Amyloidosis Research Consortium Cardiac Amyloidosis Survey: Results from Patients with AL and ATTR Amyloidosis and Their Caregivers

Isabelle Lousada[1], Mathew S. Maurer[2], Melissa Warner[1], Spencer Guthrie[3], Kristen Hsu[1], Martha Grogan[4]

[1]Amyloidosis Research Consortium, Boston, MA, USA; [2]Columbia University, New York, NY, USA; [3]Aurora Bio, San Francisco, CA, USA; [4]Mayo Clinic, Rochester, MN, USA

BACKGROUND

- Cardiac amyloidosis is a severe, progressive, and fatal disease caused by accumulation of misfolded proteins (amyloid) in cardiac tissue.
- Three main types of amyloidosis can result in cardiac amyloidosis: AL amyloidosis (AL), wildtype ATTR amyloidosis (wtATTR), and hereditary ATTR amyloidosis (hATTR).
- AL is caused by misfolded immunoglobulin light chains, while hATTR and wtATTR are caused by misfolded transthyretin.
- Delays in diagnosis are frequent due to non-specific initial symptoms and lack of disease awareness.
- Challenges associated with diagnosis were captured in a series of surveys conducted by the Amyloidosis Research Consortium (ARC), which asked questions about the patient and caregiver journey to diagnosis.

OBJECTIVE

- To gain insight into patient experiences with delays and errors in the diagnostic pathway for cardiac amyloidosis.

METHODS

- Patient and caregiver surveys created by ARC were posted on ARC's website and given to the Amyloidosis Foundation, Amyloidosis Support Groups, and individual physicians for distribution to individuals affected by cardiac amyloidosis.
- Translated surveys were made available to increase the range of targeted populations.

RESULTS

Demographics

Table 1. Demographics of respondents

	Respondents, N (%)
Type of Amyloidosis	
AL	482 (65%)
wtATTR	91 (12%)
hATTR	123 (17%)
Other	29 (4%)
Unsure	20 (3%)
Region	
Asia-Pacific (APAC)	54 (7%)
European Union (EU)	161 (22%)
North America (NA)	529 (71%)
Sex	
Male	475 (64%)
Female	255 (34%)
Age	
18-25	1 (0%)
26-40	18 (2%)
41-55	130 (17%)
56-70	377 (51%)
71 or older	203 (27%)
Ethnicity	
White / Caucasian	595 (80%)
Black / African American / Black British	31 (4%)
Asian / Pacific Islander / Asian British	19 (3%)
Hispanic / Latino	14 (2%)
Native American	8 (1%)
Other	69 (9%)
Mixed race	17 (2%)
Total	**745**

- At the time of analysis there were 745 total responses.
- This analysis focuses on respondents who reported having AL, wtATTR, or hATTR with cardiac involvement (N=696).
- Of these responses, 405 (58%) were patients and 290 (42%) were caregivers.

Organ Involvement

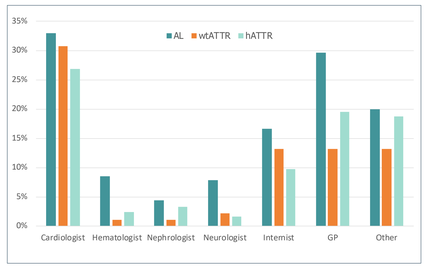
- All patients reported cardiac involvement. In addition, other common organ involvement is reported below in Table 2.

Table 2. Common extra-cardiac organ involvement

	AL	wtATTR	hATTR
Kidney	271 (56%)	21 (23%)	23 (19%)
Nerves	173 (36%)	20 (22%)	81 (66%)
Liver	79 (16%)	12 (13%)	29 (24%)
GI	190 (39%)	8 (9%)	49 (40%)
Skin	88 (18%)	12 (13%)	12 (10%)
Other	130 (27%)	19 (21%)	20 (16%)

- The most common extra-cardiac involvement was kidney for AL (56%) and nerves for hATTR (66%). In wtATTR, both kidney (23%) and nerves (22%) were frequently reported.
- GI involvement was also common in AL and hATTR (39% and 40% respectively).
- Absence of extra-cardiac involvement was seen most commonly in wtATTR (40%).
- 27% of all patients reported involvement of ≥3 organs.

Figure 1. Misdiagnosing physician by type



Misdiagnosis and incorrect treatment

- Overall 326 (47%) patients received ≥1 misdiagnoses before being correctly diagnosed with amyloidosis.
- Cardiologists were the most common misdiagnosing physician across all types (Figure 1).
- Unspecified heart failure was the most common misdiagnosis across all types (23%) and was most common in wtATTR (32%).
- 6% of all patients reported misdiagnosis with a psychiatric condition including stress, depression, and hypochondria.
- A majority of patients (75%) received treatment for their misdiagnosis.
- Treatment with beta blockers and/or ace inhibitors, which are poorly tolerated in amyloidosis[1], was common in all patients (35%) and most common in wtATTR (51%).
- Of patients that were prescribed ace inhibitors and/or beta blockers, 15% reported starting after their diagnosis of amyloidosis, of which 66% are still taking them.

Clinical presentation

- Reported clinical presentation was similar, regardless of type. The most common presenting symptoms across all types were shortness of breath (60%) and fatigue (58%), with hATTR patients also commonly reporting neuropathy (37%).
- Diagnosis of carpal tunnel before diagnosis of amyloidosis was common across all types (38%) and was most common in ATTR (64% of wtATTR and 61% of hATTR). 38% of patients reported ≥6 years between their diagnosis of carpal tunnel and amyloidosis.
- 27% of wtATTR patients and 15% of hATTR patients went undiagnosed for >4 years.

Diagnosis

- 60% of patients saw ≥3 different physicians and 41% saw ≥4 before they were correctly diagnosed, with AL most commonly reporting ≥5 (Figure 2).
- 32% of patients reported seeing ≥2 cardiologists before their diagnosis (Figure 3).
- Diagnosis by a cardiologist was common in all types (43%) and most common in wtATTR (75%).
- 48% of patients diagnosed within the past 2 years were diagnosed by a cardiologist compared to 35% of patients diagnosed more than 2 years ago. Both patients diagnosed ≥2 and ≤2 years ago commonly saw 5 or more doctors before being diagnosed correctly (26%).
- Diagnosis by a cardiologist was more common in the EU, 49%, than North America (NA), 36%.
- Diagnostic procedures varied between types (Figure 4A). The most common procedures were cardiac MRI in AL (60%), heart biopsy in wtATTR (69%), and cardiac MRI and fat pad biopsy in hATTR (55% and 54%).
- In the EU, imaging was more commonly used than in NA, with 52% of patients receiving ≥1 imaging test compared to 38% respectively (Figure 4B).
- Fat pad biopsy was the most commonly reported diagnostic biopsy and was more common in NA (44%) than the EU (32%).

Disease burden

- 56% of patients were hospitalized for their cardiac amyloidosis (56% in AL, 65% in wtATTR, 52% in hATTR).
- 19% of patients had to travel >2 hours to get diagnosed and 24% report air travel for their treatment.
- 96% of caregivers were either family members or spouses / partners of patients.
- Of caregivers of deceased patients, 55% report the patient died unexpectedly and only 48% were offered a palliative care consultation.

Figure 2. Number of different physicians seen before diagnosis. Patients saw numerous different physicians before receiving the correct diagnosis.

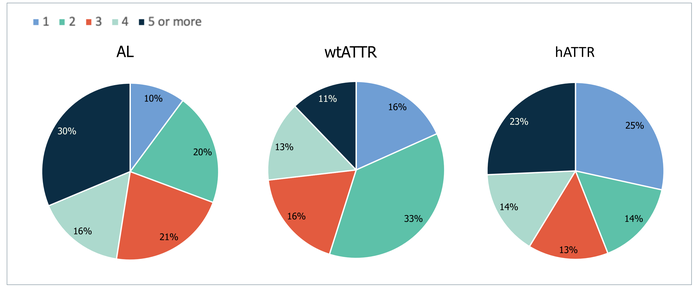


Figure 3. Number of cardiologists seen before diagnosis. Many patients had to see more than one cardiologist before receiving the correct diagnosis.

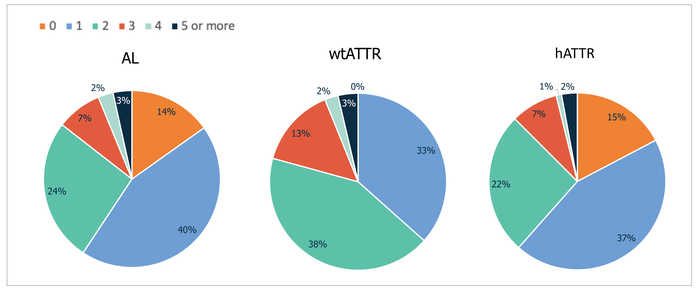
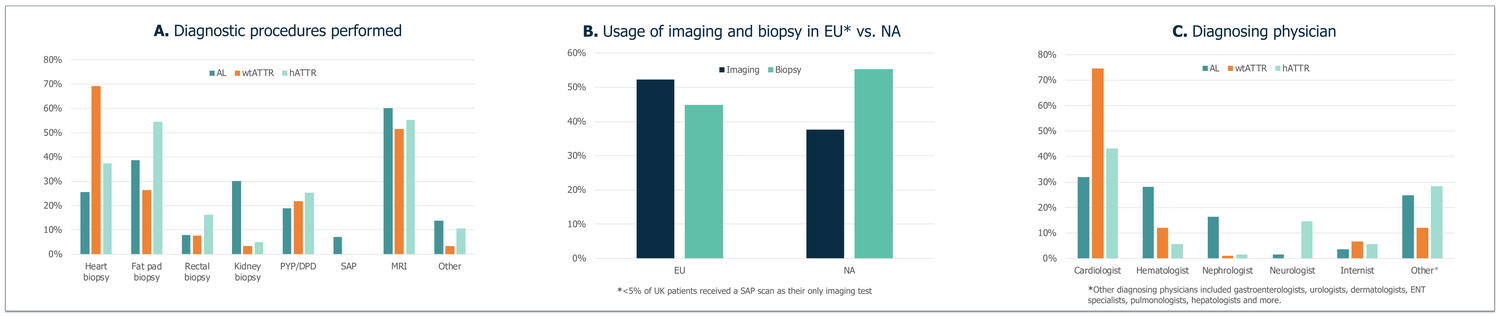


Figure 4. Comparison of diagnostic procedures and diagnosing physicians across different types and regions.



CONCLUSIONS

- Patients with cardiac amyloidosis are commonly misdiagnosed. Misdiagnosing physicians tend to focus on treating presenting symptoms individually, which causes delays in diagnosis and patients to receive incorrect treatments, typically for their cardiac involvement, that can worsen symptoms and reduce survival.
- Ace inhibitors and beta blockers, which are poorly tolerated in amyloidosis[1], are still frequently prescribed to patients even after they have been diagnosed, highlighting the need for continuing physician education.
- Diagnosis by cardiologists is increasing over time, however, patients still frequently see 5 or more doctors before they are diagnosed correctly.
- Comparison of diagnostic procedures performed shows lack of a standardized diagnostic pathway and continued reliance on heart biopsy, fat pad biopsy, and cardiac MRI. PYP/DPD scans, which are non-invasive, inexpensive, and reliable, are underutilized in the diagnosis of amyloidosis. Increasing the use of PYP/DPD may help improve early diagnosis.
- While one might expect hATTR patients to be diagnosed quickly due to the familial component, a high percentage went undiagnosed after the start of symptoms, showing a demand for better understanding and awareness across the health care provider and patient community.
- Patient and physician education around initial symptoms is crucial in facilitating earlier diagnosis. Understanding of early signs, such as carpal tunnel[2], and early symptoms are vital to improving diagnosis and care.

REFERENCES

[1]Siepen F et al. ISA 2016; Jul 3-7, 2016; Uppsala, Sweden. Abstract PA98.
[2]Ikram et al. Journal of Cardiac Failure. 2017 Aug; 23(8): S11-S12

Presented at the 23rd annual Heart Failure Society of America; September 13-16, 2019; Philadelphia, PA