

Transthyretin Cardiac Amyloidosis: The Disease, Misdiagnosis, and Treatments

There is reasonable evidence to suggest that ATTR is not only misdiagnosed but that it is much more prevalent than previously thought. Because of this, diagnostic methods must be improved and the approach to therapeutics should come to reflect the true nature of the disease.

What is ATTR:

A disease caused by the misfolding and aggregation of the protein transthyretin, originally produced in the liver, in various organs around in the body but most prominently in the heart. The aggregation of transthyretin amyloids in the heart causes cardiomyopathy, i.e. your heart cannot pump blood as well, with symptoms worsening over time. There are two main types of ATTR: wild-type (wt) which is spontaneous and variance/familial(f/v) which is inherited. ATTRwt is found primarily in the elderly population, with some studies suggesting that it is present in 25% of people over 80. ATTRv/f comprises a variety of different mutations. The most prominent mutation in the United States being Val122Ile, which is carried by ~4.0% of the African-American population. A person with ATTR has a life expectancy of 2.5 to 3.5 years after diagnosis.

Kazi DS, Bellows BK, Baron SJ, Shen C, Cohen DJ, Spertus JA, Yeh RW, Arnold SV, Sperry BW, Maurer MS, Shah SJ. Cost-Effectiveness of Tafamidis Therapy for Transthyretin Amyloid Cardiomyopathy. *Circulation*. 2020 Apr 14;141(15):1214-1224. doi: 10.1161/CIRCULATIONAHA.119.045093. Epub 2020 Feb 12. PMID: 32078382; PMCID: PMC7156331.

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Misdiagnosis and Diagnosis:

ATTR has been called the “great imitator” due to its symptoms mimicking those of much more common diseases such as heart failure. ATTR mimics other diseases so well that it is frequently misdiagnosed as other diseases like heart failure first before a correct diagnosis. This is a problem for a variety of reasons, chief among them being that the administration of proper treatment is delayed and that treatments for heart failure aggravate the symptoms of ATTR. There currently exist proposed diagnostic methods for practitioners involving new technology and techniques but they have yet to be implemented for a variety of reasons.

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Treatment and Care:

There currently exist three classes of treatment for ATTR, both actual and theoretical. The first are gene silencers that work by preventing the production of transthyretin in the liver. No current gene silencers are available to the public, all potential drugs are in trial. The second class are transthyretin stabilizers which work by preventing transthyretin from forming amyloids. There are currently transthyretin stabilizers available to the public in the form of Diflusinal and Tafamids. The third class are amyloid disruptors that work by causing amyloid deposits to degrade and break up. There are currently no amyloid disruptor drugs available to the public and no ongoing trials. Currently the best drug on the market, in the United States, is Tafamids, which extends a patient's life by ~1.5 quality years on average. However Tafamids costs approximately \$250,000 per year, a cost that is not feasible for widespread use of the drug.

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