



Recurrent Syncope: Unveiling Hidden Perils

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Introduction

- Mr. S
- 76 year- old
- Father of four children (grown ups)
- Former heavy vehicle driver
- From Colombo suburbs



Background history of,

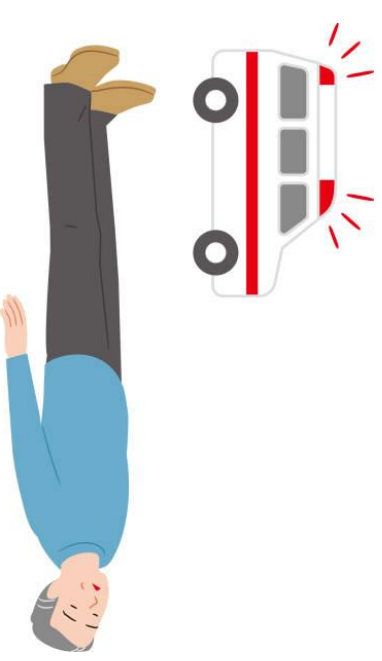
- Hypertension
- Dyslipidaemia
- Pulmonary tuberculosis- smear positive, treatment completed 25 years back
- Independent on Basic and Instrumental ADL



Presenting complain

- He presented to Emergency Treatment Unit (ETU) with a fall following sudden transient loss of consciousness
- Occurred while waiting at the bus stop
- No proceeding ill health
- He had waited at the bus stop around 20 minutes when he felt lightheadness, and nausea
- Could remember feeling unwell and sweating
- Then went “blank” was how the patient described it and could not remember anything afterwards
- He had fell on the ground, hit forehead on the pavement resulting in a laceration
- No undue pain suggestive of fractures or dislocations

- He denied proceeding chest pain, palpitations, dizziness or aura
- There were no acute onset neurological symptoms such as visual changes, weakness, headache or neck pain
- According to eye witness; brief period of LOC around 1-2 minutes and spontaneously regained the consciousness
- No abnormal limb movements
- No lateral tongue biting, incontinence or post- ictal drowsiness



- Several episodes of LOC had occurred during last three weeks; around 2-3 episodes per week
- Two of those had resulted in falls
- In other instances, as he was getting the prodromal symptoms he was able to sit down on a chair, bed or floor depending on the circumstances
- Those episodes were not specifically associated with standing from lying down position, turning the neck, prolonged standing, cough or micturition
- Among the two previous falls last fall had occurred 4 days prior to the index admission
- It had occurred while cleaning the house
- He felt the lightheadness, grabbed a window bar and tried to sit down before losing consciousness, but had failed resulting a fall
- When he regained the consciousness was lying on the floor and able to get up on his own
- He attributed these symptoms to exhaustion and did not seek medical attention

Upon assessment by the ETU team.....



- Patient was conscious and rational
- There was a bleeding forehead laceration for which suturing had been arranged
- Pulse rate was 68 bpm which was regular
- Blood pressure recorded as 100/60 mmHg
- ECG showed sinus rhythm with no evidence of conduction delay or changes to suggest acute ischaemia
- Possible hypoglycemia had been excluded as capillary blood sugar on admission was 120 mg/dl

During further assessment.....

- Patient admitted to have gradual onset exercise intolerance and fatigue for last 8 months
- Moderate exertional dyspnea (NYHA class 2)
- Also admitted slowly progressive bilateral lower limb swelling for last 6 months
- But there was no orthopnea or paroxysmal nocturnal dyspnea
- He had noticed passage of frothy urine recently, but denied having change in urine volume or haematuria
- He denied LOA, LOW, fever or night sweats
- No history of cold intolerance or recent weight gain to suggest hypothyroidism
- No history of chronic cough

Comprehensive Geriatric Assessment

Mood:

- He had low mood (felt sad all the time and find it difficult to feel pleasure from previously pleasurable activities), but reactive
- He did not have active or passive suicidal ideas

Cognition:

- No complaints related to impaired cognition

Sleep:

- Experienced sleep disturbances- difficulty in initiation of sleep and frequent awakening during night

Mini Nutritional Assessment

MNA[®]

Nestlé
NutritionInstitute

- No vision or hearing impairment
- Good dentition

- No dysphagia/ GORD symptoms

- Bowel habits were normal

- Appetite was normal

- No recent loss of weight

- Consumed a rice based diet containing adequate amount of protein and calories

- Diet contained adequate amount of dietary fibers and micronutrients

- Non vegetarian

- **Mini Nutritional Assessment: 12/14 (normal nutritional status)**

Complete the screen by filling in the boxes with the appropriate numbers. Total the numbers for the final screening score.

Screening

Last name: First name:

Sex: Age: Weight, kg: Height, cm: Date:

A Has food intake declined over the past 3 months due to loss of appetite, digestive problems, chewing or swallowing difficulties?

0 = severe decrease in food intake
1 = moderate decrease in food intake
2 = no decrease in food intake

B Weight loss during the last 3 months

0 = weight loss greater than 3 kg (6.6 lbs)
1 = does not know
2 = weight loss between 1 and 3 kg (2.2 and 6.6 lbs)
3 = no weight loss

C Mobility

0 = bed or chair bound
1 = able to get out of bed / chair but does not go out
2 = goes out

D Has suffered psychological stress or acute disease in the past 3 months?

0 = Yes
2 = no

E Neuropsychological problems

0 = severe dementia or depression
1 = mild dementia
2 = no psychological problems

F1 Body Mass Index (BMI) (weight in kg) / (height in m²)

0 = BMI less than 19
1 = BMI 19 to less than 21
2 = BMI 21 to less than 23
3 = BMI 23 or greater

IF BMI IS NOT AVAILABLE, REPLACE QUESTION F1 WITH QUESTION F2.
DO NOT ANSWER QUESTION F2 IF QUESTION F1 IS ALREADY COMPLETED.

F2 calf circumference (CC) in cm

0 = CC less than 31
3 = CC 31 or greater

Screening score (max. 14 points)

12-14 points: Normal nutritional status
8-11 points: At risk of malnutrition
0-7 points: Malnourished

Save Print Reset

Geriatric Depression Scale (Short Form)

Delirium:

Confusion Assessment Method (CAM) criteria
negative

MMSE: 26/30

Orientation 10/10

Registration 3/3

Recall 2/3

Attention and calculation 5/5

Language 5/8

Copying 1/1

GDS: 10/15 (moderate depression)

Patient's Name: _____ Date: _____

Instructions: Choose the best answer for how you felt over the past week.

No.	Question	Answer	Score
1.	Are you basically satisfied with your life?	YES / NO	
2.	Have you dropped many of your activities and interests?	YES / NO	
3.	Do you feel that your life is empty?	YES / NO	
4.	Do you often get bored?	YES / NO	
5.	Are you in good spirits most of the time?	YES / NO	
6.	Are you afraid that something bad is going to happen to you?	YES / NO	
7.	Do you feel happy most of the time?	YES / NO	
8.	Do you often feel helpless?	YES / NO	
9.	Do you prefer to stay at home, rather than going out and doing new things?	YES / NO	
10.	Do you feel you have more problems with memory than most?	YES / NO	
11.	Do you think it is wonderful to be alive?	YES / NO	
12.	Do you feel pretty worthless the way you are now?	YES / NO	
13.	Do you feel full of energy?	YES / NO	
14.	Do you feel that your situation is hopeless?	YES / NO	
15.	Do you think that most people are better off than you are?	YES / NO	
TOTAL			

Scoring:

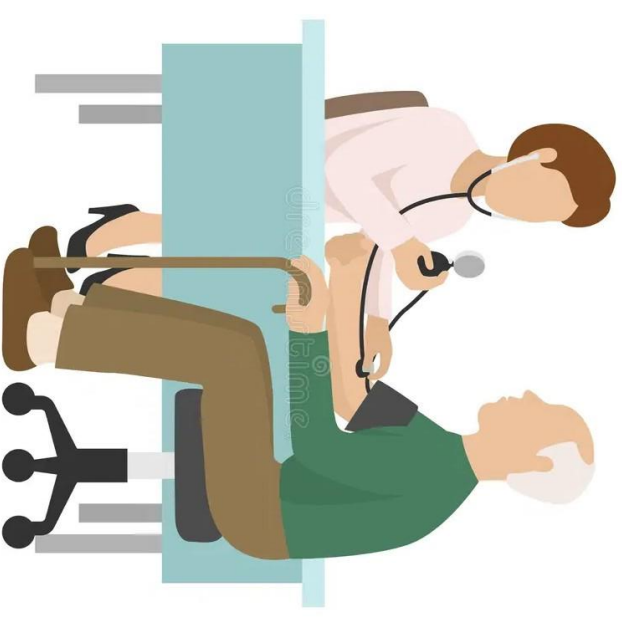
Assign one point for each of these answers:

- | | | | | |
|--------|--------|--------|---------|---------|
| 1. NO | 4. YES | 7. NO | 10. YES | 13. NO |
| 2. YES | 5. NO | 8. YES | 11. NO | 14. YES |
| 3. YES | 6. YES | 9. YES | 12. YES | 15. YES |

A score of 0 to 5 is normal. A score above 5 suggests depression.

Past medical history

- Hypertension diagnosed 10 years back
- On treatment with good compliance
- Dyslipidemia diagnosed 3 years back
- Smear positive pulmonary tuberculosis diagnosed 25 years back
- Standard ATT has been completed
- No history of reactivations



- No history of past surgeries
- No known allergies

Routine medications included,

- Amlodipine 10 mg daily
- Losartan 50 mg twice a day
- Atorvastatin 10 mg nocte



Social history

- Past history of smoking twenty pack years, stopped 25 years back when he was diagnosed with TB
- Consumed 2 units of alcohol per week
- Lived in his own house with wife and youngest son who was unmarried
- Primary care giver for his 65 year old wife who is fully dependent for last one year, following a hemorrhagic stroke
- Significant care giver burden (Using 22 item Zarit burden interview- score of 45)
- Respite care giver for the wife was the younger son
- Previously a heavy vehicle driver, but unemployed for last one year
- No stable source of income
- Financial support was from children
- Receiving government welfare benefits

22 Item Zarit Burden Interview

The Zarit Burden Interview

- 0 : NEVER
 1 : RARELY
 2 : SOMETIMES
 3 : QUITE FREQUENTLY
 4 : NEARLY ALWAYS

Question	Score
1 Do you feel that your relative asks for more help than he/she needs?	0 1 2 3 4
2 Do you feel that because of the time you spend with your relative that you don't have enough time for yourself?	0 1 2 3 4
3 Do you feel stressed between caring for your relative and trying to meet other responsibilities for your family or work?	0 1 2 3 4
4 Do you feel embarrassed over your relative's behaviour?	0 1 2 3 4
5 Do you feel angry when you are around your relative?	0 1 2 3 4
6 Do you feel that your relative currently affects our relationships with other family members or friends in a negative way?	0 1 2 3 4
7 Are you afraid what the future holds for your relative?	0 1 2 3 4
8 Do you feel your relative is dependent on you?	0 1 2 3 4
9 Do you feel strained when you are around your relative?	0 1 2 3 4
10 Do you feel your health has suffered because of your involvement with your relative?	0 1 2 3 4
11 Do you feel that you don't have as much privacy as you would like because of your relative?	0 1 2 3 4
12 Do you feel that your social life has suffered because you are caring for your relative?	0 1 2 3 4

Question	Score
13 Do you feel uncomfortable about having friends over because of your relative?	0 1 2 3 4
14 Do you feel that your relative seems to expect you to take care of him/her as if you were the only one he/she could depend on?	0 1 2 3 4
15 Do you feel that you don't have enough money to take care of your relative in addition to the rest of your expenses?	0 1 2 3 4
16 Do you feel that you will be unable to take care of your relative much longer?	0 1 2 3 4
17 Do you feel you have lost control of your life since your relative's illness?	0 1 2 3 4
18 Do you wish you could leave the care of your relative to someone else?	0 1 2 3 4
19 Do you feel uncertain about what to do about your relative?	0 1 2 3 4
20 Do you feel you should be doing more for your relative?	0 1 2 3 4
21 Do you feel you could do a better job in caring for your relative?	0 1 2 3 4
22 Overall, how burdened do you feel in caring for your relative?	0 1 2 3 4

Interpretation of Score:

- 0 - 21 little or no burden
 21 - 40 mild to moderate burden
 41 - 60 moderate to severe burden
 61 - 88 severe burden

Concerns of patient

- Patient was concerned about recurrent episodes of LOC
- Believed those might have caused by lack of rest
- Expected a cure for his symptoms, so he could continued to care for his wife

Examination findings

BMI 23.8 kg/m²

Pale, anicteric

Periorbital oedema

No palpable lymph nodes or salivary gland enlargement

No finger clubbing

Significant lower limb pitting oedema - Grade 3

Also noted to have soft tissue swelling of scrotum

CVS:

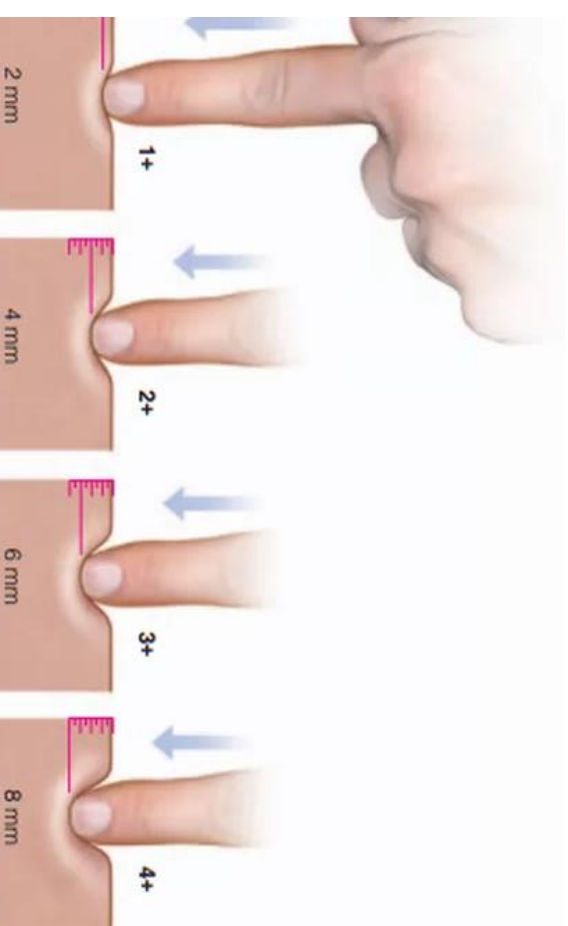
Jugular venous pulse not elevated

PR 64 beats per minute, regular

BP 110/70 mmHg in supine position and 100/70 on standing

DR, **heart sounds were muffled**

No murmurs



RS:

Oxygen saturation was 96% on ambient air

Dullness to percussion and diminished breath sounds at the lung bases

Abdomen:

no organomegaly/other masses, no ascites

Musculoskeletal:

normal



Neurology:

GCS 15

B/L pupils were equal and reactive to light

Fundoscopic examination- No optic disc oedema

No neck stiffness/ kernig sign negative

Cranial nerve examination normal

Cerebellar signs negative

UL and LL tone, power and reflexes normal

No sensory impairment



Mobility and balance:

- Gait normal
- TUG- 16 seconds
- Chair rise test- 15 seconds
- Grip strength- good
- 4 point balance test- 4/4

Fracture risk assessment:

FRAX score (without BMD)

MOP # risk: 4.3% Hip # risk: 1.9%

FRAX[®] Fracture Risk Assessment Tool

Home Calculation Tool Paper Charts FAQ References CE Mark English

Calculation Tool

Please answer the questions below to calculate the ten year probability of fracture with BMD.

Country: Sri Lanka Name/ID: About the risk factors

Questionnaire:

- Age (between 40 and 90 years) or Date of Birth
Age: 76 Y: M: D:
- Sex
 Male Female
- Weight (kg)
64
- Height (cm)
164
- Previous Fracture
 No Yes
- Parent Fractured Hip
 No Yes
- Current Smoking
 No Yes
- Glucocorticoids
 No Yes
- Rheumatoid arthritis
 No Yes
- Secondary osteoporosis
 No Yes
- Alcohol 3 or more units/day
 No Yes
- Femoral neck BMD (g/cm²)
Select BMD

10. Secondary osteoporosis No Yes

11. Alcohol 3 or more units/day No Yes

12. Femoral neck BMD (g/cm²)
Select BMD

BMI: 23.8
The ten year probability of fracture (%)
without BMD

Major osteoporotic	4.3
Hip Fracture	1.9

Weight Conversion

Pounds → Kg

Height Conversion

Inches → cm

00025296
Individuals with fracture risk assessed since 1st June 2011

The Lawton Instrumental Activities of Daily Living Scale

Functional Capacity:

- Independent on BADL (assessed with Barthel index)

- Lawton instrumental activity scale- 6/8

A. Ability to Use Telephone

1. Operates telephone on own initiative; looks up and dials numbers..... 1
2. Dials a few well-known numbers..... 1
3. Answers telephone, but does not dial..... 1
4. Does not use telephone at all..... 0

E. Laundry

1. Does personal laundry completely 1
2. Launders small items, rinses socks, stockings, etc..... 1
3. All laundry must be done by others 0

B. Shopping

1. Takes care of all shopping needs independently 1
2. Shops independently for small purchases..... 0
3. Needs to be accompanied on any shopping trip 0
4. Completely unable to shop 0

F. Mode of Transportation

1. Travels independently on public transportation or drives own car..... 1
2. Arranges own travel via taxi, but does not otherwise use public transportation 1
3. Travels on public transportation when assisted or accompanied by another 1
4. Travel limited to taxi or automobile with assistance of another..... 0
5. Does not travel at all 0

C. Food Preparation

1. Plans, prepares, and serves adequate meals independently..... 1
2. Prepares adequate meals if supplied with ingredients..... 0
3. Heats and serves prepared meals or prepares meals but does not maintain adequate diet..... 0
4. Needs to have meals prepared and served..... 0

G. Responsibility for Own Medications

1. Is responsible for taking medication in correct dosages at correct time..... 1
2. Takes responsibility if medication is prepared in advance in separate dosages..... 0
3. Is not capable of dispensing own medication..... 0

D. Housekeeping






1. Maintains house alone with occasion assistance (heavy work)..... 1
2. Performs light daily tasks such as dishwashing, bed making..... 1
3. Performs light daily tasks, but cannot maintain acceptable level of cleanliness..... 1
4. Needs help with all home maintenance tasks..... 1
5. Does not participate in any housekeeping tasks..... 0





H. Ability to Handle Finances

1. Manages financial matters independently (budgets, writes checks, pays rent and bills, goes to bank); collects and keeps track of income..... 1
2. Manages day-to-day purchases, but needs help with banking, major purchases, etc..... 1
3. Incapable of handling money 0

Scoring: For each category, circle the item description that most closely resembles the client's highest functional level (either 0 or 1).

CLINICAL FRAILTY SCALE

	1	VERY FIT People who are robust, active, energetic and motivated. They tend to exercise regularly and are among the fittest for their age.
	2	FIT People who have no active disease symptoms but are less fit than category 1. Often, they exercise or are very active occasionally, e.g., seasonally.
	3	MANAGING WELL People whose medical problems are well controlled , even if occasionally symptomatic, but often are not regularly active beyond routine walking.
	4	LIVING WITH VERY MILD FRAILTY Previously "vulnerable," this category marks early transition from complete independence. While not dependent on others for daily help, often symptoms limit activities . A common complaint is being "slowed up" and/or being tired <u>during the day</u> .
	5	LIVING WITH MILD FRAILTY People who often have more evident slowing , and need help with high order instrumental activities of daily living (finances, transportation, heavy housework). Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation, medications and begins to restrict light housework.

	6	LIVING WITH MODERATE FRAILTY People who need help with all outside activities and with keeping house . Inside, they often have problems with stairs and need help with bathing and might need minimal assistance (cuing, standby) with dressing.
	7	LIVING WITH SEVERE FRAILTY Completely dependent for personal care , from whatever cause (physical or cognitive). Even so, they seem stable and not at high risk of dying (within ~6 months).
	8	LIVING WITH VERY SEVERE FRAILTY Completely dependent for personal care and approaching end of life. Typically, they could not recover even from a minor illness.
	9	TERMINALLY ILL Approaching the end of life. This category applies to people with a life expectancy <6 months , who are not otherwise living with severe frailty . (Many terminally ill people can still exercise until very close to death.)

SCORING FRAILTY IN PEOPLE WITH DEMENTIA

The degree of frailty generally corresponds to the degree of dementia. Common symptoms in **mild dementia** include forgetting the details of a recent event, though still remembering the event itself, repeating the same question/story and social withdrawal.

In **moderate dementia**, recent memory is very impaired, even though they seemingly can remember their past life events well. They can do personal care with prompting.

In **severe dementia**, they cannot do personal care without help.

In **very severe dementia** they are often bedfast. Many are virtually mute.



Clinical Frailty Scale ©2005–2020 Rockwood, Version 2.0 (EN). All rights reserved. For permission: www.geriatricmedicine.ca
Rockwood K et al. A global clinical measure of fitness and frailty in elderly people. CMAJ 2005;173:489–495.

Frailty scale 4 Living with very mild frailty

Problems

- Recent onset recurrent syncope and falls in an independently functioning older adult with only mild frailty
- Slowly progressive bilateral lower limb edema with associated pleural effusion and pericardial effusion with no features of heart failure
- Primary care giver for the spouse resulting significant care giver burden and moderate depression
- Socioeconomic issues with lack of financial stability and independence in the older age



INVESTIGATIONS

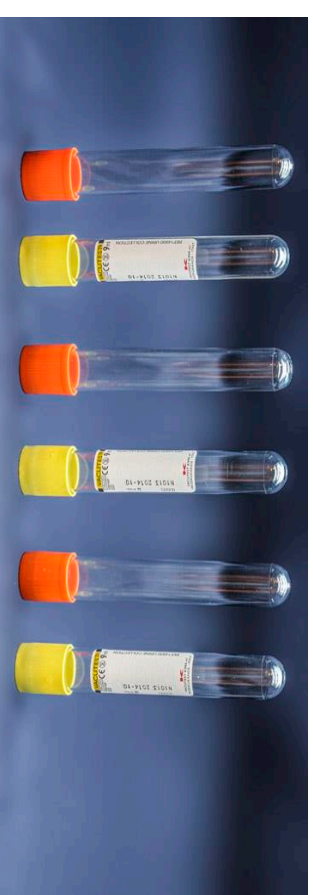
WBC	7.6 (N 65%, L 27%, E 3%)
HB	9.3
MCV	88
PLT	257

Normocytic normochromic anemia. Evidence of chronic inflammatory process with moderate rouleux formation

Total Protein	52 g/L	(60- 83)
Albumin	17 g/L	(34- 54)
Globulin	45 g/L	(23- 34)
ALT	45 U/L	(7- 56)
AST	35 U/L	(8- 33)

ESR	87 mm
CRP	12 mg/dL (<6)

Creatinine	2.3 mg/dL	(0.7- 1.3)
eGFR	27.6	
Sodium	138 mEq/L	(135- 145)
Potassium	3.7 mEq/L	(3.5- 5.2)
Albumin corrected calcium	2.6 mmol/L	(2.2- 2.7)
Magnesium	0.96 mmol/L	(0.85- 1.10)



ECG	Sinus rhythm. HR 64 bpm. Normal voltage complexes No acute ischaemic changes	
High sensitive troponin I	Negative	
NT pro BNP	315 pg/mL (<450)	
24 hour holter monitoring	Intermittent high grade atrio-ventricular block with spontaneously reverting back to sinus rhythm	

FBS	86 mg/dL	(80- 100)
HBA1c	5.6%	(< 5.7)
TSH	2.6 mU/L	(0.4- 4.1)



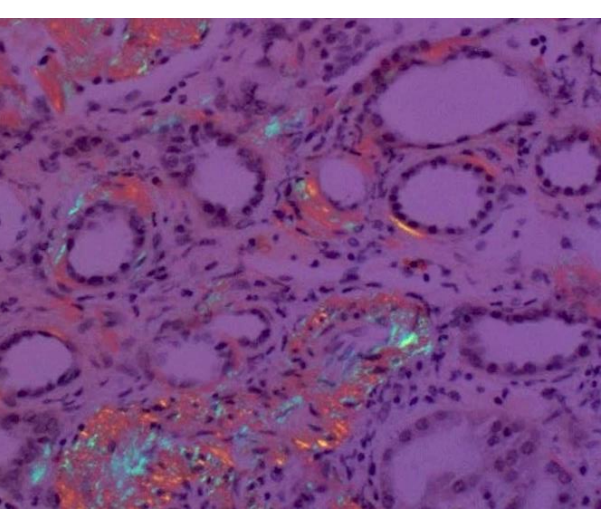
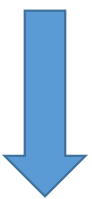
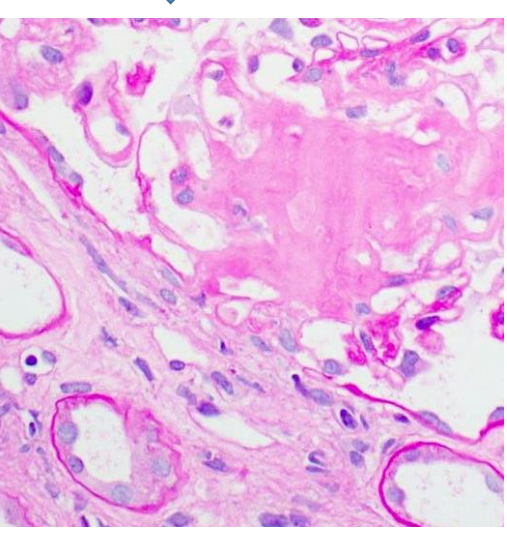
UFR	Protein +++ Pus cells 2-3 Red cells Nil	
Urine protein: creatinine ratio	7.06 mg/mg (>3.5)	
24 hour urine protein	4266 mg/ 24 hours (<150)	
Urine Acid Fast Bacilli staining	Negative	
Urine Bence Jones proteins	Positive	

Chest radiograph	Moderate pulmonary edema and bilateral pleural effusions
Transthoracic echocardiography	Concentric hypertrophy of the left ventricle. Diastolic dysfunction. LV ejection fraction of 65%. Thin rim of pericardial fluid
Ultrasound scan abdomen	No hepatomegaly or splenomegaly. Kidney sizes were normal. Slightly increased renal echogenicity

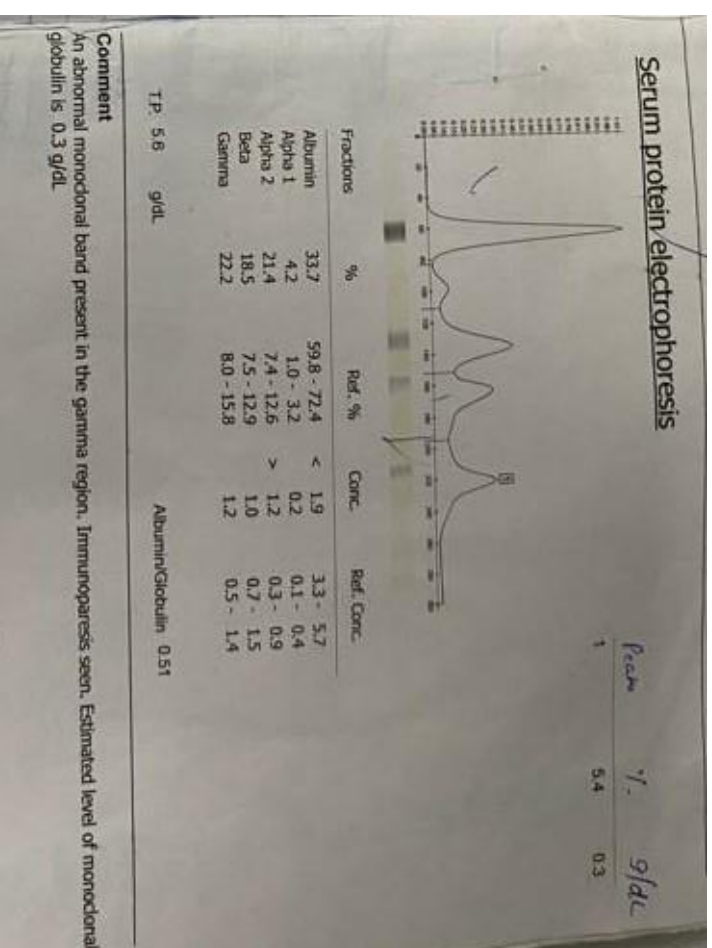


Interferon Gamma Release Assay	Negative
ANA	Negative
Complement C3 and C4 levels	Normal
ANCA	Negative

- Because of nephrotic range proteinuria renal biopsy was arranged
- Renal biopsy showed amorphous material deposited in the mesangium of the glomeruli and the blood vessel walls which was not stained by the immuno stain used.
- Use of Congo red highlighted eosinophilic material in salmon pink colour and light apple green birefringent was present under polarized light which was suggestive of **amyloid deposition**
- Abdominal fat pad biopsy revealed only mature adipose tissues only and was negative for amyloid deposition



- Serum protein electrophoresis showed an abnormal monoclonal band in the gamma region with immunoparesis
- Serum free light chain assay showed monoclonal gammopathy of lambda light chains
- **Bone marrow aspiration showed 20% plasma cells.** No evidence of amyloid deposition in bone marrow
- X- Ray skeletal survey did not show any lytic lesions
- But whole body MRI showed multiple T1 low T2 and STIR high signal intensities in T8, T11 and L3 vertebral bodies **suggestive of multiple myeloma**



Conclusion

- Diagnosis of AL amyloidosis associated with multiple myeloma with renal and cardiac involvement was made depending on the clinical context and investigation findings
- Cardiogenic syncope due to intermittent high grade AV block in the background of cardiac amyloidosis

Management

- Multidisciplinary team meeting was arranged with the participation of the consultant haematologist, cardiologist, nephrologist and psychiatrist
- Permanent cardiac pacemaker implantation was arranged considering the high risk of progression to complete heart block
- Diagnosed with moderate depression and started on antidepressants
- He was not a candidate for autologous stem cell transplant
- As for definitive treatment chemotherapy with CyBORD (cyclophosphamide + bortezomib + dexamethasone) was planned
- Family meeting was arranged and patient and family members were explained regarding the diagnosis and treatment plan

Follow up

- Unfortunately, he did not have favorable hematologic or clinical responses, and continued to decline functionally over the next few months
- PPM was functioning properly, but had several hospital admissions with worsening heart failure which were managed symptomatically with diuretics
- Renal functions were also declining gradually, but he did not consent
- for renal replacement therapy



- Ten months after his initial diagnosis patient had presented with sepsis following lower respiratory tract and urinary tract infections
- Detected to have persistent hypotension with hypoglycaemia (45mg/dl), hyponatraemia (128mmol/l) and elevated potassium level (5.4 mmol/l)
- Patient was managed as for hypoadrenalism with IV steroids for which he had a favorable response initially
- However patient rapidly deteriorated and succumbed to septic shock
- Pathological postmortem was not consented
- ??? Sepsis induced adrenal insufficiency
- ??? Adrenal amyloidosis



AL Amyloidosis

- AL systemic amyloidosis occurs as a result of abnormal light chain protein deposition
- Approximately 20% of patients with AL amyloidosis present with coexisting multiple myeloma, while the rest are diagnosed with other plasma cell dyscrasias
- The heart (82%) and kidneys (68%) are the most common sites of deposition
- Additionally, the liver, nervous system, and gastrointestinal tract are often involved

- AL amyloidosis occurs more commonly in the elderly
- The average age of a patient with AL amyloidosis is 64 years, with an age range of 50-80 years
- Two-thirds of the elderly patients with AL amyloidosis are males

- The clinical diagnosis of AL amyloidosis is quite challenging and often delayed due to variable, nonspecific symptoms depending upon the organs involved
- Clinical presentations that should lead to consideration of amyloidosis includes,
 - ✓ non-diabetic nephrotic range proteinuria
 - ✓ cardiac failure without aortic stenosis or hypertension
 - ✓ unexplained peripheral neuropathy
- Very specific signs such as macroglossia and periorbital purpura is often not present



Raccoon eyes



Subcutaneous
nodules and plaques



Macroglossia



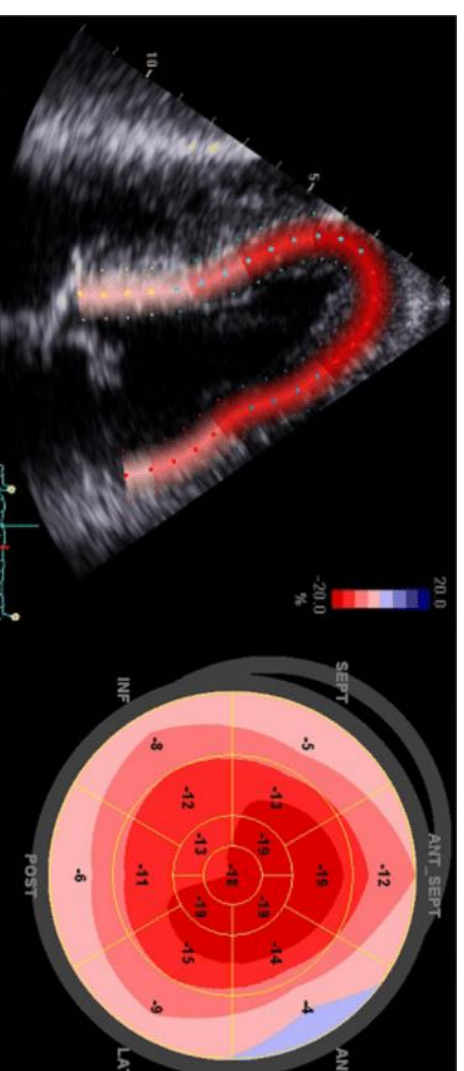
- The median time from symptom onset to clinical diagnosis is approximately seven months
- **It took around eight months to confirm the diagnosis and start definitive treatment in our patient !!!!!**
- Earlier amyloidosis diagnosis correlates with improved clinical outcomes because of end organ damage
- Renal involvement in amyloidosis is associated with an increase in morbidity and mortality

- A biopsy is the gold standard for diagnosis and it should be performed when amyloidosis is suspected
- The biopsy may be performed on a fat pad, bone marrow, or other suspected organs.
- Staining with hematoxylin and eosin as well as periodic Acid-Schiff (PAS) may detect the depositions outside the cells as shapeless pink material
- Congo red staining with apple-green birefringence under polarized light is pathognomonic for amyloid protein deposition

Cardiac Amyloidosis

- Cardiac amyloidosis (CA) causes an infiltrative restrictive cardiomyopathy
- Most common CA types are light chain amyloidosis (AL) caused by monoclonal immunoglobulin light chains and transthyretin amyloidosis (ATTR)
- Cardiac amyloidosis should be suspected in patients with:
 - ✓ Unexplained LV hypertrophy
 - ✓ Patients with aortic stenosis with features associated with cardiac amyloidosis
 - ✓ Patients with symptoms or signs typical of AL or ATTR amyloidosis and HF
 - ✓ Patients with a condition highly associated with cardiac amyloidosis (eg, systemic AL amyloidosis)

- Echocardiography is the initial imaging test of choice for diagnosis of cardiac amyloidosis
- Infiltration of the ventricular walls produces an appearance of hypertrophy (commonly biventricular) with nondilated or small ventricles
- Reduction in global longitudinal strain (a measure of systolic function) is one of the earliest markers
- characteristic pattern of relative apical sparing of longitudinal strain → preserved apical longitudinal shortening and impaired basilar shortening
- **“Cherry on top” pattern**
- high sensitivity (93 percent) and specificity (82 percent) for cardiac amyloidosis



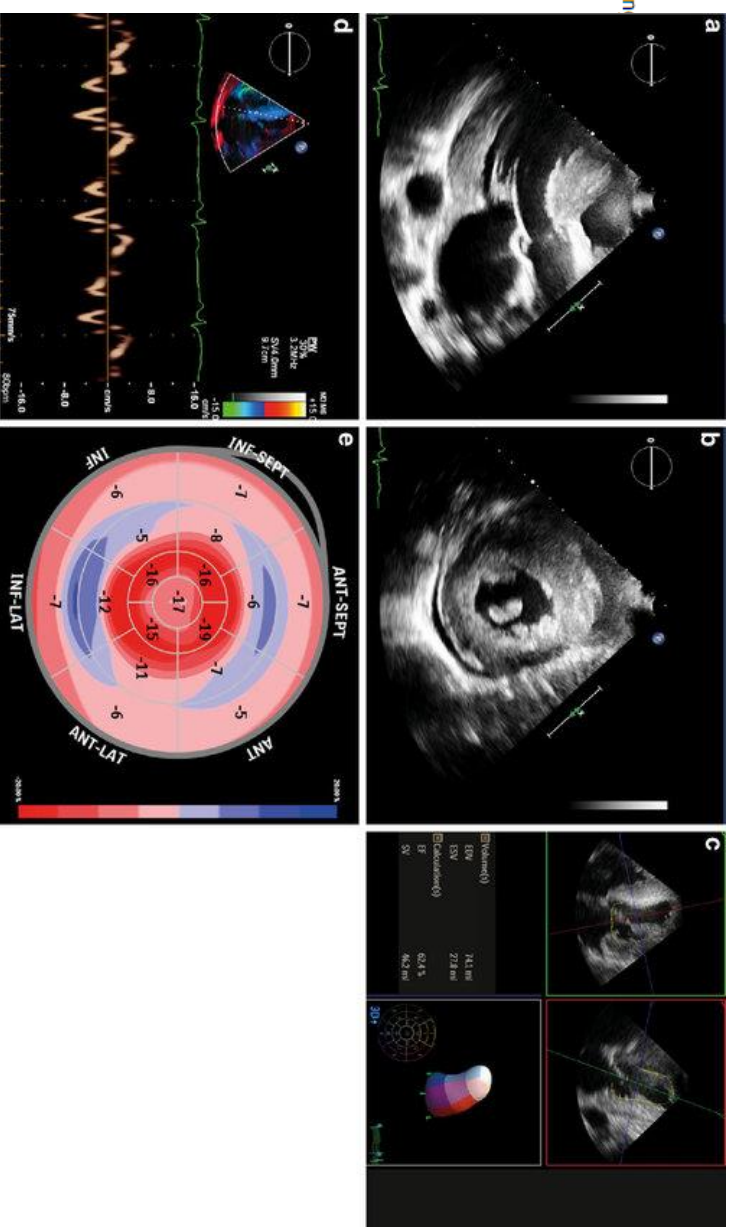


Practical recommendations for the diagnosis and management of transthyretin cardiac amyloidosis

Vasiliki Bistola¹ · John Parissis¹ · Emmanouil Foukarakis² · Pipitsa N. Valsamaki³ · Aris Anastasakis⁴ · Georgios Koutsis⁵ · Georgios Efthimiadis⁶ · Efstathios Kastritis⁷

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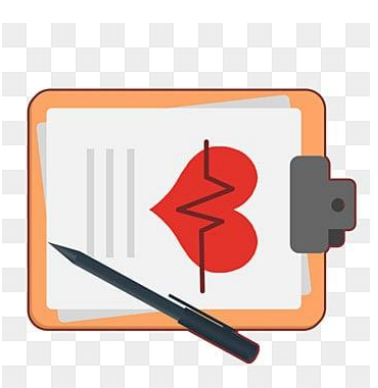
	Sensitivity ^a	Specificity ^a
*LV hypertrophy	100%	0
†Atrial dilatation	44%	93%
**AV valve & IAS thickening	Suggestive	Not specific
#DD grade ≥II	Suggestive	Not specific
*Depressed TDI velocities	Highly suggestive	Not specific
§GLS ≥-15	88%	72%
¶Relative apical sparing >1	38%	93%



Typical echocardiographic findings of cardiac amyloidosis and their diagnostic accuracy (sensitivity and specificity)

- Cardiovascular magnetic resonance (CMR) is a key test in the diagnosis of cardiac amyloidosis
- Cardiac amyloidosis has a highly characteristic appearance on CMR imaging performed with late gadolinium enhancement
- Three progressive LGE patterns are identified in cardiac amyloidosis,
 - None
 - Subendocardial
 - Transmural
- These patterns correlate with the degree of myocardial infiltration
- Endomyocardial biopsy is required only in selected patients
- Tissue biopsy is not required when other findings are diagnostic for the presence and type of cardiac amyloidosis

Treatment



- Treatment of AL renal amyloidosis is focused on elimination of the monoclonal proteins and the plasma cell clones with chemotherapeutic agents which may help to prevent organ damage
- All patients with newly diagnosed AL amyloidosis need to be assessed to determine eligibility for autologous hematopoietic cell transplantation
- For many years standard treatment of patients with AL amyloidosis who were not candidates for HCT was melphalan and prednisone
- This has been replaced currently with bortezomib-based regimens

- Preferred combination is daratumumab, cyclophosphamide, bortezomib, and dexamethasone (dara-CyBord)
- This has been shown in a phase 3 trial (ANDROMEDA) which demonstrated that addition of daratumumab to CyBord deepened responses and delayed major organ deterioration



ORIGINAL ARTICLE



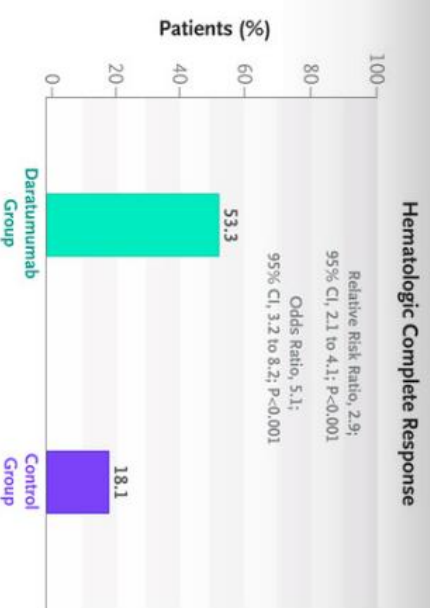
Daratumumab-Based Treatment for Immunoglobulin Light-Chain Amyloidosis

Authors: Efsthios Kastiris, M.D., Giovanni Palladini, M.D., Monique C. Minnema, M.D., Ashutosh D. Wechalekar, M.D., Arnaud Jaccard, M.D., Hans C. Lee, M.D., Vaishali Sanchorawala, M.D., **49**, for the ANDROMEDA Trial Investigators* Author Info & Affiliations

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CONCLUSIONS
The addition of daratumumab to standard therapy with bortezomib, cyclophosphamide, and dexamethasone was associated with a significantly higher frequency of hematologic complete response than standard therapy alone.



Most Common Adverse Events of Grade 3 or 4

	Daratumumab Group (N=193)	Control Group (N=188)
Lymphopenia	13.0%	10.1%
Pneumonia	7.8%	4.3%
Cardiac Failure	6.2%	4.8%
Diarrhea	5.7%	3.7%

- If daratumumab is not available, preferred regimens would be cyclophosphamide, bortezomib, and dexamethasone (CyBord) or bortezomib, melphalan, and dexamethasone (BMD)

- For AL amyloidosis, CyBord is usually administered on a 28-day cycle

Bortezomib	1.3 to 1.5 mg/m² subcutaneous	once a week
Cyclophosphamide	500 mg (total dose) by mouth	once a week
Dexamethasone	20 to 40 mg by mouth	once a week

- If available, daratumumab-hyaluronidase (1800 mg daratumumab with 30,000 units hyaluronidase) is administered subcutaneously,
 - once a week for cycles 1 and 2
 - then every two weeks for cycles 3 through 6
 - then every four weeks until disease progression or for a maximum of two years



Normal functioning and activity. No assistance needed.	100	No impact on normal functioning.
	90	Minor impact on functioning. Normal activity.
Unable to maintain occupation and normal functioning. Differing amounts of care needed.	80	Some impact on functioning. More effort for normal functioning.
	70	No impact on self care. Unable to maintain normal activity / occupation.
Unable to do self care. Requires some form of hospitalization. Advanced disease state.	60	Some impact on self care. May require some assistance.
	50	Requires assistance with ADLs. Requires recurrent medical appointments and visits.
	40	Severely impaired function. Requires a lot of assistance with ADLs.
	30	Disabled. Requires hospitalization.
	20	Hospital bound. Advanced disease state.
	10	Bed bound. Approaching death.
	0	Death.

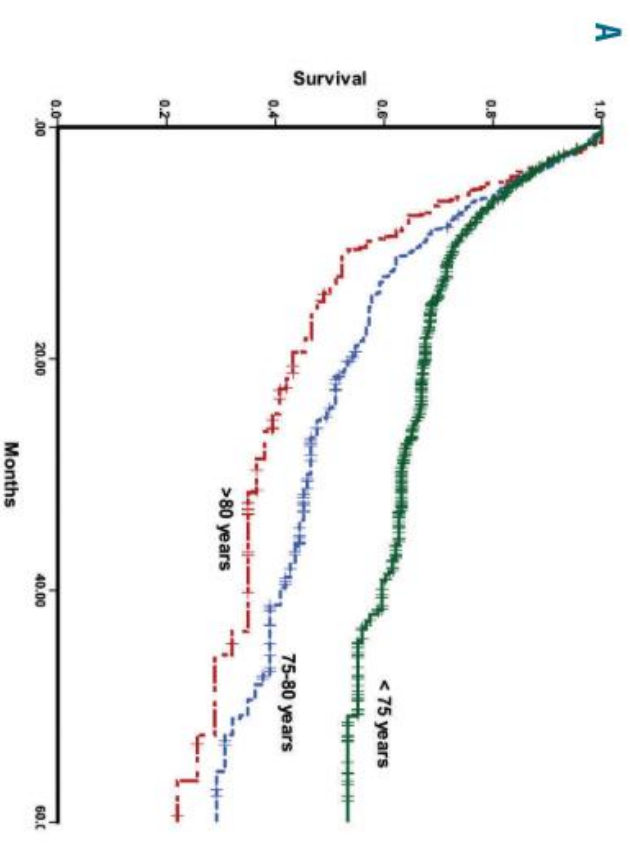
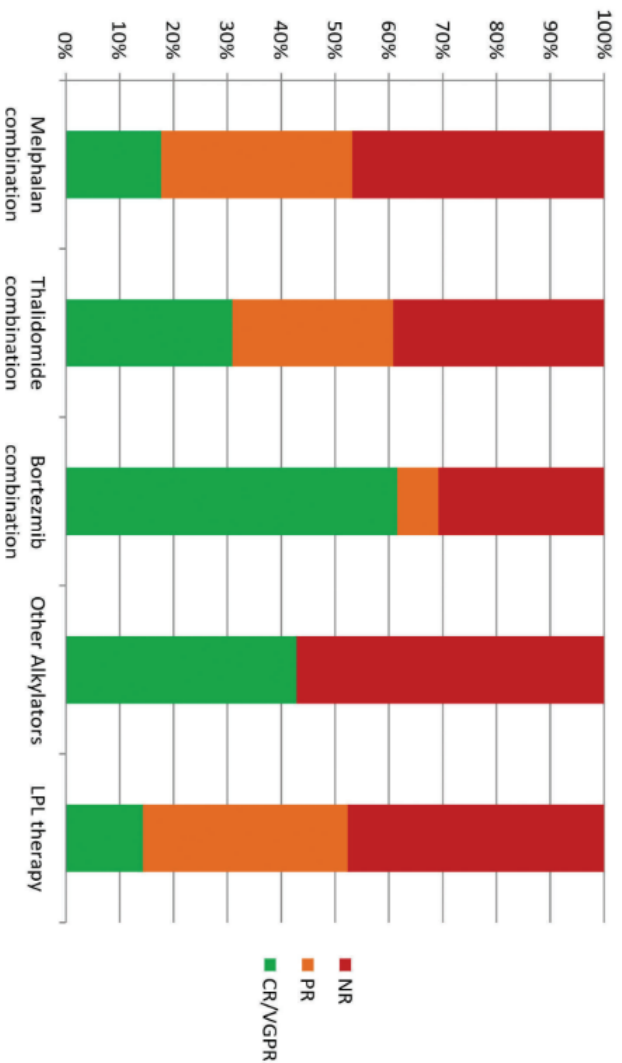


- **Unfortunately poor treatment outcomes seen in elderly !!!!!**
- May be due to their advanced ages, time delay in diagnosis, aggressive pathogenesis of AL amyloidosis, and poor Karnofsky performance scores
- Patients that have a coexisting MIM have a worse prognosis than patients who do not
- Patients with glomerular involvement in the renal biopsy are at increased risk of end-stage renal disease
- These patients may require renal replacement therapy or kidney transplantation with the progression of the disease

Clinical profile and treatment outcome of older (>75 years) patients with systemic AL amyloidosis

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Summary

- Multifactorial evaluation and intervention is recommended in older patients with syncope and unexplained falls because more than one possible etiology may be present
- It is important to consider amyloidosis as a differential diagnosis in evaluating elderly patients presenting with lower extremity edema or presyncope/ syncope with unexplained LVH as earlier diagnosis correlates with improved clinical outcomes

THANK YOU

