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], Simon Gibbs[4], Ute Hegenbart[5], Kristen Hsu[1], Martha Grogan[6]

[1]Amyloidosis Research Consortium, Boston, MA, USA; [2]Columbia University, New York, NY, USA; [3]Biopharma Strategic Consulting, USA; [4]The Victorian and Tasmanian Amyloidosis Service, Australian Amyloidosis Network, Australia; [5]Amyloidosis Center, University Hospital Heidelberg, Germany; [6]Mayo Clinic, Rochester, MN, USA

BACKGROUND

- Cardiac amyloidosis is a severe, progressive, and fatal disease caused by the 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 buildup of 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 diagnosing amyloidosis were captured in a series of patient-focused survey studies 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

- Patients and caregiver surveys created by ARC were made available on the ARC website and were also 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	469 (67%)
wtATTR	70 (10%)
hATTR	114 (16%)
Other	28 (4%)
Unsure	18 (3%)
Region	
Asia-Pacific	54 (8%)
European Union	119 (17%)
North America	526 (75%)
Sex	
Male	453 (62%)
Female	253 (36%)
Age	
18-25	1 (0%)
26-40	18 (3%)
41-55	127 (18%)
56-70	362 (52%)
71 or older	183 (26%)
Ethnicity	
White / Caucasian	582 (83%)
Asian	16 (2%)
Black	26 (4%)
Hispanic / Latino	15 (2%)
Native American	7 (1%)
Other	59 (8%)
Total	**699**

- At the time of analysis there were 699 total responses.
- This analysis focuses on respondents who reported having AL, wtATTR, or hATTR (N=653), with cardiac involvement.
- Of these responses, 372 (57%) were patients, 281 (43%) were caregivers.

Organ Involvement

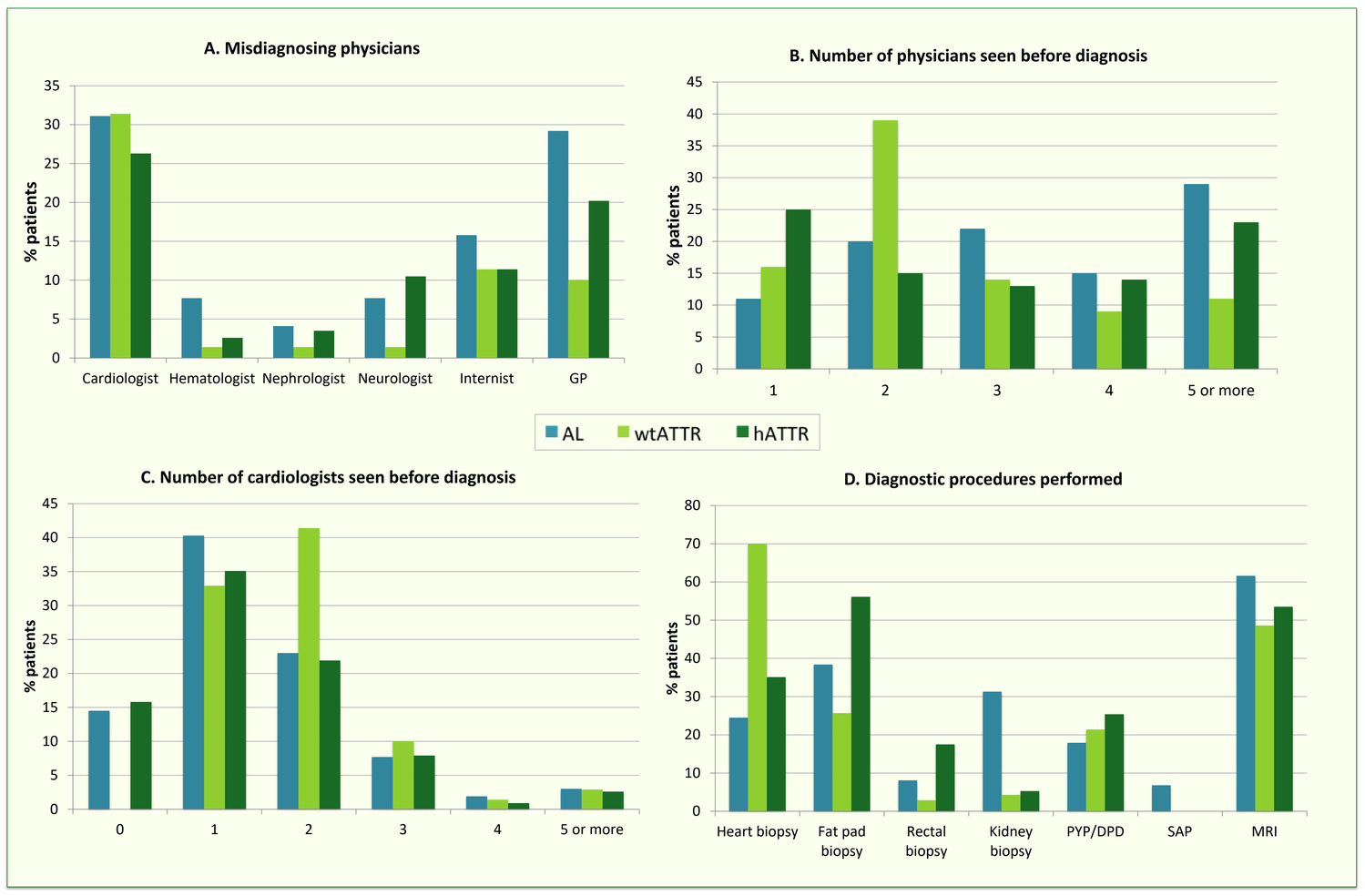
- All patients reported as having cardiac involvement. In addition to cardiac involvement, other common organ involvement is reported below in Table 2.

Table 2. Common extra-cardiac organ involvement

	AL	wtATTR	hATTR
Kidney	260 (55%)	14 (20%)	19 (17%)
Nerves	160 (34%)	16 (23%)	79 (69%)
Liver	72 (15%)	10 (14%)	26 (23%)
GI	178 (38%)	6 (9%)	48 (42%)
Skin	81 (17%)	8 (11%)	10 (9%)

- The most common extra-cardiac organ involvement for AL was kidney (55%) and nerves for wtATTR and hATTR (23% and 69% respectively).
- Many patients had solely cardiac involvement, most commonly in wtATTR (57%).
- More than one third of patients with AL and hATTR reported having ≥3 organs involved.

Figure 1. Responses show numerous misdiagnoses, physician consultations, and diagnostic procedures before diagnosis.



Missed diagnosis and Misdiagnosis

- Overall 294 (45%) patients (42% in AL, 39% in wtATTR, 44% in hATTR) received ≥1 misdiagnoses before being correctly diagnosed with amyloidosis.
- Cardiologists were the most common misdiagnosing physician across all types followed by general practitioners and internists (Figure 1A).
- A majority of patients saw ≥3 different physicians (59%) before they were correctly diagnosed (Figure 1B), with many seeing >1 cardiologist as well (37%) (Table 1C).
- Unspecified heart failure or heart disease was a common misdiagnosis across all types (24%) and most common in wtATTR patients (33%).
- The next most common misdiagnoses were all cardiac related: hypertrophic cardiomyopathy (11%), high blood pressure (5%), and heart arrhythmias (5%).
- A majority of misdiagnosed patients (77%) received treatment for their misdiagnosis.
- Treatment with beta blockers and ace inhibitors, which are poorly tolerated in amyloidosis[1], was common, being reported in 27% and 17% of all patients respectively and 31% and 20% of misdiagnosed patients.

Diagnosis

- The clinical presentation was similar, regardless of type.
- The most common presenting symptoms across all types were shortness of breath (57%) and fatigue (57%), with the exception of neuropathy for hATTR patients (41%).
- Diagnosis of carpal tunnel before diagnosis of amyloidosis was common across all types (36%) and was most common in ATTR (64% of wtATTR and 57% of hATTR) with 43% of patients reporting ≥6 years between their diagnosis of carpal tunnel and their diagnosis of amyloidosis.
- While AL patients were most commonly diagnosed within 1 year of symptom onset (47%) and rarely reported undiagnosed symptoms for >4 years (6%), ATTR patients more commonly went undiagnosed for >4 years (25% in wtATTR, 16% in hATTR).

Figure 2. Time between symptom onset and diagnosis

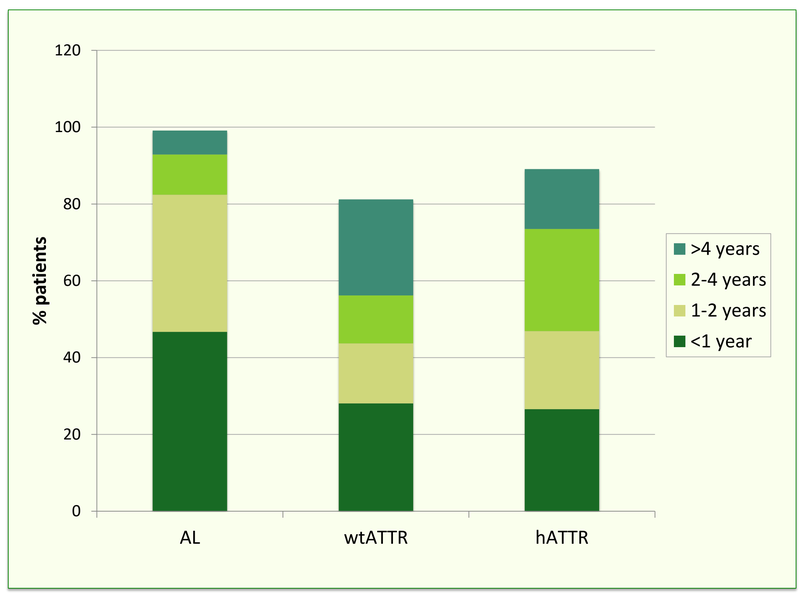
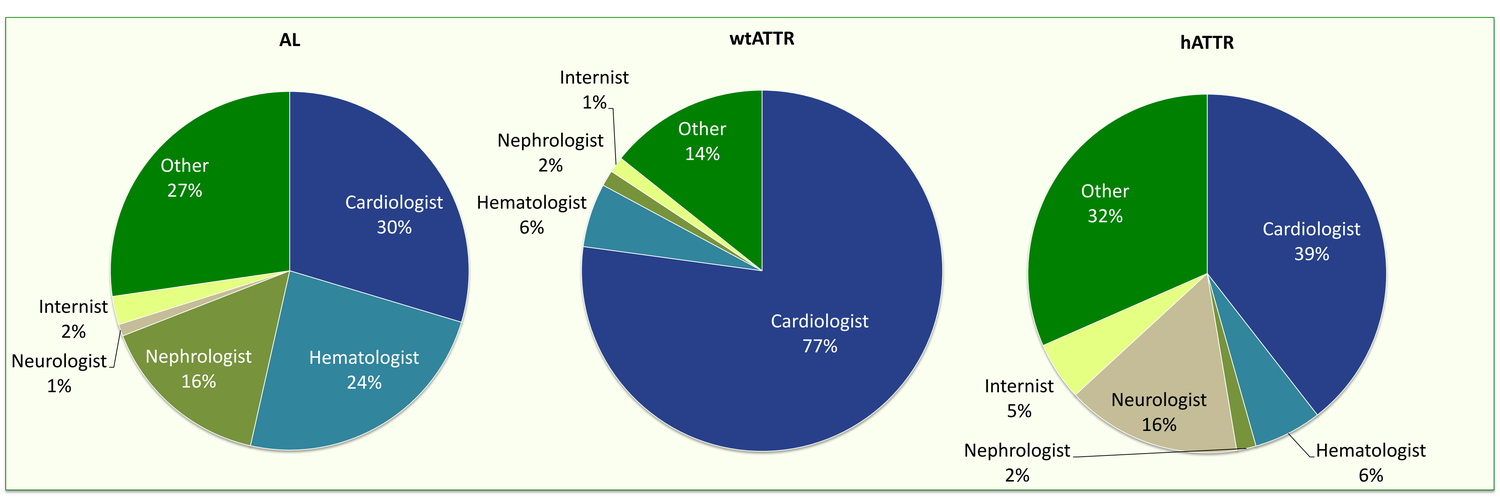


Figure 3. Breakdown of diagnosing physician by type of amyloidosis



Disease Burden

- 54% of all patients were hospitalized for their cardiac amyloidosis (54% of AL, 61% of wtATTR, and 50% of hATTR).
- 19% of patients had to travel over 2 hours to their diagnosing physician, and 25% of patients have had to take a plane in order to seek treatment.
- 95% of caregivers were either family members or spouses / partners of patients. Of caregivers of deceased patients, 57% say the patient died unexpectedly and 48% were offered a palliative care consultation.

CONCLUSION

- Patients with cardiac amyloidosis are commonly misdiagnosed, which is frequently associated with their cardiac involvement. Misdiagnosing physicians tend to focus on treating presenting symptoms individually, which causes a delay in diagnosis and patients to receive incorrect treatments, that can worsen symptoms and reduce survival.
- The comparison of diagnostic procedures performed shows an underuse of PYP/DPD in the diagnosis of amyloidosis. PYP/DPD scans are non-invasive, inexpensive, and reliable. Increasing the use of PYP/DPD scans may help improve earlier diagnosis among patients.
- While one might expect hATTR patients to be more quickly diagnosed due to the familial component, a high percentage of hereditary patients went undiagnosed after the start of symptoms, which shows a demand for better understanding and awareness across both the health care provider and patient community.
- Patient and physician education around initial symptoms is crucial in facilitating earlier diagnosis. Understanding of early presenting symptoms such as carpal tunnel and catching early symptoms in hATTR patients are vital to improving diagnosis and care.

REFERENCES

[1]Siepen F et al. ISA 2016; Jul 3-7, 2016; Uppsala, Sweden. Abstract PA98.

http://bit.ly/2pl7Nfp

Presented at the XVIth International Symposium on Amyloidosis; March 26-29, 2018; Kumamoto, Japan