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

**Amyloidosis Research Consortium**

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

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**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), wild-type ATTR amyloidosis (wATTR), and hereditary ATTR amyloidosis (hATTR).
- AL is caused by misfolded immunoglobulin light chains, while hATTR and wATTR are caused by misfolded transthyretin.
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**RESULTS**

**Demographics**

Table 1. Demographics of respondents

<table>
<thead>
<tr>
<th>Type of Amyloidosis</th>
<th>AL</th>
<th>ATTR</th>
<th>WT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respondents, % (N/1)</td>
<td>46% (181)</td>
<td>91% (323)</td>
<td>52% (195)</td>
</tr>
<tr>
<td>Region</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asia/Pacific (AP)</td>
<td>31% (77)</td>
<td>26% (97)</td>
<td>38% (147)</td>
</tr>
<tr>
<td>Europe (EU)</td>
<td>40% (97)</td>
<td>32% (121)</td>
<td>21% (80)</td>
</tr>
<tr>
<td>North America (NA)</td>
<td>30% (74)</td>
<td>28% (107)</td>
<td>34% (128)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>67% (124)</td>
<td>61% (222)</td>
<td>65% (259)</td>
</tr>
<tr>
<td>Female</td>
<td>33% (71)</td>
<td>39% (144)</td>
<td>35% (129)</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>65-74</td>
<td>30% (69)</td>
<td>36% (132)</td>
<td>28% (106)</td>
</tr>
<tr>
<td>25-64</td>
<td>20% (46)</td>
<td>12% (44)</td>
<td>21% (81)</td>
</tr>
<tr>
<td>&lt;25</td>
<td>6% (14)</td>
<td>7% (25)</td>
<td>7% (29)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>60% (139)</td>
<td>56% (208)</td>
<td>57% (212)</td>
</tr>
<tr>
<td>Asian</td>
<td>16% (37)</td>
<td>19% (74)</td>
<td>18% (68)</td>
</tr>
<tr>
<td>Black/African American</td>
<td>21% (49)</td>
<td>22% (83)</td>
<td>16% (61)</td>
</tr>
<tr>
<td>Other</td>
<td>8% (18)</td>
<td>9% (34)</td>
<td>7% (24)</td>
</tr>
<tr>
<td>Total</td>
<td>100% (233)</td>
<td>100% (378)</td>
<td>100% (395)</td>
</tr>
</tbody>
</table>

**Delays in diagnosis**

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

**Clinical presentation**

- Reported clinical presentation was similar, regardless of type. The most common presenting symptoms across all types were shortness of breath (50%) and fatigue (50%), with ATTR patients commonly reporting neuropathy (37%).
- Diagnosis of cardiac tumors before diagnosis of amyloidosis was common across all types (38%) and was most common in ATTR (48% of wATTR and 61% of hATTR). 38% of patients reported ≥6 years between their diagnosis of cardiac tumors and amyloidosis.
- 27% of hATTR patients and 19% 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 ≥3 (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 wATTR (75%).

**Challenges associated with diagnosis**

- Patients had to see more than one physician before being diagnosed correctly (26%).
- Most common diagnosis was misdiagnosed (41%), followed by misdiagnosis of carpal tunnel and amyloidosis.
- AL (46%) had the most common misdiagnosis across all types (23% and was most common in hATTR (28%)).
- Cardiologists were the most common misdiagnosing physician (43%) and most common in hATTR (49%).

**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).
- Unspecific heart failure was the most common misdiagnosis across all types (23%) and was most common in wATTR (32%).
- 6% of all patients reported misdiagnosed 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 α-blockers, which are poorly tolerated in amyloidosis, was common in all patients (33%) and most common in hATTR (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.

**Figure 1. Misdiagnosing physician by type**

**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.**

**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, are still frequently prescribed to patients even after they have been diagnosed, highlighting the need for continuing physician education.
- Diagnosis by cardiologists is evolving 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/PDPD scans, which are non-invasive, inexpensive, and reliable, are underutilized in the diagnosis of amyloidosis. Increasing the use of PYP/PDPD may help improve early diagnosis.

**REFERENCES**

1. Ikram et al. Journal of Cardiac Failure. 2017 Aug; 23(8): S11
2. Siepen F et al. ISA 2016; Jul 3
3. Amyloidosis Research Consortium Cardiac Amyloidosis Survey: Results from Patients with AL and ATTR Amyloidosis and Their Caregivers
4. Presented at the 23rd annual Heart Failure Society of America; September 13-16, 2019; Philadelphia, PA

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