Trends in Diagnostic Testing in Medicare Patients With Wild-Type Transthyretin Cardiac Amyloidosis

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INTRODUCTION

- Transthyretin amyloid cardiomyopathy (ATTR-CM) is a progressive, debilitating disease that is often misdiagnosed or diagnosed late in the disease course, leading to a potentially worse prognosis.[1,2]
- Importantly, many patients with wild-type ATTR-CM (ATTRwt-CM) are being diagnosed noninvasively, using nuclear imaging and monoclonal protein testing,[3] but concerns have been raised that some may receive this diagnosis based on incomplete evaluations (ie, not based on current consensus recommendations[4]).
- In this study, conducted using a cohort of US Medicare Fee-for-Service (FFS) patients, we explored the frequency and cadence of diagnostic testing that patients with undiagnosed ATTR-CM underwent.

METHODS

- Study design: Noninterventional, retrospective study.
- Data set: De-identified administrative claims data from the Centers for Medicare and Medicaid Services Medicare Fee for Service database.
- Diagnosis/clinical characteristic identification: International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) diagnosis codes.
- Definitions
  - Study period: January 2016–December 2022.
  - Identification period: January 2018–December 2022.
  - Index date: Earliest date of ATTR-CM diagnosis code use during the identification period.
- Cohorts: Eligibility criteria are shown in **Table 1.**
- Primary analysis: Diagnostic testing in patients with ATTRwt-CM.

Table 1: Summary of eligibility criteria

Criteria	Patients with probable ATTR-CM n=35,055	Patients with ATTRwt-CM n=2050
Inclusion	≥1 ICD-10-CM diagnosis code: • ATTR-CM (E85.0, E85.1, E85.2, E85.4)[a] • ATTRwt-CM (E85.82)[a] • Other amyloidosis (E85.89)[a] • Unspecified amyloidosis (E85.9)[a] • Heart failure[b] (I50) or cardiomyopathy[b] (I42 and I43)	≥1 ICD-10-CM diagnosis code: • ATTRwt-CM[a] (E85.82) • Heart failure[b] (I50) or cardiomyopathy[b] (I42 and I43)
	Age ≥65 y[b]	Age ≥65 y[b]
	≥2 y continuous enrollment in Medicare Parts A, B, and D, with full medical and drug coverage[b]	≥2 y continuous enrollment in Medicare Parts A, B, and D, with full medical and drug coverage[b]
Exclusion	≥1 ICD-10-CM code • Light chain (AL) amyloidosis[c] (E85.81)	≥1 ICD-10-CM code: • Light chain (AL) amyloidosis[c] (E85.81) • Other amyloidosis[c] (E85.89) • Organ-limited amyloidosis[c] (E85.4) • Unspecified amyloidosis[c] (E85.9)
	Prescription claim for ≥1 of the following agents: bendamustine, bortezomib, carfilzomib, cyclophosphamide, daratumumab, elotuzumab, ixazomib, lenalidomide, melphalan, pomalidomide, thalidomide, venetoclax[c,d]	Prescription claim for ≥1 of the following agents: bendamustine, bortezomib, carfilzomib, cyclophosphamide, daratumumab, elotuzumab, ixazomib, lenalidomide, melphalan, pomalidomide, thalidomide, venetoclax[c,d]
	≥1 ICD-10-CM code for multiple myeloma[c] (C90.0) or a plasma cell dyscrasia[c] (E88.09)	≥1 ICD-10-CM code for multiple myeloma[c] (C90.0) or a plasma cell dyscrasia[c] (E88.09)

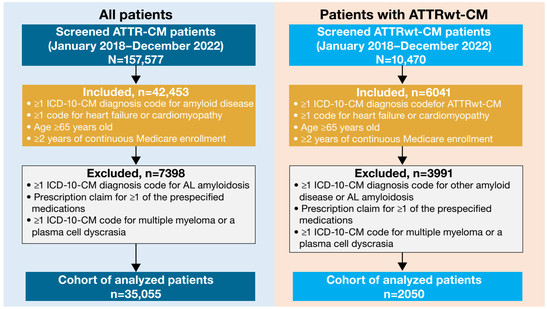
[a] During the identification period.
[b] On or before the index date.
[c] During the study period.
[d] Treatments identified using National Drug Codes.
ATTR-CM=transthyretin amyloid cardiomyopathy; ATTRwt-CM=wild-type transthyretin amyloid cardiomyopathy; ICD-10=International Classification of Diseases, Tenth Revision, Clinical Modification

RESULTS

Cohort Identification and Patient Characteristics

- Of 35,055 patients who initially satisfied eligibility criteria, 2050 were included in the ATTRwt-CM cohort (**Figure 1**).

Figure 1: Summary of patient cohort identification



ATTR-CM=transthyretin amyloid cardiomyopathy; ATTRwt-CM=wild-type transthyretin amyloid cardiomyopathy; ICD-10-CM=International Classification of Diseases, Tenth Revision, Clinical Modification

- In patients with ATTRwt-CM, the mean (SD) age was 80.0 (6.9) years and 76% were men (**Table 2**).

Table 2: Demographic and other characteristics

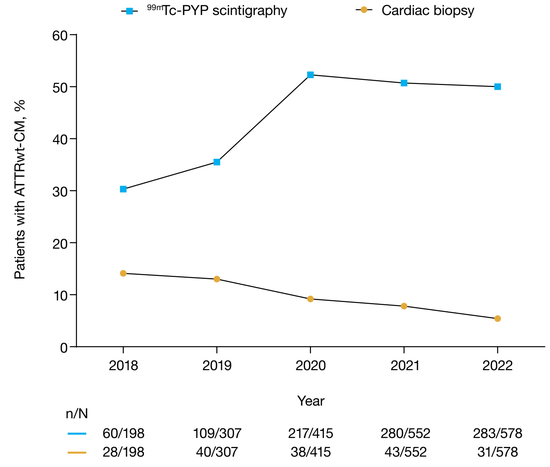
Characteristic	Patients with probable ATTR-CM n=35,055	Patients with ATTRwt-CM n=2050
Age, mean (SD), y	79.3 (7.2)	80.0 (6.9)
Sex, n (%)		
Male	20,006 (57.1)	1547 (75.5)
Female	15,049 (42.9)	503 (24.5)
Race, n (%)		
White	26,668 (76.1)	1599 (78.0)
Black	5061 (14.4)	310 (15.1)
Asian	867 (2.5)	34 (1.7)
Hispanic	1621 (4.6)	56 (2.7)
North American Native	71 (0.2)	<11[a] (<0.5)
Other	767 (2.2)	48 (2.3)
Region, n (%)		
Northeast	10,386 (29.6)	608 (29.7)
Midwest	7467 (21.3)	441 (21.5)
West	5921 (16.9)	371 (18.1)
South	11,229 (32.0)	624 (30.4)
Unknown	52 (0.2)	<11[a] (<0.5)

See Table 1 for inclusion/exclusion criteria for patients with probable ATTR-CM and ATTRwt-CM.
[a] n<11 are not shown for privacy protection (as required by the CMS).
ATTR-CM=transthyretin amyloid cardiomyopathy; ATTRwt-CM=wild-type transthyretin amyloid cardiomyopathy; CMS=US Centers for Medicare and Medicaid Services

Diagnostic Testing in Patients With ATTRwt-CM

- Total new diagnoses per year nearly tripled from 2018 (n=198) to 2022 (n=578).
- Technetium-99m pyrophosphate (^{99m}Tc-PYP) scintigraphy was performed in 30% of patients at the start of the study period (2018) and 49% by the end (2022) (**Figure 2**).
  - ^{99m}Tc-PYP scintigraphy use peaked in 2020 (52%).

Figure 2: Proportions of patients undergoing ^{99m}Tc-PYP scintigraphy and cardiac biopsy for ATTRwt-CM by diagnosis year



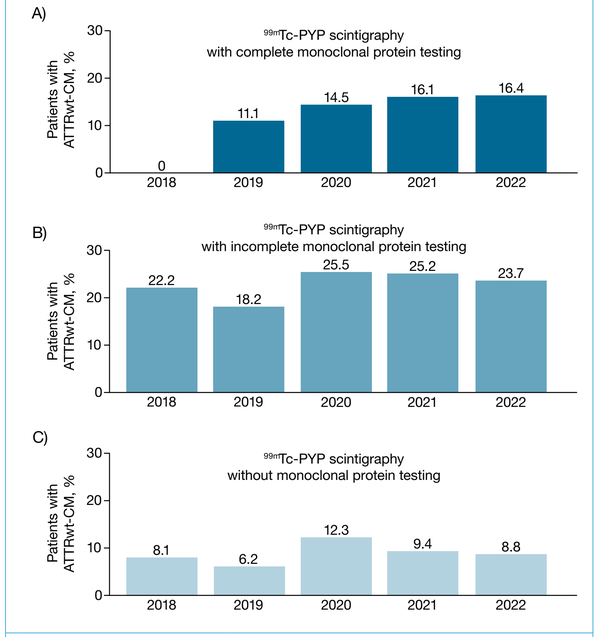
^{99m}Tc-PYP=technetium-99m pyrophosphate scintigraphy; ATTRwt-CM=wild-type transthyretin amyloid cardiomyopathy

- Cardiac biopsy use declined from 14% in 2018 to 5% in 2022 (**Figure 2**).
- Across the study period, 14% of patients with ATTRwt-CM underwent the recommended noninvasive diagnostic testing (based on the consensus algorithm[5]) comprised of ^{99m}Tc-PYP scintigraphy and complete monoclonal protein testing.
  - This recommended approach was followed in 0% and 16% of diagnosed patients in 2018 and 2022, respectively (**Figure 3A**).
  - Scintigraphy was performed with incomplete monoclonal protein testing in 22% and 24% of diagnosed patients in 2018 and 2022, respectively (**Figure 3B**).
  - Scintigraphy was performed without monoclonal protein testing in 8% and 9% of diagnosed patients in 2018 and 2022, respectively (**Figure 3C**).

CONCLUSION

- Based on Medicare claims data, most patients diagnosed with ATTRwt-CM have not been diagnosed utilizing consensus-recommended pathways.

Figure 3. Patterns in scintigraphy and monoclonal protein testing for ATTRwt-CM by diagnosis year



^{99m}Tc-PYP=technetium-99m pyrophosphate scintigraphy; ATTRwt-CM=wild-type transthyretin amyloid cardiomyopathy

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DISCLOSURES

CP, HC, and AE: Employee/stockholder of Pfizer. **CG, AR, DS, and SS:** Employee of Genesis Research Group, which received funding from Pfizer. **RW:** Alexion, Alnylam, AstraZeneca, BridgeBio, Intellia, Ionis, Janssen, Novo Nordisk, and Pfizer.

ACKNOWLEDGMENTS

This study was supported by Pfizer. Medical writing support was provided by Donna McGuire of Engage Scientific Solutions and was funded by Pfizer.

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Presented at the XIX International Symposium on Amyloidosis (ISA), May 26–30, 2024, Rochester, MN, USA