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Quality of Life of Patients with Variant and Wild-Type Transthyretin Amyloidosis

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INTRODUCTION / OBJECTIVES

- Transthyretin amyloidosis (ATTR) is a fatal disease caused by the misfolding of the protein, transthyretin (TTR).
- ATTR amyloidosis can be caused by more than 130 genetic mutations (ATTRv) or age-related (ATTRwt). The most commonly occurring variant in the United States is in the Val122Ile (p.Val142Ile) gene, which is estimated to be carried in 3-4% of African-Americans.
- ATTRwt is more common in older white males and most commonly presents in the heart as cardiomyopathy (CM).
- ATTRv can present as either predominately CM or peripheral neuropathy (PN) or a mixed phenotype.
- Prior studies have shown a high burden of disease in ATTR amyloidosis patients, but the majority of those studies were done before the availability of disease-targeting therapies (2011 for PN in Europe; 2018 for PN and 2019 for CM in the US).
- This study examined ATTR-related quality of life (QOL) among patients with ATTRv and ATTRwt in the setting of advanced diagnostics and new therapies.

MATERIAL / METHODS

- The Amyloidosis Research Consortium (ARC) conducted a multi-country online survey of patients with ATTR amyloidosis in 2023.
- Survey measures included demographics, disease characteristics, and the Transthyretin Amyloidosis Quality of Life (ATTR-QOL) questionnaire.
- The ATTR-QOL measures the symptoms and impact of ATTR amyloidosis health-related quality of life. Concepts measured include symptom frequency and severity, as well as impacts on daily activities, social/role functioning, emotional wellbeing, and physical functioning. Both modules have a 4-week recall period. Scores range from 0-100; a higher score indicates greater impact.
- Differences by genotype were evaluated with t-tests.

RESULTS

- Of the 309 ATTR amyloidosis respondents included in this analysis, the majority (n=220 [71%]) had ATTRwt. Of the 89 ATTRv patients, 37 had the Thr60Ala (T60A) TTR mutation, 34 had the Val30Met (V30M) TTR mutation, and 18 had the Val122Ile (V122I) TTR mutation. (Table 1)
- The majority of ATTRwt patients lived in the United States, 192 (87%) and all, 18 (100%) of the V122I patients also lived in the United States. United States residency was reported in 29 (78%) and 18 (53%) in ATTRT60A and ATTRV30M patients, respectively.
- Mean (standard deviation [SD]) age was 66 (7), 66 (12), and 63 (14) years for ATTRT60A, ATTRV30M, and ATTRV122I patients, respectively, and 77 (8) years for ATTRwt patients.
- Most of the ATTRwt patients were retired, 135/169 (80%). 10/32 (31%) of ATTRT60A patients were currently employed and 5/16 (31%) of ATTRV122I patients were not able to work because of ATTR amyloidosis.
- Heart involvement was reported among the vast majority of ATTRwt patients, 204 (93%), and varied by genotype in ATTRv patients, with 32 (86%), 16 (47%), and 12 (67%), in ATTRT60A, ATTRV30M, and ATTRV122I patients, respectively.
- 85-90% of ATTRv patients and one-third (75 [34%]) of ATTRwt patients reported nervous system involvement.
- Mean (SD) years since ATTR diagnosis were 4 (4) for ATTRwt, ATTRT60A, and ATTRV122I patients and 7 (6) for ATTRV30M patients.
- The majority of ATTRwt patients were currently taking tafamidis, 111 (83%), while ATTRv patients most commonly reported taking tafamadis, vutrisiran, or patisiran. (Table 2)
- Of those ATTR amyloidosis patients currently on treatment, at least two thirds have been on that treatment for a year or more.
- The mean frequency of cardiac symptoms and other symptoms (which included largely ocular and CNS symptoms) in the past four weeks was highest in ATTRV122I patients compared to the other genotypes. (Figure 1).
- ATTRV122I patients had the highest mean ATTR-QOL impact score (44.7[24.7]), indicating the greatest impact; ATTRwt patients had the lowest (24.4 [20.1]) ATTR-QOL impact score, indicating the lowest impact. (Figure 2)
- Mean Daily Activities and Social/Role Functioning scores were higher among ATTRV1221 patients ($p<0.05$).
- While not statistically significant, Emotional Wellbeing and Physical Functioning scores were also highest among ATTRV122I patients.

Transthyretin amyloidosis has a significant impact on patients' quality of life.

The greatest impact on quality of life was seen in emotional wellbeing.

Despite the being on therapy, patients with ATTR amyloidosis continue to frequently experience cardiac and neuropathic symptoms.

The impact on quality of life and symptom frequency varied across ATTR amyloidosis genotype with a greater impact seen in ATTRv patients with the Val122Ile TTR mutation.

RESULTS (continued)

Table 1: Demographic and Disease Characteristics of ATTR Amyloidosis Patients

	ATTRwt, N = 220	ATTRT60A, N = 37	ATTRV30M, N = 34	ATTRV122I, N = 18
Gender – Male*	**201** (92%)	**19** (51%)	**21** (62%)	**7** (39%)
Age [mean (SD)]*	**76.48** (7.74)	**66.41** (7.04)	**66.29** (12.25)	**63.33** (14.08)
Race – White*	**209** (95%)	**37** (100%)	**33** (97%)	**9** (50%)
Education - College Degree*	**167** (77%)	**21** (57%)	**20** (61%)	**15** (83%)
Employment Status - Retired*	**135** (80%)	**17** (53%)	**21** (75%)	**8** (50%)
Country of Residence - United States*	**192** (87%)	**29** (78%)	**18** (53%)	**18** (100%)
Region*				
Asia-Pacific	**10** (4.5%)	**1** (2.7%)	**2** (5.9%)	**0** (0%)
Europe	**9** (4.1%)	**3** (8.1%)	**10** (29%)	**0** (0%)
North America	**201** (91%)	**33** (89%)	**20** (59%)	**18** (100%)
South America	**0** (0%)	**0** (0%)	**2** (5.9%)	**0** (0%)
Organ Involvement				
Heart*	**204** (93%)	**32** (86%)	**16** (47%)	**12** (67%)
Nervous system*	**75** (34%)	**32** (86%)	**29** (85%)	**16** (89%)
Gastrointestinal system*	**35** (16%)	**23** (62%)	**15** (44%)	**10** (56%)
Kidney*	**16** (7.3%)	**1** (2.7%)	**7** (21%)	**5** (28%)
Ocular*	**8** (3.6%)	**3** (8.1%)	**6** (18%)	**5** (28%)
Other*	**6** (2.7%)	**2** (5.4%)	**2** (6.5%)	**2** (11%)
Average Time Since Diagnosis [mean SD)]*	**3.63** (4.13)	**4.16** (3.69)	**7.34** (6.19)	**4.37** (2.56)

*Indicates variables are statistically significant ($p<0.05$) between genotype

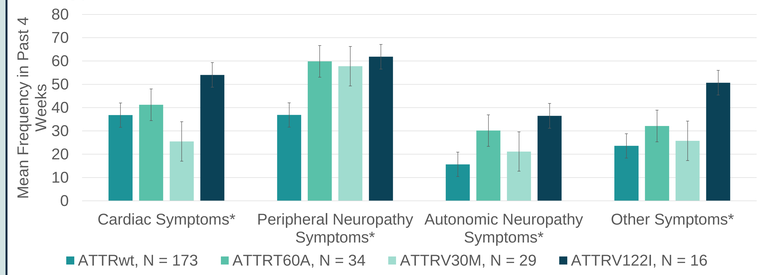
RESULTS (continued)

Table 2: Current Treatment of ATTR Amyloidosis Patients by Genotype

	ATTRwt, N = 134	ATTRT60A, N = 27	ATTRV30M, N = 24	ATTRV122I, N = 13
Current Treatment Use				
Tafamidis*	**111** (83%)	**11** (41%)	**5** (21%)	**4** (31%)
Vutrisiran*	**1** (0.7%)	**14** (52%)	**8** (33%)	**8** (62%)
Patisiran*	**2** (1.5%)	**8** (30%)	**9** (38%)	**4** (31%)
Inotersen*	**0** (0%)	**1** (3.7%)	**2 (8.3%)**	**0 (0%)**
Other	**37** (28%)	**7** (26%)	**6 (25%)**	**1 (7.7%)**
None	**6** (4.5%)	**0** (0%)	**1 (4.2%)**	**2 (15%)**
Time on Current Treatment*				
Less than 3 months	**6** (4.8%)	**3** (11%)	**2 (9.1%)**	**0 (0%)**
3 to 12 months	**25** (20%)	**6** (22%)	**3 (14%)**	**3 (30%)**
1 to 2 years	**34** (27%)	**4** (15%)	**5 (23%)**	**1 (10%)**
More than 2 years	**59** (48%)	**14** (52%)	**12** (55%)	**6** (60%)

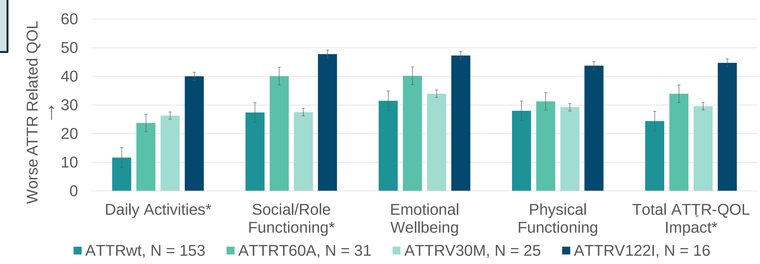
*Indicates variables are statistically significant ($p<0.05$) between genotype

Figure 1: Mean ATTR-QOL Symptom Frequency by ATTR Amyloidosis Genotype



*Indicates variables are statistically significant ($p<0.05$) between genotype

Figure 2: Mean ATTR – QOL Impact Scores by ATTR Amyloidosis Genotype



*Indicates variables are statistically significant ($p<0.05$) between genotype

SUMMARY / CONCLUSION

- ATTR amyloidosis has an impact on patients' QOL.
- The results of this study suggest that disease burden differs across genotype, with the greatest impact among ATTRV122I patients.
- With currently available treatments, patients with ATTR amyloidosis continue to be burdened with cardiac and peripheral neuropathy symptoms.
- Further studies are needed to better understand the impact of genotype on ATTR-related quality of life.

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