Health Related Quality of Life among Patients with Transthyretin Amyloidosis: A Systematic Literature Review

ANTHOLOGY
transforming ATTR care through practice-changing evidence

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Diego Delgado[1]; Nitin Shivappa[2]; Firas Dabbous[3]; Divya Shridharmurthy[3]; Eric Wittbrodt[2]; Krister Järbrink[4]

[1]Division of Cardiology and Transplant, UHN, Toronto, ON, Canada, [2]Cardiovascular, Renal and Metabolism (CVRM) Evidence, BioPharmaceuticals Medical, AstraZeneca, Wilmington, DE, USA, [3]Data Analytics, Real World Evidence, Evidera, IL, USA, [4]Cardiovascular, Renal and Metabolism (CVRM) Evidence, BioPharmaceuticals Medical, AstraZeneca, Gothenburg, Sweden

Background

- Amyloid transthyretin (ATTR) amyloidosis is a rare, progressive disease characterized by the abnormal buildup of amyloid deposits composed of misfolded transthyretin protein in the body's organs and tissues.
- ATTR-PN (polyneuropathy) and ATTR-CM (cardiomyopathy) are two most common types with distinct clinical symptoms, each further categorized into hereditary (ATTRv) and wild forms (ATTRwt).
- If left untreated or mismanaged, ATTR amyloidosis imposes a significant impact on patient survival and health-related quality of life (HRQoL). Timely diagnosis and treatment can extend mean life expectancy considerably; therefore, early identification, diagnosis, and timely treatment are critical.

Objectives

The aims of this systematic literature review (SLR) were:

- To identify instruments used to measure HRQoL among ATTR amyloidosis patients
- To summarize the HRQoL in ATTR amyloidosis patients overall and by phenotype

Methods

- Searches were conducted in Medline and Embase for studies published between 01/2018 and 04/2023.
- Two reviewers screened titles and abstracts; a third resolved discrepancies. Similar process was followed for full-text assessment.
- Two reviewers extracted data independently, validated by a third reviewer. Disagreements were settled through discussion.
- Eligible studies were observational, longitudinal or database/registry studies, SLRs, or meta-analyses conducted on patients with ATTR amyloidosis with reported outcomes on HRQoL, clinical trials on ATTR amyloidosis treatments were excluded.

Results

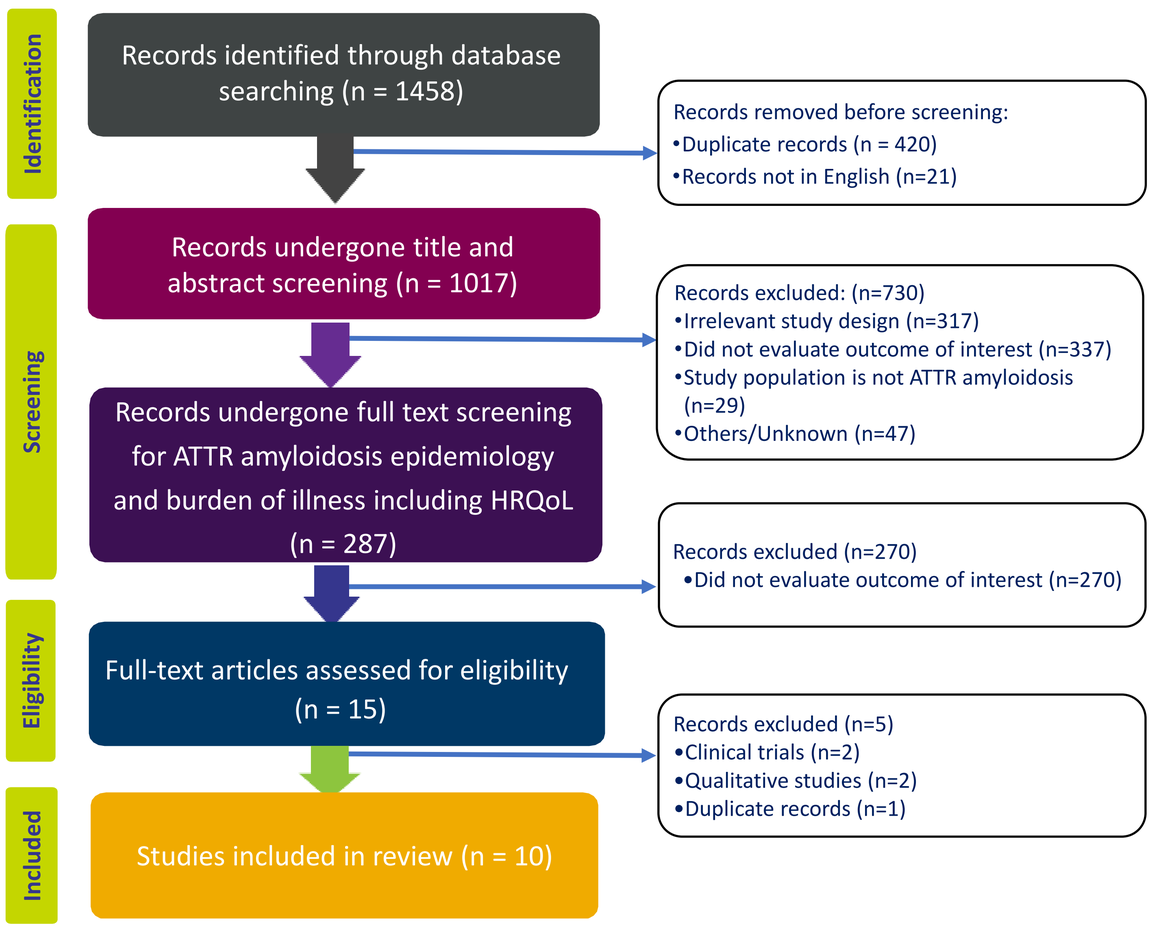

Figure 1. PRISMA diagram outlining the identification of studies included

This study was part of a broader SLR that aimed to summarize the evidence on the epidemiology, and burden of illness of ATTR amyloidosis. Therefore, we initially included 1458 studies and screened 1017 abstracts.

Phenotype specific HrQoL instruments

- The Norfolk Quality of Life-Diabetic Neuropathy (Norfolk QoL-DN) questionnaire (total score range -4 to 136, with higher scores indicating worse QoL) was the most broadly used instrument (n=6). The mean total score among patients with ATTR-PN ranged from 23.4 to 74.1.
- The Kansas City Cardiomyopathy Questionnaire (KCCQ) (overall summary score range 0 to 100, with higher scores indicating better health) was most widely used (n=3) among patients with ATTR-CM. The overall summary score ranged between 43 and 58.

Generic health state instruments

- One study used SF-12 V2 and reported a physical health component summary score (range 0 to 100, with higher scores indicating better health) of 23.4 for all patients with ATTR amyloidosis. The SF-12 summary scores are normalized to have a mean of 50 and a standard deviation of 10 in the general US population.
- The HRQoL, as assessed by the EuroQol-5Dimensions-3Levels (EQ-5D-3L) index score (range 0 to 1) derived from the five items of the EQ-5D-3L questionnaire ranged from 0.66 to 0.83 in two studies. The US population norm for the EQ-5D-3L index score (median) is 0.94.

Table 1. HRQoL by type of ATTR amyloidosis and instrument

Author, year	Population	Patient reported outcome measure	Descriptive statistic reported	Score	Time of assessment
Zadok & Kornowski. 2023	ATTRwt-CM, ATTRv-CM	KCCQ-OSS	Median (IQR) [n]	40 (22, 86) [16]	At tafamidis initiation among diagnosed
Lane et al. 2019	ATTRwt-CM	KCCQ-OSS	Mean (CI) [n]	58 (53–62) [158]	At 12 months from diagnosis
	V122I-ATTRv-CM	KCCQ-OSS	Mean (CI) [n]	55 (45–55) [158]	At 12 months from diagnosis
	Non-V122I-ATTRv-CM	KCCQ-OSS	Mean (CI) [n]	56 (40–72) [158]	At 12 months from diagnosis
Ishii et al. 2020	ATTRv-PN	Norfolk QoL-DN total score[Ŧ]	Mean (SD) [n]	53.3 (37.0) [81]	At tafamidis initiation among those diagnosed
Reines et al. 2021	ATTRv-PN	Norfolk QoL-DN total score	Mean (min-max) [n]	46.6 (-0.5 - 123) [19]	Within 12 months of diagnosis
Bolte et al. 2020	ATTRv-PN	WHODAS 2.0 disability score	Median (IQR) [n]	16 (8–41) [38]	At study enrollment among diagnosed
Mundayat et al. 2018	ATTRv-PN	Norfolk QoL-DN total score	Mean (SD) [n]	23.4 (23.7) [252]	At tafamidis initiation among diagnosed
Dispenzieri et al. 2022	ATTRv-PN ATTRwt-PN	Norfolk QoL-DN total score	Mean (SD) [n]	33.3 (29.2) [2472]	At study enrollment among diagnosed
		EQ-5D-3L EQ-VAS	Mean (SD) [n] Mean (SD) [n]	0.7 (0.2) [2461] 65.2 (20.5) [2423]	
	ATTRwt-PN	Norfolk QoL-DN total score	Mean (SD) [n]	23.9 (20.9) [742]	
		EQ-5D-3L EQ-VAS	Mean (SD) [n] Mean (SD) [n]	0.8 (0.2) [753] 65.5 (19.3) [743]	
Luigetti et al. 2022	ATTRv-PN, Mixed ATTR-PN	Norfolk QoL-DN total score	Mean (SD) [n]	74.1 (29.5) (23)	At inotersen initiation among diagnosed
Valle et al., 2021	ATTRv carriers	Norfolk QoL-DN total score	Mean (min-max) [n]	6.9 (12 - 46) [86]	At study enrollment among diagnosed
Stewart et al. 2018*	ATTR-CM	KCCQ-OSS	Mean (SD) [n]	35.4 (16.5) [11]	At study enrollment among diagnosed
		EQ-5D-3L EQ-VAS	Mean (SD) [n] Mean (SD) [n]	0.83 (0.2) [6] 63.2 (12.7) [6]	
		SF-12v2 PCS-12	Mean (SD) [n]	32.0 (9.5) [6]	
		SF-12v2 MCS-12	Mean (SD) [n]	54.2 (8.6) [6]	
	ATTR-PN	KCCQ-OSS	Mean (SD) [n]	57.4 (18.9) [6]	
		EQ-5D-3L EQ-VAS	Mean (SD) [n] Mean (SD) [n]	0.71 (0.2) [27] 59.6 (20.7) [27]	
		SF-12v2 PCS-12	Mean (SD) [n]	34.4 (11.7) [27]	
		SF-12v2 MCS-12)	Mean (SD) [n]	45.8 (10.1) [27]	
	Both ATTR-CM and ATTR-PN	KCCQ-OSS	Mean (SD) [n]	43.2 (20.0) [17]	
		EQ-5D-3L EQ-VAS	Mean (SD) [n] Mean (SD) [n]	0.66 (0.2) [11] 46.2 (19.8) [11]	
		SF-12v2 PCS-12	Mean (SD) [n]	23.4 (7.3) [11]	
		SF-12v2 MCS-12	Mean (SD) [n]	47.2 (11.2) [11]	
	ATTR-CM, ATTR-PN and both	Norfolk QoL-DN total score	Mean (SD) [n]	61.8 (30.5) [44]	

*Data reported for patients in the US only.
[Ŧ]Instrument not specified in article and to be confirmed by author.
KCCQ= Kansas City Cardiomyopathy questionnaire, Norfolk QoL-DN= Norfolk Quality of Life- Diabetic Neuropathy questionnaire, WHODAS 2.0= World Health Organization Disability Assessment Schedule 2.0, SF-12v2= 12-Item Short Form Health Survey, version 2, EQ-5D-3L= EuroQoL-5 Dimensions-3 Levels questionnaire

Discussion

- Overall summary scores for disease-specific and generic health instruments indicated substantial burden of illness in people with ATTR amyloidosis.
- As treatments for ATTR amyloidosis have become widely available, ATTR amyloidosis has gained increased attention and sparked newfound hope in patients who previously had limited therapeutic options.
- Thus, it is essential that healthcare providers and payers can make informed decisions when prioritizing options both within and beyond the ATTR amyloidosis therapeutic area.
- Given that ATTR amyloidosis is a fatal disease, it is imperative that treatments remain accessible and should not be compromised due to challenges in prioritizing between therapeutic areas.
- There is an imminent need to gain additional understanding on how HRQoL is best captured to inform healthcare providers and other stakeholders.

Conclusions

- Presently, the usage of available instruments to assess HRQoL in patients with ATTR amyloidosis is highly limited and often restricted to specific subgroups.
- Given the broad manifestations of the disease and increased recognition of patients with mixed symptoms, there is a need for better understanding of available instruments' capability to capture the impact of ATTR amyloidosis on patients' HRQoL and enable an informed prioritization.

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