Transthyretin Cardiomyopathy (TTR-CM) Disease Information Fact Sheet

What is TTR-CM?

Transthyretin cardiomyopathy (TTR-CM) is a rare, progressive and universally fatal disease associated with restrictive cardiomyopathy and progressive heart failure, with life expectancy averaging three to five years from diagnosis. The two types of TTR-CM – TTR familial amyloid cardiomyopathy (TTR-FAC), the hereditary form of the disease, and wild-type TTR cardiomyopathy (wild-type TTR-CM), a non-hereditary form of the disease that is also sometimes referred to as Senile Systemic Amyloidosis (SSA).4

What is the difference between TTR-FAC and wild-type TTR-CM?

Both types of TTR-CM share common pathophysiology of TTR tetramer destabilization leading to amyloid deposition in the heart and cardiac symptoms.1,4,5,6

Patients with TTR-FAC typically experience symptom onset in their 50s or 60s.4 The most prevalent mutation is V122I, and affects primarily African-Americans or people of African descent worldwide.4 More than 27 other mutations leading to TTR-CM have been identified.7 Because TTR-FAC is a hereditary disease, family members may also be at risk for developing the disease.6 Awareness of this rare disease among physicians and the general public is very low, and it often takes years from onset of symptoms for a patient to receive an accurate diagnosis.2,8

Patients with wild-type TTR-CM usually experience symptom onset over the age of 60, and are primarily male.2 Due to the lack of a genetic marker, diagnosis of wild-type TTR-CM is even more difficult than diagnosis of TTR-FAC.8

What causes TTR-CM?

TTR-CM (both TTR-FAC and wild-type TTR-CM) is caused when “transthyretin”, a transport protein that naturally circulates in the blood, becomes unstable and misfolds. The misfolded protein can build up in the heart as amyloid fibrils, which causes the heart muscle to become stiff, resulting in heart failure.1,5,6

What are the symptoms of TTR-CM?

Symptoms include the typical signs and symptoms associated with heart failure, such as shortness of breath and peripheral (e.g., ankle) edema.9

What are the challenges in diagnosing TTR-CM?

TTR-CM is typically diagnosed by heart failure specialists in expert centers. Overall awareness of TTR-CM is very low among cardiologists and general physicians.8

The actual number of patients with TTR-CM is unknown.2 It is currently estimated that there are 800-1,000 diagnosed patients with the disease worldwide.10 Though TTR-CM is a rare disease, it is likely vastly under-diagnosed.2

TTR-CM at a Glance

-- It is currently estimated that there are approximately 800-1,000 diagnosed patients with TTR-CM worldwide, though the actual number of patients with TTR-CM is presently unknown.2,10

-- TTR-CM typically occurs in patients during adulthood:
  - TTR-FAC typically occurs in patients in their 50s or 60s.4
  - Wild-type TTR-CM typically occurs in patients in their 60s and 70s.2

-- Awareness of the disease among cardiologists is low, and TTR-CM patients are often misdiagnosed as hypertensive heart failure patients.8,12

-- Because TTR-FAC is a hereditary disease, family members may also be at risk for developing the disease.4
How is TTR-CM diagnosed?

Symptoms include the typical signs and symptoms associated with heart failure, such as shortness of breath and peripheral (e.g., ankle) edema. These symptoms are very non-specific, and often a diagnosis of TTR-CM may be delayed for years. An ECG (electrocardiogram) and echocardiogram (heart ultrasound) may provide clues to the diagnosis. Cardiac MRI and scintigraphy may also be helpful in the diagnosis of TTR-CM. Genetic testing can be used to identify gene carriers with mutations associated with TTR-FAC. Definitive confirmation of TTR-CM is typically done through a cardiac biopsy (performed by a sub-specialist).

Are there any treatments available for TTR-CM?

There are currently no approved treatments for TTR-CM. Symptomatic management with traditional heart failure treatments does not address the underlying cause of disease and, in some cases, may be harmful.

What is the difference between TTR-CM and Transthyretin Familial Amyloid Polyneuropathy (TTR-FAP)?

TTR-CM and TTR-FAP are two distinct phenotypical expressions of the same underlying condition, TTR amyloidosis. The underlying pathology of TTR-CM and TTR-FAP is the same: destabilization of transthyretin, leading to formation of amyloid that is subsequently deposited in tissues – the heart or the nerves – leading to symptoms of heart failure and polyneuropathy.

Some mutations in the TTR gene lead to mostly cardiac symptoms, while others are specific to polyneuropathy. Several mutations cause symptoms of both TTR-CM and TTR-FAP. Wild-type TTR amyloidosis is usually limited to the heart and the nerves are not affected.