

Amyloidosis Research Consortium Cardiac Amyloidosis Survey: Results From Patients With AL Amyloidosis and Their Caregivers

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BACKGROUND

- Cardiac amyloidosis is a severe, progressive, fatal disease
 - Light chain (AL) amyloidosis is a multiorgan disease caused by an accumulation of misfolded immunoglobulin light chain. Although the heart is involved most often, other organs, such as the kidneys, gastrointestinal tract, and nervous system, can also be significantly impacted
 - Initial symptoms of cardiac amyloidosis, such as weight loss and fatigue, are often nonspecific, resulting in delays in diagnosis
 - The level of cardiac involvement is the main prognostic factor for early death in patients with AL and other cardiac amyloidoses; many patients with primary renal, gastrointestinal, or nerve amyloidosis eventually die of cardiac involvement
 - Health-related quality of life of patients with AL amyloidosis is significantly impacted, particularly for those with cardiac involvement¹
- The challenge of accurate and timely diagnosis of AL amyloidosis was recently highlighted in a patient-focused survey conducted by the Amyloidosis Research Consortium (ARC), which examined the patient journey to diagnosis and treatment²
 - Most patients (63%) experience delays in diagnosis of ≥ 6 months
 - 31.8% of respondents in the survey visited ≥ 5 different physicians before receiving a correct diagnosis
 - Hematologists/oncologists were most likely (34.1%) to make a correct diagnosis; however, for the 443 patients reporting missed diagnosis across ≥ 1 physician visits, 223 hematologists and 220 cardiologists did not diagnose the condition accurately
 - Patients with cardiac involvement may experience more substantial delays in diagnosis³
- Such delayed diagnosis can negatively impact the prognosis of patients and may be fatal
 - Up to 30% of patients with AL amyloidosis die within 6 months of diagnosis; death is attributed primarily to advanced cardiac involvement⁴⁻⁶

OBJECTIVE

- To understand delays, errors, and inconsistencies in the diagnostic pathway for patients with cardiac AL amyloidosis and validate these findings against caregiver responses

METHODS

- Patients with all types of amyloidosis, their family members, and their caregivers were invited to participate in an online survey through email, mailing lists, and social media channels of the ARC, the Amyloidosis Foundation, and Amyloidosis Support Groups
 - The present analysis was limited to AL amyloidosis
- The survey consisted of 36 questions for patients and 37 questions for caregivers and was developed by ARC and made available online to participants in January 2017
- Caregiver survey responses were used to validate patient survey results

RESULTS

Participants

- In this AL amyloidosis subanalysis, 137 patients and 176 caregivers (61 caregivers of deceased patients and 115 caregivers of living patients) completed the survey
- Characteristics of patient respondents are provided in **Table 1**

Table 1. Characteristics of Patient Respondents (N = 137)

Patient Respondents	Responses, n (%)
Female	75 (54.7)
Age, years	
26-40	3 (2.2)
41-55	23 (16.8)
56-70	89 (65.0)
≥ 71	22 (16.1)
Ethnicity	
American Indian or Alaska Native	1 (0.7)
Asian or Pacific Islander	3 (2.2)
Black or African American	6 (4.4)
Hispanic or Latino	3 (2.2)
White/Caucasian	112 (81.8)
Prefer not to answer	5 (3.6)
Other	7 (5.1)
Time since diagnosis	
<1 year	24 (17.5)
1-2 years	32 (23.4)
3-5 years	40 (29.2)
6-10 years	29 (21.2)
≥ 11 years	12 (8.8)
Organ involvement ^a	
Heart	137 (100)
Kidney	75 (54.7)
Gastrointestinal	60 (43.8)
Nerves	41 (29.9)
Liver	20 (14.6)
Skin	20 (14.6)
Other ^b	49 (35.8)

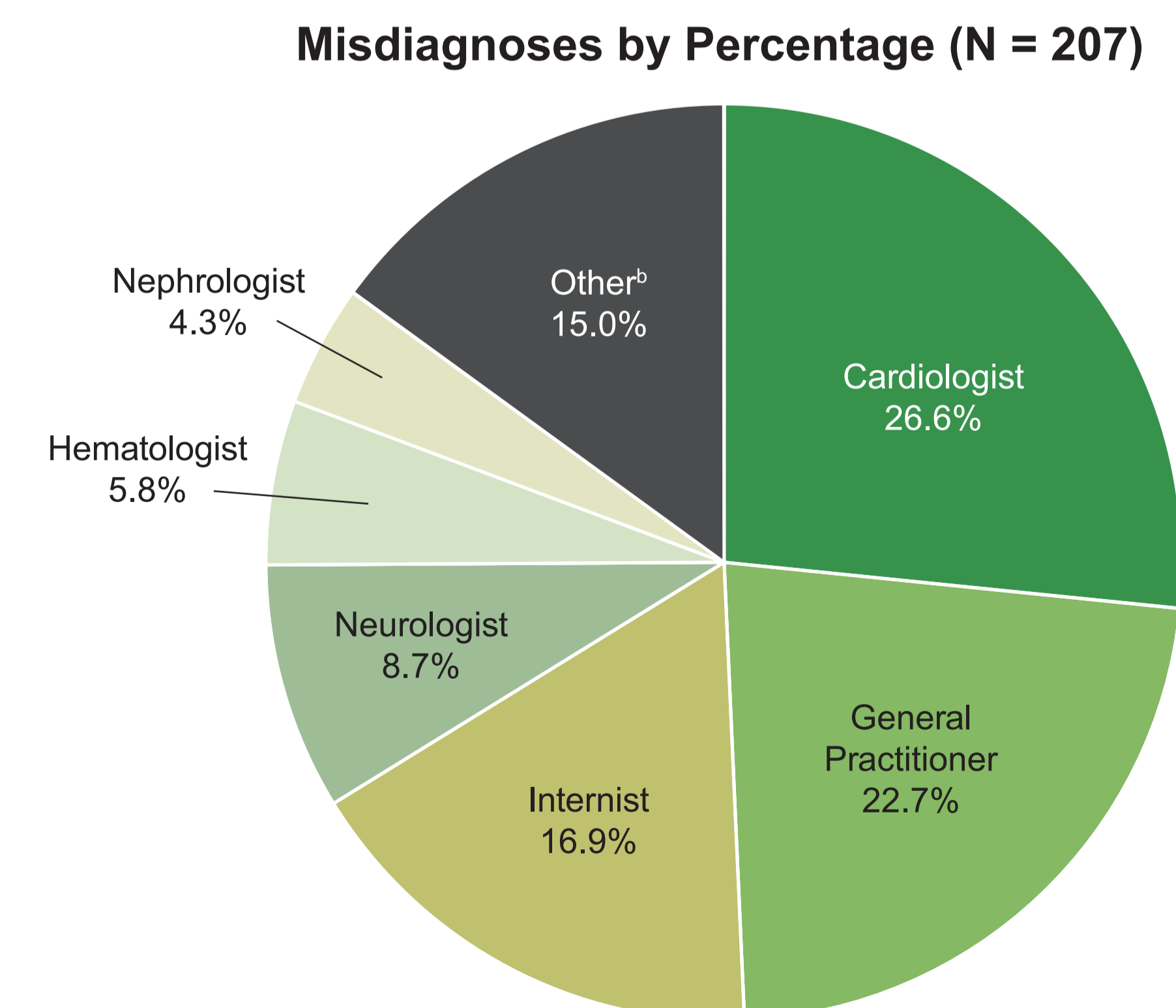
^aRespondents could check all answers that applied.

^bResponses included lung, bladder, spleen, muscles, salivary glands, and thyroid gland.

Missed Diagnosis and Misdiagnosis

- Before a correct diagnosis was made, 43.8% (n = 60) of patients received incorrect diagnoses—predominantly by cardiologists and general practitioners—of ≥ 1 other conditions (**Figure 1**)

Figure 1. Patients: Which type of doctor told you that you had something other than amyloidosis?^a



^aRespondents could check all answers that applied.

^bOther responses included dermatologist, endocrinologist, gastroenterologist, infectious disease specialist, oncologist, oral surgeon, otolaryngologist, pulmonologist, podiatrist, rheumatologist, surgeon, and urologist.

- Nearly all patients who received misdiagnoses (83.3%; n = 50/60) reported undergoing treatment for their misdiagnosed condition; treatments included medications, surgical procedures (ablations, pacemakers, angioplasty/stents, nerve surgery, myectomy), and speech therapy
 - Patients who received misdiagnoses were at times prescribed beta-blockers, calcium channel blockers, or angiotensin-converting enzyme inhibitors, which may contribute to early mortality and worsening of symptoms⁷
 - These medications were prescribed in 45 (32.8%) patients before correct diagnosis and in 37 (27.0%) patients after correct diagnosis
- More than 75% of patients visited ≥ 3 different physicians before they received a correct diagnosis, suggesting substantial numbers of missed opportunities for diagnosis

Diagnosis

- Fatigue (94 [68.6%]), shortness of breath (89 [65.0%]), and edema (69 [50.4%]) were the initial symptoms prompting the first doctor's visit for $>50\%$ of patients
 - Of note, one-third of patients experienced carpal tunnel syndrome (45 [32.8%])
 - Carpal tunnel syndrome diagnosis preceded AL diagnosis by >2 years in 32 (71.1%) patients; it may be an early symptom of AL amyloidosis
- Patients reported that biopsy of fat pad (75 [54.7%]), kidney (41 [29.9%]), or heart (40 [29.2%]) was the predominant diagnostic test performed
- Most caregivers and patients reported that the correct diagnosis was made most often by hematologists and nephrologists and that they visited a multitude of physicians before receiving the correct diagnosis (**Figure 2**)
 - Patients reported traveling great distances for diagnosis; 25 (18.2%) traveled ≥ 2 hours to visit the physician who diagnosed AL amyloidosis
- Responses from caregivers of patients with AL amyloidosis who died indicated even more visits—to ≥ 5 distinct physicians—before the correct diagnosis; significantly fewer cardiologists made the correct diagnosis (**Figure 2**)

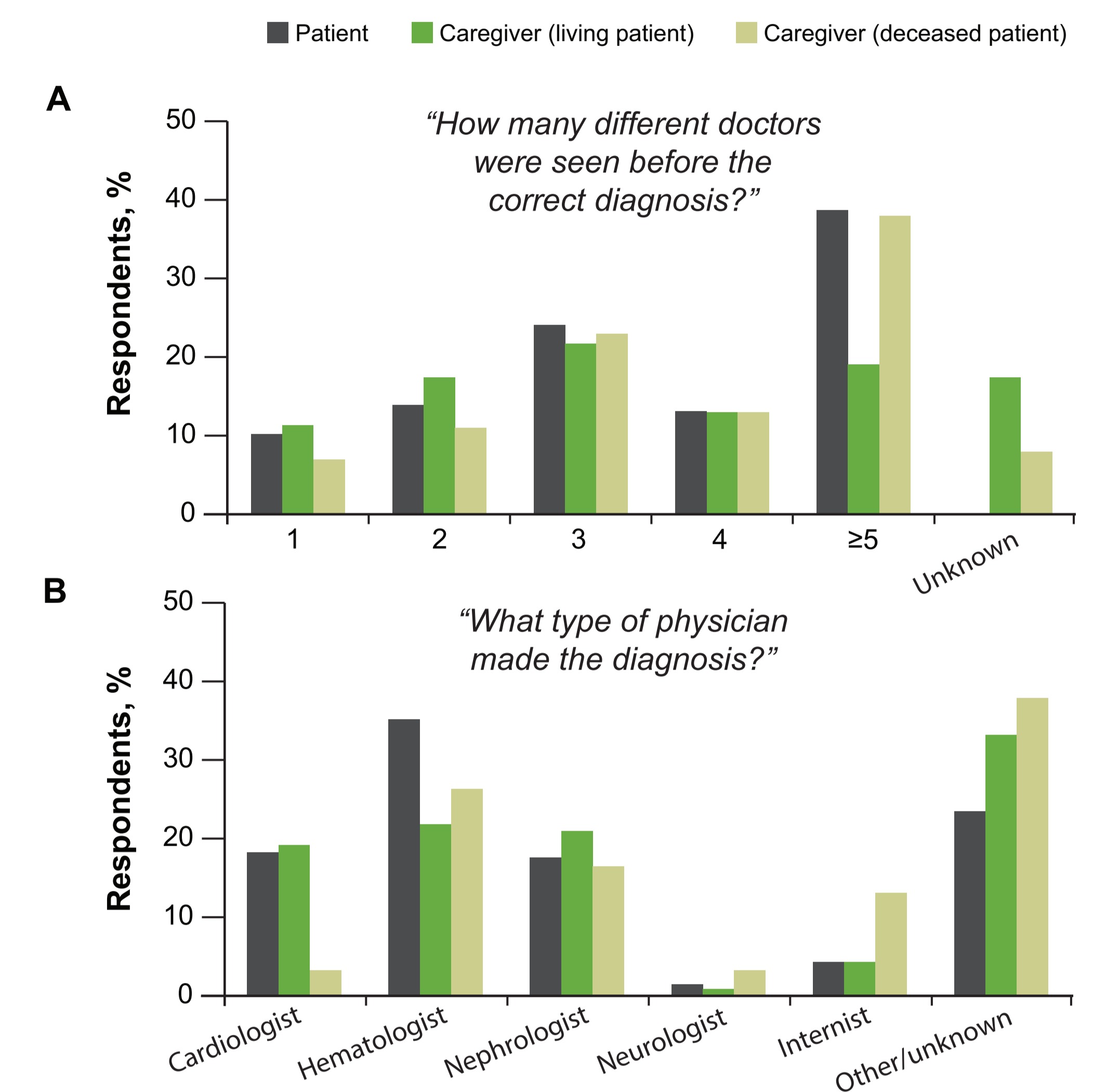
CONCLUSIONS

- This first survey of caregiver and patient experiences with AL amyloidosis shows alignment of responses and validates our patient-directed research
- Patients with cardiac AL amyloidosis frequently receive misdiagnoses and sometimes undergo incorrect, poorly tolerated treatments, which may worsen their symptoms and reduce their survival
- Awareness of AL amyloidosis among all specialists is vital
 - Recognition of cardiac AL amyloidosis is crucial because of the increased delays in diagnosis and the risk for death
- We speculate that many patients die of delays before receiving a diagnosis. It is vitally important that AL amyloidosis be diagnosed earlier

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Figure 2. Patient (N = 137) and caregiver (N = 176; n = 61 deceased patients and 115 living patients) responses show alignment on the substantial numbers of physicians consulted before diagnosis and the predominant diagnoses by cardiologists, hematologists, and nephrologists.



Disease Burden

- Hospitalization was common; 76 (55.5%) patients reported hospitalization for cardiac amyloidosis
 - Of these patients, 35 reported hospitalization for cardiac amyloidosis in the year before survey completion
- Moreover, 43 (31.4%) patients reported the need for air travel for expert physician consultation

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