The Relative Burden of AL Amyloidosis on Health-Related Quality of Life

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BACKGROUND

- The SF-36v2® Health Survey (SF-36v2) is a widely used, generic, patient-reported outcome survey that can describe and quantify the impact of disease and its treatment on health-related quality of life (HRQoL)[1]
- Amyloid light chain (AL) amyloidosis is a complex, rare disease characterized by misfolded amyloid protein deposits in tissue and vital organs
- Accumulation of amyloid deposits in the body can lead to organ toxicity, irreversible organ damage, and death; however, patients' experiences of the disease vary broadly because of the heterogeneity of organ involvement and dysfunction[2,3]
- The presence and extent of cardiac involvement is a critical, organ-related prognostic factor that has significant treatment implications[4]
- HRQoL may be substantially affected in patients with newly diagnosed AL amyloidosis who are in the early stages of the treatment process and might not have experienced hematologic or organ response[5]
- Little is known about the impact of AL amyloidosis on HRQoL[5,6]

OBJECTIVES

- To compare the HRQoL profile of patients with AL amyloidosis overall with that of a US general normative population
- To examine the relative burden of AL amyloidosis among key subgroups of patients hypothesized to have greater severity of disease: those whose AL amyloidosis has been recently diagnosed and those with cardiac involvement

METHODS

Data Sources

Patients With AL Amyloidosis

- The SF-36v2 was administered in an online, noninterventional, longitudinal study of adults (≥18 years of age) with self-reported AL amyloidosis (N = 341) using the Optum Smart Measurement® System
- These analyses used cross-sectional data from the initial study survey collected in 2015
- 2 patient advocacy groups helped to support recruitment efforts that consisted of social media posts and emails highlighting the study participation opportunity

US General Population Norms

- Data were drawn from a 2009 Internet-based HRQoL-norming study
- Study participants were recruited from the Knowledge Panel® (Knowledge Networks [Burnaby, BC, Canada], now GfK Custom Research, LLC), a probability-based sample of noninstitutionalized US adults
- 4036 persons completed the SF-36v2 to provide normative estimates of HRQoL for the US population (USP). Because some data were missing, the sample size ranged from 4024 to 4036 for specific SF-36v2 scores

Measures

SF-36v2® Health Survey

- The SF-36v2 is a 36-item, self-report measure of generic HRQoL. The standard (4-week recall) version was used for this study[1]
- It allows for the calculation of 8 domains of functional health and well-being
  - Physical functioning (PF)
  - Role limitations due to physical health problems (RP)
  - Bodily pain (BP)
  - General health (GH)
  - Vitality (VT)
  - Social functioning (SF)
  - Role limitations due to emotional health problems (RE)
  - Mental health (MH)
- Scores on all domains are used to calculate summary measures for overall physical and mental health
  - Physical Component Summary (PCS)
  - Mental Component Summary (MCS)
- Each scale/summary measure is calculated and standardized to 50 ± 10 (mean ± SD). Thresholds for clinically meaningful differences on the scales range from 2 to 4
- For all scales, a score of 50 is the average in the USP; higher scores represent better functioning

Statistical Analysis

- USP data were adjusted to the age and sex distribution of the AL amyloidosis patient sample using separate ordinary least-squares regression models, with each SF-36v2 scale or summary score a dependent variable
- Analysis of variance was used to compare the SF-36v2 scores of patients with AL amyloidosis with scores of the age- and sex-adjusted USP
- Using the same method, we compared the burden of disease of 2 key patient subgroups with the burden of disease of the USP
  - Patients with a recent diagnosis (within the past year) (n = 52)
  - Patients with cardiac involvement (n = 178)

RESULTS

- Study participants varied in terms of demographics and clinical characteristics, such as type of organ involvement, years since diagnosis, and response to treatment. Demographic information and clinical characteristics of the patients surveyed are provided in **Table 1**

Table 1. Demographic and Disease Characteristics of Patients With AL Amyloidosis

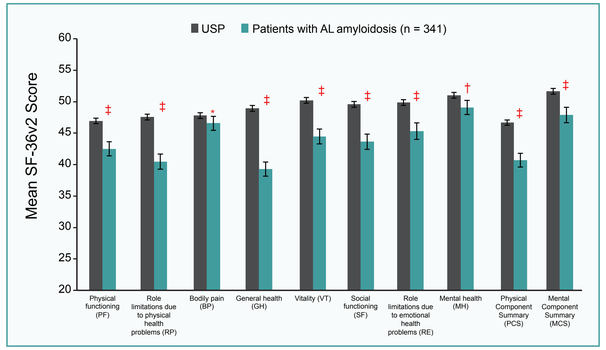
Characteristics	Patients With AL Amyloidosis N = 341	
	n	%
Age, years		
Mean (SD)	60.6 (10.2)	
Range (median)	23–85 (61)	
Gender (n = 340)[a]		
Male	160	47.1
Female	180	52.9
Race/Ethnicity		
White	304	89.1
Other	37	10.9
Education (n = 322)[a]		
≤High school diploma or GED	26	8.1
Some college (<4 years; associate's or technical degree)	99	30.7
Bachelor's degree	109	33.9
Graduate degree	88	27.3
Marital status (n = 330)[a]		
Married	271	82.1
Other	59	17.9
Employment status (n = 300)[a]		
Currently employed	115	38.3
Time since diagnosis		
Mean (SD)	4.5 (4.0) years	
Range (median)	1 month–28 years (3.5 years)	
Organs/systems impacted[b]		
Heart (cardiac)	178	52.2
Kidney	214	62.8
Liver	49	14.4
Nervous system	126	37.0
Gastrointestinal	148	43.4
Other	117	34.3
Number of organs involved		
1	95	27.9
2	89	26.1
≥3	157	46.0
Most recent hematologic response status		
No response to treatment	23	6.7
Partial hematologic response or partial remission	126	37.0
Complete hematologic response or complete remission	141	41.3
Do not know	51	15.0

[a]Frequencies <341 were due to missing data; percentages were based on available data.
[b]Multiple response options were allowed.

Comparison of Patients With AL Amyloidosis and the USP

- Compared with USP norms, patients with AL amyloidosis had significantly worse HRQoL, as demonstrated by their scores from all SF-36v2 domain scales and both PCS and MCS ($P < 0.05$ for all) (**Figure 1**)
- The largest decrement was in GH, where the mean for patients with AL amyloidosis (39.3) was 1 SD worse than for the USP (49.0) (Cohen's *d*, –0.654; $P < 0.001$)
- Large decrements (>0.5 SD in AL amyloidosis patients vs USP) also were seen in RP (40.5 vs 47.6), VT (44.5 vs 50.2), SF (43.6 vs 49.6), and PCS (40.7 vs 46.7)

Figure 1. Mean SF-36v2 scores of patients with AL amyloidosis and of the USP.

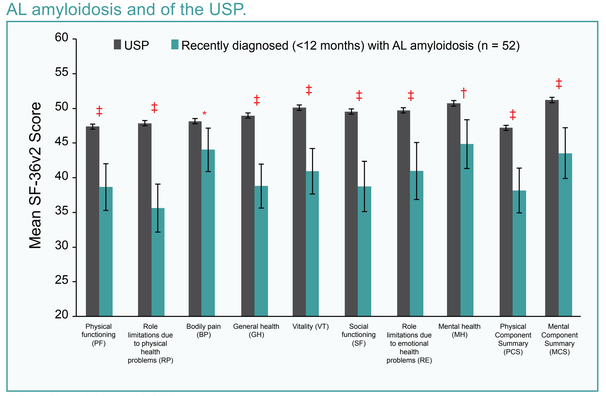


*USP > AL amyloidosis, $P < 0.05$.
†USP > AL amyloidosis, $P < 0.01$.
‡USP > AL amyloidosis, $P < 0.001$.
Note: Error bars indicate 95% confidence intervals. USP adjusted to the age and gender distribution of the patients.
USP sample size varied by scale: PF, n = 4034; RP, n = 4027; BP, n = 4027; GH, n = 4036; VT, n = 4028;
SF, n = 4029; RE, n = 4026; MH, n = 4028; PCS, n = 4024; MCS, n = 4024.

Comparison of Patients With Recently Diagnosed AL Amyloidosis and the USP

- Patients with a recent diagnosis of AL amyloidosis exhibited large decrements in each of the SF-36v2 domain scales and in PCS and MCS ($P < 0.05$ for all) compared with the USP (**Figure 2**)
- Mean scores for all domains except BP were ≥0.5 SD lower in patients with AL amyloidosis than in the USP; 3 domain scores were ≥1 SD lower (RP, GH, SF)

Figure 2. Mean SF-36v2 scores of patients with recently diagnosed AL amyloidosis and of the USP.



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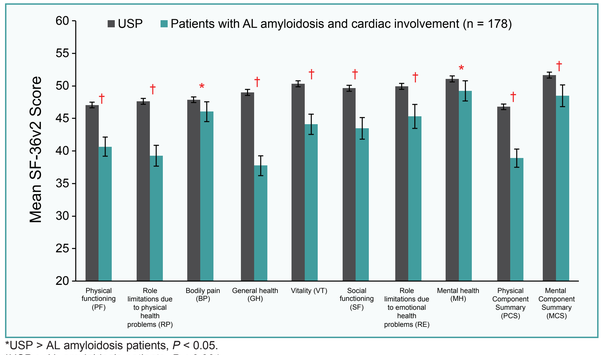
SF, n = 4029; RE, n = 4026; MH, n = 4028; PCS, n = 4024; MCS, n = 4024.

Comparison of Patients With AL Amyloidosis and Cardiac Involvement and the USP

- Compared with the USP, patients who had AL amyloidosis and cardiac involvement also reported large decrements in each of the SF-36v2 domain scales and the PCS and MCS ($P < 0.05$ for all) (**Figure 3**)
- Among patients with AL amyloidosis and cardiac involvement, 5 domain scores and 1 summary measure score (PF, RP, GH, VT, SF, and PCS) were ≥0.5 SD lower than in the USP

Figure 3. Mean SF-36v2 scores of patients with AL amyloidosis and cardiac involvement and of the USP.



*USP > AL amyloidosis patients, $P < 0.05$.
†USP > AL amyloidosis patients, $P < 0.001$.
Note: Error bars indicate 95% confidence intervals. USP adjusted to the age and gender distribution of patients.
USP sample size varied by scale: PF, n = 4034; RP, n = 4027; BP, n = 4027; GH, n = 4036; VT, n = 4028;
SF, n = 4029; RE, n = 4026; MH, n = 4028; PCS, n = 4024; MCS, n = 4024.

CONCLUSIONS

- We present direct evidence regarding how patients with AL amyloidosis feel and function in daily life based on a well-defined and reliable assessment
- The patient sample is broad, representing persons with a range of organ involvement and including both patients with newly diagnosed disease and long-term survivors
- Results from all surveyed patients show noteworthy HRQoL deficits across all areas of physical and mental functioning compared with the USP
  - The extent of impairment was even greater for patients who received diagnoses within the past year and for those with cardiac involvement
- Decrements were statistically significantly worse than those of a matched population norm and exceeded thresholds for clinically meaningful differences
- The largest effects were observed in aspects related to physical functioning and well-being. General health and role limitations related to physical health were among the greatest deficits observed overall and in each key subgroup
- Understanding the burden of AL amyloidosis can help physicians identify ancillary treatments and services that may ease patients' disease burden and ultimately improve their HRQoL

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