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CARDIAC AMYLOIDOSIS:

A Comprehensive Clinical Resource for Cardiovascular Nurses

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ABSTRACT

Background: Cardiac amyloidosis (CA) is a relatively rare and often undiagnosed cause of infiltrative cardiomyopathy. Although CA patients can present with heart failure-like symptoms, it is important for cardiovascular nurses to have a comprehensive understanding of the unique features of CA and the care of these patients across the illness trajectory.

Purpose: Our goals are to increase awareness of CA and to provide cardiovascular nurses with an evidence-based, clinical resource on the care of patients with CA.

Methods: This document is grounded in a review of recent evidence and practices guidelines, as well as the clinical insights of a team of cardiovascular nurses and nurse practitioners from across Canada, with experience in caring for CA patients.

Conclusion: This resource, including current evidence related to the pathophysiology, risk factors, clinical manifestations, diagnostic evaluation, medical and nursing management, and key clinical practice points, will ideally optimize care and outcomes for the unique CA patient population.

KEY TERMS

Cardiac amyloidosis; clinical practice; nursing; nursing practice; pathophysiology; risk factors; clinical manifestations; diagnostic evaluation; medical management

1 BACKGROUND

Amyloidosis is a relatively rare, systemic disease caused by the misfolding of proteins and subsequent deposits of amyloid protein fibrils in various tissues of the body, most commonly in the heart and kidneys, but also in the liver, nerves, digestive tract, and lungs (Cuddy & Falk, 2020). In cardiac amyloidosis (CA), aggregation of amyloid in the interstitium of the heart may cause stiffening of the heart muscle with progressive cardiac dysfunction and heart failure (HF; Bistola et al., 2021). Based on a recent systematic review and meta-analysis (N = 11 studies; 3303 patients), See et al. (2022) concluded that a considerable proportion (13.7%) of patients with HF have underlying CA.

Over 30 different proteins have been implicated in amyloidosis; however, the two most common types, immunoglobulin light chain amyloidosis (AL amyloidosis) and transthyretin amyloidosis (ATTR), account for 95% of CA (Donnelly & Hanna, 2017). Clinically, both AL amyloidosis and ATTR are often camouflaged within patients with other common cardiovascular diseases, including HF, aortic stenosis (AS), and cardiac arrhythmias (Fine, Falk et al., 2020). Consequently, CA, and ATTR, in particular, are often undiagnosed (de Marneffe et al., 2022). Advances in diagnostics and emerging novel therapies are dramatically improving early recognition, diagnosis, and treatment options for these patients; however, epidemiological research, including data from a recent Alberta study (Sepehrvand et al., 2022), suggests that the incidence and prevalence of CA in Canada have increased over the past decade.

Cardiovascular nurses working in primary, acute, chronic, and palliative care settings play a key role in the care of patients with CA. Based on our review of the literature, only one recent publication, which focused on oncology nursing (Fogaren et al., 2022), has addressed the nursing perspective of CA. Therefore, the purpose of this document is to increase nurses' awareness and to provide cardiovascular nurses, in particular, with a current, evidence-based, and comprehensive nursing resource related to CA nursing care. Accordingly, this document is based on a review of recent evidence and clinical practices guidelines, as well as the CA-related clinical experiences of a team of cardiovascular nurses and nurse practitioners (NPs) from across Canada. We have included an overview of the pathophysiology, risk factors, clinical manifestations, diagnostics, medical and nursing management, and most importantly, key clinical practice points for caring for patients with CA in various settings, and across the illness trajectory. Our goal is that the knowledge gleaned from this document will facilitate the provision of optimal nursing care and improve outcomes for the CA patient population.

2 PATHOPHYSIOLOGY & RISK

The two most common types of CA are: 1) Transthyretin amyloidosis (ATTR), which includes the two subtypes of wild-type amyloidosis (wtATTR) and hereditary amyloidosis (hATTR), and 2) light chain amyloidosis (AL amyloidosis; Griffin et al., 2021; see Table 1). Transthyretin

amyloidosis, the most common form of systemic amyloidosis, occurs because of misfolding and deposition of a liver-derived protein (i.e., transthyretin [TTR]) as amyloid in various organs, including the heart. In wtATTR, the disease process occurs over decades and is therefore most common in the elderly. Although amyloid deposits occur in the soft tissues of ligaments and tendons, causing such issues as carpal tunnel syndrome, rupture of the biceps tendon, or spinal stenosis, the main pathologic deposits occur in the heart, resulting in CA (Cuddy & Falk, 2020; de Marneffe et al., 2022). While the mechanism by which the normal TTR causes these pathogenic amyloid deposits remains unclear, research evidence suggests that wtATTR is not only prevalent in the elderly, but it is also a leading cause of HF in the aging population (Mohamed-Salem et al., 2018; Sipe et al., 2016).

TABLE 1

Summary of Cardiac Amyloidosis (CA) 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	Median age > 70	Variable - 30 to > 60 (depends on genotype) Median age = 39
Sex	Male > Female	Male > Female	Male = Female
Genetics ethnicity	No	No	Yes
Classic/ Defining Clinical Features	• multi-system • autonomic dysfunction • bleeding/bruising • periorbital edema	• primarily cardiac • carpal tunnel syndrome • lumbar spinal stenosis • spontaneous bicep tendon rupture	• FHX – autosomal dominant inheritance • depends on variant • polyneuropathy • glaucoma/dry eyes
Cardiac Clinical Features	**CA in ~ 50%** • HFpwEF; diastolic dysfunction • atrial & ventricular arrhythmias • heart blocks	**CA in ~ 100%** • HFpEF symptoms • 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 tx	• slowly progressive	• depends on mutation/stage • median survival: 3–12 yrs

Note: CA = cardiac amyloidosis; HFpEF = heart failure with preserved ejection fraction.
From: Cuddy & Falk (2020); de Marneffe et al., 2022; Fine, Davis, et al., (2020); John (2018)

Patients with hATTR are born with a pathologic mutation in the TTR gene, which leads to accelerated amyloid deposits, commonly in the nervous system and the heart (Cuddy & Falk, 2020). Although hATTR is found in all ethnic groups, individuals with certain ethnicities/ geographical backgrounds appear to be more vulnerable. For example, in the United States, the most common mutation with predominantly cardiac involvement is present in 3-3.5% of individuals of African Descent (Buxbaum & Ruberg, 2017). Numerous other mutations have been identified, with age at presentation and male-to-female differences varying based on the genotype (Cuddy & Falk, 2020).

Light chain amyloidosis (AL amyloidosis) is caused by plasma cell dyscrasias in the bone marrow, which in turn result in the production of misfolded immunoglobulin light chains and aggregation of amyloid fibrils in the extracellular spaces of tissues. While AL amyloidosis is rare, cardiac AL amyloidosis affects slightly more men than women (3:2), most often between the fifth and seventh decade (Bistola et al., 2021). Importantly, cardiac involvement in patients with AL amyloidosis is reportedly seen in 50 – 75% of cases and the prognosis is generally worse than other types of CA (de Marneff et al., 2022; Falk et al., 2016).

Regardless of the pathogenesis, as the CA progresses, the amyloid deposits expand the extracellular space and stiffen the heart, which leads to restrictive physiology with diastolic dysfunction, and ultimately manifesting clinically as HF syndrome. Cardiac and peripheral autonomic dysfunction, as well conduction system abnormalities, are also hallmarks of CA, commonly resulting in postural hypotension, and arrhythmias such as atrial fibrillation (AF; Fine. Davis et al., 2020; Yamada et al., 2020). In addition, amyloid deposits within various areas of the heart may result in angina and AS (Fine, Davis et al., 2020).

KEY POINT

Amyloidosis is a systemic disease, which often affects multiple body systems, including the heart - leading to multi-system clinical manifestations, and specifically HF and conduction abnormalities.

3 CLINICAL PRESENTATION

Historically, CA has been under-diagnosed due, in part, to the multiple organ systems affected. The diagnosis of CA may be delayed because patients are referred to multiple specialists for their varied complaints involving different organ systems (Law & Gilmore, 2022; Martinez-Naharro et al., 2018; Zhang et al., 2020;). Moreover, because several types of amyloidosis are more common in older patients with other comorbidities, a diagnosis of CA may not be at the forefront (Fine, Davis et al., 2020; Porcari et al., 2020). The delayed diagnosis will likely limit the type of treatments offered to patients; therefore, knowledge of the presenting signs and symptoms that may be associated with CA is important for cardiovascular nurses, particularly in primary and acute care settings.

The clinical presentation of patients with CA may initially be somewhat nonspecific. For example, symptoms such as fatigue and weakness may be attributed to aging or other comorbidities, rather than the impaired cardiac function and arrhythmias associated with CA-related HF (Donnelly & Hanna, 2017). Although these patients typically exhibit signs and symptoms related to HF with preserved ejection fraction (HFpEF), including dyspnea on exertion, they may also present with right sided HF symptoms, including fluid retention with peripheral edema and ascites (Donnelly & Hanna, 2017). Disease progression may result in refractory HF signs and symptoms and worsening left ventricular function, leading to HF with a reduced ejection fraction (HFrEF), and patients experiencing increasing severity of their HF symptoms, as well as postural hypotension related dizziness and syncope (see Table 2).

Cardiac arrhythmias, including AF, are more commonly seen in wtATTR-CA. While a cardioembolic stroke resulting from AF may be the initial sign of CA, (Donnelly & Hanna, 2017), bundle branch and complete heart blocks, which are more commonly seen in ATTR-CA, can also be early manifestations of CA (Donnelly & Hanna, 2017). Patients may also initially present with angina in the presence of normal coronary arteries. While this angina may be due to diffuse ischemia (Donnelly & Hanna, 2017), it can also be attributed to small vessel disease caused by perivascular amyloid infiltration associated impaired vasodilation (John, 2018).

As many other organs are commonly affected by amyloidosis, CA patients will often present with a history that reflects the systemic disease process (see Tables 1 & 2). Several key non-specific warning signals should raise suspicion of potential CA and warrant further investigation (see Table 2). For example, age and ethnicity/geographic location are predisposing factors in hATTR-CA; A history of carpal tunnel syndrome, or biceps tendon rupture, may precede cardiac-related symptoms in wtATTR-CA (de Marneffe et al., 2022; Donnelly & Hanna 2017; Fine, Davis et al., 2020; Vaxman & Gertz, 2020). A diagnosis of low flow/low gradient AS, perhaps requiring a transcatheter aortic valve replacement (TAVR; Vaxman & Gertz 2020), should also raise suspicion, especially when associated with other seemingly unrelated symptoms, such as spinal stenosis, peripheral neuropathy, visual disturbances, gastrointestinal symptoms (e.g. chronic diarrhea or constipation), weight loss, and non-diabetic nephrotic syndrome (see Tables 1 & 2; Donnelly & Hanna, 2017; Porcari et al., 2017; Vaxman & Gertz, 2020).

TABLE 2

Key Non-Specific Warning Signals for Cardiac Amyloidosis

AL CA & ATTR	
Intolerance to beta blockers and/or ACE inhibitors/ARBs/ARNIs ↓ BP in patients with previous HTN Dysautonomia (e.g., orthostatic hypotension, GI disturbances [e.g., anorexia, nausea, constipation, diarrhea], erectile dysfunction)	
AL CA	**ATTR**
• Renal insufficiency • Abnormal bruising/bleeding • Macroglossia and/or periorbital edema • Autonomic dysfunction • MGUS • Multiple myeloma	• Hx of carpal tunnel syndrome, bicep tendon rupture, spinal stenosis • Afro-American >60, with HFpEF; no hx of HTN • New dx of aortic stenosis in elderly • FHx of ATTR • Peripheral neuropathy

ACE =Angiotensin Converting Enzyme; ARB=Angiotensin Receptor Blocker;
ARNI = Angiotensin Receptor-Neprilysin Inhibitor;
AL-CA =Light chain cardiac amyloidosis;
ATTR = Transthyretin cardiac amyloidosis;
HTN = hypertension; MGUS = Monoclonal gammopathy of undetermined significance.

From: Fine, Davis et al., 2020; Donnelly & Hanna, 2017; Porcari et al., 2017; Vaxman & Gertz, 2020).

KEY POINT

Patients with CA may present as other common cardiac and non-cardiac conditions; however, nurses with knowledge of the clinical signs and symptoms and astute nursing assessment skills, which include a comprehensive history and physical exam, can identify important clues to the diagnosis and early treatment of CA.

4 DIAGNOSTIC EVALUATION

It is important for nurses who are involved in the care of CA patients to be knowledgeable about the diagnostic tests for CA. Nurses play an essential role in educating patients and their family members about these diagnostic tests, preparing patients for the tests, and providing support to newly diagnosed patients and their families. Moreover, depending on their scope of practice, clinic nurses and nurse practitioners (NPs) may be responsible for ordering the initial diagnostic tests necessary to make a differential diagnosis of AL-CA vs wtATTR-CA or hATTR-CA (see Figure 1).

The Canadian Cardiovascular Society/Canadian Heart Failure Society (CCS/CHFS) position statement (Fine, Davis et al., 2020) advises that routine initial diagnostic tests for suspected CA in HF patients should include a 12-lead EKG and lab work for cardiac biomarkers (i.e., troponin, and BNP/NTproBNP). While the EKG findings in patients with CA will most commonly show low voltage and left ventricular (LV) hypertrophy (Maurer et al., 2019; Murtagh et al., 2005), AF with abnormal conduction and ectopy are nonspecific findings in these patients (see Table 2; Fine, Davis et al., 2020). It is also not uncommon to detect chronically elevated cardiac biomarkers in patients with CA (Fine, Davis et al., 2020).

Additional non-invasive imaging diagnostics including transthoracic echocardiogram (TTE), cardiac magnetic resonance imaging (MRI), and cardiac nuclear scintigraphy (e.g., pyrophosphate [PYP] scan) play a pivotal role in the diagnosis of CA. Echocardiography is often the first imaging diagnostic test performed on patients presenting with HF; however, early features of CA could be missed with this test (Dorbala et al., 2020). While the echocardiogram will identify LV wall thickness, particularly in patients with ATTR-CA, as well as diastolic dysfunction in both ATTR-CA and AL-CA, these findings are neither specific nor sensitive for amyloidosis (de Marneffe et al., 2022; Dorbala et al., 2020). However, a cardiac MRI can differentiate hypertrophic cardiomyopathy from ATTR-CA (Dorbala et al., 2020). Although endomyocardial biopsy remains the gold standard for diagnosing all subtypes, the PYP scan is now replacing cardiac biopsies to diagnose ATTR-CA, (Dorbala et al., 2020).

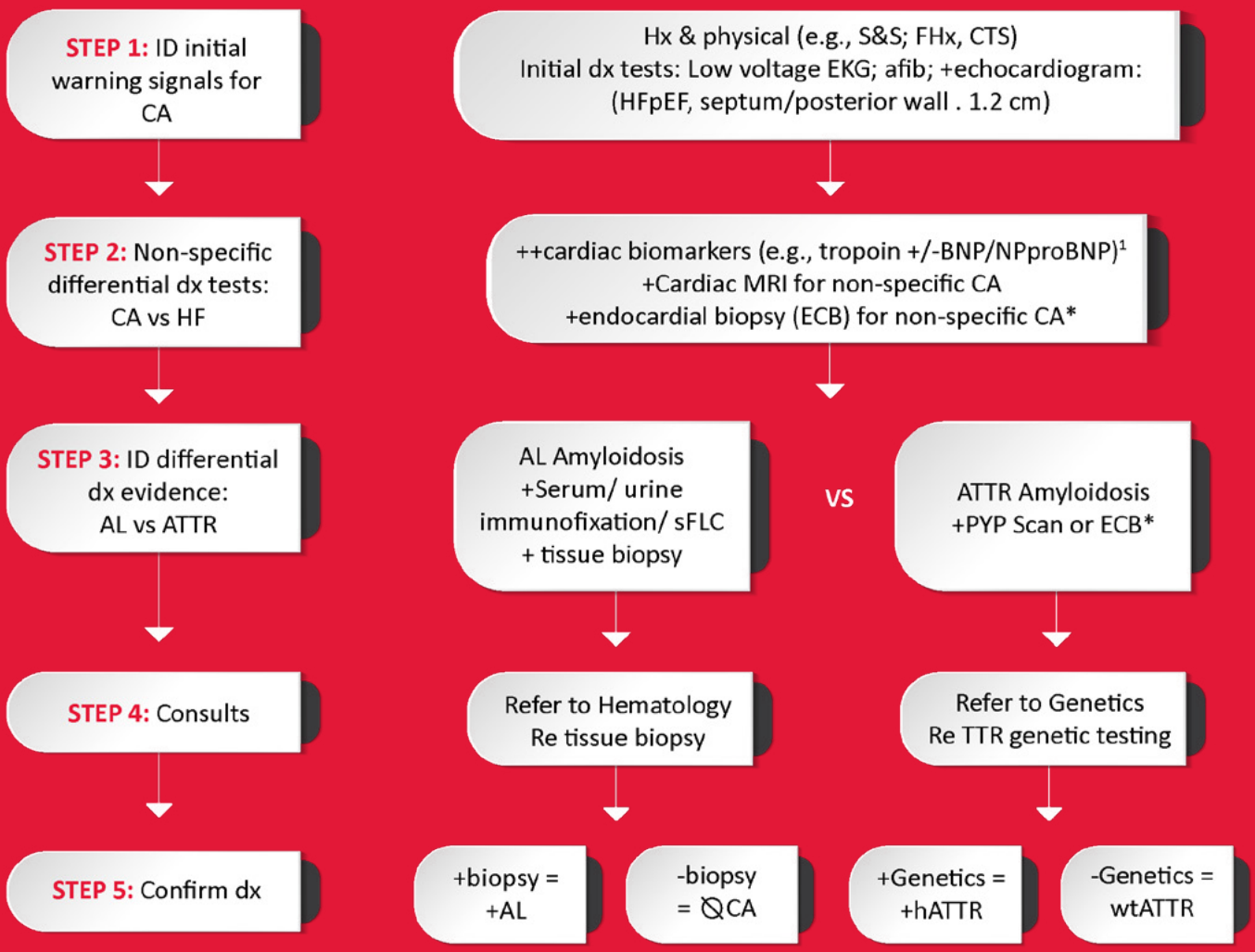
Additional diagnostic tests may be ordered to determine the specific type of CA. Serum and urine immunofixation tests are important in the diagnosis of AL amyloidosis (de Marneffe et al., 2022; Fine, Davis et al., 2020). If AL-CA is suspected, a tissue biopsy is needed to confirm the diagnosis; This could include a bone marrow biopsy, or an abdominal fat pad, rectum, colon, or lip biopsy. As well, an endomyocardial biopsy is recommended when other diagnostics are not conclusive, but the clinical suspicion is still high for CA (Fine, Davis et al., 2020). Finally, genetic testing is recommended to rule out hATTR (Fine, Davis et al., 2020).

KEY POINT

It is important for nurses to be well- informed about the specific diagnostic tests for CA as they play a pivotal role in diagnostic process, including educating and supporting patients and their families prior to, during, and following the diagnosis.

FIGURE 1

Cardiac Amyloidosis: Steps to a Differential Diagnosis



Note: CTS = carpal tunnel syndrome;
NTproBNP = N-terminal-pro B-type natriuretic peptide;
sFLC = serum free light chain assay;
PYP scan = m99Tc technetium pyrophosphate scan.

[1] cardiac enzymes are persistently & disproportionately higher in CA than HF.

***While ECB is the gold standard for non-specific dx of CA, generally not recommended unless non-invasive test results are unclear, or non-invasive tests such as PYP scan not available.

From: Donnelly & Hanna, 2017; Fine, Davis et al., 2020.

5 MEDICAL MANAGEMENT

Individuals with CA usually present with the clinical syndrome of HF, because of the CA-related restrictive cardiomyopathy. As CA is a progressive disease, signs and symptoms become increasingly severe and refractory to conventional HF management strategies (e.g., dietary and fluid restrictions), therefore requiring more aggressive medical management. In addition, treating the frequent arrhythmias associated with CA and exploring options for disease modifying agents are central to the medical management of these patients. Importantly, the overall goal of medical management is to reduce the burden of clinical symptoms, slow the disease process, and help these patients to optimize their quality of life (Fogaren et al., 2022).

MANAGING THE CARDIAC SYMPTOMS

Managing Heart Failure

Heart failure is the hallmark cardiovascular presentation for patients with CA. The patient may present with either left and/or right sided HF symptoms, such as shortness of breath (SOB), orthopnea, paroxysmal nocturnal dyspnea (PND), peripheral edema, abdominal bloating, weakness, and fatigue (Fine, Davis et al., 2020). Managing the symptoms of volume overload can be challenging because of the reduced stroke volume and cardiac output (Kittleson et al., 2020). Loop diuretics (e.g., Furosemide; Bumetanide) are frequently used to alleviate congestion and are often combined with potassium sparing diuretics (e.g., mineralocorticoid receptor antagonists [MRAs]; e.g., Spironolactone), and/or thiazide diuretics (e.g., Metolazone,). These diuretics, along with fluid and sodium restrictions are considered the mainstay of HF symptom management (Fine, Davis et al., 2020); However, the aggressive use of diuretics can result in decreased cardiac output, further lowering BP and renal function; therefore, a stepwise approach, with close monitoring of vital signs and bloodwork is preferred (Bistola et al., 2021).

It is also important to note that, due to the progressive restrictive cardiomyopathy and varying degrees of autonomic dysfunction, other traditional HF guideline directed medical therapies, including beta-blockers (BBs), angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), calcium channel blockers (CCBs), and digoxin are generally poorly tolerated by CA patients (Fine, Davis et al., 2020). Importantly, medical management is individualized, with multiple considerations, including patient status, physician preference, and cost to the patient.

Managing Arrhythmias

Arrhythmias, most commonly AF and conduction abnormalities (e.g. various degrees of heart block), are a frequent consequence of CA. Atrial fibrillation may be the initial manifestation of CA, particularly in patients with wtATTR (Donnelly & Hanna, 2017). While the ventricular rate in CA-related AF is usually controlled because of amyloid infiltrating the atrioventricular conduction system, when rapid ventricular rates do occur, they are poorly tolerated due to decreased stroke volume. (Bistola et al., 2021). Similar to managing non-CA HF, many of the typical medications used to treat arrhythmias (e.g., BBs, CCBs, digoxin) should be used with

caution or avoided altogether in patients with CA because of their negative inotropic effects, limited data, and associated risks (Fine, Davis et al., 2020). However, Amiodarone, which is usually well-tolerated, may be considered for pharmacologic conversion to sinus rhythm or for rate control if patients remain symptomatic with other rate control medications (Bistola et al., 2021; de Marneffe et al., 2022; Kittleson et al., 2020). Electrical cardioversion may also be an option, with success rates reportedly similar to patients with non-CA AF (i.e., up to 90–94%; El-Am et al., 2019). Refractory AF shows benefits with AV node ablation; however, there is limited data and experience for catheter ablation for CA-related AF (Cheung, 2020; Giancaterino, 2020).

Importantly, patients with CA, both with and without AF, are at increased risk for thrombus and embolus formation (Bistola et al., 2021; Giancaterino, 2020). Amyloid infiltration results in atrial dilation, hemostasis, and the consequent risk of left atrial thromboembolism (Fine, Davis et al., 2020; Giancaterino, 2020; Mints, 2018,). According to the 2020 CCS/CHFS position statement, despite the lack of data to support a specific anticoagulation strategy, anticoagulation for patients with CA and AF is recommended (Fine, Davis et al., 2020)

Based on a focused review, Giancaterino et al. (2020) concluded that ventricular arrythmias are common in patients with CA, with non-sustained ventricular tachycardia (NSVT) reportedly greater than 70% in these patients. Moreover, studies have shown that sudden cardiac death is as high as 50% in patients with CA (Giancaterino et al., 2020). Current guidelines generally support ICDs being offered to CA patients for secondary, but not primary prevention (Bistola et al., 2021; Fine, Davis et al., 2020; John, 2018).

Although the prevalence of conduction abnormalities in CA patients is high, the pathophysiology is not well understood (Giancaterino et al., 2020). Common conduction abnormalities in CA patients include 1st-degree AV block and intraventricular bundle branch blocks. While routine follow-up EKGs of these patients are crucial to identify any progression of the blocks, the initial symptom is often syncope (co-author: DB). Permanent pacemakers are commonly indicated for CA patients with significantly symptomatic conduction disease; however, prophylactic pacing in the CA population has not been shown to improve outcomes (Giancaterino et al., 2020).

KEY POINT

Medical management of cardiac signs and symptoms and arrhythmias may vary considerably in CA vs non-CA patients. Therefore, it is critically important for cardiovascular nurses to be well-informed of the individual/unique differences in managing these patients.

DISEASE MODIFYING THERAPIES

Medical treatment options for managing patients with CA may include disease-modifying therapies. To ensure the provision of optimal care, nurses working with patients receiving these medications must be aware of their actions and potential adverse effects. This knowledge also enables nurses to effectively educate patients regarding rationale for these medications, as well as possible untoward effects.

While AL-CA is usually managed with chemotherapy protocols (e.g., bortezomib, combined with dexamethasone & low-dose cyclophosphamide), autologous stem cell transplantation may also be considered when oral regimens have failed (de Marneffe et al., 2022; Fine, Davis et al., 2020). These therapies mitigate disease progression by arresting the production of abnormal free light chains and preserving organ function (Bianchi et al., 2021). However, if left untreated, AL cardiac amyloidosis progresses rapidly and has an extremely poor prognosis (Cuddy & Falk, 2020).

The progression of ATTR–CA can be altered by two types of therapies: stabilizing and silencing agents. Novel transthyretin-targeted (TTR) stabilizing therapies prevent the breakdown of TTR tetramers into unstable monomers. For example, tafamidis, an orally administered TTR stabilizer, is prescribed for individuals diagnosed with wtATTR-CA or hATTR-CA with functional classification of NYHA I to III HF symptoms (Fine, Davis et al., 2020). Silencing TTR RNA agents (e.g., Inotersen & Patisiran) also inhibit the progression and possibly reverse amyloid burden in hATTR amyloidosis patients. The 2020 CCS/CHFS position statement recommends the use of these medications for patients who have hATTR amyloidosis with associated ambulatory polyneuropathy (Fine, Davis et al., 2020). However, further clinical trials are needed to examine the safety and efficacy of these therapies.

Disease modifying therapies are dramatically improving the prognosis for CA patients (Fine, Falk et al., 2020). As well, ongoing studies on new disease modifying therapies for the treatment of CA are reasons for optimism. However, further research is required to determine next steps in the treatment of this complex disease.

KEY POINT

It is important for nurses working with CA patients to be aware of the actions, and adverse effects of novel disease modifying therapies, as well as the emerging evidence of effective and timely treatment for these patients

ADVANCED THERAPIES

Advanced and aggressive therapies, such as cardiac transplantation and implantation of a biventricular assist device (BiVAD) are potential options for patients who struggle with intractable symptoms of CA. An earlier retrospective study on the outcome of heart transplantation in patients with CA (N = 69; Kpodonu et al., 2005) found that these patients had reduced survival compared to patients transplanted for other conditions. However, in a more recent retrospective

study (N=23), Guendouz et al. (2022) found that heart transplantation, either alone or with liver and kidney transplant, was a viable treatment option for select patients diagnosed with severe CA. Of note, the role of BiVADs as a bridge to transplantation appears to have similar outcomes to patients transplanted without a BiVAD; however, further research with larger, prospective studies, and longer follow-up is still required (Chen et al., 2021).

KEY POINT

When considering advanced interventions for patients with CA, the complexity of their condition, the challenges of recovery, and the possibility of negative consequences must be considered and communicated to patients and their families.

6 DISEASE COURSE

The type of CA provides insight into the typical disease course/progression (see Table 2). For example, median survival for untreated AL-CA from onset of HF to death is approximately five months (Cuddy & Falk, 2020). With treatment, and achievement of hematologic remission with chemotherapy or stem cell transplantation, survival of patients with AL-CA can be extended to several years (Cuddy & Falk, 2020). In most cases, wtATTR is a disease of aging and progresses slowly; however, sudden onset of refractory HF may develop after the initial slow progression phase (Bistola et al., 2021). The median survival of wtATTR-CA is approximately 3.5 years after diagnosis, depending on the degree of HF (Cuddy & Falk, 2020). While the disease course and prognosis of hATTR-CA is influenced by gene mutation and the geographic region, survival from onset of symptoms ranges from 7 to 12 years. (Cuddy & Falk, 2020). Recent advances in treatments and earlier recognition are extending the survival of patients with CA (Fine, Falk et al. 2020), highlighting the importance of early diagnosis and treatment for these patients. However, for the patients with advanced CA and those who do not respond well to advanced therapies, early referrals to palliative care may have a favorable impact on their quality of life (Fine, Davis et al., 2020).

KEY POINT

Although advances in diagnostics and treatment are improving CA patients' quality of life and outcomes, nurses play an important role in openly communicating with CA patients and their families about their disease course and prognosis.

7 NURSING CONSIDERATIONS

Cardiac amyloidosis is a unique, relatively rare, and complex disease. Therefore, nurses caring for this patient population in the clinical setting require comprehensive nursing knowledge and skills related its unique pathophysiology, history and physical assessment findings, diagnostics, disease course, and medical and nursing management. Moreover, educating CA patients and their families, as well as teaching novice nurses about this disease is central to optimal care. Finally, to date, no apparent nursing research related to CA has been published in the scientific literature; therefore, there is an urgent need for nursing-related research in this area.

CLINICAL PRACTICE

As amyloidosis affects multiple systems, with varying symptoms and treatments, caring for patients with CA can be challenging for healthcare providers (Fine, Davis et al., 2020). A key role for CV nurses in all clinical areas is to be aware of early, multi-system signs, as well as the worsening cardiac-related symptoms of HF and various arrhythmias. Nurses also provide care that accommodates the unique challenges of the progressive nature of CA. Furthermore, nurses are well-positioned to have difficult conversations with patients and their families regarding prognosis and goals of care and palliation, and to introduce these conversations early in a plan of care for patients with end stage CA (Tsukanov & Fabbro, 2016).

Multi-disciplinary teams are invaluable for the provision of comprehensive and collaborative care of patients with CA. Given nurses' unique role in providing direct patient care and ensuring patients' quality of care, as well as managing a variety of healthcare resources, nurses are ideally situated to assess the need to engage other members of the healthcare team. Therefore, nurses play an integral role in coordinating multi-disciplinary teams to address patients' physical, social, psychological, and spiritual needs in the clinical setting. In addition, nurse clinicians, clinical nurse specialists (CNS), and NPs in particular, because of their advanced level of knowledge and expanded scope of practice, are invaluable as leaders of the healthcare team, ensuring the provision of seamless care for these patients within the acute and chronic care, critical care, palliative care, and community settings.

Ideally, all aspects of care for CA patients, including assessment, diagnostics, medical and nursing management, and ongoing monitoring, as well as psychosocial and spiritual care should take place in a specialized clinical setting that provides individualized, comprehensive care to CA patients and their families. This setting should include a multi-disciplinary team, led by nurses with experience and specialization in managing patients with CA (Fogaren et al., 2022). Although still relatively new in Canada, centralized CA clinics and nurse managed CA clinics, in particular, are emerging across this country. For example, in Calgary, the Cardiac Amyloidosis Clinic was officially established in January 2022; however, CA patients had been managed in a Cardio-Oncology Clinic since 2013. This Clinic is devoted to caring for the three main types of CA (i.e., AL-CA, wtATTR-CA and hATTR-CA) patients. The Clinic is managed by nurse clinicians, who are RNs with experience and expertise in caring for this patient population. While the Clinic is overseen by a Cardiologist, standard guidelines have been developed for nursing staff. Although the nurse clinicians do not prescribe medications, protocols enable them to be relatively

autonomous, and allow for independent and innovative thinking in the care of CA patients (co-author DB).

This is an exciting time for nurses in this field as new and innovative disease management strategies and treatment options are emerging to improve longevity and quality of life outcomes for these patients. As cardiovascular nurses are ideally positioned to participate in and manage specialized clinics for CA patients, it is important to advocate for this important role.

EDUCATION

Education for patients with CA and their families is a critically important aspect of care, from diagnosis to end of life. As the primary point of care, nurses educate patients about their diagnostic procedures and various aspects of their medical management, including medications, interventions, and novel therapies. Providing clear and consistent messaging and facilitating access to available resources is an important role for nurses, with the goal to alleviate a measure of the psychological suffering and stress in these individuals and their families. Support groups can also provide information and assistance for patients and their families who are trying to come to terms with their disease (Kendall, 2010). Importantly, the groundwork for CA support groups in Canada is currently being initiated by nurses in several centers. Initially, these support groups will be nurse led, with the goal for the patients and families to assume the leading role in the future (co-author: DB).

Nurses caring for patients with CA, across clinical settings and in the community, must have a comprehensive understanding of the pathophysiology, risk factors, clinical manifestations, diagnostic evaluation, medical management and nursing considerations of CA patients across the illness trajectory. The nursing team plays an important role in ensuring that novice nurses receive this education and are mentored by their experienced colleagues to ensure that they are providing optimal care to this unique patient population. Ongoing education for all nursing staff working with CA patients regarding novel and emerging medical therapies is also essential to achieving and maintaining standards of care.

FUTURE NURSING RESEARCH

Over the past several decades, burgeoning evidence has changed the face of CA patient care, with dramatic advances towards achieving the goal of earlier and more effective treatments for these patients. However, there is a conspicuous dearth of nursing research in this area. Studies exploring and evaluating the role of specialized nurses, including nurse clinicians, CNSs, and NPs in the care of this complex patient population are needed. As well, further research regarding the specific physical and psychological needs of CA patients and their families, and how nurses can support, educate, and provide the optimal nursing care to improve patient outcomes, are urgently needed.

KEY POINT

Cardiovascular nurses play a pivotal role in supporting the care of these complex patients within clinical practice, education, and research.

8 CONCLUSION

Cardiac amyloidosis is a unique, relatively rare, and under-diagnosed disease. The often complex patient presentation, diagnostics, and medical management require cardiovascular nurses to have astute nursing assessment skills and the ability to safely and effectively implement the treatment plan, as well to provide education and supportive care to patients and their families. To this end, cardiovascular nurses must be aware of the current, evidence-based, key practice points for caring for patients with CA in various settings and across the illness trajectory. This knowledge will enable nurses to provide optimal nursing care and improve outcomes for the CA patient population.

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