Cardiac Amyloidosis:
An Overview for Patients

Presented by:

Canadian Council of Cardiovascular Nurses

Conseil canadien des infirmières et infirmiers en soins cardiovasculaires

Cardiac amyloidosis

- Amyloidosis is a rare disease caused by a protein called amyloid that misfolds and builds up in organs, such as the heart and kidneys.
- While the misfolded amyloid proteins typically accumulate in the soft tissues of ligaments and tendons, the main buildup that causes amyloid disease occurs in the tissues of the heart, causing cardiac amyloidosis (which is also referred to as CA).
- CA is often undiagnosed in patients with other common heart diseases or symptoms of heart failure (also referred to as HF), but new and advanced therapies are largely improving the ability to recognize and diagnose CA.

CA has been increasing in Canada in recent years, so it is important to raise awareness of the disease in hopes of optimizing care and improving outcomes for patients with CA.

Pathophysiology & risk

There are 2 common types of CA:

Light chain amyloidosis
(also referred to as AL amyloidosis)

Transthyretin amyloidosis
(also referred to as ATTR)

Wild-type amyloidosis
(also referred to as wtATTR)

- Disease develops over decades
- Most common in elderly (>70 years of age) but also significantly affects the aging population

Hereditary amyloidosis
(also referred to as hATTR)

- Patients born with mutation in the transthyretin gene
- Amyloid builds up, most often in the heart and nervous system
- Affects all ethnic groups, but higher risk in certain ethnic groups and geographic regions

Refer to Table 1 for a summary of CA

- Although AL amyloidosis is uncommon, AL amyloidosis in the heart is more frequent in men than women (3:2 ratio).
- Notably, 50%–75% of patients with AL amyloidosis also experience heart issues.
- Regardless of how the disease develops, CA can stiffen the heart muscle and can cause cardiac dysfunction or HF.

Table 1: Summary of cardiac amyloidosis features

Features/ risk factors	Light chain cardiac amyloidosis (AL-CA)	Transthyretin cardiac amyloidosis (ATTR-CA)	
		Wild-type (wtATTR-CA)	Variant/hereditary transthyretin (hATTR-CA)
Age of onset	Median age >60 years	Median age >70 years	Variable: 30 to >60 years (depends on genotype) Median age = 39 years
Sex	Male > Female	Male > Female	Male = Female
Genetics ethnicity	No	No	Yes
Classic/defining clinical features	• Multisystem • Autonomic dysfunction • Bleeding/bruising • Periorbital edema	• Primarily cardiac • Carpal tunnel syndrome • Lumbar spinal stenosis • Spontaneous bicep tendon rupture	• Family history – autosomal dominant inheritance • Depends on variant • Polyneuropathy • Glaucoma/dry eyes
Cardiac clinical features	**CA in ~50%** • HFpEF; diastolic dysfunction • Atrial & ventricular arrhythmias • Heart blocks	**CA in ~100%** • HFpEF symptoms • Atrial arrhythmias • Heart blocks • Aortic stenosis	**CA depends on variant** **100% in VA-122ile** • Conduction disorders • Atrial fibrillation • Aortic stenosis
Disease course	• More rapid progression • Poor prognosis, but improving with new treatment	• Slowly progressive	• Depends on mutation/stage • Median survival 3–12 years

CA = cardiac amyloidosis; HFpEF = heart failure with preserved ejection fraction

Clinical presentation

- The following factors may lead to CA underdiagnosis or delayed diagnosis:
  - Several organs being affected
  - Patients referred to several doctors/specialists for concerns involving varying organs
  - Presenting with symptoms of other types of amyloidosis that are more frequent in older patients with other diseases or medical conditions
- Although patients with CA may have signs and symptoms of other common conditions, key nonspecific signs (shown below) could provide clues for potential CA.

Key nonspecific warning signals for cardiac amyloidosis

AL-CA & ATTR

Intolerance to beta blockers and/or ACE inhibitors/ARBs/ARNIs	Lower blood pressure in patients with previous HTN	Dysautonomia (eg, orthostatic hypotension, gastrointestinal disturbance [eg, anorexia, nausea, constipation, diarrhea], erectile dysfunction)

AL-CA

- Renal insufficiency
- Abnormal bruising/bleeding
- Macroglossia and/or periorbital edema
- Autonomic dysfunction
- MGUS
- Multiple myeloma

ATTR

- History of carpal tunnel syndrome, bicep tendon rupture, spinal stenosis
- African American >60 years, with HFpEF; no history of HTN
- New diagnosis of aortic stenosis in elderly
- Family history of ATTR
- Peripheral neuropathy

ACE = angiotensin-converting enzyme; AL-CA = light chain cardiac amyloidosis; ARB = angiotensin receptor blocker; ARNI = angiotensin receptor-neprilysin inhibitor; ATTR = transthyretin cardiac amyloidosis; HFpEF = heart failure with preserved ejection fraction; HTN = hypertension; MGUS = monoclonal gammopathy of undetermined significance

Diagnostic evaluation

- The Canadian Cardiovascular Society/Canadian Heart Failure Society (also referred to as CCS/CHFS) suggests initially conducting an electrocardiogram and laboratory testing in patients with HF suspected of having CA.
- Other noninvasive tools that may be used to diagnose CA include cardiac magnetic resonance imaging, cardiac nuclear scintigraphy, and transthoracic echocardiogram.
- Endomyocardial biopsy is the standard diagnostic tool for CA, but its use is generally recommended only when noninvasive test results are unclear or noninvasive diagnostic tools are unavailable.
- Additional tests (eg, serum and urine immunofixation tests for AL amyloidosis) may be conducted to further identify specific types of CA.

Medical management

- Although CA commonly presents with HF, CA is a progressive disorder that often presents with increasingly severe symptoms that may require more intense medical treatment than only conventional HF treatment strategies.
- Medical management of CA is therefore important to reduce the overall burden of CA symptoms, slow down disease progression, and improve quality of life in patients with CA.

Managing cardiac symptoms

- HF and arrhythmias (ie, abnormal heartbeat) are frequently associated with CA. Patients may experience symptoms such as shortness of breath, swelling, abdominal bloating, fatigue, atrial fibrillation (ie, irregular/fast heartbeat), and conduction abnormalities.
- Medical management of HF and arrhythmias may vary significantly in patients with versus without CA.
  - HF symptoms are typically managed by use of diuretics (also known as water pills) or restrictions in fluid and sodium intake.
  - However, other conventional HF medical management strategies, including angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, beta-blockers, calcium channel blockers, and digoxin, are not typically well tolerated in patients with CA.
  - Similarly, many treatments used for non-CA arrhythmias (eg, beta blockers, digoxin) may be of concern in patients with CA due to associated risks and negative inotropic effects on the heart. For atrial fibrillation patients with CA, the CCS/CHFS recommends anticoagulation therapy (also known as blood thinners).
- Medical management strategies are therefore commonly personalized for each patient.

Disease modifying and advanced therapies

- Disease modifying therapies may further be used for treatment in patients with CA, with studies reporting significant improvement in disease prognosis.
  - Chemotherapy may be used to stop the progression of cardiac AL amyloidosis (also referred to as AL-CA) and preserve organ function. Additionally, an autologous stem cell transplant could potentially be performed if oral treatment fails.
  - For ATTR-CA, stabilizing and silencing therapies may be used to modify the progression of the disease.
- For patients who are dealing with difficult or stubborn CA symptoms, other advanced therapies include a heart transplant or use of a biventricular assist device.

Disease course

- CA disease course or progression may be inferred from the type of CA (ie, AL-CA or ATTR; refer to Table 1).
- Median survival for patients with untreated AL-CA is approximately 5 months after the onset of HF.
- Median survival among patients with ATTR disease ranges from approximately 3.5 years to 12 years after symptom onset, depending on the type of disease (ie, wild-type or hereditary) and the degree of HF.
- Advanced therapies and early diagnosis of CA are therefore crucial in extending survival among patients with CA. For instance, treatment of AL-CA may extend patient survival to several years after the onset of HF compared with approximately 5 months without treatment.

Conclusion

The relatively uncommon and complex CA disease is underdiagnosed. Medical treatment options, such as advanced therapies, may extend survival in patients with CA.

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Where can I find more information?

For more information on this project, please refer to the full manuscript:

- **Full manuscript:** Cardiac Amyloidosis: A Comprehensive Clinical Resource for Cardiovascular Nurses
- **Link to article:** https://cccn.ca/education-health/cardiac-amyloidosis
- **Full article citation:** Groenewegen-Beukeboom M, et al. Cardiac amyloidosis: a comprehensive clinical resource for cardiovascular nurses. *Canadian Journal of Cardiovascular Nursing*. 2023;33(1):4–12.