

# ATTR Cardiac Amyloidosis\*

## Considerations for Identification and Diagnosis

\*Also known as transthyretin amyloid cardiomyopathy or ATTR-CM.



**ATTR-CM is an underrecognized cause of heart failure with preserved ejection fraction (HFpEF) in older adults<sup>1</sup>**

## DISEASE BURDEN



**Heart failure (HF) is a leading cause of hospitalization and is associated with high morbidity and mortality postdiagnosis.<sup>2</sup> Many patients with heart failure present with multiple comorbidities.<sup>3</sup>**

- **6.9 million** people are living with HF in the United States, and this number is expected to rise to nearly **8.5 million** by 2030<sup>4†</sup>
- Approximately **23% of Medicare patients** with a diagnosis of HF were readmitted to the hospital within 30 days<sup>5‡</sup>
- In one study, **51.5% of HF patients** had **HFpEF**<sup>6</sup>
- Once diagnosed, untreated patients with ATTR-CM have a median survival of ~3 to 5 years<sup>7</sup>

**ATTR-CM is a life-threatening, progressive, infiltrative rare disease that can often be overlooked as a cause of heart failure.<sup>8</sup>**

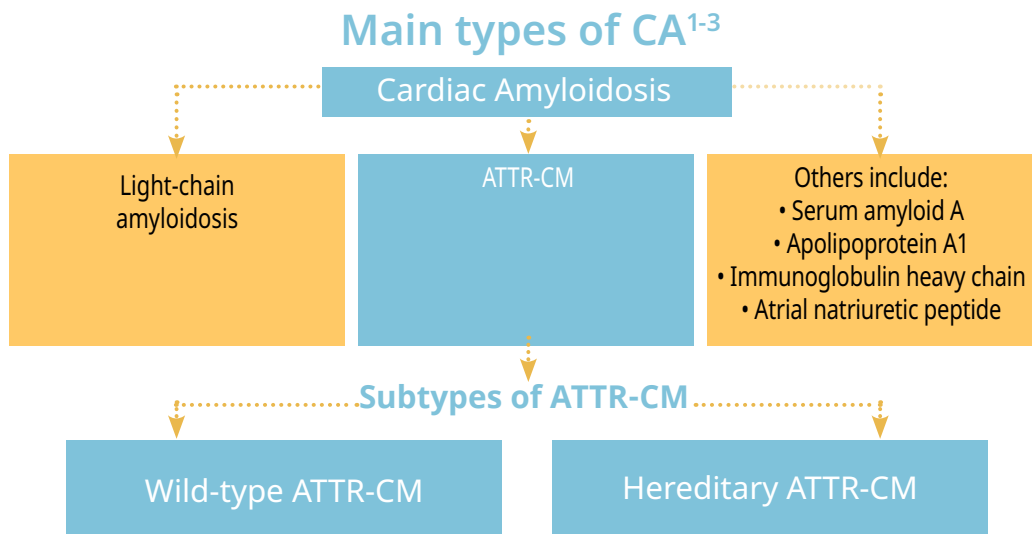
**Abbreviation:** ATTR, transthyretin amyloidosis.

<sup>†</sup>American Heart Association estimate.

<sup>‡</sup>Retrospective study of Medicare fee-for-service beneficiaries aged 65 years or older hospitalized with HF, acute myocardial infarction, or pneumonia from January 1, 2008, through December 31, 2014.<sup>5</sup>

# ATTR CARDIAC AMYLOIDOSIS (ATTR-CM) OVERVIEW

Two types of cardiac amyloidosis (CA)—light-chain amyloidosis (AL) and ATTR-CM—make up ~95% of all CA diagnoses<sup>1</sup>



There are 2 types of ATTR-CM—wild type and hereditary<sup>1</sup>:

## Wild-type ATTR-CM\* (wtATTR)



### Associated with aging<sup>4,5</sup>

- Most often affects White men over the age of 60<sup>6-8</sup>
- May be the most common form of ATTR-CM<sup>8</sup>

## Hereditary ATTR-CM† (hATTR)



### Caused by a change (or “mutation”) in one of your genes<sup>9</sup>

- Passed down from a relative<sup>7</sup>
- Affects both men and women, with symptoms beginning as early as 50 to 60 years old<sup>10</sup>
- There are more than 120 known mutations that cause hATTR; the most common mutation in the United States is V122I<sup>1,3</sup>

**Abbreviation:** ATTR, transthyretin amyloidosis.

\*Formerly known as senile cardiac amyloidosis, senile systemic amyloidosis, or age-related amyloidosis.<sup>6</sup>

†May also be known as mutant variant ATTR, ATTRm amyloidosis, mutant ATTR amyloidosis, or hereditary amyloidosis.<sup>1</sup>

# SUSPICION OF ATTR CARDIAC AMYLOIDOSIS (ATTR-CM)



- More than **50% of hATTR patients and 39% of wtATTR patients received a misdiagnosis**<sup>1</sup>
- **~75%** of those patients received treatment for the misdiagnosed condition<sup>1</sup>



## In Witteles et al, further evidence to support a suspicion of ATTR-CM includes the following **red flags**<sup>1</sup>:

- Reduction in longitudinal strain with apical sparing
- Discrepancy between left ventricular thickness and QRS voltage (with a lack of left ventricular hypertrophy on an electrocardiogram)
- Atrioventricular block, in the presence of increased left ventricular wall thickness
- Echocardiographic hypertrophic phenotype with associated infiltrative features, including increased thickness of the atrioventricular valves, interatrial septum, and right ventricular free wall
- Marked extracellular volume expansion, abnormal nulling time for the myocardium, or diffuse late gadolinium enhancement on cardiac magnetic resonance imaging
- Symptoms of polyneuropathy and/or dysautonomia
- History of bilateral carpal tunnel syndrome
- Mild increase in troponin levels on repeated occasions



## Patients affected by ATTR-CM may have multiorgan system involvement and may present with clinical symptoms related to various systems, including musculoskeletal, ocular, neurologic (peripheral and autonomic), and cardiovascular<sup>2-4</sup>

- ~1 in 10 patients over the age of 60 with HFpEF were found to have ATTR-CM<sup>5,6</sup>
- In one study, **1 in 6 patients aged 65 years and older** with severe symptomatic aortic stenosis undergoing transcatheter aortic valve replacement had ATTR-CM (16% overall and 22% of men)<sup>7</sup>
- 6% of patients with myocardial hypertrophy of unknown cause had hATTR<sup>8</sup>
- **69%** of patients diagnosed with ATTR-CM **had atrial fibrillation**<sup>9</sup>
- In 2 studies among patients with wtATTR, **46% to 49% had carpal tunnel syndrome**<sup>10,11</sup>
- **Total knee and hip arthroplasty** was **3 to 5 times more common** among patients with ATTR-CM than for age- and sex-matched controls<sup>12</sup>
- **24% of tissue samples removed during surgery for rotator cuff repair** were found to have wtATTR deposits<sup>13</sup>
- **ATTR** deposits have been identified in resected tissues in patients undergoing lumbar spinal stenosis surgery<sup>14</sup>

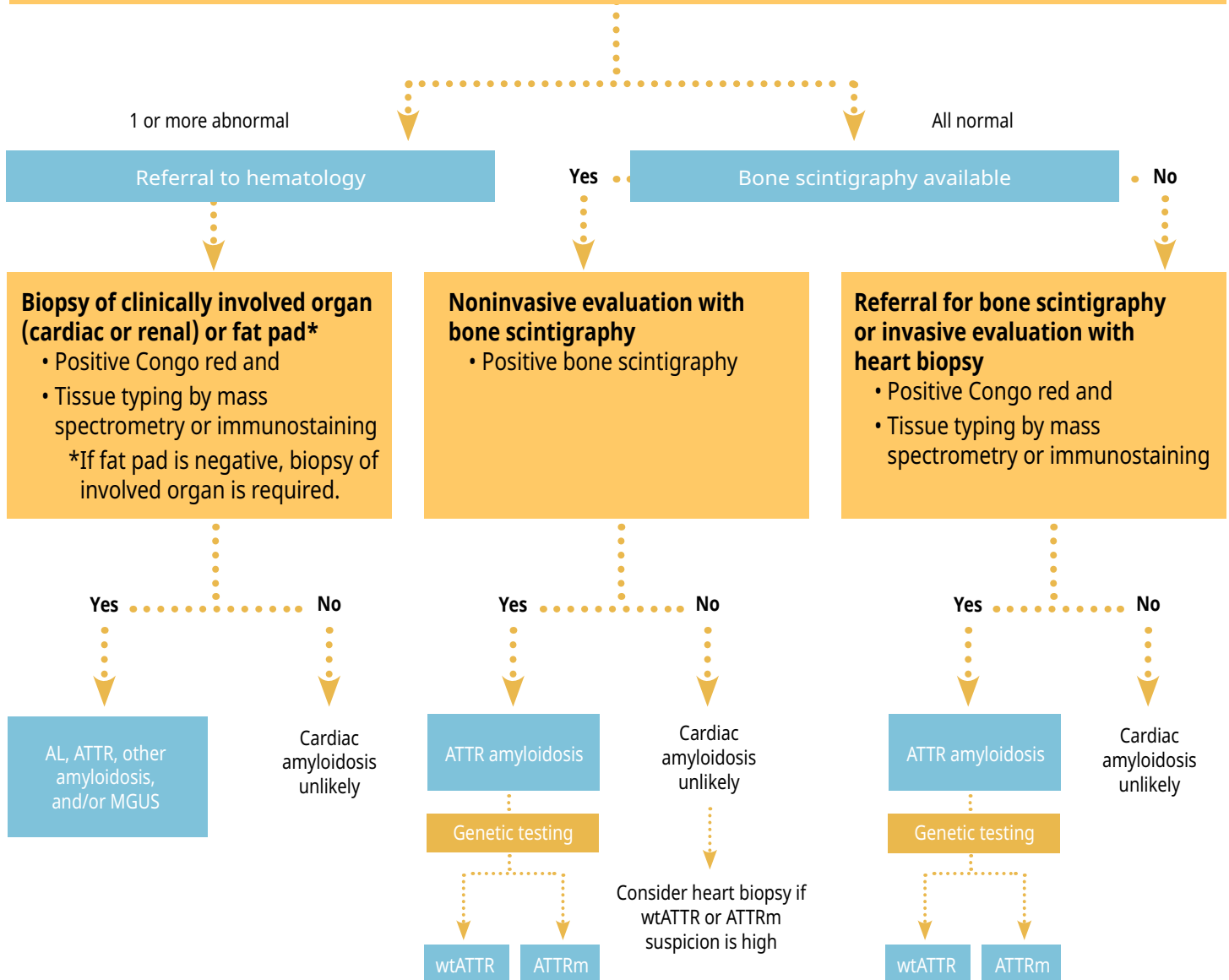
# DIAGNOSIS OF ATTR CARDIAC AMYLOIDOSIS (ATTR-CM)

Once ATTR-CM is suspected, a definitive diagnosis can be achieved through a noninvasive or invasive diagnostic approach<sup>1,2</sup>

Symptoms, ECG, echocardiogram, MRI, or biomarkers suggestive of cardiac amyloidosis<sup>1,2</sup>

**Screen for the presence of a monoclonal protein. Order the following 3 tests:**

- Serum kappa/lambda free light-chain ratio (abnormal if ratio is <0.26 or >1.65)
- Serum protein immunofixation (abnormal if monoclonal protein is detected)
- Urine protein immunofixation (abnormal if monoclonal protein is detected)



**Abbreviations:** AL, light-chain amyloidosis; ATTR, transthyretin amyloidosis; ATTRm, mutant transthyretin amyloidosis; ECG, electrocardiogram; MGUS, monoclonal gammopathy of undetermined significance; MRI, magnetic resonance imaging; wtATTR, wild-type ATTR-CM.

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# SUSPICION AND DIAGNOSIS OF ATTR CARDIAC AMYLOIDOSIS (ATTR-CM)



## A review of noninvasive and invasive approaches for suspicion and diagnosis of ATTR-CM<sup>1</sup>

### Tools used to raise suspicion:

#### Echocardiogram

- Plays a major role in noninvasive diagnosis because of its assessment of structure and function and its pervasive use for patients with concerning cardiac symptoms<sup>2</sup>
- Showcases increased left ventricular wall thickness<sup>2</sup>
- Suspicion of ATTR-CM may include echocardiographic hypertrophic phenotype with associated infiltrative features, including increased thickness of the atrioventricular valves, interatrial septum, and right ventricular free wall<sup>3</sup>

#### Cardiac Magnetic Resonance (CMR)

- Plays an important role in noninvasive diagnosis because it provides tissue characterization in addition to high-resolution morphologic and functional assessment<sup>2</sup>
- Offers value in 2 clinical scenarios<sup>2</sup>:
  - Differentiation of cardiac amyloidosis from other cardiomyopathies
  - Potential early detection of cardiac amyloidosis
- CMR with late gadolinium enhancement may be relatively contraindicated in patients with suspected cardiac amyloidosis and concomitant renal failure<sup>2</sup>

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### Tools used to make a definitive diagnosis:

#### PYP Cardiac Imaging (Nuclear Scintigraphy)

- A noninvasive, readily available diagnostic tool with high sensitivity and specificity for ATTR-CM when combined with testing to rule out AL<sup>4,5</sup>
- Uses <sup>99m</sup>Tc-pyrophosphate (<sup>99m</sup>Tc-PYP), a radioactive tracer used as an adjunct in the diagnosis of ATTR-CM<sup>4,5</sup>
- A multicenter international study of scintigraphy at amyloidosis centers of excellence demonstrated 100% specificity for ATTR-CM using visual grade 2 or 3 with concurrent testing to rule out AL<sup>5</sup>

#### Endomyocardial Biopsy (EMB)

- An invasive, traditional approach for diagnosing cardiac amyloidosis; however, the need for specialized centers and expertise may contribute to diagnostic delay<sup>4,5</sup>
- Potential EMB complications, although rare, can include<sup>6</sup>:
  - Arrhythmia
  - Perforation with pericardial tamponade
  - Pneumothorax

**ATTR-CM can be a burden to both patients and health systems because of its protracted diagnosis or misdiagnosis resulting from a poor understanding of the disease, heterogeneity of clinical characteristics, or misconceptions about diagnosis and treatment.<sup>3</sup>**

**Early and accurate diagnosis can improve patient care.<sup>3</sup>**

**THERE ARE MANY EXCELLENT RESOURCES ON ATTR CARDIAC AMYLOIDOSIS (ATTR-CM) FOR YOU, YOUR PATIENTS, AND THEIR LOVED ONES. FIND SUPPORT FROM THESE TRUSTED AMYLOIDOSIS ORGANIZATIONS:**



**Amyloidosis Support Groups**

[www.amyloidosisupport.org](http://www.amyloidosisupport.org)

- Provides education for patients through live support groups in 30 cities
- Provides patient education through virtual webinars and patient support groups on Facebook



**Amyloidosis Research Consortium**

[www.arci.org](http://www.arci.org)

- Provides comprehensive support and information for patients
- Accelerates development of and access to new and innovative treatments
- Drives research that will have the greatest impact on patients



**Amyloidosis Foundation**

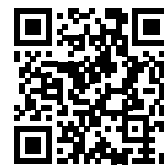
[www.amyloidosis.org](http://www.amyloidosis.org)

- Supports research for an earlier diagnosis
- Educates medical professionals
- Provides patients with a comprehensive range of services

**Additional Resources**

PROGRAM	DESCRIPTION	HOW TO ACCESS
Your Heart's Message	To learn more about ATTR-CM and the resources available to patients (support groups)	<a href="http://www.yourheartsmessage.com">www.yourheartsmessage.com</a>
Transthyretin Cardiac Amyloidosis	Website HCPs can access for ATTR-CM information	<a href="https://transthyretincardiacamyloidosis.pfizerpro.com">https://transthyretincardiacamyloidosis.pfizerpro.com</a>

**Click here to get more information on ATTR-CM:**



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