# Novel Treatment Strategies for Patients With Heart Failure – Diagnosis and Management of Amyloid Associated HF

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# Comparison of Subtypes of Amyloid Cardiomyopathy

| Amyloid Type | Systemic Amyloidosis | Transthyretin (TTR) Amyloidosis | |
|---|---|---|---|
| **Subtype** | **AL** | **ATTRm** | **ATTRwt** |
| **Protein deposited** | Light chain | Mutated TTR protein | wtTTR monomers |
| **Disease etiology** | Plasma cell dyscrasia with ↑ light chains | Familial mutation of TTR | Common in elderly aged >75 years |
| **Specific features** | Kidney, heart, and liver affected | V122I common in African Americans | Carpal tunnel<br>Male dominance |
| **Median survival** | 1-3 years | 2 years | 4-6 years |
| **Prognostic factors** | Cardiac function, BNP, troponin | Duration, ↓LVEF | BNP, uric acid, ↓LVEF, ↑ wall thickness |

AA, amyloid A amyloidosis; AL, light-chain amyloidosis; ATTRm, mutated transthyretin amyloidosis; ATTRwt, wild-type transthyretin amyloidosis; BNP, brain natriuretic peptide; HR, heart rate; LVEF, left ventricular ejection fraction; TTR, transthyretin.

Adapted from Liu PP, Smyth D. Circulation. 2016;133:245-247.

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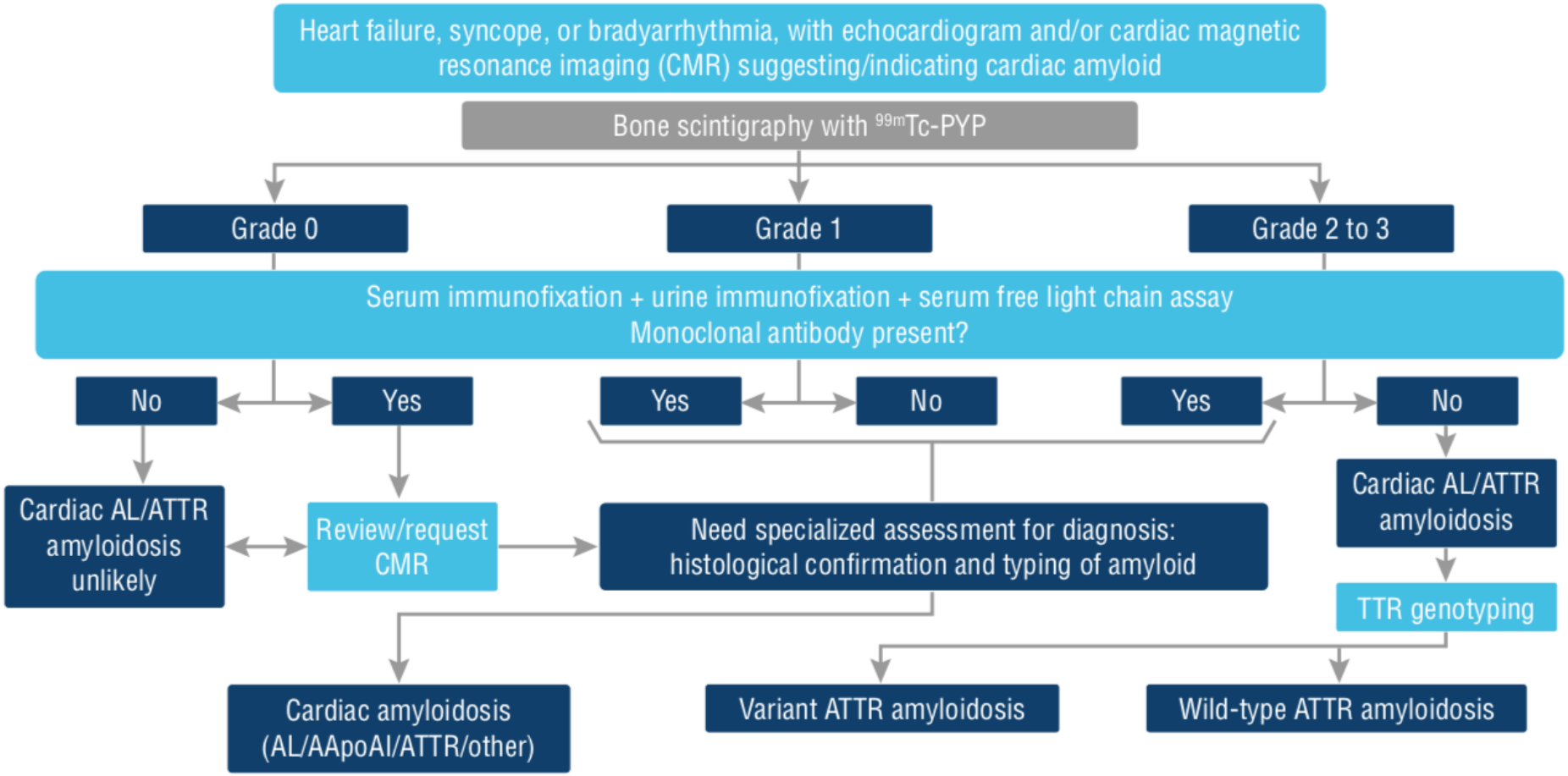
# Diagnosis: Suspected Amyloid Cardiomyopathy




Gillmore JD, et al. Nonbiopsy diagnosis of cardiac transthyretin amyloidosis. *Circulation*;133(24):2404-2412. https://tinyurl.com/CircGillmore

# Red Flags: Transthyretin Amyloid Cardiomyopathy

- ☑ Heart failure with preserved ejection fraction without hypertension
- ☑ Low-flow low-gradient aortic stenosis
- ☑ Bilateral carpal tunnel syndrome
- ☑ Lumbar spinal stenosis
- ☑ Atraumatic rupture of biceps tendon
- ☑ Suspected late-onset hypertrophic cardiomyopathy
- ☑ Intolerance to standard heart failure therapies (ACEi/ARB, beta blockers)
- ☑ Low voltage or low voltage-to-mass ratio on electrocardiogram
- ☑ Pseudoinfarct pattern on electrocardiogram
- ☑ Persistent low-level troponin elevation without angina
- ☑ Unexplained increased wall thickness (especially discordance between wall thickness and ECG voltage)
- ☑ Late gadolinium enhancement on cardiac MRI
- ☑ Apical sparing on echocardiography or MRI strain rate imaging

Modified from *J Card Fail* 22(12), Brunjes DL, et al. Transthyretin cardiac amyloidosis in older Americans, 996-1003. Copyright 2016, with permission from Elsevier.

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# Symptom-Directed Treatment Is Limited

e care aimed at symptomatic

**Congestive Symptoms**
- Loop diuretics and thiazides in combination with mineralocorticoid receptor antagonist

**Cardiomyopathy Medications**
- Avoid β-blockers, ACEi, and ARB

→
- Do not modify disease progression
- Can result in worsening fatigue and hypotension

**Atrial Arrhythmias**
- Amiodarone
- Catheter ablation

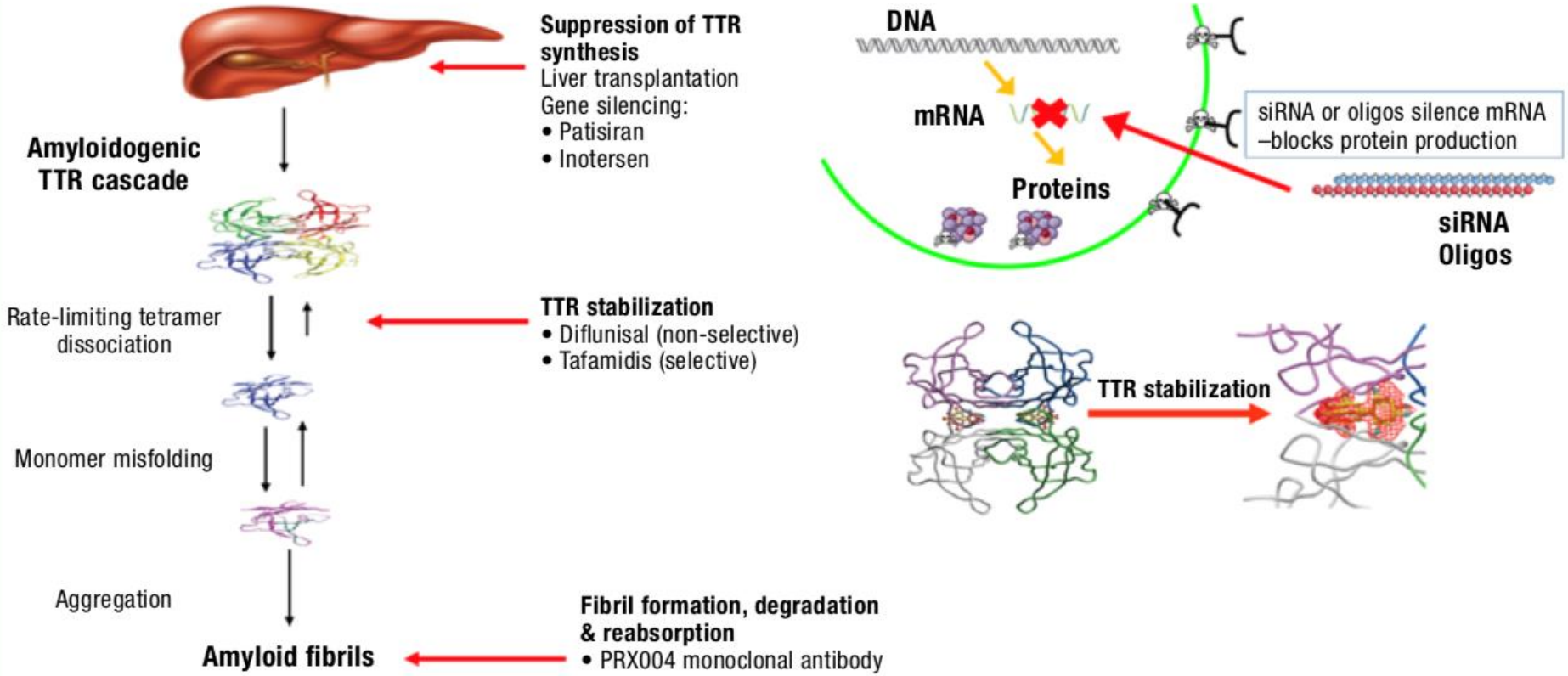
→
- Calcium channel blockers are contraindicated (bind to the amyloid fibrils)
- Digoxin can cause cardiac toxicity (progressive accumulation in amyloid-rich heart despite normal serum levels)
- Catheter ablation has high recurrence rate, necessitating AV ablation with permanent pacemaker placement in refractory cases

**Hypotension**
- α-1 blocker midodrine and compression stockings

ACEi, Angiotensin converting enzyme inhibitors; ARB, Angiotensin II receptor blockers; AV, atrioventricular.

Halatchev IG et al. J Thorac Dis 2018;10(3):2034-2045.

# Medication Targets in TTR Amyloid Cascade




Modified from Maurer MS, et al. Addressing common questions encountered in the diagnosis and management of cardiac amyloidosis. *Circulation;*135(14):1357-1377. https://tinyurl.com/CircMaurer