

Amyloidosis Program of Calgary



ATTR Disease Progression Monitoring Guideline

Listed below are a series of parameters whereby the occurrence of new or worsening of one or more may indicate progression of transthyretin amyloidosis (ATTR). This list is intended as a guide for clinicians caring for ATTR patients. Clinical judgment is needed to determine the magnitude of change as clinically relevant, and whether such change is associated with ATTR disease.

The frequency of assessment is also subject to clinical judgment, but a general recommendation would be annually for cardiac parameters and biannually for neurologic examinations with nerve conduction studies done yearly. Similarly, therapeutic changes made in response to worsening of below parameters is also subject to clinical judgment and beyond the scope of this document to describe.

For neurologic symptoms/signs, serial use of objective questionnaires/scales may be helpful in disease monitoring and to catch early symptoms of worsening neuropathy. Two such scales are the COMPASS31 and R-ODs. The COMPASS31 questionnaire is a useful tool for autonomic symptom monitoring that can be filled out by patients at each visit¹. Similarly, general disability from motor and sensory symptoms in neuropathy can be measured using the R-ODS questionnaire².

Systemic/Functional

- Unintentional weight loss
- Excessive fatigue

Ocular

- Blurred vision due to vitreous opacities

- Retinal detachment

Dysautonomia

- Orthostatic lightheadedness
- Diarrhea/constipation
- Sexual dysfunction
- Urinary retention
- Sweating/skin temperature regulation abnormalities

Musculoskeletal/Soft Tissue (Impingement)

- Carpal tunnel syndrome (CTS)
- Spinal stenosis
- Joint/tendon dysfunction – biceps tendon, rotator cuff

Cardiac

Clinical

- Cardiovascular hospitalization – heart failure or arrhythmia
- Worsening outpatient heart failure
- Outpatient diuretic dose
- New York Heart Association (NYHA) class change
- Other clinical heart failure sign/symptom (orthopnea, paroxysmal nocturnal dyspnea, etc)
- Worsening outpatient arrhythmia
- Pre/syncope
- Heart block/pacemaker implant
- Symptomatic tachyarrhythmia/implantable cardioverter-defibrillator (ICD) implant

Laboratory

- N-terminal pro/B-type natriuretic peptide (NTpro/BNP)
- Troponin
- Estimated glomerular filtration rate

Imaging

- Left ventricular wall thickness
- Global longitudinal strain
- Left ventricular ejection fraction
- Cardiac magnetic resonance imaging – extracellular volume

Neuro

Clinical

- Progression in numbness and/or weakness. Note that worsening pain alone is not a reliable marker of disease progression.
- Progression in gait difficulties; need for a new gait or mobility aid
- Increasing falls, especially at night or in dim light
- Worsening hand dexterity, dropping or difficulty handling objects
- Worsening scores on objective patient questionnaires (see above – COMPASS31, R-ODs)

Neurologic Examination

- Worsening of large or small fiber sensory findings
- Worsening muscle weakness on objective strength testing; consider tracking grip strength using a dynamometer
- Progressive reflex loss
- Progressing muscle wasting (outside of CTS related muscles – as above progression of CTS/spinal stenosis often occurs independently of ATTR disease progression and can occur despite stability of other ATTR symptoms)
- New or progression in orthostatic drop on postural vitals

Electrophysiologic

- Significant (based on laboratory normal range) worsening in compound muscle action potential/sensory nerve action potential (CMAP/SNAP) amplitudes or development of new large fiber neuropathy findings
- Newly abnormal RR interval or sympathetic sweat response in nerve conduction studies (NCS)
- New or worsening autonomic dysfunction on formal autonomic testing

References

1. Sletten et al. COMPASS 31: A Refined and Abbreviated Composite Autonomic Symptom Score. Mayo Clinic Proceedings, 2012.
2. van Nes et al. Rasch-built Overall Disability Scale (R-ODS) for immune-mediated peripheral neuropathies. Neurology, 2011.

Both of these tools are freely available at <https://www.hattrevaluationtools.eu/>