What is Transthyretin Cardiomyopathy?

Transthyretin Cardiomyopathy (TTR-CM) is a rare, underdiagnosed condition that leads to progressive heart failure.1,4 The average life expectancy for people with TTR-CM is 3 to 5 years from diagnosis.5

About TTR-CM

TTR-CM is a type of cardiac amyloidosis that is caused by destabilization of a transport protein called “transthyretin,” which is composed of 4 identical subunits (a “tetramer”).

Heart failure occurs when unstable tetramers dissociate, resulting in misfolded proteins that aggregate into amyloid fibrils and deposit in the heart.1,6

What Types of TTR-CM Exist?

Wild Type (wtTTR-CM): In wild-type TTR-CM, there is no mutation of the TTR protein; however, with age, the protein becomes unstable and misfolds, accumulating as amyloid in the heart.7

More than 90 percent of patients with TTR cardiomyopathy have wtTTR-CM, which is not inherited and usually affects men after age 60.4

Familial Amyloid Cardiomyopathy (TTR-FAC): The inherited form of TTR-CM, referred to as TTR-FAC, is caused by a mutation in the TTR gene, which causes the protein to misfold. TTR-FAC can occur in people in their 50s and 60s. There are more than 27 identified TTR gene mutations that can cause TTR-FAC; the most common (V122I) in the United States is seen in African Americans or people of African descent.6

What are the Symptoms of TTR-CM?

TTR-CM symptoms are often similar to those of more common causes of heart failure, which can lead to misdiagnosis.8

TTR-CM symptoms may include:

- Shortness of breath
- Fainting
- Fatigue
- Swelling/edema of the lower legs and ankles due to the heart’s inability to properly pump fluid through the body
- Atrial fibrillation (irregular heartbeat)8
Low Awareness Adds to a Difficult Diagnosis

Awareness of TTR-CM is low among both the general public and healthcare professionals; therefore, the condition often is overlooked. As a result, most patients with TTR-CM either never receive a definitive diagnosis or remain undiagnosed for many years until the disease has significantly progressed.

Wild-type TTR-CM can be more difficult to diagnose than the hereditary form since there is no family history or genetic marker for the disease.

How is TTR-CM Diagnosed?

Once TTR-CM is suspected, a cardiac biopsy and genetic test for type of TTR variant (WT or variant) are normally performed for a definitive diagnosis.

Common non-invasive assessments such as EKG, ECG, or cardiac MRI may be used to identify patients at risk for the disease.

More recently, other non-invasive tests have been studied to confirm the presence of amyloid in the heart, including scintigraphy (a form of diagnostic test used in nuclear medicine).

How is TTR-CM Treated?

There are currently no medications specifically indicated and approved for the treatment of TTR-CM.

Management of TTR-CM patients include:

**Symptom Management:** When treating their TTR-CM patients, healthcare providers are limited to options that focus on management of symptoms, such as fluid retention and atrial fibrillation. However, traditional heart failure medications, such as angiotensin-converting enzyme (ACE) inhibitors or calcium channel blockers, do not address the underlying cause of TTR-CM. In some cases, these drugs may even be harmful because they decrease heart function in patients whose hearts are already compromised.

**Heart and Liver Transplants:** In very rare cases, liver or heart transplants may be considered in younger, healthier patients. A liver transplant will remove the major source of the variant TTR protein, while a heart transplant replaces the damaged organ. However, TTR-CM patients are usually older and not in good health as a result of the disease, making these procedures risky.

If you think you may have TTR-CM, speak with your doctor to learn more about your options. Early identification of TTR-CM is essential for doctors to determine the best path forward to meet the individual medical needs of each patient.

In fact, it is estimated that less than 1% of people with TTR-CM are diagnosed.

Currently, TTR-CM is primarily diagnosed in select Centers of Excellence.