Light Chain Amyloidosis: Patient Experience Survey From the Amyloidosis Research Consortium

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BACKGROUND

- Amyloidosis is a rare disorder characterized by the accumulation of misfolded proteins, causing progressive organ damage.[1,2] There are several types of systemic amyloidoses; light chain (AL) amyloidosis is the most common[3,4]
- The estimated incidence of AL amyloidosis is 8 to 12 people per million per year.[4-6] In addition, an estimated 10% to 15% of cases occur in association with multiple myeloma.[3] Based on the incidence data, approximately 30,000 to 45,000 patients are living with AL amyloidosis in the United States and the European Union
- The clinical presentation of AL amyloidosis can vary widely and depends on the extent and number of organs affected. Initial symptoms are often nonspecific (eg, weight loss, fatigue). As the disease progresses, symptoms reflect the organs involved, most commonly the heart and the kidneys[7]
- The goal of treatment for patients with AL amyloidosis should be to preserve and improve organ function with a safe and effective disease-modifying therapy
- Despite recent advances in AL amyloidosis diagnostic tools and treatment, the early mortality rate remains high, with 1-year mortality rates around 30%. Unfortunately, by the time a diagnosis is made and treatment is initiated, the disease has often become advanced[7]
- In the absence of approved therapies for AL amyloidosis, physicians use off-label multiple myeloma therapies that target the abnormal plasma cells that produce the pathogenic proteins.[7-9] However, these treatments can be associated with significant adverse events, and patients often die before experiencing benefit from them.[7] There is an urgent need to expedite clinical trials that evaluate safe and effective treatment options for these patients
- Despite the significant effects of AL amyloidosis on patient quality of life, data describing those effects are limited. Detailing the patient experience may identify ways to improve patient care and disease outcomes

OBJECTIVE

- The primary aim of this study was to gather data on the AL amyloidosis patient experience to foster understanding of the challenges in establishing a diagnosis of AL amyloidosis and of the barriers to accessing appropriate care

METHODS

- Patients with amyloidosis, their family members, and their caregivers were invited to participate in an anonymous online survey through email and social media channels of the Amyloidosis Foundation (www.amyloidosis.org) and an amyloidosis awareness group on Facebook (www.facebook.com/AmyloidosisFoundation)
- The 16-question survey was developed by the authors and was available online to participants from January 29 to February 5, 2015
- The initial survey consisted of 16 questions covering demographic information, type of amyloidosis, symptoms, organ involvement, diagnosis, amyloidosis education, and clinical trial awareness
- After the initial survey was completed, participants with AL amyloidosis who provided contact information were sent an 8-question follow-up survey by email
- The follow-up survey consisted of 8 questions covering amyloidosis treatments, treatment tolerance, and quality of life before and after treatment

RESULTS

Participants

- The initial survey was completed by 533 participants; 58% identified themselves as patients, 34% identified themselves as family members, and 8% identified themselves as caregivers taking the survey on behalf of the patients (**Table 1**)
- Most respondents were female (62%) and were between 50 and 69 years of age (62%)
- The follow-up survey was completed by 201 participants

Table 1. Characteristics of Survey Respondents

Characteristics	Respondents n = 533
Type of respondent, n (%) n = 515	
Patient	298 (57.8)
Family member	174 (33.8)
Caregiver	43 (8.4)
Sex, n (%) n = 519	
Female	323 (62.2)
Male	196 (37.8)
Age group, n (%) n = 524	
25-34 years	23 (4.4)
35-44 years	59 (11.3)
45-54 years	96 (18.3)
55-64 years	190 (36.3)
65-74 years	120 (22.9)
75 years or older	36 (6.9)
Median age at diagnosis, years (range)	57 (20-83)
Type of amyloidosis, n (%) n = 484	
AL amyloidosis	347 (71.7)
AA amyloidosis	23 (4.8)
Hereditary transthyretin-related amyloidosis	35 (7.2)
Hereditary non–transthyretin-related amyloidosis	6 (1.2)
Other	25 (5.2)
Unknown	48 (9.9)
Organ involvement, n (%) n = 469	
Heart	172 (36.7)
Kidneys	132 (28.1)
Liver	15 (3.2)
Gastrointestinal tract	27 (5.8)
Nervous system	26 (5.5)
Multiple organ involvement	97 (20.7)

AA, inflammatory.

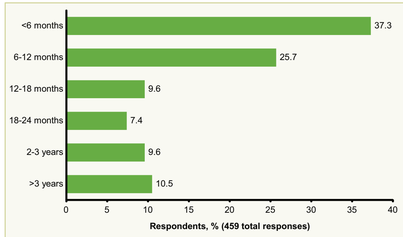
Amyloidosis Symptoms and Organ Involvement

- Initial symptoms were most commonly fatigue, shortness of breath, weakness, neuropathy, and swelling of the legs and/or tongue
- Most respondents reported the heart (37%) or kidneys (28%) as the major organ affected, with involvement of the liver (3%), gastrointestinal tract (6%), or nervous system (6%) reported less frequently (**Table 1**)
  - Multiple organ involvement was reported by 21% of respondents

Diagnosis of Amyloidosis

- The median age at diagnosis was 57 years (range, 20-83 years)
- AL amyloidosis was the most common diagnosis, reported by 72% of respondents (**Table 1**)
  - Other types of amyloidosis included AA (inflammatory) amyloidosis (5%), hereditary transthyretin-related amyloidosis (7%), hereditary non–transthyretin-related amyloidosis (1%), other (5%), or unknown (10%)
- Most respondents received a diagnosis of amyloidosis within 1 year of initial symptoms (63%), whereas diagnosis was delayed for more than 1 year in 37% (**Figure 1**)

Figure 1. Time from initial symptoms to diagnosis of amyloidosis.



- A substantial proportion of respondents reported visiting 5 or more physicians before receiving the diagnosis of amyloidosis (32%); only 8% received the diagnosis after visiting 1 physician (**Figure 2**)
- Respondents most commonly received the correct diagnosis from a hematologist/oncologist (34%); nephrologists and cardiologists provided the correct diagnosis for 23% and 19% of respondents, respectively (**Figure 3**)

Figure 2. Number of physician visits before establishment of a diagnosis.

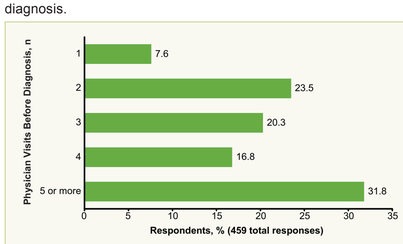
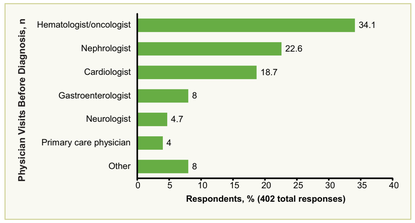


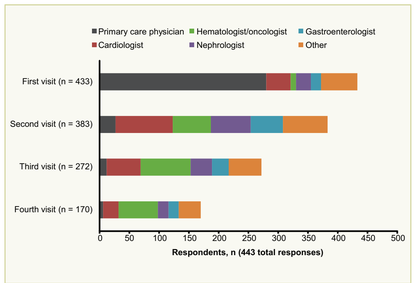
Figure 3. Specialty of diagnosing physician.



"Other" includes internists, hepatologists, ophthalmologists, and dermatologists.

- The first doctor seen was usually a primary care physician (65%) (**Figure 4**)
- Respondents were then often referred for a second visit to a cardiologist (25%), hematologist/oncologist (17%), nephrologist (18%), or gastroenterologist (14%) (**Figure 4**)
  - Cardiologists, hematologists/oncologists, and nephrologists had the most opportunities to diagnose amyloidosis for respondents referred to their specialties
  - Respondents also visited other specialists, including internists, neurologists, hepatologists, ophthalmologists, and dermatologists
- Respondents saw cardiologists more frequently than hematologists/oncologists and nephrologists, though cardiologists diagnosed the condition much less frequently

Figure 4. Types of physicians visited before a diagnosis of amyloidosis.

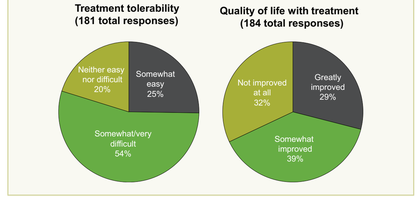


- 63% of respondents had been evaluated at an amyloidosis center (452 total responses), but only 44% received treatment at an amyloidosis center (444 total responses)

AL Amyloidosis Diagnosis and Treatment

- Among the participants with AL amyloidosis who completed the follow-up survey, 39% reported low quality of life before diagnosis, 31% reported average quality of life, and 30% reported great quality of life (199 total responses)
- When asked how the diagnosis of amyloidosis made the patient feel, 63% reported feeling frightened, 31% depressed, 31% numb, 29% powerless, 26% hopeless, 19% relieved, and 18% angry (200 total responses)
- For patients with AL amyloidosis who responded to the follow-up survey, treatment consisted of chemotherapy in 63% of respondents, stem cell transplantation in 39%, and solid organ transplantation in 8%. Other treatments were also reported by 58% of respondents (198 total responses)
- When asked how well treatment was tolerated, 54% reported that it was somewhat or very difficult, 20% reported neither easy nor difficult, and 25% reported somewhat easy (181 total responses) (**Figure 5**)
- Quality of life was greatly improved with treatment for 29% of respondents, somewhat improved for 39%, and not improved at all for 32% (184 total responses) (**Figure 5**)

Figure 5. Treatment tolerance and quality of life improvement with treatment.



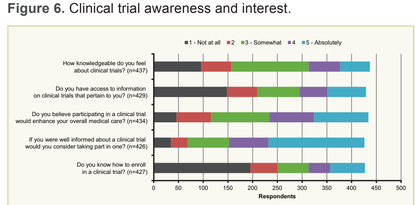
Amyloidosis Education

- Among 427 respondents who answered a question pertaining to information or educational material received at the time of diagnosis about their specific amyloidosis type, 39% reported receiving the center's own printed handouts, 34% received another organization's disease or treatment literature, 29% received information on support groups, 24% received clinical trial information, and 40% reported receiving no information or educational material

Clinical Trial Awareness

- In the initial survey, participants were asked to score their answers regarding clinical trial knowledge and access on a scale of 1 to 5, from "Not at all" (score 1) to "Absolutely" (score 5)
- A significant number of respondents felt uninformed about clinical trials and felt they did not have access to pertinent clinical trial information, with 72% indicating a score of 3 or less regarding knowledgeability and 68% indicating a score of 3 or less regarding access to clinical trial information (**Figure 6**)
- Nevertheless, almost half (46%) said they believed that a clinical trial would enhance their medical care (score of 4 or more), and 46% reported that they would absolutely consider enrolling in a clinical trial if they were well informed (**Figure 6**)
- In the follow-up survey, 19% of respondents reported that they had participated in a clinical trial (190 total responses)

Figure 6. Clinical trial awareness and interest.



CONCLUSIONS

- Establishing an early and accurate diagnosis of amyloidosis is a challenge for patients. These data demonstrate that most patients require multiple physician visits to different medical specialists, often spanning more than 1 year
- Although AL amyloidosis is typically considered a disease of the elderly (older than 60 years of age), the median age of respondents in our survey was 37 years, with 34.0% younger than 55 years of age and 15.6% younger than 45 years of age
  - It appears these younger patients are significantly underdiagnosed
- Consistent with the literature,[7] most respondents experienced heart or kidney involvement. Because of the high incidence of cardiac symptoms (including shortness of breath) associated with AL amyloidosis, primary care physicians often refer their patients to cardiologists
- These data suggest that physicians in all medical specialties have difficulty establishing a diagnosis of AL amyloidosis. Increasing physician awareness of the signs and symptoms and the appropriate evaluation of AL amyloidosis has the potential to improve patient outcomes
- Considering 54% of respondents had difficulty tolerating treatment and only 30% of respondents reported a definite improvement in quality of life, there is a need for therapies clearly associated with treatment benefit
- Survey responses indicate that patient awareness of clinical trials and patient education about the disease can be considerably improved, especially since responders indicated a high willingness to participate in clinical trials. There are a number of opportunities to enhance patient care, such as providing education and information to help patients feel empowered and knowledgeable about their diagnosis and treatment plan and increasing access to support groups and relevant clinical trials
- Data from this study and other studies can help identify areas in which diagnosis is delayed or missed and can illustrate the need for early, accurate diagnosis of amyloidosis to help improve disease management and survival outcomes

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