,7 10^{12}/l,
HBG 148 g/l, PLT 212 10^9 /l
Na 132 ↓ K 3.9, Ca 1.2
LFT: ALT 3 x ULR, AST 2.5 x ULR, TSB 3x ULR ↑
Albumin 33 g/l ↓
INR 1.5 ↑
Cr 1.4 mg/dl ↑, **GFR 37.7 mL/min/1.73 m²**↓
NT pro BNP 1419 pg/ml ↑
hsTn I 175.3 pg/ml ↑
24 hour protein in urine 4200 mg/24hour ↑



- ✓Disproportionally low QRS voltage;
- ✓Atrial fibrillation
- ✓Unexplained LV thickness ≥ 12 mm
- ✓Idiopathic pericardial effusion.
- ✓A decrease in GLS with a distinctive apical sparing pattern ,GLS ≥ −15.1%
- ✓reduced s’ , e’ , and a’ velocities
- ✓Persistent troponin elevation and disproportionately high NT-proBNP

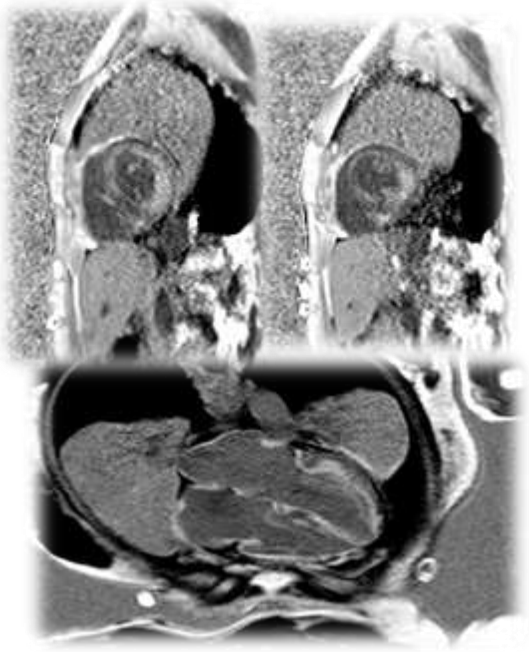
Which infiltrative cardiomyopathy is suspected?

1. Sarcoidosis,
2. Haemochromatosis
3. Cardiac amyloidosis √
4. Fabry disease

What tests would you order next?

1. SPEP, UPEP, Serum free light chain
2. Cardiac MRI √
3. Cardiac pyrophosphate scan
4. Order all 3 tests

Cardiac MRI



Diffuse late gadolinium enhancement.

What is the next?

2023 ACC Expert Consensus Decision Pathway on Cardiac Amyloidosis1083

FIGURE 3 Diagnostic Algorithm for Cardiac Amyloidosis

Clues from history, ECG, echocardiogram, CMR (see text and Table 1)

- *SPEP/UPEP not as sensitive as IFE*
- *mal K/L ratio in severe kidney disease: 0.54-3.30*

Free kappa light chains 393↑

Free lambda light chains 13.8

Ration free light chains 28.5 ↑

- *Cardiac scintigraphy could be ordered simultaneously for efficiency but must be interpreted in the context of the negative monoclonal protein screen*
- *Avoid false positives: SPECT imaging to exclude blood pool uptake*
- *Avoid false negatives: consider biopsy if scan is negative/equivocal but clinical suspicion is high*

Fat biopsy Congo red –
Cardiac biopsy Congo red + kappa Lch subtype

Yes

Consultation with hematologist
Biopsy (affected organ/surrogate site)
- Positive Congo red
- Tissue typing by mass spectrometry

AL-CM (see Figure 11)

No

Tc-99m-PYP
- Grade 2/3 uptake

No

Cardiac amyloidosis unlikely

Yes

ATTR-CM

Genetic testing

ATTRv-CM

ATTRwt-CM

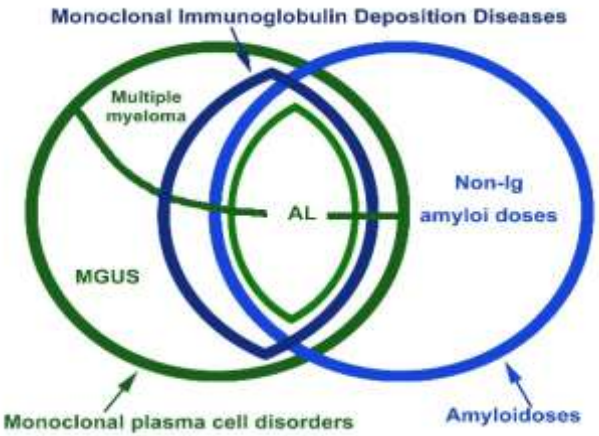
AL-CM = amyloid monoclonal immunoglobulin light chain cardiomyopathy; ATTR-CM = amyloid transthyretin cardiomyopathy; ATTRv-CM = variant transthyretin amyloid cardiomyopathy; ATTRwt-CM = wild-type transthyretin amyloid cardiomyopathy; CMR = cardiac magnetic resonance; ECG = electrocardiogram; IFE = immunofixation electrophoresis; K/L = kappa/lambda; PYP = pyrophosphate; SPECT = single-photon emission computed tomography; SPEP/UPEP = serum/urine protein electrophoresis.

Hematological workup

HFpEF , AL AMYLOIDOSIS

Hematological workup

Plasma total protein 76,1 g/l
Ig G 1830 Mg/dl
Ig A 118 Mg/dl
Ig M 145 Mg/dl
Paraprotein- negative
Albumin 51%
Globulin 48%
α 1 4.5%
α 2 12.0%
β 10.2%
γ 22.7%
A/G 1.0
M gradient - negative
Bence jones protein – negative



Symptom	Myeloma	AL amyloidosis
Bone pain, especially in your spine or chest	Common	Rare
Bone fractures, brittle bones and bone lesions	Common	Rare
Hypercalcemia (elevated calcium levels in the blood)	Common	Rare
Nausea	Less common (in AL amyloidosis, it is most commonly a sign of stomach involvement; in myeloma, hypercalcemia can cause this)	
Constipation	Common (in AL amyloidosis, it is most commonly a sign of intestine involvement; in myeloma, hypercalcemia can cause this)	
Diarrhoea	Common	
Loss of appetite	Common (in AL amyloidosis, it is most commonly a sign of stomach involvement)	
Unexplained weight loss	Common (in AL amyloidosis, it is most commonly a sign of stomach and intestine involvement)	
Dizziness, feeling light-headed	Common (can be caused by anaemia and fatigue)	
Anaemia (deficiency in the number or quality of red blood cells)	Common (due to myeloma cells interfering with the blood-cell-making activities of the bone marrow)	Rare

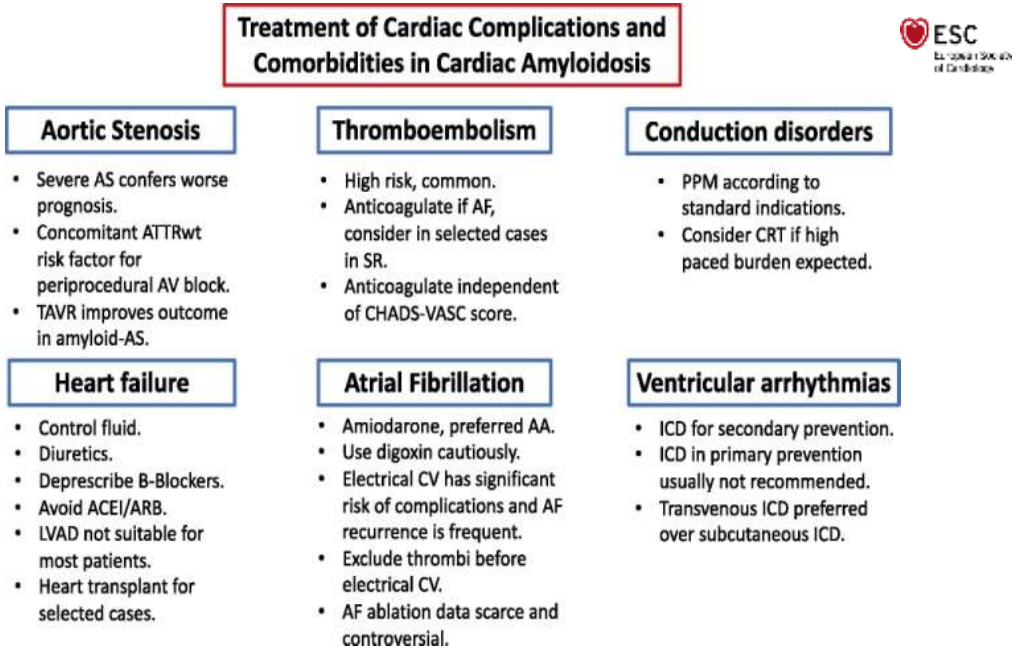
Symptom	Myeloma	AL amyloidosis
Fatigue	Common (due to abnormal blood counts, affected digestive functioning, kidney problems and a weakened immune system)	
Frequent infections	Common (due to a weakened immune system)	No
Excessive thirst	Rare	
Shortness of breath	Common (due to a weakened immune system)	No
Heart palpitations	No	Common (especially from exercising/ walking up and down stairs; if cardiovascular complications are present, these are related to poor prognosis)
Swollen tongue	No	This is a distinctive symptom of AL amyloidosis (referred to as macroglossia and occurs when the disease affects the oral cavity)
Bleeding of the skin around the eyes or in skin folds, also called purpura skin	No	This is a distinctive symptom of AL amyloidosis
Bloating or excessive gas	Less common	Common (a sign that the stomach or intestines are affected by the disease)
Peripheral neuropathy (damage to the peripheral nervous system; weakness or numbness in your legs)	Not common at early stages but can arise later (usually as an adverse event of anti-plasma cell therapies)	Common (a sign of nerve involvement, carpal tunnel syndrome in both hands can be a sign of AL amyloidosis)
Renal failure	Common	Rare
Excessive bubbles in the urine/foaming urine	Can occur in cases of cast nephropathy (renal impairment)	Common (due to proteinuria, when kidneys are involved)
Oedema	No	Common (mostly a sign of kidney involvement)

TREATMENT

Which statement is not correct concerning HF treatment of patients with cardiac amyloidosis :

1. Usually larger doses of diuretics are required but optimal fluid balance is difficult to achieve as these patients are preload dependent.
2. Ace-I , ARB , beta blockers are well tolerated V
3. As an antiarrhythmic (AA) drug the best choice is digoxin V
4. Amiodarone is preferred AA drug
5. ICD is recommended as a primary prevention of SCD V

1. **Torasemide 100 mg**
2. **Rivaroxaban 15 mg**
3. **Amyodaron 100 mg**

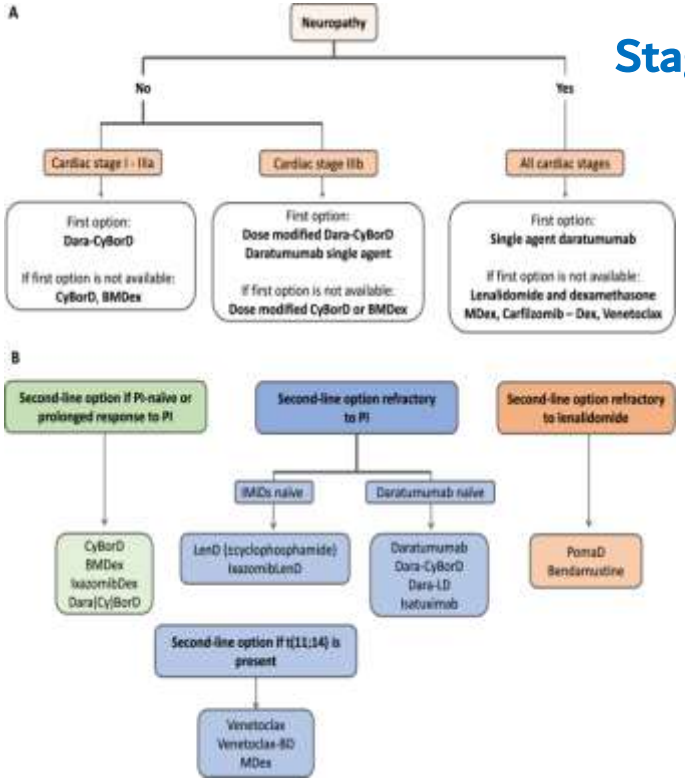


Eur Heart J, Volume 42, Issue 16, 21 April 2021, Pages 1554–1568, https://doi.org/10.1093/eurheartj/ehab072

Staging of cardiac and renal damage in AL amyloidosis

Staging system	Markers and thresholds	Stages	Outcomes*
Cardiac[34,35]	NT-proBNP >332 ng/L cTnT >0.035 ng/mL (or cTnI > 0.01 ng/mL)	I. no markers above the cutoff II. one marker above the cutoff IIIa. both markers above the cutoff and NT-proBNP <8500 ng/L IIIb. both markers above the cutoff and NT-proBNP >8500 ng/L	I. median survival not reached, 60% surviving 10 years II. median survival 49 months IIIa. median survival 14 months IIIb. median survival 5 months
Revised Mayo Clinic [36]	NT-proBNP >1800 ng/L cTnT >0.025 ng/mL dFLC >180 mg/L	I. 0 markers above the cutoff II. 1 marker above the cutoff III. 2 markers above the cutoff IV. 3 markers above the cutoff	I. median survival not reached, 55% surviving 10 years II. median survival 57 months III. median survival 18 months IV. median survival 6 months
Renal[37]	eGFR <50 mL/min per 1.73 m^2 proteinuria >5 g/24h	I. both eGFR above and proteinuria below the cutoffs II. either eGFR below or proteinuria above the cutoffs III. both eGFR below and proteinuria above the cutoffs	I. 1% risk of dialysis at 2 years II. 12% risk of dialysis at 2 years III. 48% risk of dialysis at 2 years

cTn, cardiac troponin; dFLC, difference between involved (amyloidogenic) and uninvolved circulating free light chain; eGFR, estimated glomerular filtration rate; NT-proBNP, N-terminal pro-natriuretic peptide type-B. *Observed in 1065 patients with AL amyloidosis newly diagnosed at the Pavia Amyloidosis Research and treatment center.

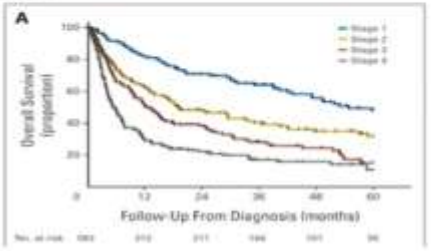


Stage III a

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Revised Prognostic Staging System for Light Chain Amyloidosis Incorporating Cardiac Biomarkers and Serum Free Light Chain Measurements

- Mayo Stage 2012
  - NT-ProBNP 1,800 pg/mL
  - cTnT 0.025 ng/mL, and
  - FLC-diff 18 mg/dL



EHA-ISA Guidelines for Stem Cell Transplantation in AL Amyloidosis

Eligibility Criteria
- Age >18 and <70 years
- At least one vital organ involvement
- Left ventricular ejection fraction ≥40% and NYHA class <III
- Oxygen saturation ≥95% on room air and DLCO >50%
- Supine systolic blood pressure ≥90 mm Hg
- ECOG performance status score ≤2
- Direct Bilirubin <2 mg/dL
- NTproBNP <5000 pg/mL
- Troponin I <0.1 ng/mL, Troponin T <0.06 ng/mL, hs-Troponin T <75 ng/mL

Induction Therapy
- Consider if bone marrow plasmacytosis >10%
- Bortezomib based regimen 2-4 cycles
- Defer SCT if hematologic CR achieved with induction therapy

Stem Cell Mobilization and Collection
- G-CSF at 10-16 mcg/kg/day (single or split dose)
- Plerixafor on demand or planned
- Avoid cyclophosphamide

Risk-Adapted Melphalan Dosing

	MEL 200[a]	MEL 200 vs non-SCT regimens[b]	MEL 140
Age (years)	≤65	66-70	
Cardiac stage	I	II	
eGFR (mL/min/m^2)	>50	30-50	≤30[c]

[a] *must meet all criteria*
[b] *multidisciplinary discussion recommended*
[c] *increased risk of AKI and ESRD during the peri-SCT period; may consider if on a stable chronic dialysis schedule*

A pair of wooden Shoes, by Vincent van Gogh

“For sale: baby shoes never worn." **Ernest Miller Hemingway**

“ Did not arrive for the scheduled visit. Found dead at home. Fatal end ”

TAKE HOME MESSAGE

- ✓ Always understand the cause behind heart failure
- ✓ Atrial arrhythmias can be an initial manifestation of cardiac amyloidosis
- ✓ Accurate subtyping is a critical step in appropriate management of patients with AL amyloidosis
- ✓ Tailor therapy to the individual patient taking into account :
- anticipated toxicities of various agents
- extent and degree of organ involvement
- availability of various agents
- ✓ Close monitoring and multidisciplinary management involving oncologists, cardiologists,nephrologist

H O P E

A previously hopeless disease has now rapidly become a treatable and possibly curable condition.