Quality of Life Considerations and Multidisciplinary Team-Based Care for Patients with hATTR Amyloidosis

Brett W. Sperry, MD
Advanced Heart Failure & Transplantation
Director, Cardiac Amyloidosis Program
Saint Luke's Mid America Heart Institute
@BrettSperryMD

American Heart Association.

Disclosures

- Pfizer – consultant, speaker
- Alnylam – consultant
- Eidos/BridgeBio – consultant

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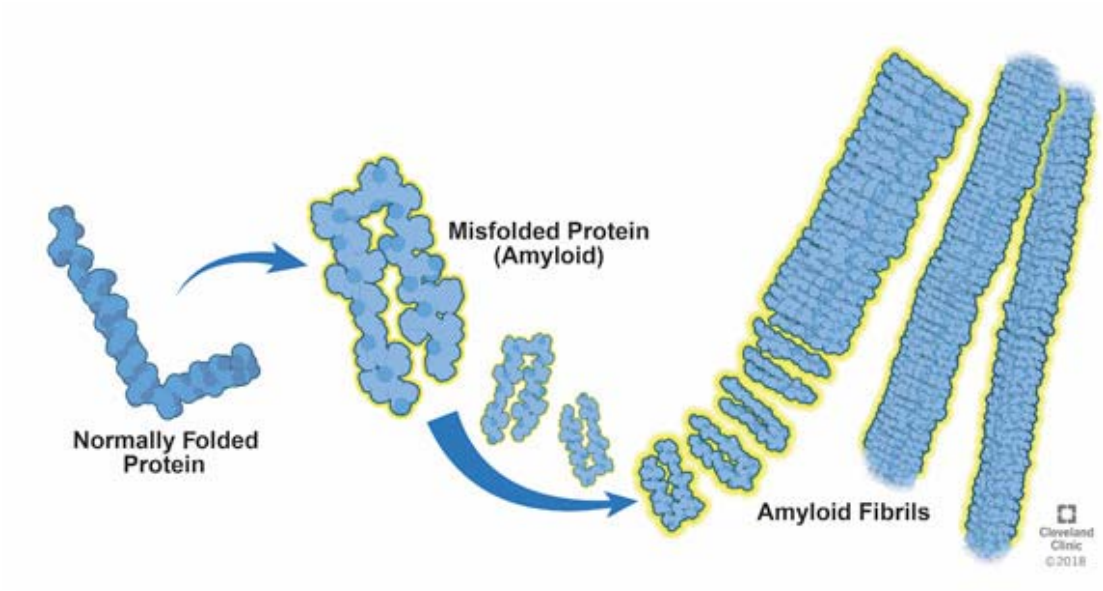
What is amyloidosis?



https://my.clevelandclinic.org/departments/cancer/depts/amyloid

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.

Kholova et al, JCP, Feb 2005.

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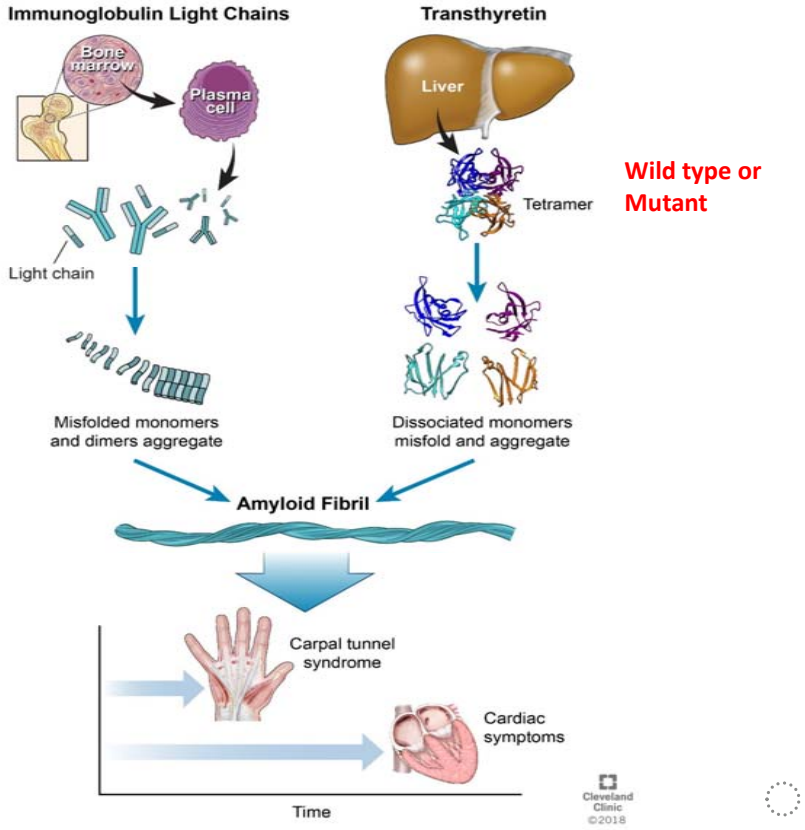
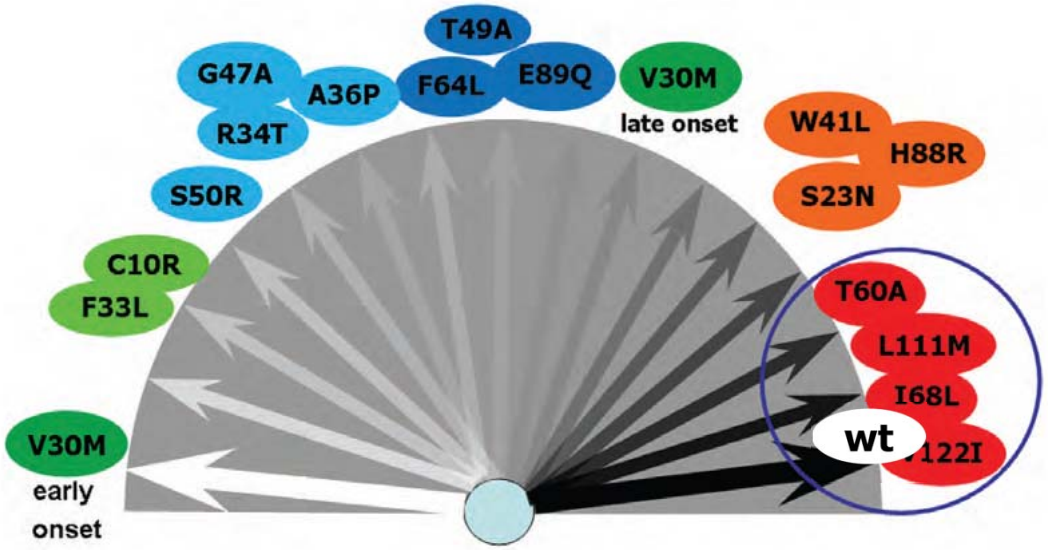
2 Main Types of Systemic Amyloidosis

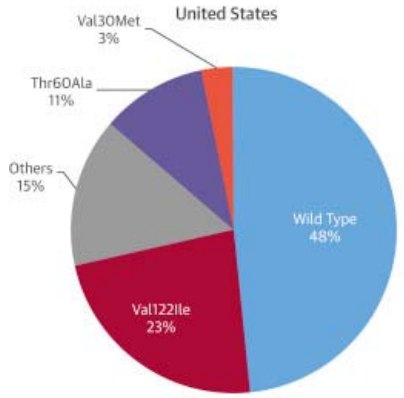


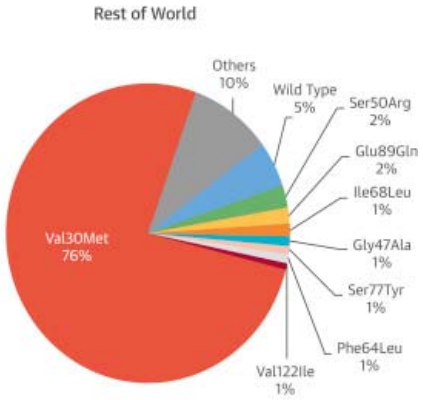
Donnelly, Hanna, Sperry, Seitz. JHS 2019: 44(10) 868-876.

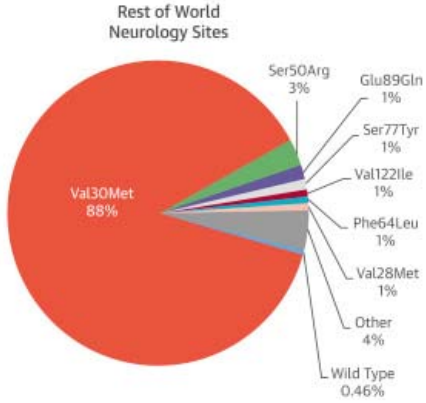
Mutations of hATTR amyloidosis

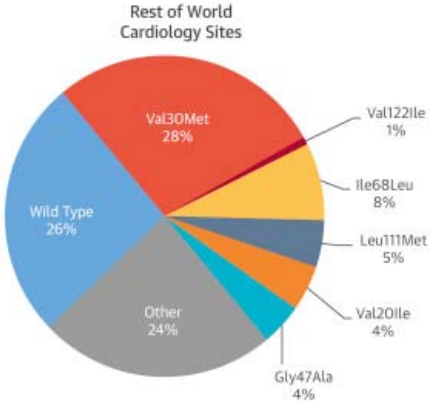


Rapezzi et al. EHJ (2013) 34,520-528.









THAOS Registry

Symptoms of ATTR amyloidosis

CARDIAC FINDINGS

- Increased LV (and RV) wall thickness
- Low voltage ECG relative to LV thickness
- Heart failure with preserved or mildly decreased EF
- De-escalation of BP meds
- Atrial arrhythmias
- Persistently elevated NTproBNP & troponin
- Aortic stenosis (particularly low-flow low-gradient)

NON-CARDIAC FINDINGS

- Age (>60 years for ATTR-CM)
- Men more common than women
- Bilateral carpal tunnel syndrome
- Spinal stenosis
- Biceps tendon rupture
- Peripheral neuropathy
- Autonomic neuropathy
- Chronic kidney disease / proteinuria
- Periorbital purpura, glossomegaly

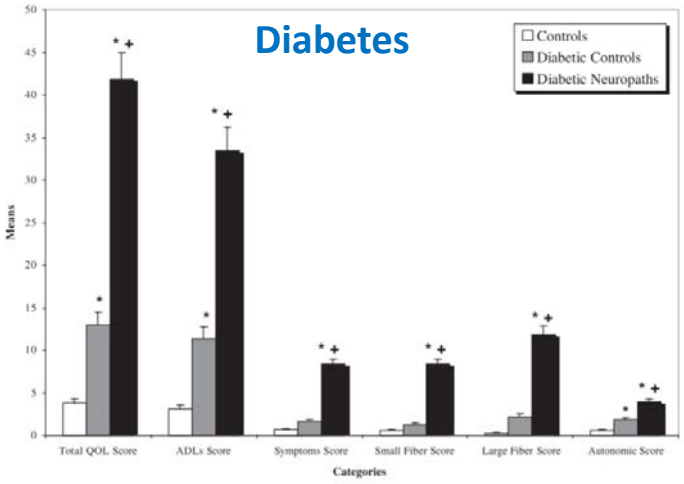
Outline

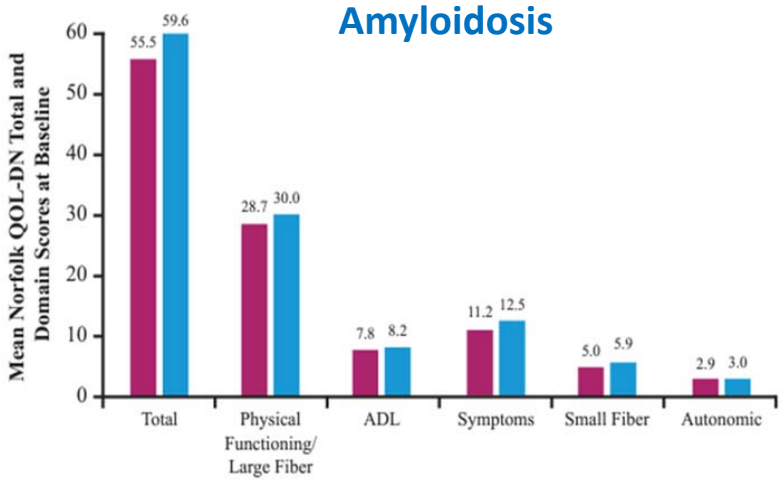
- Quality of life in ATTR amyloidosis
- Multidisciplinary care
- How to create an amyloidosis center

What do we know about quality of life in hATTR amyloidosis?

Polyneuropathy QOL – Norfolk QOL-DN

Baseline Data





Vinik et al., Diabetes Technology & Therapeutics 2005;7(3), 497–508.

Obici et al., Amyloid 2020;27(3):153-162.

Polyneuropathy QOL – Norfolk QOL-DN

Total QOL

- ADL score = mix of small fiber, large fiber, and autonomic questions
- Symptoms = duration of symptoms and # medications used
- Large fiber neuropathy = electric shocks and weakness
- Small fiber neuropathy = numbness, tingling, pins/needles
- Autonomic neuropathy

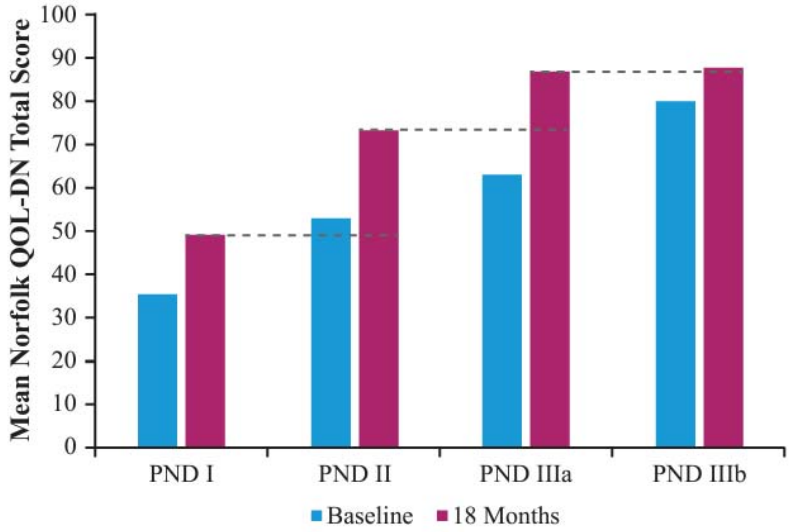
PND Score

1. Only sensory disturbances
2. Motor impairment but ambulates without aid

3A. Walking with the help of 1 stick

3B. Walking with the help of 2 sticks

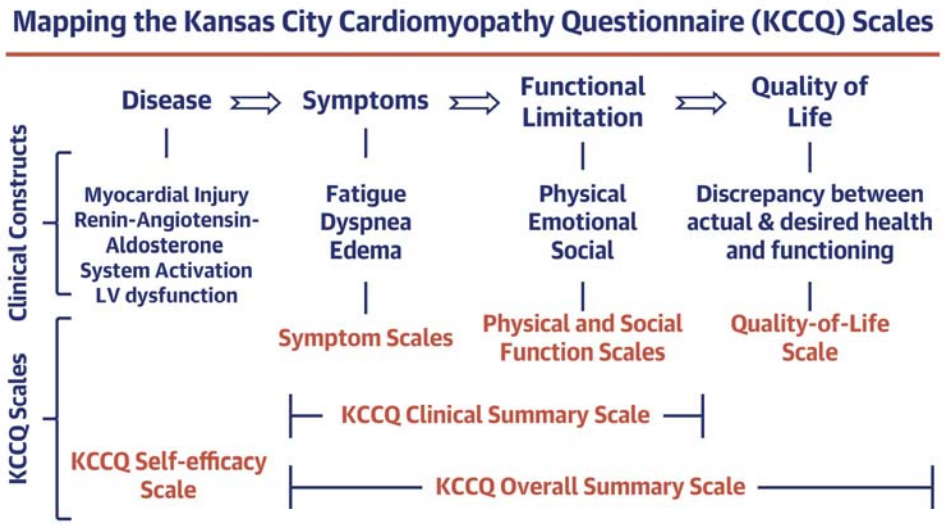
4. Wheelchair bound



Obici et al., Amyloid 2020;27(3):153-162.

Cardiomyopathy QOL

CENTRAL ILLUSTRATION: Conceptual Mapping of the Kansas City Cardiomyopathy Questionnaire to Different Manifestations of Heart Failure



Spertus, J.A. et al. J Am Coll Cardiol. 2020;76(20):2379-90.

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Cardiomyopathy QOL

Baseline Data from ATTR-ACT

Kansas City Cardiomyopathy Questionnaire, EQ-5D, and patient global assessment scores at baseline

Variable	Stabilizer	Placebo
KCCQ domains, mean (SD)		
Quality of Life	62.63 (24.73)	59.98 (24.65)
Social Limitation	63.36 (28.96)	63.10 (28.97)
Physical Limitation	69.07 (22.77)	68.24 (24.18)
Total Symptoms*	73.45 (20.27)	72.11 (20.64)
Symptom Burden	73.58 (20.72)	73.31 (20.82)
Symptom Frequency	73.41 (21.85)	70.90 (22.49)
Self-efficacy	83.10 (20.86)	80.16 (21.42)
Symptom Stability	52.10 (16.18)	49.30 (15.64)
KCCQ summary scores, Mean (SD)		
Clinical Summary†	71.34 (20.04)	70.15 (20.51)
Overall Summary‡	67.28 (21.36)	65.90 (21.74)
EQ-5D, mean (SD)		
EQ-5D-3L Index Score	0.80 (0.16)	0.80 (0.15)
EQ VAS	68.30 (18.57)	66.50 (17.76)
PGA§		
Normal, not at all ill	43 (16.3%)	21 (11.9%)
Borderline ill	52 (19.7%)	28 (15.8%)
Mildly ill	49 (18.6%)	39 (22.0%)
Moderately ill	72 (27.3%)	55 (31.1%)
Markedly ill	35 (13.3%)	26 (14.7%)
Severely ill	9 (3.4%)	3 (1.7%)
Among the most extremely ill	1 (0.4%)	0

EQ VAS = EQ visual analog scale; KCCQ = Kansas City Cardiomyopathy Questionnaire; PGA = patient global assessment; SD = standard deviation.

Adapted from Hanna M, et al. Am J Cardiol. 2021 Feb 15;141:98-105.

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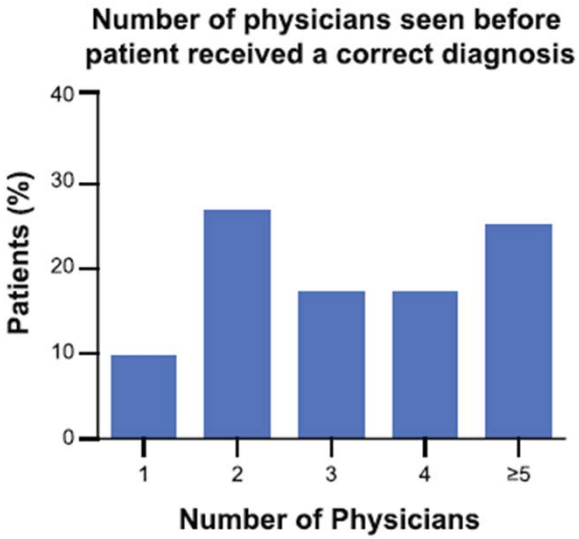
Outline

- Quality of life in ATTR amyloidosis
- Multidisciplinary care
- How to create an amyloidosis center

Multidisciplinary care is needed for diagnosis

Multiple Clinicians

- In ATTR, only 1/3 to 1/2 of patients have a correct diagnosis made within 6 months.
- Only 10% of patients are diagnosed by the first clinician they see.



Lousada I, Comenzo RL, Landau H, Guthrie S, Merlini G. Patient experience with hereditary and senile systemic amyloidoses: a survey from the Amyloidosis Research Consortium. Orphanet J Rare Dis. 2015;10(Suppl 1):P22 Pl

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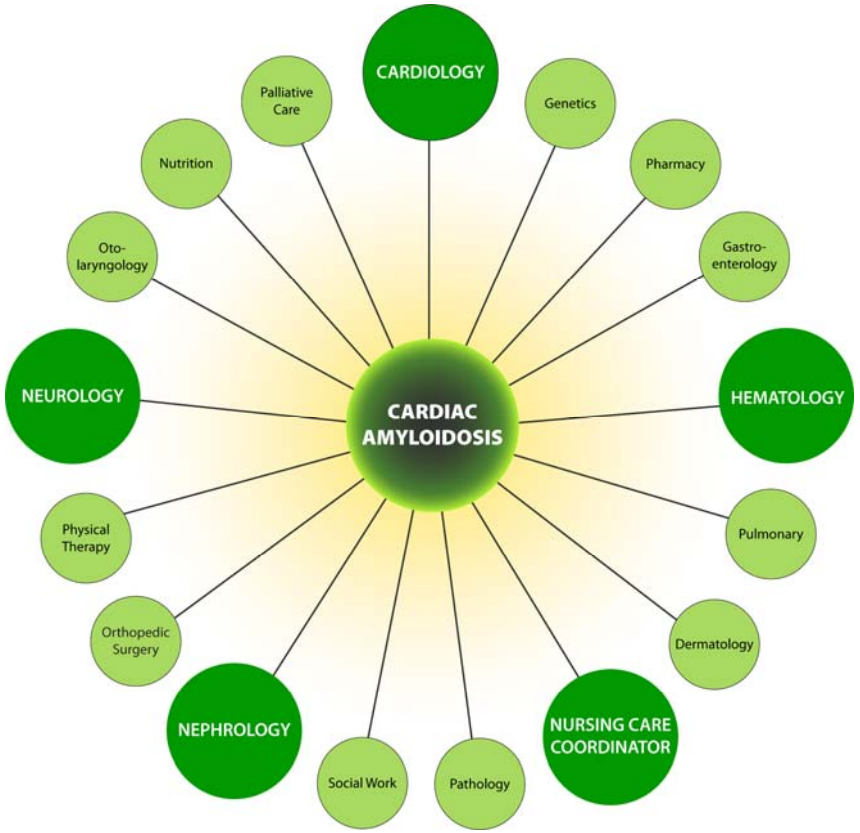
Diagnosis can be made from multiple specialties



Sperry BW, et al. Comprehensive approach to cardiac amyloidosis care: considerations in starting an amyloidosis program. Heart Fail Rev. 2021 Aug 30.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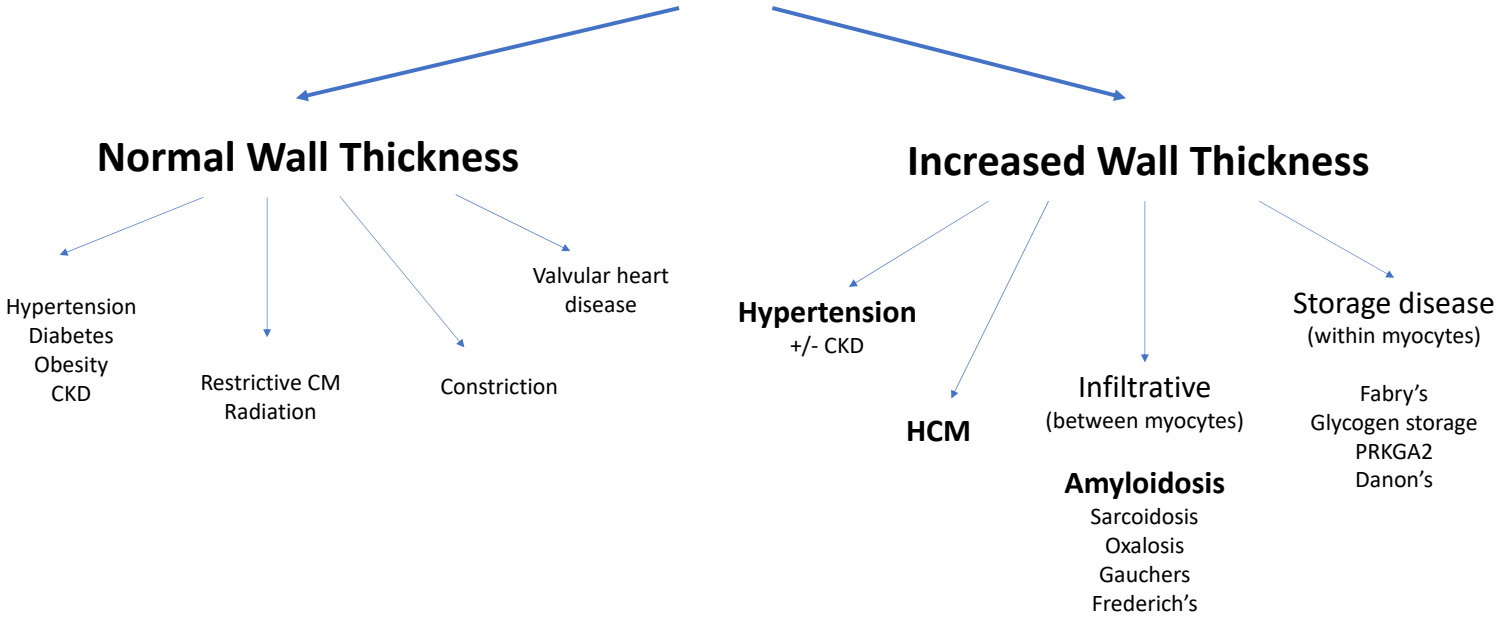
amyloid?
Reply
Reply All
Forward
RS
Raza, Shahzad
To Sperry, Brett W
Hi Brett, can you look at this echo and tell me if it looks like amyloidosis?
Shahzad
20

Heart Failure with Preserved Ejection Fraction



Borlaug. Evaluation and management of heart failure with preserved ejection fraction. Nature Reviews Cardiology, 2020: 17, 559-573.

Symptoms of ATTR amyloidosis

CARDIAC FINDINGS

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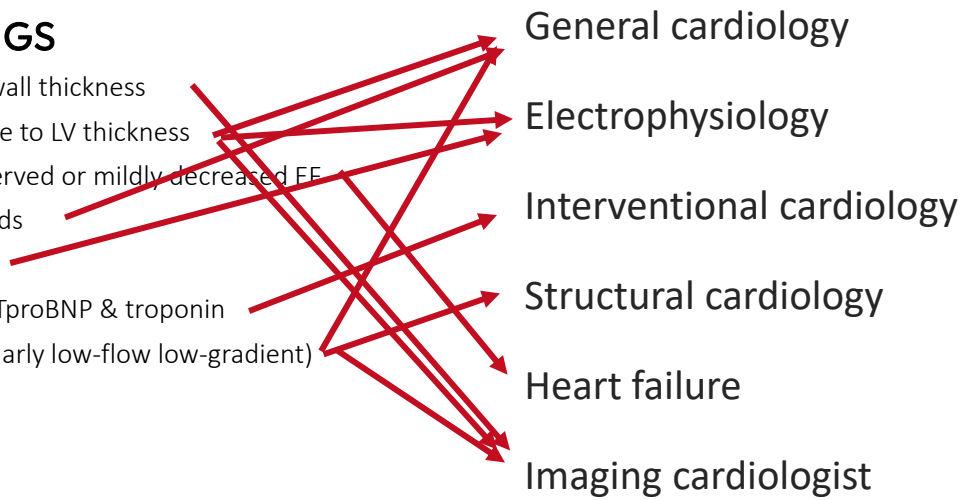
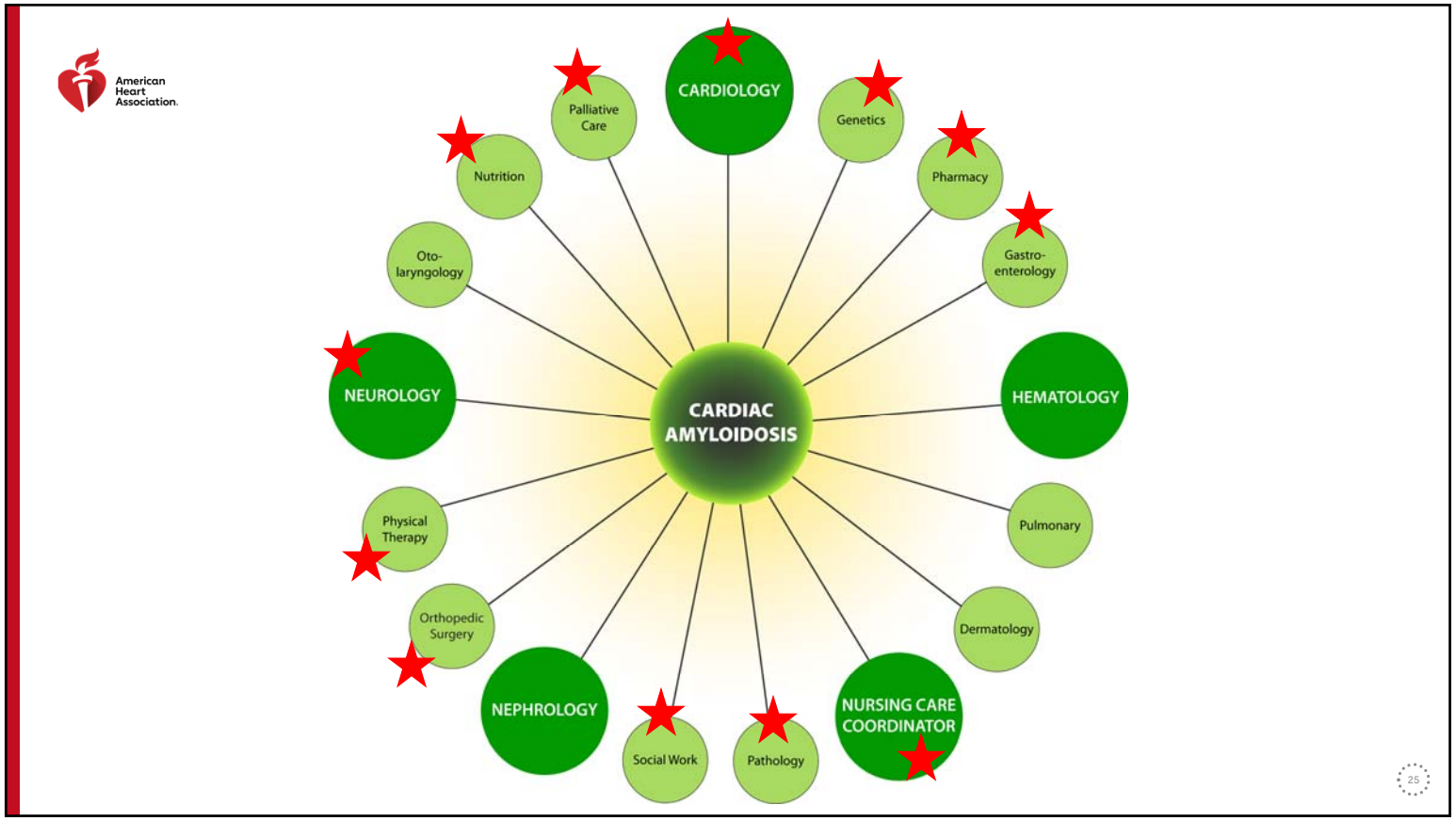


Multidisciplinary team is needed for longitudinal care

Case

65-year-old male with hATTR amyloidosis from V30M mutation

- Aortic stenosis s/p TAVR
- Cardiomyopathy with diastolic heart failure
- Severe polyneuropathy with weakness and inability to ambulate without assistance
- Constipation and diarrhea
- Weight loss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CARDIOLOGY
Palliative Care
Genetics
Nutrition
Pharmacy
Oto-laryngology
Gastro-enterology
NEUROLOGY
CARDIAC AMYLOIDOSIS
HEMATOLOGY
Physical Therapy
Pulmonary
Orthopedic Surgery
Dermatology
NEPHROLOGY
Social Work
Pathology
NURSING CARE COORDINATOR
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Outline

- Quality of life in ATTR amyloidosis
- Multidisciplinary care
- **How to create an amyloidosis center**

Heart Failure Reviews
https://doi.org/10.1007/s10741-021-10163-0

Check for updates

Comprehensive approach to cardiac amyloidosis care: considerations in starting an amyloidosis program

Brett W. Sperry[1] · Julie A. Khoury[2] · Shahzad Raza[3] · Julie L. Rosenthal[4]

Accepted: 17 August 2021

Canadian Journal of Cardiology 37 (2021) 674–678

Training/Practice
Contemporary Issues in Cardiology Practice

Establishing a Cardiac Amyloidosis Clinic: A Practical Primer for Cardiologists

Margot K. Davis, MD, MSc,[a] Nowell M. Fine, MD, SM,[b] Gary R. Small, MBBCh, PhD,[c] Katherine Connolly, MD,[d] Debra Bosley, BScN,[b] Shelley Zieroth, MD,[e] and Sean A. Virani, MD, MSc, MPH[a]

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STEPS TO STARTING AN AMYLOIDOSIS PROGRAM

STEP 1	• Identify multidisciplinary stakeholders
STEP 2	• Develop overarching program goals
STEP 3	• Create institutional buy-in
STEP 4	• Emphasize program growth and development

Sperry BW et al. Comprehensive approach to cardiac amyloidosis care: considerations in starting an amyloidosis program. Heart Fail Rev 2021.

1. Identify stakeholders

- Cardiologist
- Hematologist
- Neurologist
- Nephrologist
- Nursing care coordinator

Sperry BW et al. Comprehensive approach to cardiac amyloidosis care: considerations in starting an amyloidosis program. Heart Fail Rev 2021.

2. Develop overarching program goals

- Mission statement
- Multidisciplinary meetings
- Amyloid clinic

Sperry BW et al. Comprehensive approach to cardiac amyloidosis care: considerations in starting an amyloidosis program. Heart Fail Rev 2021.

3. Create institutional buy-in

- Amyloid consults generate significant downstream testing and referrals
- More resources are needed than standard cardiac patients
  - Care coordination
  - Patient assistance paperwork
  - 2x as many patient contacts/messages as other HF patients
  - Clinical trials

Sperry BW et al. Comprehensive approach to cardiac amyloidosis care: considerations in starting an amyloidosis program. Heart Fail Rev 2021.

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4. Program growth and development

- Education
  - Fellows/residents and colleagues within the cardiology practice
  - Local cardiologists and potential referring physicians
  - Patients
- Early identification
  - Increased physician education
  - Screening patients with carpal tunnel syndrome
  - Screening patients with HFpEF or aortic stenosis
  - EMR AI screening
  - Amyloidosis order set
- Multidisciplinary clinic and availability for Inpatient consultation
- Partnering with national organizations
- Clinical trials

Sperry BW et al. Comprehensive approach to cardiac amyloidosis care: considerations in starting an amyloidosis program. Heart Fail Rev 2021.

Summary

- Neuropathic QOL is poor in patients with hATTR-PN and significantly worse than diabetic PN
- Cardiac QOL is poor in patients with ATTR-CM and generally worse at baseline than patients enrolled in contemporary heart failure trials
- A multidisciplinary team is needed for diagnosis and longitudinal care of patients with amyloidosis
- Tips to start and maintain an amyloidosis program


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Thank You.
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