

Transthyretin amyloid cardiomyopathy (ATTR-CM)

ATTR-CM: An Underdiagnosed Cause of Heart Failure

Transthyretin amyloid cardiomyopathy, or **ATTR-CM**, is a rare and life-threatening condition that affects the heart and is associated with heart failure.^{1,2}

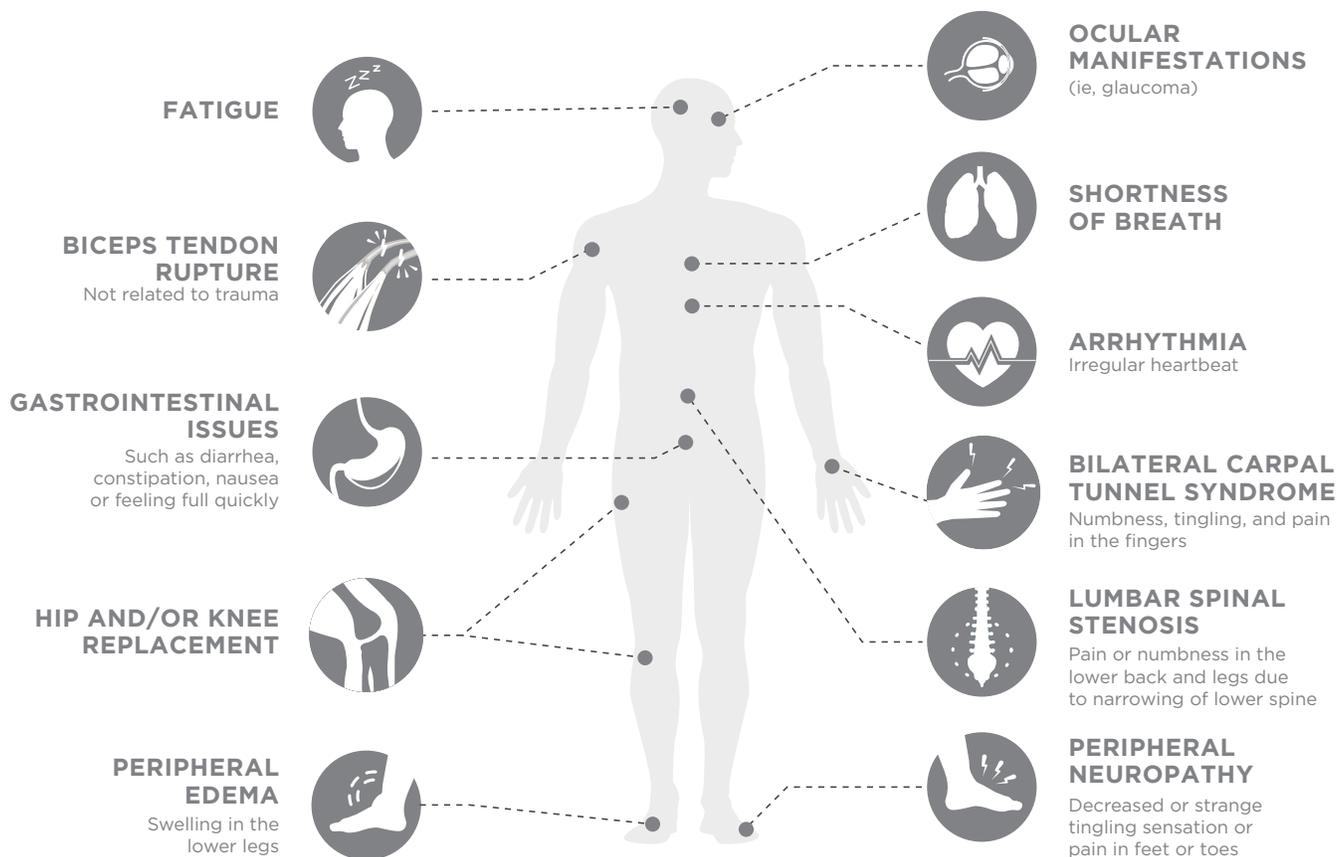
It is the result of misfolding proteins that become unstable, resulting in the creation of amyloid fibrils which build up in the heart and other parts of the body.^{1,2}

The buildup of misfolded proteins causes the heart muscle to stiffen over time, eventually leading to **heart failure**.^{1,2}

Signs and Symptoms of ATTR-CM

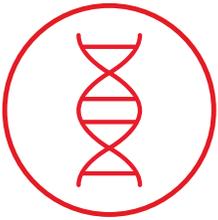
Symptoms often mimic other more common types of heart failure and can include shortness of breath, fatigue, and swelling of the ankles, but may also include other symptoms related to buildup of amyloid fibrils throughout the body, such as carpal tunnel syndrome and peripheral neuropathy.

Often the disease is diagnosed only after symptoms have become severe. Patients should talk to their cardiologist about ATTR-CM if they have heart failure and experience any of these signs and symptoms.³⁻¹¹



Two Sub-types of ATTR-CM^{1,2,5,12,13}

Hereditary (hATTR-CM), also known as variant



Hereditary ATTR-CM occurs due to a mutation in the transthyretin gene.

It can occur in people as early as their **50s and 60s**. Not all people with a *TTR* mutation will develop hATTR-CM.

Wild-type (wtATTR-CM)



The **wild-type** form of ATTR-CM is associated with aging and is thought to be the most common form of ATTR-CM.

Visual effect only.

Challenges and Impact



In ATTR-CM, receiving a correct diagnosis has historically been difficult because disease awareness is low among healthcare professionals, and misdiagnosis is common because patients often present with symptoms similar to more common causes of heart failure.¹⁴



ATTR-CM is significantly under or misdiagnosed, making it difficult to characterize worldwide prevalence. It is believed that only 1–2% of people with the disease are diagnosed.¹⁵ Education is important to help recognize symptoms and improve diagnosis.¹⁴



Without treatment, the average life expectancy for people with ATTR-CM is approximately 2–3.5 years from diagnosis.^{16,17}

Learn More & Find Support

Amyloidosis Research Consortium:
<http://www.arci.org>

Amyloidosis Foundation:
www.amyloidosisresearchfoundation.org

Amyloidosis Alliance:
<http://www.amyloidosisalliance.org/>

Amyloidosis Support Groups:
<http://amyloidosisupport.org>

MacKenzie's Mission:
<http://mm713.org/>

One Amyloidosis Voice:
<http://www.oneamyloidosisvoice.com/>

1. Maurer MS, Elliott P, Comenzo R, Semigran M, Rapezzi C. Addressing common questions encountered in the diagnosis and management of cardiac amyloidosis. *Circulation*. 2017;135(14):1357-1377. 2. Siddiqi OK, Ruberg FL. Cardiac amyloidosis: an update on pathophysiology, diagnosis and treatment. *Trends in Cardiovascular Medicine*. 2017;1050-1738. 3. Geller HI, Singh A, Alexander KM, Mirto TM, Falk RH. Association Between Ruptured Distal Biceps Tendon and Wild-Type Transthyretin Cardiac Amyloidosis. *JAMA*. 2017;318(10):962-963. doi:10.1001/jama.2017.9236. 4. Nativi-Nicolau J, Maurer MS. Amyloidosis cardiomyopathy: update in the diagnosis and treatment of the most common types. *Curr Opin Cardiol*. 2018;33(5):571-579. 5. Ruberg FL, Berk JL. Transthyretin (TTR) cardiac amyloidosis. *Circulation*. 2012;126(10):1286-1300. 6. Bishop E, Brown EE, Fajardo J, Barouch LA, Judge DP, Halushka MK. Seven factors predict a delayed diagnosis of cardiac amyloidosis. *Amyloid*. 2018;25(3):174-179. doi:10.1080/13506129.2018.1498782. 7. Coelho T, Maurer MS, Suhr OB. THAOS – the transthyretin amyloidosis outcomes survey: initial report on clinical manifestations in patients with hereditary and wild-type transthyretin amyloidosis. *Curr Med Res Opin*. 2013(29):1:63-76. 8. Westermark P, Westermark GT, Suhr OB, Berg S. Transthyretin-derived amyloidosis: probably a common cause of lumbar spinal stenosis. *Ups J Med Sci*. 2014;119(3):223-228. 9. Yanagisawa A, Ueda M, Sueyoshi T, et al. Amyloid deposits derived from transthyretin in the ligamentum flavum as related to lumbar spinal canal stenosis. *Mod Pathol*. 2015;28(2):201-207. 10. Rubin J, Alvarez J, Teruya S. Hip and knee arthroplasty are common among patients with transthyretin cardiac amyloidosis, occurring years before cardiac amyloid diagnosis: can we identify affected patients earlier? *Amyloid*. 2017;24(4):226-230. 11. Maurer MS, Elliott P, Merlini G, et al. Design and Rationale of the Phase 3 ATTR-ACT Clinical Trial (Tafamidis in Transthyretin Cardiomyopathy Clinical Trial). *Circ Heart Fail*. 2017;10(6):e003815. doi:10.1161/CIRCHEARTFAILURE.116.003815. 12. González-López E, Gallego-Delgado M, Guzzo-Merello G, et al. Wild-type transthyretin amyloidosis as a cause of heart failure with preserved ejection fraction. *Eur Heart J*. 2015;36(38):2585-2594. 13. Swiecicki PL, Zhen DB, Mauermann ML, et al. Hereditary ATTR amyloidosis: a single-institution experience with 266 patients. *Amyloid*. 2015;22(2):123-131. 14. Rapezzi C, Lorenzini M, Longhi S, et al. Cardiac amyloidosis: the great pretender. *Heart Failure Reviews*. 2015;20(2):117-124. 15. 2018 Internal Analysis. Data on File Pfizer Inc. 16. Connors LH, Sam F, Skinner M, et al. Heart failure due to age-related cardiac amyloid disease associated with wild-type transthyretin: a prospective, observational cohort study. *Circulation*. 2016;133(3):282-290. 17. Grogan M, Scott CG, Kyle RA, et al. Natural history of wild-type transthyretin cardiac amyloidosis and risk stratification using a novel staging system. *J Am Coll Cardiol*. 2016;68:1014-1020.