Burden of Transthyretin Amyloid Cardiomyopathy in Treatment-Naïve Patients by Heart Failure Severity: Results From a Large, Non-Interventional, Real-World Study

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INTRODUCTION

- Transthyretin amyloid cardiomyopathy (ATTR-CM) is a progressive condition that leads to heart failure.[1]
- Initial studies have suggested that patients with transthyretin amyloidosis experience a multidimensional burden; however, most have focused on patients with the variant form of the disease, which can have a predominantly neurologic phenotype. Few studies have specifically evaluated burden in patients with ATTR-CM.[2-12]
- This multicenter, international, real-world survey study aimed to comprehensively evaluate the burden of ATTR-CM in patients naïve to disease-modifying treatment. It further aimed to explore this burden in patients with different severities of heart failure.[13]

METHODS

- This large, cross-sectional, noninterventional study recruited patients (aged 18–89 years) with diagnosed ATTR-CM and untreated with disease-modifying therapy from international amyloidosis centers of excellence and referral centers between July 2021 and August 2022.[13]
  - Symptomatic standard of care therapy was permitted, but patients must not have had a heart or liver transplant, a left ventricular mechanical assist device, or have a diagnosis of immunoglobulin light chain amyloidosis.
- Patients completed surveys on various aspects of disease burden, including on symptom intensity during the last 7 days (0–10, where higher indicates increasing intensity), their ability to walk, and the impact of ATTR-CM on their daily living. Patients also completed several established patient-reported outcome surveys (**Table 1**).

Table 1: Patient-reported outcome surveys

Survey	Measure of	Scoring
23-item Kansas City Cardiomyopathy Questionnaire (**KCCQ**)	Health status	KCCQ Overall Summary (**KCCQ-OS**), Total Symptoms (**KCCQ-TS**), and Clinical Summary (**KCCQ-CS**) scores were each transformed on to a 0 to 100 scale. Higher scores indicate better health status, less symptom burden, and less symptom-related physical limitation, respectively, in the past 2 weeks. KCCQ scores were interpreted as 0 to 24 = poor; 25 to 49 = fair; 50 to 74 = good; and 75 to 100 = excellent.[14,15]
12-Item Short Form Health Survey (**SF-12**)	Health status	Responses inform the physical (**PCS**) and mental component summary (**MCS**) scores, each with a range of 0 to 100. Higher scores indicate better health status. Median scores for patients aged ≥75 y are PCS 39 (25th percentile: 29, 75th percentile: 48) and MCS 54 (40, 59).[16]
Hospital Anxiety and Depression Scale (**HADS**)	Symptoms of anxiety and depression	Responses inform the anxiety (**HADS-A**) and depression (**HADS-D**) subscale scores. Subscale scores range from 0 to 21, where higher scores indicate more severe symptoms. A score ≥8 was considered to potentially represent clinically relevant anxiety or depression.[17]

- The recruiting investigator provided information from the patient's medical record on their age, sex, transthyretin genotype, time since diagnosis, current symptoms (yes/no to a list), New York Heart Association (NYHA) functional classification, and left ventricular ejection fraction.
- Findings were summarized descriptively for the overall patient population and by NYHA class (I/II or III; no patients were NYHA class IV). No statistical analyses were performed.

RESULTS

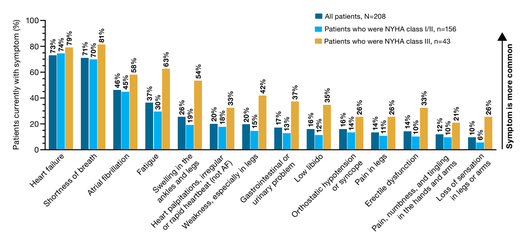
- 208 patients in Europe, Australia, Canada, and Russia were recruited to the study and provided responses.
- Patients had a median age of 81 years and 86% were male. The population was relatively newly diagnosed and 91% of the patients with genetic testing data had wild-type ATTR-CM.
  - Overall, 78% of patients with NYHA classifications had class I/II heart failure and 22% had class III heart failure (**Table 2**).
- Patients experienced transthyretin amyloidosis symptoms affecting multiple systems (**Figure 1**).
  - The numerical proportion of patients experiencing each symptom was higher among patients who were NYHA class III vs I/II.
- Patients reported that the neurologic symptoms of tingling, numbness or pain in the limbs, and muscle weakness, had the highest median intensities (3/10) over the last 7 days (**Figure 2**).
  - The median severity of many symptoms was numerically higher in patients who were NYHA class III vs I/II.

Table 2: Demographics and clinical characteristics

	Patients N=208	Patients who were NYHA class I/II n=156	Patients who were NYHA class III n=43
Age, median (min, max), y	81.0 (46, 90)	81.0 (46, 90)	81.0 (47, 90)
Sex, n (%)			
Male	179 (86)	136 (87)	34 (79)
Female	29 (14)	20 (13)	9 (21)
Years since diagnosis, median (IQR)	0.5 (0.1–1.3)[a]	0.5 (0.1–1.3)[b]	0.3 (0.1–1.2)
Type of ATTR-CM, n (%)	n=155 with data	n=119 with data	n=29 with data
Wild-type	141 (91)	109 (92)	25 (86)
Variant	14 (9)	10 (8)	4 (14)
NYHA class, n (%)	n=199 with data	n=156 with data	n=43 with data
I	36 (18)	36 (23)	0
II	120 (60)	120 (77)	0
III	43 (22)	0	43 (100)
IV	0	0	0
Left ventricular ejection fraction, n (%)	n=197 with data	n=149 with data	n=42 with data
≥55%	103 (52)	80 (54)	20 (48)
40% to 54%	77 (39)	56 (38)	18 (43)
≤39%	17 (9)	13 (9)	4 (10)

[a]n=207; [b]n=155.
ATTR-CM=transthyretin amyloid cardiomyopathy; IQR=interquartile range; NYHA=New York Heart Association

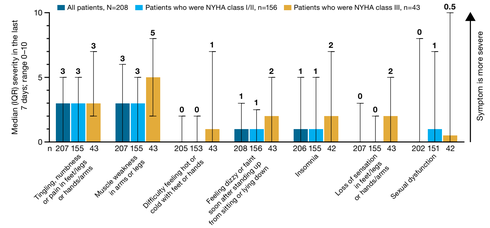
Figure 1: Current symptoms



Nine patients did not have a recorded NYHA classification and are not included in the subgroups. Current symptoms reported in ≥20% of patients in any group are shown.
AF=atrial fibrillation; NYHA=New York Heart Association

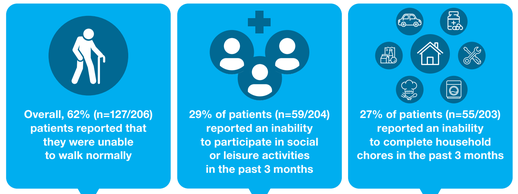
- 62% of patients were unable to walk normally due to ATTR-CM (**Figure 3**). Disease symptoms prevented some patients from completing their daily tasks.
  - The proportion of patients unable to walk normally or who had been unable to complete their daily tasks was higher among those who were NYHA class III vs I/II.
- Median KCCQ-OS, -TS, and -CS scores in the overall patient population suggested a good health status among patients with ATTR-CM (**Figure 4**).
  - Patients who were NYHA class III had numerically lower KCCQ scores than patients who were NYHA class I/II, suggesting a poorer health status, a higher burden of symptoms, and more symptom-related physical limitations.
- Median SF-12 scores in the overall patient population were marginally lower than expected for people of a similar age in the general population (**Figure 5**).
  - Both PCS and MCS scores were numerically lower in patients who were NYHA class III vs I/II.
- The HADS-A and HADS-D scores, respectively, were 5 and 6 in all patients (n=205 and n=204).
  - Among patients who were NYHA class III, 67% (n=29/43) had clinically relevant HADS-D score (≥8). This proportion was 32% (n=49/152) in patients who were NYHA class I/II.

Figure 2: Symptom severity



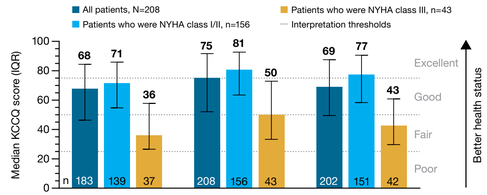
Median is annotated on the top of each bar. The whiskers show the IQR. Shows symptoms with a severity ≥1 in any group. Some groups have a median of 0.
Nine patients did not have a recorded NYHA classification and are not included in the subgroups.
IQR=interquartile range; NYHA=New York Heart Association

Figure 3: Limitation on daily activities



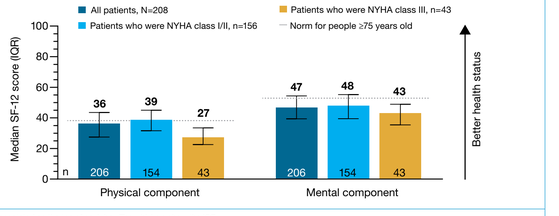
NYHA=New York Heart Association

Figure 4: KCCQ scores



Median is annotated on the top of each bar. The whiskers show the IQR.
Nine patients did not have a recorded NYHA classification and are not included in the subgroups.
IQR=interquartile range; KCCQ-CS/OS/TS=Kansas City Cardiomyopathy Questionnaire Clinical Summary/Overall Summary/Total Symptoms; NYHA=New York Heart Association

Figure 5: SF-12 scores



Median is annotated on the top of each bar. The whiskers show the IQR.
Nine patients did not have a recorded NYHA classification and are not included in the subgroups.
IQR=interquartile range; NYHA=New York Heart Association; SF-12=12-item Short Form Health Survey

Limitations

- Interpretation of the findings is based on observed numerical differences, and should not be extrapolated outside the patient population surveyed, which mainly comprised patients with untreated and relatively newly diagnosed wild-type ATTR-CM.

CONCLUSIONS

- This large, multinational, real-world study demonstrated that untreated ATTR-CM is a burden to patients. Most aspects of burden appeared to be higher in patients with more symptomatic heart failure.[13]
- An array of symptoms were common and often bothersome in patients with ATTR-CM. Patients frequently reported restricted mobility and difficulty undertaking social and household activities.
- Our findings are consistent with the previously published association between higher NYHA classification and lower KCCQ-OS score in patients with heart failure.[14, 18, 19]
- In patients who were NYHA class I/II, KCCQ scores were consistent with previous findings in patients with heart failure, and SF-12 findings also included an age-expected decline in physicality.[10-12, 14-15] Patients who were NYHA class III reported lower-than-expected mental and physical health for their age.[10,15]

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DISCLOSURES

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