Prevalence and Characteristics of Transthyretin Amyloid Cardiomyopathy in Patients With Hypertrophic Cardiomyopathy: Final Analysis of the TTRACK Study

Nicolas Piriou[1], Perry Elliott[2], Thibaud Damy[3], Roberto Barriales-Villa[4], Francesco Cappelli[5], Carmen Munteanu[6], Catherine Bahus[6], Denis Keohane[6], Pablo Mallaina[6], Pablo Garcia-Pavia[7]

[1]Nantes University Hospital, Nantes, France; [2]University College London, London, UK; [3]Assistance Publique-Hôpitaux de Paris, Henri Mondor University Hospital, Créteil, France; [4]Complexo Hospitalario Universitario A Coruña, A Coruña, Spain; [5]Careggi University Hospital, Florence, Italy; [6]Pfizer Inc, New York, NY, USA; [7]Hospital Universitario Puerta de Hierro Majadahonda, Madrid, Spain

BACKGROUND

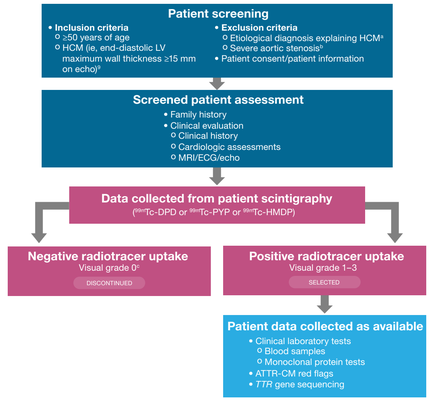
- Transthyretin amyloid cardiomyopathy (ATTR-CM) is a progressive, fatal disease with 2 main phenotypes: variant (ATTRv-CM) and wild type (ATTRwt-CM).[1]
- Although the exact frequency of ATTR-CM is unknown, the disease is more common than previously thought.
- If ATTR-CM is left untreated, median survival from the time of diagnosis is limited for patients with[2-4]:
  - ATTRv-CM: 2.6-5.8 years.
  - ATTRwt-CM: 3.6-4.8 years.
- Delayed diagnosis and misdiagnosis of ATTR-CM are common.[5-7] The diagnosis of ATTR-CM is challenging for several reasons, including:
  - The perceived rarity of disease.
  - Features that overlap with those of more common diseases.
  - Its broad clinical spectrum.
  - Clinicians' lack of familiarity with clinical clues ("red flags").
- Although ATTR-CM remains under-recognized as a cause of heart failure,[5] awareness is increasing.
- Radionuclide scintigraphy and monoclonal protein tests can now provide non-biopsy diagnosis in appropriate clinical scenarios.[7]
- Early diagnosis may allow for prompt disease-modifying treatment and improved clinical outcomes.[8]
- The TTRACK study (NCT03842163) was conducted to improve our knowledge of ATTR-CM in patients with hypertrophic cardiomyopathy (HCM) of unknown etiology.[9]
- The objectives of this study were to (1) estimate the prevalence of ATTR-CM using radionuclide scintigraphy and (2) assess clinical characteristics related to the disease.

METHODS

Study Design

- Design: This was a multicenter, noninterventional epidemiologic study (**Figure 1**).
- Sites: 20 centers in 11 countries across 3 continents.
- Final analysis date range: July 2018–October 2022.
- Scintigraphy assessment: cardiac uptake of bisphosphonate radiotracers (**Figure 1**, **Table 1**).

Figure 1: TTRACK study flow



[a] Sarcomeric hypertrophic cardiomyopathy, myeloma, Fabry disease, sarcoidosis, any type of amyloidosis.
[b] Aortic valve area <1.0 cm^2.
[c] Visual grade 0 / 1 / 2 / 3=absent / mild / moderate / high radiotracer uptake.
^{99m}Tc-DPD / HMDP / PYP=technetium-99m 3,3-diphosphono-1,2-propanodicarboxylic acid / hydroxymethylene diphosphonate / pyrophosphate; ATTR-CM=transthyretin amyloid cardiomyopathy; ECG=electrocardiogram; echo=echocardiogram; HCM=hypertrophic cardiomyopathy; LV=left ventricular; SPECT=single photon emission computed tomography; *TTR*=transthyretin

Table 1: Visual grading system used to define cardiac uptake of bisphosphonate radiotracers[10]

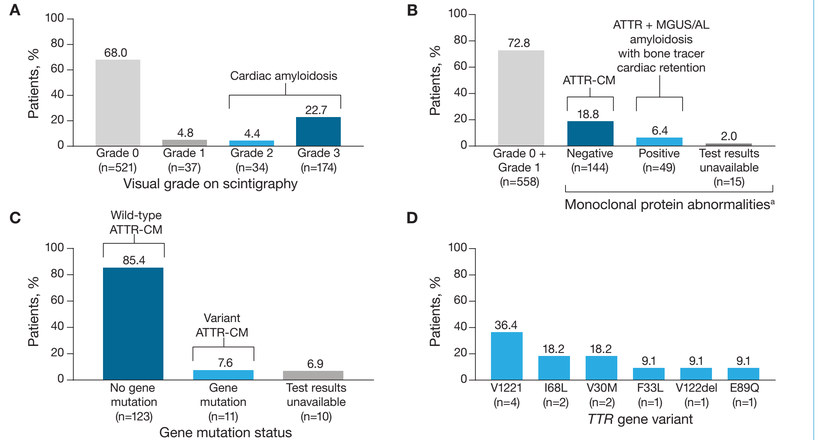
Visual grade	Level of cardiac uptake
0	No cardiac uptake
1	Mild: uptake less than bone
2	Moderate: uptake equal to bone
3	High: uptake greater than bone

RESULTS

Patient Disposition

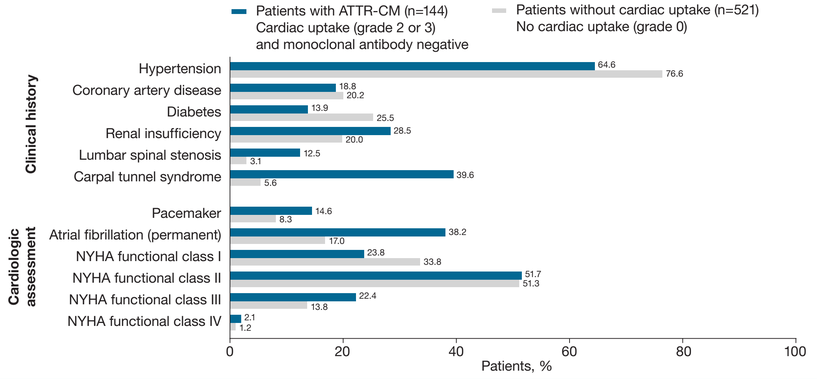
- 766 patients with scintigraphy data were eligible for the study. Of these:
  - 521 (68.0%) patients had no cardiac uptake.
  - 245 (32.0%) patients had cardiac uptake.
  - 208 (27.2%) patients had moderate or high uptake (cardiac amyloidosis) (**Figure 2A**).
  - 144 (18.8%) patients had moderate or high cardiac uptake and negative monoclonal protein findings (ATTR-CM) (**Figure 2B**).

Figure 2: Patient disposition by (A) visual grade on scintigraphy, (B) monoclonal protein test findings, (C) *TTR* genetic test findings, and (D) *TTR* gene variant



[a] In grades 2 + 3 (n=208). AL=light chain; ATTR-CM=transthyretin amyloid cardiomyopathy; CA=cardiac amyloidosis; MGUS=monoclonal gammopathy of undetermined significance

Figure 3: Clinical characteristics of patients with unexplained HCM and ATTR-CM vs no cardiac uptake



ATTR-CM=transthyretin amyloid cardiomyopathy; HCM=hypertrophic cardiomyopathy; NYHA=New York Heart Association

- Patients (n=144) by ATTR-CM subtypes:
  - No *TTR* gene variants: 123 (85.4%) patients had ATTRwt-CM (**Figure 2C**).
  - *TTR* gene variants: 11 (7.6%) patients had ATTRv-CM (**Figure 2C**).
  - The most common *TTR* gene variant was V122I (p.V142I; **Figure 2D**).

Clinical Characteristics

- Patients with ATTR-CM vs no cardiac uptake had higher rates of several clinical conditions (**Figure 3**):
  - Carpal tunnel surgery: 39.6% vs 5.6%.
  - Lumbar spinal stenosis: 12.5% vs 3.1%.
  - Renal insufficiency: 28.5% vs 20.0%.
  - Atrial fibrillation: 38.2 % vs 17.0%.
  - Pacemaker implantation: 14.6% vs 8.3%.
  - New York Heart Association functional class III: 22.4% vs 13.8% and class IV: 2.1% vs 1.2%.

CONCLUSIONS

- In the final analysis of the TTRACK study, 19% (n=144/766) of patients aged ≥50 years with unexplained HCM based on 2014 ESC guidelines[9] (end diastolic left ventricular maximum wall thickness ≥15 mm) had scintigraphy/monoclonal protein findings indicative of ATTR-CM.
- Several clinical conditions, including carpal tunnel surgery, lumbar spinal stenosis, pacemaker implantation, and atrial fibrillation, were more common in patients with ATTR-CM compared with patients with no cardiac uptake.
- Additional information about the prevalence and clinical characteristics of ATTR-CM in patients with HCM is critical to improving knowledge and facilitating detection of this debilitating but treatable disease.

REFERENCES

1. Rapezzi C, et al. Nat Rev Cardiol 2010;7:398-408. **2.** Lane T, et al. Circulation 2019;140:16-26. **3.** Gillmore JD, et al. Eur Heart J 2018;39:2799-896. **4.** Gregan M, et al. J Am Coll Cardiol 2016;68:1014-20. **5.** Ruberg FL, et al. J Am Coll Cardiol 2019;73:2872-91. **6.** Witteles RM, et al. JACC Heart Fail 2019;7:709-16. **7.** Kittleson MM, et al. J Am Coll Cardiol 2023;81:1076-126. **8.** Maurer MS, et al. N Engl J Med 2018;379:1007-16. **9.** Elliott PM, et al. Eur Heart J 2014;35:2733-79. **10.** Perugini E, et al. J Am Coll Cardiol 2005; 46:1076-84.

DISCLOSURES

NP: Alnylam and Pfizer. **PE:** Alnylam and Pfizer. **TD:** Alnylam, GlaxoSmithKline, Pfizer, and Prothena. **RBV:** Consultancy fees from Alnylam, Amicus, Bristol Myers Squibb, Chiesi, Cytokinetics, Pfizer, and Sanofi. **FC:** Akcea, Alnylam, Novo Nordisk, and Pfizer. **CM, CB, DK, and PM:** Employee of Pfizer and holds stock/stock options. **PGP:** Alexion, Alnylam, AstraZeneca, ATTRalus, Bridgebio, General Electric, Intellia, Ionis, Neurimmune, Novo Nordisk, and Pfizer.

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