

Predictors of Burden in Caregivers to Patients With Untreated Transthyretin Amyloid Cardiomyopathy

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INTRODUCTION

- A recent real-world survey study evaluated the multidimensional burden of transthyretin amyloid cardiomyopathy (ATTR-CM) in 208 pairs of patients treated with symptomatic but not disease-modifying therapy and their unpaid primary caregivers, recruited from amyloidosis centers of excellence in 7 countries.¹
- The study found untreated ATTR-CM was a mental and physical burden on both patients and their caregivers. This burden was higher for both groups when patients had more symptomatic heart failure.¹
- Identifying predictors of ATTR-CM burden could help improve the approach to treatment for patients and better inform ways to support their caregivers.
- The aim of this post hoc analysis was to evaluate items from the recent international survey study as predictors of burden in caregivers to patients with ATTR-CM.

METHODS

- The original international survey study took place between July 2021 and August 2022.¹
- This post hoc analysis used univariate and multivariate analyses to evaluate selected study items as predictors of caregiver burden, as measured by their Zarit Burden Interview (ZBI) score (**Figure 1**).
 - Univariate associations were confirmed with a *t*-test, linear or ordinal logistic regression, and Pearson correlation coefficient, as appropriate.
 - The full multivariate models included all variables and were then optimized using forward selection and CV Press criteria with 8-fold cross-validation to identify the best predictors.
- Hierarchical linear regression analyses were used to explore potential moderators on the relationship identified between the patient's Kansas City Cardiomyopathy Questionnaire–Overall Summary (KCCQ-OS) score and the caregiver's continuous ZBI score. Evaluated moderators are shown in **Table 1**.
 - A significant moderator was defined as a variable where:
 - the interaction term showed a statistically significant relationship with the caregiver's ZBI score, and
 - there was a clinically significant change in the regression coefficient when the covariate was included in the model.

Table 1: Evaluated moderators

Patient's variables	Caregiver's variables
- HADS-A and HADS-D scores - PROMIS Fatigue score - SF-12 PCS and MCS scores - NYHA functional class - Severity of specific symptoms over the last 7 days (rated 0–10 with increasing severity) - Presence of specific symptoms associated with ATTR-CM	- Age - Relationship to patient - Sex - Hours per week spent with patient - Number of years providing care - If they live with the patient - HADS-A and HADS-D scores - PROMIS Fatigue score - SF-12 PCS and MCS scores - Whether the patient needs help with a range of daily activities

ATTR-CM=transthyretin amyloid cardiomyopathy; HADS-A=Hospital Anxiety and Depression Scale Anxiety subscale; HADS-D=Hospital Anxiety and Depression Scale Depression subscale; NYHA=New York Heart Association; PROMIS=Patient-Reported Outcomes Measurement Information System; SF-12 PCS/MCS=12-item Short Form Health Survey Physical Component Summary/Mental Component Summary

Figure 1: Items evaluated and outcome measures

Evaluated items		Outcome measures of burden
Demographics	All items were included in each outcome model	
	Relationship to the patient - spouse or other	Caregiver's ZBI score - continuous
	Sex - female or male	Caregiver's ZBI categorical score - 0–20 (little to no burden) or 21–60 (mild to moderate burden)
Caregiving duration	Caregiver and patient live together - yes or no	
	Hours per week that the caregiver spends with the patient - continuous	
	Number of years that the caregiver has provided care - continuous	
Patient's clinical characteristics	Patient's NYHA functional class - I or II or III	
	Patient's KCCQ-OS score - continuous	
	Patient's HADS-A score - continuous	
	Patient's HADS-D score - continuous	

HADS-A=Hospital Anxiety and Depression Scale Anxiety subscale; HADS-D=Hospital Anxiety and Depression Scale Depression subscale; KCCQ-OS=Kansas City Cardiomyopathy Questionnaire–Overall Summary; NYHA=New York Heart Association; ZBI=Zarit Burden Interview

RESULTS

Caregivers and Patients

- Paired data for 208 patients and 208 caregivers were included in the analysis.
- Most caregivers in the original study were female (85%) and the spouse (59%) of the patient, with a median ZBI score of 13 (**Table 2**).
- Most patients were male (86%) and elderly (median age 81 years), with symptomatic heart failure (**Table 3**). Nearly all patients (91%) with genotyping data had wild-type transthyretin. Patients' median KCCQ-OS score was 68, and Hospital Anxiety and Depression Scale subscale (HADS) scores were <8.

Univariate Models

- In the unadjusted univariate models, the patient's New York Heart Association (NYHA) class, KCCQ-OS, and HADS subscores were significantly ($P<0.05$) and independently associated with caregiver's continuous or categorical ZBI scores.

Full Multivariate and Optimized Models

- In the full multivariate models, the patient's KCCQ-OS score was the only significant ($P<0.05$) predictor of the caregiver's ZBI score.
- The final optimized models included only the patient's KCCQ-OS score as a predictor of the caregiver's continuous (regression coefficient: -0.26 [95% CI: -0.33 , -0.20]) and categorical (odds ratio for no burden vs mild to moderate burden: 0.96 [95% CI: 0.94, 0.97]) ZBI score (**Figure 2**).

Moderators

- None of the evaluated variables had a statistically and clinically significant moderator effect on the relationship identified between the patient's KCCQ-OS score and the caregiver's continuous ZBI score.

Table 2: Key caregiver characteristics¹

	All caregivers N=208
Age, y	
Mean (SD)	66 (12.2)
Median (min, max)	68 (32, 88)
Sex, n (%)	
Male	32 (15.4)
Female	176 (84.6)
Relationship to the patient, n (%)	
Spouse	122 (58.7)
Adult child	77 (37.0)
Parent	2 (1.0)
Sibling	1 (0.5)
Other	6 (2.9)
Caregiver and patient live in the same house, n (%)	138 (66.3)
No. hours caregiver and patient spend together in a week, median (IQR) [n=196]	71 (14.0–168.0)
No. years caregiver has provided care to patient, median (IQR) [n=166]	1.5 (0.0–3.0)
ZBI score	
Median (IQR)	13 (3.0–24.0)
Categorical burden by score, n (%)	
Little or none (0–20)	134 (64.4)
Mild to moderate (21–40)	63 (30.3)
Moderate to severe (41–60)	11 (5.3)
Severe (61–88)	0

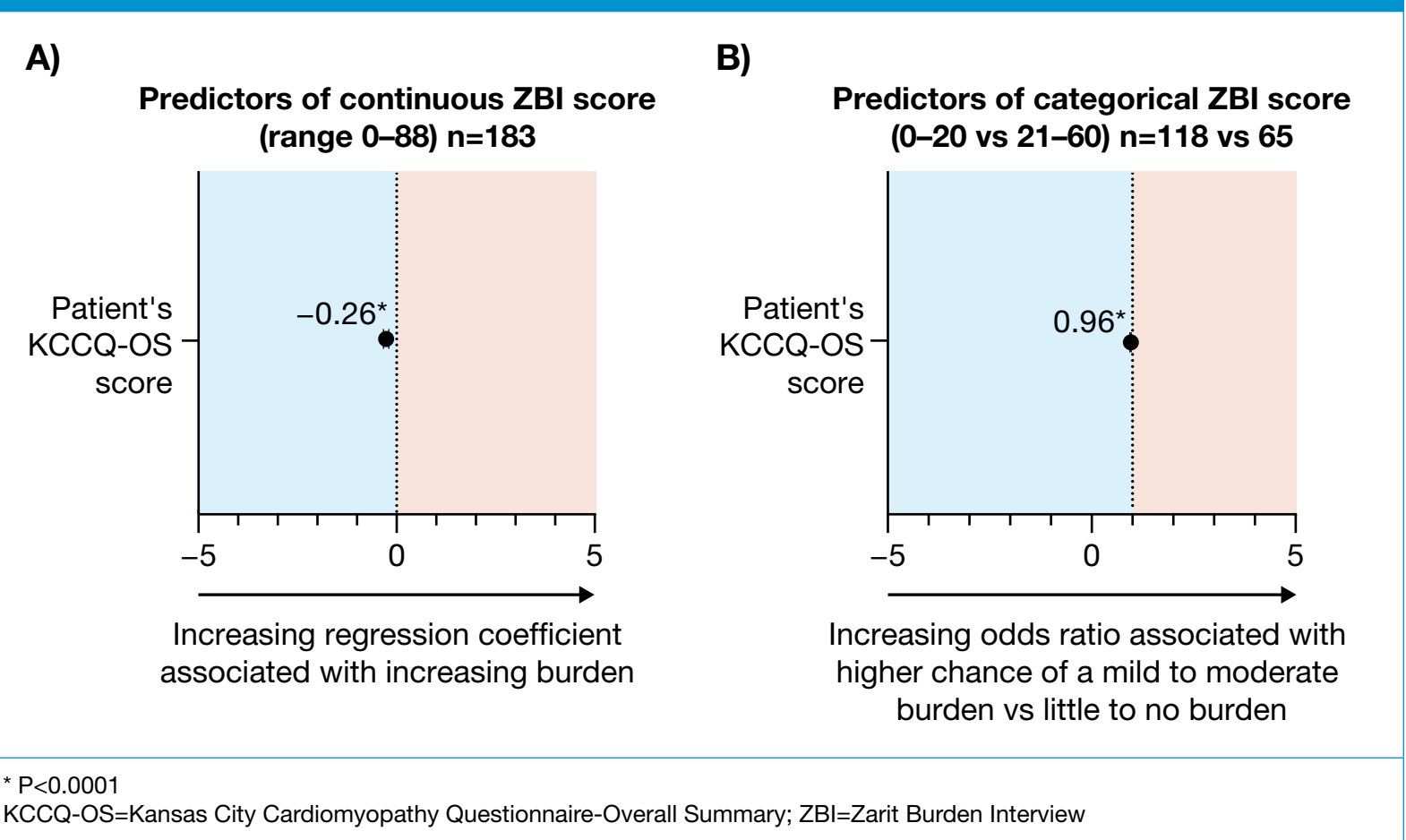
IQR=interquartile range; min, max=minimum, maximum; ZBI=Zarit Burden Interview

Table 3: Key patient characteristics¹

	All caregivers N=208
Age, y	
Mean (SD)	80 (7.0)
Median (min, max)	81 (46, 90)
Sex, n (%)	
Male	179 (86.1)
Female	29 (13.9)
<i>Transthyretin</i> genotype, n (%) [n=155]	
Wild-type	141 (91.0)
Variant	14 (9.0)
NYHA functional class, n (%) [n=199]	
I	36 (18.1)
II	120 (60.3)
III	43 (21.6)
IV	0
KCCQ-OS score, median (IQR) [n=183]	68 (46.4–84.4)
HADS score, median (IQR)	
HADS-A [n=205]	5 (3.0–8.0)
HADS-D [n=204]	6 (3.0–10.0)

HADS-A=Hospital and Depression Scale Anxiety subscale; HADS-D=Hospital Anxiety and Depression Scale Depression subscale; IQR=interquartile range; KCCQ-OS=Kansas City Cardiomyopathy Questionnaire–Overall Summary; min, max=minimum, maximum; NYHA=New York Heart Association

Figure 2: Items evaluated and outcome measures



CONCLUSIONS

- A higher caregiver burden was best predicted by poorer health status in the patient, even in the presence of potential moderators.
- Strategies that reduce a patient's symptoms and improve their health status may help reduce their burden and that experienced by their primary caregiver.

REFERENCE

- Ponti L, et al. Front Cardiovasc Med 2023;10:1238843.

DISCLOSURES

LP and KH: Nothing to disclose. **TD:** Consulting fees from Alnylam, GlaxoSmithKline, Pfizer, and Prothena; honoraria from Alnylam, Pfizer, and Prothena; research grants from GlaxoSmithKline and Pfizer; and clinical trial support from Alnylam, Ionis, and Pfizer. **EV:** His institution has received an unconditional research grant from Pfizer. **NV:** Research grant, honoraria for advisory board participation, and speaker's fees from Pfizer. **DK, RW, MI, NK, and CM:** Employees of Pfizer and hold stock/stock options. **FC:** Honoraria for advisory board participation from Pfizer, Alnylam, Novo Nordisk, and Akcea; his institution has received an unconditional research grant from Pfizer.

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