Cardiac amyloidosis is an under-recognized and potentially fatal cause of heart failure and other cardiovascular manifestations. It is caused by deposition of misfolded precursor proteins as fibrillary amyloid deposits in cardiac tissues.

Most common subtypes of cardiac amyloidosis

- **Light chain amyloidosis (AL)** – Hematologic malignancy with multisystem amyloid deposition, most often involving heart and kidney.
- **Transferrin amyloidosis (ATTR)** – Misfolding of the hepatic protein transferrin due to either a gene mutation (hereditary type, hATTR), or ageing (wild-type, wtATTR), with predominantly heart and peripheral nerve involvement.

Epidemiology

Cardiac amyloidosis is more common in older patients, and more common in men than women. AL amyloidosis has an approximate annual incidence of 10/million. hATTR is endemic in certain regions but relatively rare in Canada. wtATTR is likely underdiagnosed in older patients with heart failure and may account for over 10% of HfPEF cases in this demographic.

RED-FLAG SYMPTOMS

- New onset heart failure + one or more of the following:
  - Unexplained increase in LV wall thickness
  - Low-flow low-gradient aortic stenosis with preserved LVEF (in patients >60 years old)
  - Carpal tunnel syndrome (bilateral)
  - Established AL or ATTR in non-cardiac organ/system
  - Peripheral sensorimotor neuropathy and/or dyssautonomia

How do you investigate suspected cardiac amyloidosis?

- **Standard HF workup**: cardiac imaging (ECHO, CMR), troponin and BNP/NT-proBNP
- **Screen for plasma cell dyscrasia**: serum and urine protein electrophoresis/immunofixation; serum free light chain assay

  - If AL suspected – Hematology referral tissue biopsy
  - If ATTR suspected (AL screen negative) – Tc99m-MDP scan (if unavailable, cardiac biopsy)
  - Genetic testing if ATTR confirmed, to differentiate hATTR from wtATTR

Management

**Cardiac Sequelae**
1. Diuresis, sodium restriction for heart failure
2. Cautious use of β-blockers/ACEI/ARBs
3. Anticoagulation for atrial arrhythmias
4. Pacemaker for symptomatic bradycardia

**Disease Modifying Therapy**
1. AL – chemotherapy +/- stem cell transplant
2. wtATTR or hATTR with NYHA class III heart failure – Tafamidis
3. hATTR with polyneuropathy – Inotersen or patisiran

To learn more about Cardiac Amyloidosis please visit us at [CCS.CA](http://CCS.CA)