Poster #P-101

Burden of AL Amyloidosis and its Association with Cardiac Involvement: Initial Results from a Patient-Reported Outcome Survey

Preeti S. Bajaj;[1] Kaitlin LaGasse;[2] Avery A. Rizio;[2] Gia Huynh;[2] Kristen L. McCausland;[2] Ansgar Conrad;[1] K. Ingrid Sprinz[1]

[1]Prothena Biosciences Inc; [2]QualityMetric, an IQVIA business

INTRODUCTION

- Amyloid light chain (AL) amyloidosis is a rare, progressive, and typically fatal disease in which misfolded light chains form soluble, toxic aggregates and deposit as amyloid in organs[1,2]
  - Amyloid deposits can lead to organ damage, dysfunction, and failure
- AL amyloidosis can affect multiple organs, which contributes to heterogeneity in clinical presentation and patient experience[3]
- Among patients with AL amyloidosis, those with cardiac involvement have an elevated risk of death[1,4,5]

AIM

- To examine the burden of AL amyloidosis in newly diagnosed patients with and without cardiac involvement in a real-world setting

METHODS

- Adults with AL amyloidosis diagnosed in the past 24 months in the United States, the United Kingdom, and Canada were enrolled in a longitudinal, mixed-methods study
  - The study includes an online survey administered at 4 timepoints over 18 months and qualitative interviews with a subset of participants
  - Follow-up data collection is in progress. Results reported here are based on data from the initial online survey timepoint collected in 2022-2023; all data are patient-reported
- Patient-reported outcome (PRO) measures were used to assess disease burden, including:
  - SF-36v2® Health Survey (SF-36v2), a measure of generic health-related quality of life (HRQoL)
  - Kansas City Cardiomyopathy Questionnaire-12 Item Short Form (KCCQ-12), a measure of HRQoL specific to congestive heart failure, administered only to patients with cardiac involvement
  - Work Productivity and Activity Impairment Questionnaire: Specific Health Problem (WPAI), a measure of work and activity impacts attributed to a specific health problem (in this study, AL amyloidosis)
  - Patient Global Impression of Severity (PGI-S), a single-item, 7-point measure of disease severity
- Participants were grouped by self-reported cardiac involvement (yes/no) and number of organs involved (1, 2, ≥3) to examine differences in PRO scores across key clinical subgroups
- Differences in PRO scores were tested using parametric or nonparametric tests based on score distributions
  - For normally distributed scores: independent samples t-tests or one-way analysis of variance (ANOVA)
  - For non-normally distributed scores: Mann-Whitney or Kruskal-Wallis tests

RESULTS

- The analysis sample included 97 participants **(Table 1)**

Table 1. Participant Demographics and Clinical Characteristics (N=97)

Continuous Variables	Median (IQR)	Mean (Range)
Age, years	62 (51-67)	59.4 (28-80)
Time Since Diagnosis, months	11 (6-18)	12.2 (1-24)
Number of Organs Involved	2 (1-3)	2 (1-5)
Categorical Variables	**n (%)**	
Assigned Sex at Birth		
Female	53 (54.6%)	
Male	44 (45.4%)	
Race/Ethnicity[a]		
White or Caucasian	84 (86.6%)	
Black, African, or Caribbean	6 (6.2%)	
Other[b]	5 (5.2%)	
Hispanic, Latino, or of Spanish origin	4 (4.1%)	
Country of Residence		
United States	72 (74.2%)	
United Kingdom	14 (14.4%)	
Canada	11 (11.3%)	
Impacted Organs[a]		
Heart	56 (57.7%)	
Kidney	56 (57.7%)	
Gastrointestinal system	36 (37.1%)	
Other	23 (23.7%)	
Nervous system	19 (19.6%)	
Liver	6 (6.2%)	
Prior or Current Treatment for AL Amyloidosis Reported	90 (92.8%)	
History of Comorbid Multiple Myeloma	26 (26.8%)	

[a]Multiple responses allowed; [b]Includes categories reported by <5% of sample: Asian and American Indian, Alaska Native, or Indigenous.

RESULTS (CONTINUED)

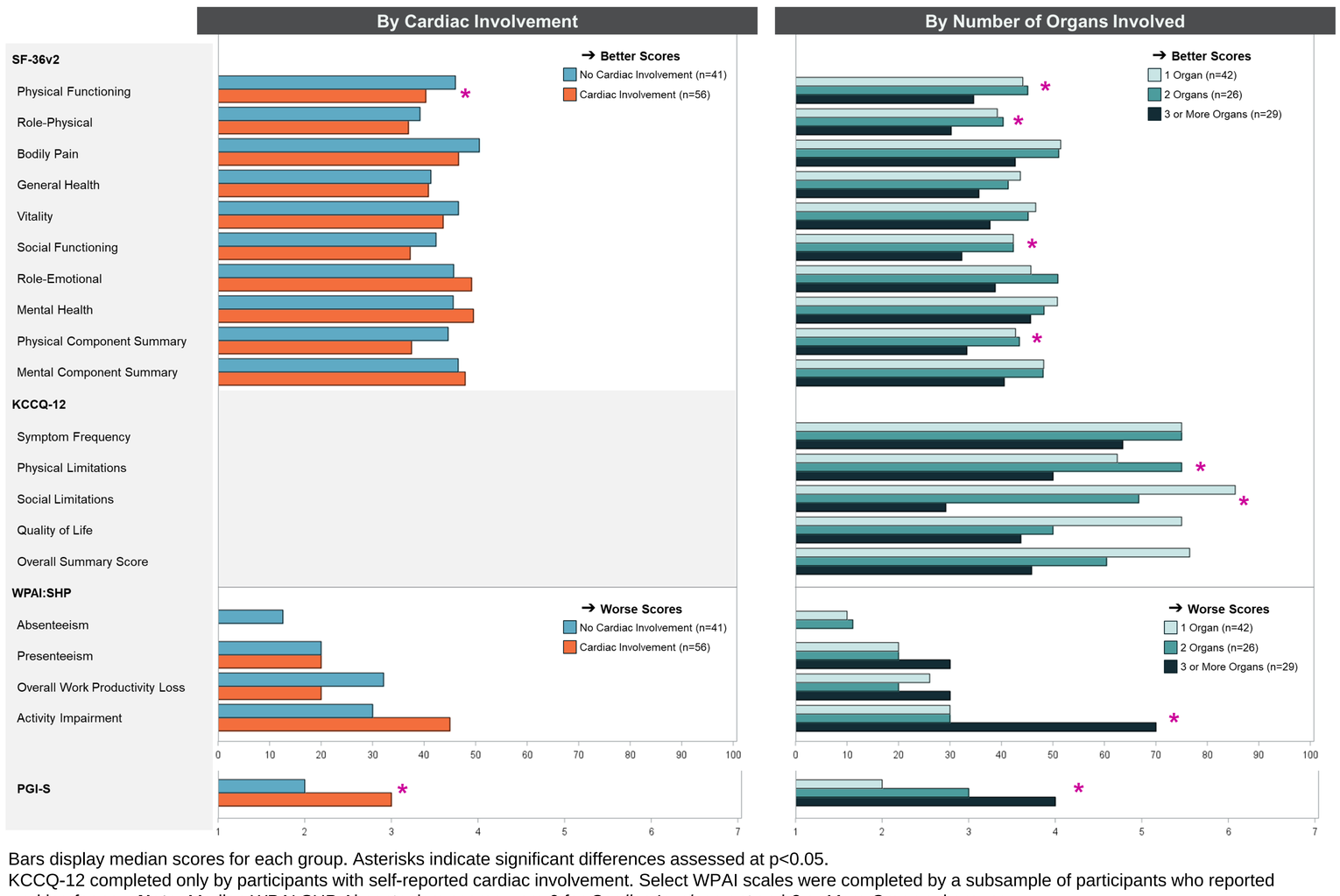
- In the full analysis sample, SF-36v2 and KCCQ-12 scores indicated deficits in HRQoL, especially in physical health and social functioning domains
  - Median SF-36v2 domain and summary scores were all below the general population normative score of 50, exceeding established thresholds for meaningful impairment for all domains except Mental Health
  - Median KCCQ-12 scores reflect "fair to good" health status (in the 50-74 range[6])
- **Figure 1** displays PRO scores stratified by key clinical subgroups
  - Participants with cardiac involvement had significantly worse SF-36v2 Physical Functioning scores and PGI-S scores than those without cardiac involvement
  - Participants with ≥3 organs involved experienced greater burden than those with fewer organs involved in multiple domains

Table 2. PRO Scores for Overall Sample (N=97)

Instrument	Median (IQR)	Mean (SD)
SF-36v2 (N=97) ↑		
Physical Functioning	42.23 (32.66 - 51.80)	41.60 (10.98)
Role-Physical	36.95 (27.96 - 48.17)	37.90 (11.82)
Bodily Pain	46.68 (38.21 - 55.55)	46.42 (10.23)
General Health	41.30 (31.79 - 47.48)	40.21 (9.54)
Vitality	43.69 (34.77 - 52.60)	43.32 (10.82)
Social Functioning	37.29 (27.26 - 47.31)	39.41 (11.93)
Role-Emotional	45.72 (35.28 - 56.17)	44.07 (11.89)
Mental Health	48.25 (40.40 - 56.10)	47.50 (9.97)
Physical Component Summary	41.01 (31.85 - 47.50)	40.19 (10.26)
Mental Component Summary	46.83 (38.40 - 54.99)	45.72 (10.40)
KCCQ-12 (N=56) ↑		
Symptom Frequency	73.96 (50.00 – 87.50)	66.26 (25.36)
Physical Limitations	62.50 (50.00 – 91.67)	62.85 (28.00)
Social Limitations	58.33 (25.00 – 100.0)	57.76 (36.19)
Quality of Life	50.00 (25.00 – 87.50)	52.46 (33.91)
Overall Summary Score	58.33 (38.37 – 89.58)	61.10 (28.07)
PGI-S (N=97) ↓	3.00 (2.00 – 4.00)	2.90 (1.59)
WPAI:SHP ↓		
Absenteeism (N=31)	0.00 (0.00 – 30.00)	20.84 (31.13)
Presenteeism (N=29)	20.00 (10.00 – 40.00)	27.93 (26.64)
Overall Work Productivity Loss (N=29)	20.00 (10.00 – 63.64)	35.77 (31.63)
Activity Impairment (N=97)	40.00 (20.00 – 70.00)	42.68 (30.29)

Arrows indicate direction of better scores. KCCQ-12 completed only by participants with cardiac involvement. Select WPAI scales were completed by a subsample of participants working for pay. **Possible score ranges:** SF-36v2 (Physical Functioning [19.26-57.54], Role-Physical [21.23-57.16], Bodily Pain [21.68-62.00], General Health [18.95-66.50], Vitality [22.89-70.42], Social Functioning [17.23-57.34], Role-Emotional [14.39-56.17], Mental Health [11.63-63.95], Physical Component Summary [5.02-79.78], Mental Component Summary [-3.33-80.09]); KCCQ-12 (0-100); PGI-S (1-7); WPAI: SHP (0-100).

Figure 1. Median PRO Scores by Cardiac Involvement and Number of Organs Involved



Bars display median scores for each group. Asterisks indicate significant differences assessed at $p<0.05$.
KCCQ-12 completed only by participants with self-reported cardiac involvement. Select WPAI scales were completed by a subsample of participants who reported working for pay. **Note:** Median WPAI:SHP Absenteeism scores were 0 for *Cardiac Involvement* and *3 or More Organ* subgroups.

CONCLUSIONS

- Participants with newly diagnosed AL amyloidosis reported significant disease burden related to symptom severity and HRQoL impacts; these observations align with prior research on HRQoL burden in AL amyloidosis[7,8]
- Participants with cardiac involvement and a greater number of organs involved experienced additional burden in symptom severity and HRQoL, including work impacts, despite prior or current treatment for AL amyloidosis
- Results demonstrate the need for better therapeutic options in these key clinical subgroups
- Limitations of this research include reliance on only patient-reported information for organ involvement, potential for selection bias in recruitment, and limited sample size within some subgroups
- Analyses of longitudinal survey data and integration with qualitative interview data may provide additional insights on the burden of AL amyloidosis

REFERENCES

1. Sanchorawala V. *N Engl J Med.* 2024;390(24):2295-2307. **2.** Merlini G, et al. *J Clin Oncol.* 2011;29(14):1924-1933. **3.** Mahmood S, et al. *Haematologica*. 2014;99(2):209-221. **4.** Staron A, et al. *Blood Cancer J.* 2021;11:139. **5.** Barrett CD, et al. *JACC Heart Fail.* 2019;7:958-66. **6.** Spertus JA, et al. *J Am Coll Cardiol*. 2020;76(20):2379-2390. **7.** Bayliss M, et al. *Orphanet J Rare Dis*. 2017;12(1):15. **8.** Sanchorawala V, et al. *Br J Haematol.* 2017;179(3):461-470.

AUTHOR DISCLOSURES

PSB, AC, and IS are employees of Prothena Biosciences Inc and shareholders of Prothena Corporation plc. KML, AAR, GH, and KLM are employees of QualityMetric, which received funding from Prothena Biosciences Inc to conduct this research.

ACKNOWLEDGMENTS

This study was sponsored by Prothena Biosciences Limited, Dublin, Ireland, a member of the Prothena Corporation plc group. We would like to thank the patients who participated in this study.

Presented at 21st International Myeloma Society Annual Meeting