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
Disclosures

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

THE OPINIONS EXPRESSED IN THIS PRESENTATION (AND/OR SLIDES) ARE SOLELY THOSE OF THE PRESENTER AND NOT NECESSARILY OF THE AMERICAN HEART ASSOCIATION / AMERICAN STROKE ASSOCIATION (AHA/ASA). THE AHA/ASA DOES NOT ENDORSE ANY SPECIFIC PRODUCTS OR DEVICES.
What is amyloidosis?

[Diagram showing the process of protein folding and misfolding to form amyloid fibrils]

https://my.clevelandclinic.org/departments/cancer/depts/amyloid
Over 30 amyloidogenic proteins

<table>
<thead>
<tr>
<th>Amyloid protein</th>
<th>Precursor</th>
<th>Distribution</th>
<th>Syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>AL</td>
<td>Immunoglobulin light chain</td>
<td>Systemic/localised</td>
<td>Primary/myeloma associated</td>
</tr>
<tr>
<td>AH</td>
<td>Immunoglobulin heavy chain</td>
<td>Systemic/localised</td>
<td>Primary/myeloma associated</td>
</tr>
<tr>
<td>AA</td>
<td>Serum amyloid A</td>
<td>Systemic</td>
<td>Secondary</td>
</tr>
<tr>
<td>AAβ, Microglobulin</td>
<td>β2 Microglobulin</td>
<td>Systemic</td>
<td>Secondary</td>
</tr>
<tr>
<td>ATTR</td>
<td>Transthyretin</td>
<td>Systemic</td>
<td>Senile systemic/familial</td>
</tr>
<tr>
<td>AANF</td>
<td>Atrial natriuretic factor</td>
<td>Localised</td>
<td>Atrial isolated</td>
</tr>
<tr>
<td>AApoA-I</td>
<td>Apolipoprotein A-I</td>
<td>Localised/systemic</td>
<td>Aortic/familial</td>
</tr>
<tr>
<td>AApoA-II</td>
<td>Apolipoprotein A-II</td>
<td>Systemic</td>
<td>Familial</td>
</tr>
<tr>
<td>Amed</td>
<td>Lactadherin</td>
<td>Localised</td>
<td>Aortic</td>
</tr>
<tr>
<td>Agel</td>
<td>Gelatin</td>
<td>Systemic</td>
<td>Familial</td>
</tr>
<tr>
<td>Alys</td>
<td>Lysozyme</td>
<td>Systemic</td>
<td>Familial</td>
</tr>
<tr>
<td>Asfb</td>
<td>Fibronectin α chain</td>
<td>Systemic</td>
<td>Familial</td>
</tr>
<tr>
<td>Acys</td>
<td>Cystatin C</td>
<td>Systemic</td>
<td>Familial</td>
</tr>
<tr>
<td>Aβl</td>
<td>Aβ protein precursor</td>
<td>Localised</td>
<td>Alzheimer’s disease, aging</td>
</tr>
<tr>
<td>ApoP</td>
<td>Prolactin</td>
<td>Localised</td>
<td>Sporadic encephalopathies</td>
</tr>
<tr>
<td>Abαl</td>
<td>Abα protein precursor</td>
<td>Localised</td>
<td>Familial dementia</td>
</tr>
<tr>
<td>Acalc</td>
<td>(Pro)calcitonin</td>
<td>Localised</td>
<td>Thyroid tumours derived from C cells</td>
</tr>
<tr>
<td>AAAPP</td>
<td>Islet amyloid polypeptide</td>
<td>Localised</td>
<td>Langerhans islets, insulinomas</td>
</tr>
<tr>
<td>Agro</td>
<td>Prolactin</td>
<td>Localised</td>
<td>Prostatic carcinomas, pituitary in elderly</td>
</tr>
<tr>
<td>Ains</td>
<td>Insulin</td>
<td>Localised</td>
<td>Iatrogenic</td>
</tr>
<tr>
<td>Ake2</td>
<td>Keratin</td>
<td>Localised</td>
<td>Familial, cornea</td>
</tr>
<tr>
<td>Alac</td>
<td>Lactadherin</td>
<td>Localised</td>
<td>Familial, cornea</td>
</tr>
</tbody>
</table>

Proteins involved in the cardiovascular system are in bold.

2 Main Types of Systemic Amyloidosis

Mutations of hATTR amyloidosis

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

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
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

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

Mapping the Kansas City Cardiomyopathy Questionnaire (KCCQ) Scales

- **Disease**
  - Myocardial Injury
  - Renin-Angiotensin-Aldosterone System Activation
  - LV dysfunction

- **Symptoms**
  - Fatigue
  - Dyspnea
  - Edema

- **Functional Limitation**
  - Physical
  - Emotional
  - Social

- **Quality of Life**
  - Discrepancy between actual & desired health and functioning
  - Symptom Scales
  - Physical and Social Function Scales
  - Quality-of-Life Scale

Cardiomyopathy QOL
Baseline Data from ATTR-ACT

<table>
<thead>
<tr>
<th>Variable</th>
<th>Stabilizer</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>KCCQ domains, mean (SD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quality of Life</td>
<td>62.63 (24.73)</td>
<td>59.98 (24.65)</td>
</tr>
<tr>
<td>Social Limitation</td>
<td>63.36 (28.96)</td>
<td>63.10 (28.97)</td>
</tr>
<tr>
<td>Physical Limitation</td>
<td>69.07 (22.77)</td>
<td>68.24 (24.18)</td>
</tr>
<tr>
<td>Total Symptoms℠</td>
<td>73.45 (20.27)</td>
<td>72.11 (20.64)</td>
</tr>
<tr>
<td>Symptom Burden</td>
<td>73.58 (20.72)</td>
<td>73.31 (20.82)</td>
</tr>
<tr>
<td>Symptom Frequency</td>
<td>73.41 (23.85)</td>
<td>70.90 (22.49)</td>
</tr>
<tr>
<td>Self-efficacy</td>
<td>83.10 (20.86)</td>
<td>80.16 (21.42)</td>
</tr>
<tr>
<td>Symptom Stability</td>
<td>52.10 (16.18)</td>
<td>49.30 (15.64)</td>
</tr>
<tr>
<td>KCCQ summary scores, Mean (SD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinical Summary</td>
<td>71.34 (20.04)</td>
<td>70.15 (20.51)</td>
</tr>
<tr>
<td>Overall Summary</td>
<td>67.28 (21.36)</td>
<td>65.90 (21.74)</td>
</tr>
<tr>
<td>EQ-5D, mean (SD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EQ-5D-3L Index Score</td>
<td>0.80 (0.16)</td>
<td>0.80 (0.15)</td>
</tr>
<tr>
<td>EQ VAS</td>
<td>68.30 (18.57)</td>
<td>66.50 (17.76)</td>
</tr>
<tr>
<td>PGA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal, not at all ill</td>
<td>43 (16.3%)</td>
<td>21 (11.9%)</td>
</tr>
<tr>
<td>Borderline ill</td>
<td>52 (19.7%)</td>
<td>28 (15.8%)</td>
</tr>
<tr>
<td>Mildly ill</td>
<td>49 (18.6%)</td>
<td>39 (22.0%)</td>
</tr>
<tr>
<td>Moderately ill</td>
<td>72 (27.3%)</td>
<td>55 (31.1%)</td>
</tr>
<tr>
<td>Markedly ill</td>
<td>35 (13.3%)</td>
<td>26 (14.7%)</td>
</tr>
<tr>
<td>Severely ill</td>
<td>9 (3.4%)</td>
<td>3 (1.7%)</td>
</tr>
<tr>
<td>Among the most extremely ill</td>
<td>1 (0.4%)</td>
<td>0</td>
</tr>
</tbody>
</table>

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

• 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.

Diagnosis can be made from multiple specialties

Hi Brett, can you look at this echo and tell me if it looks like amyloidosis?

Shahzad
Heart Failure with Preserved Ejection Fraction

Normal Wall Thickness
- Hypertension
- Diabetes
- Obesity
- CKD
- Restrictive CM
- Radiation
- Constriction
- Valvular heart disease

Increased Wall Thickness
- Hypertension
- +/- CKD
- Infiltrative
  (between myocytes)
- Amyloidosis
  Sarcoïdosis
  Oxalosis
  Gauchers
  Frederich’s
- Storage disease
  (within myocytes)
  Fabry’s
  Glycogen storage
  PRKGA2
  Danon’s

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)

General cardiology
Electrophysiology
Interventional cardiology
Structural cardiology
Heart failure
Imaging cardiologist
Multidisciplinary team is needed for longitudinal care
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
Outline

• Quality of life in ATTR amyloidosis
• Multidisciplinary care
• How to create an amyloidosis center
Comprehensive approach to cardiac amyloidosis care: considerations in starting an amyloidosis program

Brett W. Sperry¹ · Julie A. Khoury² · Shahzad Raza³ · Julie L. Rosenthal¹

Accepted: 17 August 2021
© The Author(s), under exclusive licence to Springer Science+Business Media, LLC, part of Springer Nature 2021

Training/Practice
Contemporary Issues in Cardiology Practice
Establishing a Cardiac Amyloidosis Clinic: A Practical Primer for Cardiologists

Margot K. Davis, MD, MSc,¹ Nowell M. Fine, MD, SM,² Gary R. Small, MBBCh, PhD,³ Katherine Connolly, MD,⁴ Debra Bosley, BScN,⁵ Shelley Zieroth, MD,⁵ and Sean A. Virani, MD, MSc, MPH⁵
**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
1. Identify stakeholders

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

2. Develop overarching program goals

- Mission statement
- Multidisciplinary meetings
- Amyloid clinic
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

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

• 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
Thank You.