Amyloidosis Research Consortium
COMPASS

A Newsletter for Amyloidosis Research Updates

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Amyloidosis Research Consortium Cardiac Amyloidosis Survey

Cardiac amyloidosis is a severe, progressive, and fatal disease caused by accumulation of misfolded proteins (amyloid) in cardiac tissue. Delays in diagnosis of cardiac amyloidosis 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. The objective of the study was to gain insight into patient experiences with delays and errors in the diagnostic pathway for cardiac amyloidosis.

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. Surveys were available from January 2017 until December 2018. Patients with cardiac amyloidosis or a caregiver of a patient with cardiac amyloidosis were invited to participate.

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Of 745 total responses, 696 reported having AL, wtATTR, or hATTR with cardiac involvement. The 696 who reported cardiac involvement were included in this analysis. 405 (58%) were patients and 290 (42%) were caregivers. The vast majority (96%) of caregivers were either family members or spouses / partners of patients. 37% of caregivers reported that they were responding on behalf of a deceased patient; of these, 55% report the patient died unexpectedly and 48% were offered a palliative care consultation.

	Respondents, N (%)
Type of amyloidosis	
AL	482 (69%)
wtATTR	91 (13%)
hATTR	123 (18%)
Region	
Asia-Pacific (APAC)	49 (7%)
European Union (EU)	148 (21%)
North America (NA)	499 (72%)
Sex	
Male	446 (64%)
Female	238 (34%)
Age	
18-25	0 (0%)
26-40	17 (2%)
41-55	115 (17%)
56-70	364 (52%)
71 or older	184 (26%)
Ethnicity	
White/Caucasian	556 (80%)
Black/African American/Black British	26 (4%)
Asian/Pacific Islander/Asian British	16 (2%)
Hispanic/Latino	14 (2%)
Native American	6 (1%)
Other	75 (11%)
Total	696

Table 1. Demographics of respondents

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More than 50% of patients reported involvement of at least 3 organs. In addition to cardiac organ involvement, the most common organ involvement was kidney for AL (56%) and nerves for hATTR (66%). In wtATTR, both kidney (23%) and nerve involvement (22%) were commonly reported. GI involvement was also frequently reported in AL and hATTR (39% and 40% respectively). Absence of any additional organ involvement was seen most commonly in wtATTR (40%).

The most common presenting symptoms across all types were shortness of breath (60%) and fatigue (58%), with hATTR patients also commonly reporting neuropathy symptoms (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 their diagnosis of amyloidosis. A majority of AL patients were diagnosed within 2 years of symptom onset (65%) while ATTR patients more commonly went undiagnosed for more than 4 years (27% in wtATTR and 15% in hATTR). 19% of patients had to travel over 2 hours to get diagnosed, and 24% reported having to travel by plane at some point for their treatment. 56% of all patients were hospitalized for their cardiac amyloidosis (56% in AL, 65% in wtATTR, 52% in hATTR).

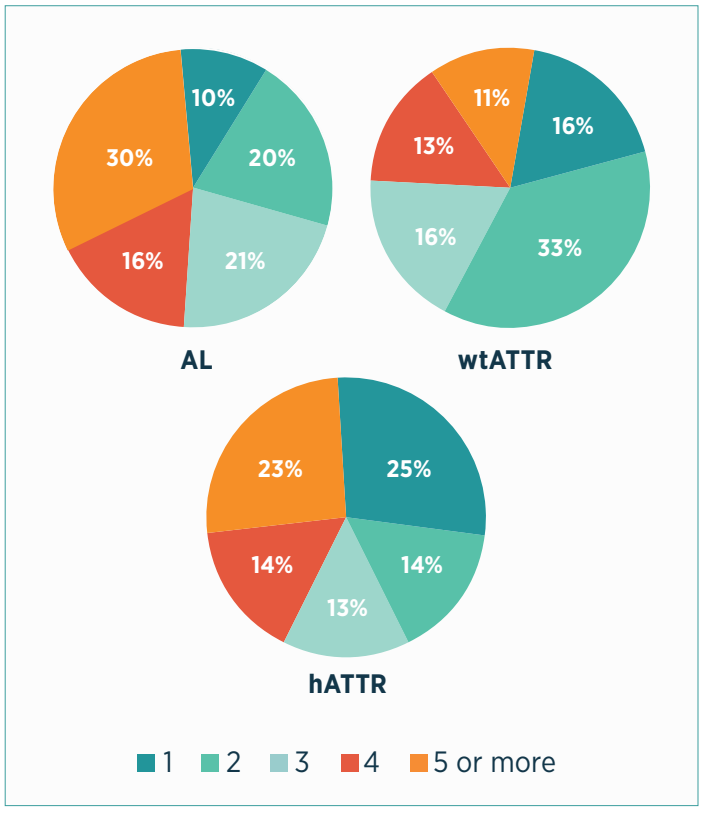

Figure 1. Number of physicians seen before diagnosis

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Figure 2a. Diagnostic procedures performed

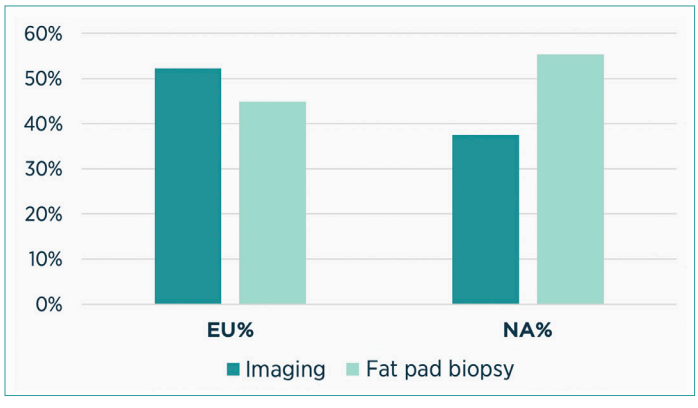

Figure 2b. Usage of imaging and biopsy in EU vs NA

most common in wtATTR (32%). 6% of patients reported misdiagnosis with a psychiatric condition including stress, depression, and hypochondria. A majority of misdaignosed patients (75%) received treatment for their misdiagnosis. Treatment with beta blockers and/or ACE inhibitors, which are poorly tolerated in amyloidosis, was common (35%) in all patients and most common (51%) in wtATTR patients.

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The majority of patients (60%) saw at least 3 different physicians before receiving a correct diagnosis. 41% saw at least 4 physicians before they were correctly diagnosed, with AL most commonly reporting ≥5 (Figure 1). About a third (32%) of patients also reported having seen 2 or more cardiologists before receiving their diagnosis of amyloidosis. Diagnosis by a cardiologist was common in all types (40%) and most common in wtATTR patients (75%). Diagnosis by a cardiologist was more common in the European Union (EU), 49%, than North America (NA), 36%.

Diagnostic procedures varied between types (Figure 2a). 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% respectively). In the EU, imaging was more commonly used than in NA, with 52% of patients receiving at least one imaging test compared to 38% respectively (Figure 2b). Fat pad biopsy was the most commonly reported diagnostic biopsy and was more common in NA (44%) than the EU (32%).

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This study highlights the challenging diagnostic journey patients with cardiac amyloidosis have historically faced and can serve as a benchmark against which the community can measure its progress in achieving earlier and more accurate diagnosis moving forward. In the absence of any treatments, there was a poor level of awareness or education around the diagnosis and management of cardiac amyloidosis within both the healthcare provider and patient communities. Patients with cardiac amyloidosis often reported seeing 5 or more doctors before receiving an accurate diagnosis. During this time, patients were commonly misdiagnosed and treated with incorrect treatments, typically for their cardiac involvement, that can worsen symptoms and reduce survival. This study showed that ACE inhibitors and beta blockers, which are poorly tolerated in amyloidosis, were frequently prescribed to patients even after they have been diagnosed, highlighting the need for continuing physician education. The comparison of diagnostic procedures performed shows there was lack of a standardized diagnostic pathway and a continued reliance on heart biopsy, fat pad biopsy, and cardiac MRI. PYP/DPD scans were largely underused at the time of this study, and while awareness campaign efforts have drastically increased the community's level of reliance on these scans in diagnosis in recent years, proper training on their use and interpretation within the diagnostic pathway is critical in ensuring that patients are diagnosed accurately and treated appropriately.

The recent approval of treatments for AL, hATTR, and wtATTR amyloidosis have ushered in a new age when it comes to the diagnosis and management of cardiac amyloidosis. While commercial interests are leading the way to increase the level of disease awareness rising among the physician community, it's critical that this general awareness and increase in speed of diagnosis come hand and hand with education on how to accurately diagnose, type, and manage the different types of cardiac amyloidosis. It will be important that as a community we measure the success of these awareness and education initiatives, identify gaps, and provide guidance where it is most needed to ensure better outcomes for patients.

Acknowledgements

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