

Canadian Cardiovascular Society Consensus Conference guidelines on heart failure – 2008 update: Best practices for the transition of care of heart failure patients, and the recognition, investigation and treatment of cardiomyopathies

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JMO Arnold, JG Howlett, A Ducharme, et al. Canadian Cardiovascular Society Consensus Conference guidelines on heart failure – 2008 update: Best practices for the transition of care of heart failure patients, and the recognition, investigation and treatment of cardiomyopathies. Can J Cardiol 2008;24(1):21-40.

Heart failure is a clinical syndrome that normally requires health care to be provided by both specialists and nonspecialists. This is advantageous because patients benefit from complementary skill sets and experience, but can present challenges in the development of a common, shared treatment plan. The Canadian Cardiovascular Society published a comprehensive set of recommendations on the diagnosis and management of heart failure in January 2006, and on the prevention, management during intercurrent illness or acute decompensation, and use of biomarkers in January 2007. The present update builds on those core recommendations. Based on feedback obtained through a national program of heart failure workshops during 2006 and 2007, several topics were identified as priorities because of the challenges they pose to health care professionals. New evidence-based recommendations were developed using the structured approach for the review and assessment of evidence that was adopted and previously described by the Society. Specific recommendations and practical tips were written for best practices during the transition of care of heart failure patients, and the recognition, investigation and treatment of some specific cardiomyopathies. Specific clinical questions that are addressed include: What information should a referring physician provide for a specialist consultation? What instructions should a consultant provide to the referring physician? What processes should be in place to ensure that the expectations and needs of each physician are met? When a cardiomyopathy is suspected, how can it be recognized, how should it be investigated and diagnosed, how should it be treated, when should the patient be referred, and what special tests are available to assist in the diagnosis and treatment? The goals of the present update are to translate best evidence into practice, apply clinical wisdom where evidence for specific strategies is weaker, and aid physicians and other health care providers to optimally treat heart failure patients, resulting in a measurable impact on patient health and clinical outcomes in Canada.

Key Words: *Cardiomyopathy; Consensus statement; Diagnosis; Disease management; Drug therapy; Etiology; Guidelines; Heart failure; Prognosis; Transition of care*

Mise à jour 2008 des lignes directrices de la conférence consensuelle sur l'insuffisance cardiaque de la Société canadienne de cardiologie : Meilleures pratiques pour la transition des soins des insuffisants cardiaques et le dépistage, l'exploration et le traitement des myocardiopathies

L'insuffisance cardiaque est un syndrome clinique qui exige normalement des soins de santé dispensés à la fois par des spécialistes et des non-spécialistes. Ce fonctionnement est avantageux, car les patients profitent d'ensembles de compétences et d'expérience complémentaires, mais il peut poser problème pour la mise sur pied d'un plan de traitement commun et partagé. En janvier 2006, la Société canadienne de cardiologie a publié une série complète de recommandations sur le diagnostic et la prise en charge de l'insuffisance cardiaque, et en janvier 2007, sur la prévention, la prise en charge pendant une maladie intercurrente et la décompensation aiguë et sur l'utilisation des biomarqueurs. La présente mise à jour se fonde sur ces recommandations de base. D'après les commentaires obtenus lors d'un programme national d'ateliers sur l'insuffisance cardiaque ayant eu lieu en 2006 et 2007, on a déterminé plusieurs sujets prioritaires en raison des défis qu'ils représentent pour les professionnels de la santé. On a élaboré de nouvelles recommandations probantes d'après la démarche structurée pour l'analyse et l'évaluation des données probantes que la Société a adoptée et déjà décrite. On a rédigé des recommandations précises et des conseils pratiques pour s'assurer des meilleures pratiques pendant la transition des soins des insuffisants cardiaques et le dépistage, *suite à la page suivante*

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Received for publication December 10, 2007. Accepted December 12, 2007

l'exploration et le traitement des myocardopathies. Les questions cliniques abordées sont : Quels renseignements le médecin traitant fournit-il en prévision d'une consultation auprès d'un spécialiste ? Quelles directives le consultant devrait-il donner au médecin traitant ? Quels processus devraient être en place pour s'assurer de respecter les attentes et les besoins de chaque médecin ? Quand on soupçonne la présence d'une myocardopathie, comment peut-on la dépister, comment doit-on l'explorer et la diagnostiquer, comment faut-il la

traiter, quand faut-il aiguiller le patient ailleurs et quels tests spéciaux peut-on utiliser pour contribuer au diagnostic et au traitement ? La présente mise à jour vise à transférer les meilleures données probantes en pratique, à appliquer la sagesse clinique lorsque les stratégies probantes sont moins solides et à aider les médecins et les autres dispensateurs de soins à traiter les insuffisants cardiaques de manière optimale, afin d'obtenir des effets mesurables sur la santé des patients et les issues cliniques au Canada.

In 2006 and 2007, the Canadian Cardiovascular Society (CCS) published guidelines on the diagnosis and management of heart failure, the prevention of heart failure, the treatment of heart failure during intercurrent illness and acute decompensation, and the use of biomarkers, such as brain natriuretic peptide (BNP) or its prohormone (NT-proBNP). Each year, as part of the CCS National Heart Failure Workshop Initiative, a series of heart failure workshops are held across the country to interactively discuss how to implement those guidelines and, through a needs assessment, to identify additional challenges facing physicians and other health care providers in their day-to-day management of patients with heart failure. Based on those discussions, the present paper addresses the important issues of transfer and transition of heart failure care, and the diagnosis and management of some specific cardiomyopathies. These topics were identified as priorities through ongoing needs assessments and evaluations provided by participants. In many of these areas, there are few randomized clinical trials and, thus, many of the recommendations and practical tips are based on consensus. However, because they remain clinical challenges, we trust that the present paper will also stimulate further discussion, research and planning in these important areas.

The authors of the present update are the Primary Panel members and were responsible for identifying the scope of this review, reviewing the literature (search conducted by the Cochrane collaboration), determining relevance and strength of evidence, and formulating recommendations, which were agreed on by consensus. The Secondary Panel members represented a broad spectrum of Canadian practitioners and reviewed the paper, providing constructive feedback to the Primary Panel. The systematic review strategy and the methods for formulating the recommendations are described in more detail on the CCS Heart Failure Consensus Conference Program Web site (www.hfcc.ca).

The objective of the CCS Heart Failure Consensus Conference 2008 update is to provide Canadian clinical practitioners with recommendations in two principal areas: the responsibilities for the transfer of care of heart failure patients between referring physicians and specialists and vice versa, as well as a diagnostic and management approach to cardiomyopathies. It is intended that the present update will complement the previous papers published in 2006 and 2007. The clinical questions addressed by the current recommendations in the present paper include: What information should a referring physician provide for a specialist consultation? What instructions should a consultant provide to the referring physician? What processes should be in place to help ensure that the expectations and needs of each physician are met? When a cardiomyopathy is suspected, how can it be recognized, how should it be investigated and diagnosed, how should it be treated, when should the patient be referred, and what special tests are available to assist in the diagnosis and treatment? In addition, practical tips are provided to aid the health care provider in the management of heart failure patients for whom evidence-based recommendations cannot easily be made, but for whom clinical experience and reports suggest a preferred approach to treatment. All recommendations and practical tips were approved by consensus of the Primary Panelists, and the paper was reviewed by both the Primary and Secondary Panelists before submission for publication.

The Consensus Conference panelists included individuals from all relevant professional groups. For the present update, the CCS included multidisciplinary representation on the Primary Panel to include members and perspectives from the following organizations:

the Canadian Pharmacists Association, the Canadian Council of Cardiovascular Nurses, the Canadian Geriatrics Society, the Canadian Society of Internal Medicine, The College of Family Physicians of Canada and the Canadian Association of Advanced Practice Nurses. The CCS Heart Failure Consensus Conference 2008 update has been developed for those seeking evidence-based recommendations for optimal heart failure care in Canada, including cardiovascular specialists, internists, primary care physicians (PCPs), allied health professionals, patients and families.

An extensive dissemination and implementation program has been developed for the CCS Heart Failure Consensus Conference Program. For example, bilingual versions of a handy 'pocket card' and a slide kit have been developed based on the 2006 and 2007 recommendations. In addition, the CCS National Heart Failure Workshop Initiative has been developed to involve Canadian clinical practitioners in ongoing use and refinement of the CCS Heart Failure Consensus Conference. Details regarding these and other initiatives can be found on the CCS Heart Failure Consensus Conference Program Web site (www.hfcc.ca).

The class of recommendation and the grade of evidence were determined as follows:

Class I: Evidence or general agreement that a given procedure or treatment is beneficial, useful and effective.

Class II: Conflicting evidence or a divergence of opinion about the usefulness or efficacy of the procedure or treatment.

Class IIa: Weight of evidence is in favour of usefulness or efficacy.

Class IIb: Usefulness or efficacy is less well established by evidence or opinion.

Class III: Evidence or general agreement that the procedure or treatment is not useful or effective and, in some cases, may be harmful.

Level of evidence A: Data derived from multiple randomized clinical trials or meta-analyses.

Level of evidence B: Data derived from a single randomized clinical trial or nonrandomized studies.

Level of evidence C: Consensus of opinion of experts and/or small studies.

TRANSITIONAL CARE

Transitional, or transition of, care is an important but sometimes overlooked or assumed aspect of patient management that promotes a series of actions to enhance continuity of care, and facilitate safe and timely transfer of patients from one level of care to another (1-3). Transitional care particularly targets patients at high risk for heart failure readmission; for example, those with previous hospitalizations, multiple comorbidities or medications, elderly patients and those with concomitant frailty, cognitive and functional impairment, depression or limited social support (1,3,4). Because the assessment of frailty, cognitive impairment and depression, as well as the role of heart failure management programs in elderly heart failure patients, were reviewed in previous CCS Consensus Conference recommendations on heart failure (5,6), the present paper addresses in more detail some of the necessary actions to help to ensure that transitional care of a heart failure patient is optimal for both the patient and the health care providers.

Responsibilities of the heart failure specialist or clinic Recommendations

- A heart failure specialist or clinic should have the capacity to accept referrals, transition of care or arrange for transfer to a

tertiary care centre within the recommended Canadian benchmarks, that is, within 24 h for hemodynamically unstable patients, less than two weeks for patients with decompensation or progression to New York Heart Association (NYHA) class IV, less than four weeks for patients in NYHA class III, and less than six weeks for patients in stable NYHA class II who are referred for chronic disease management (class IIa, level C) (Table 1).

- The components available in a heart failure clinic should address the needs of the referred patient, the referral physician and the regional health care system (class I, level C).
- Clear, collaborative and specific communication from the accepting physician to the referring physician should occur to ensure that the concerns of the referring physician are addressed, and that new heart failure management recommendations are implemented and monitored by the referring and other treating physicians as an integrated plan (class I, level C).
- Specialist recommendations should address the following: medication initiation and dose titration (when to titrate and the target dose), laboratory monitoring, common and/or serious adverse effects (eg, hypotension, bradycardia, cough, renal dysfunction, electrolyte disturbances), patient/family or caregiver education and timing of follow-up (class I, level C).

There are substantial variations in the implementation of practice guidelines among countries (8) and between cardiologists, internists and general practitioners (9,10). The majority of patients with heart failure in Canada are treated by PCPs (11). This can be advantageous because PCPs are familiar with a patient's previous health and expectations, but may be challenging because many heart failure patients have several comorbidities, will need combination drug therapy, and may require more investigations and treatments that may not be available or very familiar to PCPs. However, frequent visits to PCPs alone without attention to heart failure-specific education, intensive follow-up and optimization of medical therapy do not appear to reduce rehospitalizations or improve quality of life (12). Shared care is therefore necessary, and the CCS guidelines have previously identified the profiles of patients who should be referred to a heart failure specialist (5). Patients with new-onset heart failure should be assessed and treated with some urgency, because their mortality is high within the first few weeks after diagnosis (13).

When available and accessible, the multidisciplinary model of care in a specialized heart failure clinic is the preferred choice, although it is not currently available in all communities (5). This heart failure care, however, should complement but not replace the other comprehensive care delivered by the PCP. In a few cases, a single visit to a heart failure specialist may be sufficient, while in most cases, ongoing collaboration and shared care is necessary. In different communities, the referral may be to a heart failure specialist with relevant postgraduate training who is part of a heart failure disease management program and team, an individual cardiologist or internist with expertise in heart failure management or, in some cases, a PCP colleague, registered nurse/advanced practice nurse (RN/APN) or pharmacist with special interest and expertise in a specific areas of heart failure such as palliative care or education. Complete transfer of care to a specialist may be required for a period of time in patients with severe or complicated heart failure. As the patient's health improves, ongoing monitoring of progress can be performed by a PCP who is confident and competent in doing so, with specialist care available to support the PCP. Managing heart failure requires resources across the entire spectrum of care, and if multidisciplinary care is not available, each health care facility should have plans in place to appropriately triage heart failure patients on admission and at the time of discharge to ensure that they receive the best care locally available.

TABLE 1
Waiting time benchmarks for the evaluation of heart failure (HF) patients by an HF specialist/clinic

Triage category	Access target	Clinical scenarios
Emergent	<24 h	Acute severe myocarditis Cardiogenic shock Transplant and device evaluation of unstable patients New-onset acute pulmonary edema
Urgent	<2 weeks	Progressive HF New diagnosis of HF, unstable, decompensated NYHA IV AHA/ACC stage D Postmyocardial infarction HF Posthospitalization or emergency visit for HF
Semiurgent	<4 weeks	New diagnosis of HF, stable, compensated NYHA III AHA/ACC stage C
Scheduled	<6 weeks <12 weeks	Chronic HF disease management NYHA II NYHA I AHA/ACC stages A and B

AHA/ACC American Heart Association/American College of Cardiology; NYHA New York Heart Association. Adapted from reference 7 with permission

However, it is recognized that recommendations made by heart failure specialists following referral are not always implemented by PCPs (14). Factors that may lead to delay in implementing suggested recommendations include insufficient specificity of recommendations and any time lag for the consultation letters to reach those physicians. Telephone, fax, e-mail and Web-based access to patient information are ways to improve the quality of this interaction. Clear, collaborative and specific communication is critical to ensure that the concerns of the PCP are addressed by the specialist, and that changes and monitoring of heart failure care may be facilitated at the primary care level (14,15).

The components available in a heart failure program should address the individual needs of the referral population. Many multidisciplinary heart failure clinics adopt the nurse-coordinated model, in which the nurse may be an APN who coordinates and implements the heart failure team's medical care plan and educates the patient and the family (16). The extent to which the heart failure care is transferred to the clinic depends on the availability of components and interventions within each program. For example, if the heart failure referral population consists of elderly patients, a program is likely to be more successful if it includes some component of home care or ability to address comorbid conditions, and social and financial issues (17). Although recent data have demonstrated benefits of multidisciplinary care to reduce hospital admissions in the setting of protocol-driven, evidence-based management of heart failure (18), a remaining challenge is to identify the combination of interventions that is most effective (12,16). Also, it is not clear when or whether patients should be 'discharged' from a heart failure clinic. Some may do so if there is a treated reversible cause, if the patient is undergoing optimized treatment and is stable, if the distance to travel is long, or if the referring PCP is comfortable and competent.

Communication between the heart failure specialist and the PCP is particularly important to ensure continuity of care and the efficient use of specialist and community resources. Recommendations from the specialist must be as explicit as possible (ie, who does what and when) and appropriate for the expected and mutually agreed level of collaborative care. To ensure consistent and complete communication between specialist and PCP, a suggested template is provided (Appendix).

Practical tips

- Centres for heart failure referral should consider the use of standardized letters or forms that document relevant clinical questions, recent laboratory findings, interventions performed by the heart failure centre, and expectations for subsequent care, including adjustment of medications and further tests or monitoring.
- All recommendations should be communicated in writing and in a timely fashion. For immediate communication, consider a brief, hand-written note (or telephone call) to the PCP identifying the key recommendations.
- Specialists should instruct patients to make an appointment with their family physician soon after the specialist visit.
- All hospitals admitting patients with heart failure should have defined care maps to ensure that patients receive the best care possible within the available resources.

Responsibilities of the referring physician

Recommendations

- The referring physician should be familiar with the services provided by the heart failure clinic, should identify the urgency of the referral, the specific question(s) to be answered, the expected care/investigations to be provided, and the extent of transfer of care (class I, level C).
- The referring physician should provide a summary of concomitant medical conditions, all current medications, side effects and drug intolerances, known patient preferences regarding interventions and treatments, and other consultants involved in the patient's care (class I, level C).
- The referring physician should provide, when available, test results of serum creatinine and electrolytes, chest x-rays, previous cardiac investigations (including echocardiography, multiple gated acquisition scan, methoxyisobutyl isonitrile stress test, heart catheterization, biomarkers such as the natriuretic peptides) and other test results or consultation letters relevant to the patient's assessment and management (class I, level C).

Many models of chronic disease management programs in primary care are being developed across the country and offer great opportunities for innovative care delivery to heart failure patients and their families. In part, because a model of primary care has not been universally or clearly defined (19), the process and particularly the extent of the transfer of care may differ among different practice settings from which the patient is referred, and represents a significant shift in the care of many heart failure patients. A specialist may be consulted for clarification of diagnosis, further investigations, treatment initiation and/or recommendations, management of complicating side effects or comorbidities, regular follow-up, advice following an acute event (eg, heart failure hospitalization or acute coronary syndrome) or for a pre-operative evaluation. Optimizing the transition and integration of care processes between the PCP or referring physician and the heart failure specialist or clinic determines the success in achieving the shared goals of therapy that may improve clinical outcomes. Because the improvement in clinical outcomes of heart failure patients who are managed by cardiologists compared with PCPs is most pronounced in patients with new-onset heart failure (20), these patients in particular should be routinely referred to a multidisciplinary heart failure clinic or, if none exists, to the community heart failure specialist. Other patients who should be referred have been identified previously (5).

To facilitate the referrals, the PCP should be familiar with the operation of the specialty clinic, including the roles of the physicians and RN/ANPs, as well as the usual clinic waiting time and benchmark waiting time (7), so that the referral request is appropriately planned and written. The referring physician should provide the specific reason for the referral and all relevant history and clinical tests, as well as insights into the patient's understanding and preferences. Issues such

as depression and cognitive dysfunction should be identified. Dialogue between the referring physician and the specialty clinic before the referral is encouraged, especially when an unusual circumstance or request exists. Because many heart failure patients initially present to a health care facility, such as a hospital (21), each facility should have policies and procedures in place for the referral of eligible patients to heart failure specialists or programs.

Practical tips

- The referring physician should instruct the patient to bring to the visit the results of home monitoring, such as a diary of symptoms, home daily weights, use of as-needed diuretics, etc, as well as all their medications.
- The referring physician should advise and encourage a family member or caregiver to accompany the patient to the clinic visit to ensure that the diagnosis, prognosis and plans for treatment are clearly understood and to identify questions they wish to have answered.
- If in doubt or disagreement, the referring physician should discuss any concerns directly with the clinic staff.

Transitional care from hospital to community

Recommendations

- Hospitalized heart failure patients should be educated with their caregivers while in hospital and soon after discharge on warning signs and symptoms of worsening heart failure, self-management skills, factors that may aggravate heart failure, as well as on their medications (class I, level A).
- Effective means of communication and collaboration between the patient, caregiver and all health care providers should be identified (class I, level B).
- A written summary of discharge diagnoses, significant interventions in hospital, in-hospital complications, medications at discharge (with appropriate prescriptions), explicit instructions for medication adjustment, plans for follow-up, and delineation of respective roles and responsibilities of caregivers should be provided to the patient at the time of discharge and to the PCP within 48 h of discharge (class IIa, level B).
- Health care institutions serving heart failure patients should provide resources for, or access to, appropriate disease management care for patients recently discharged from hospital with a primary diagnosis of heart failure (class I, level C).

Meta-analyses of programs that incorporate peridischarge planning (22-26), including comprehensive predischarge education delivered by RNs/APNs and pharmacists in multidisciplinary teams have suggested that such programs reduce readmission rates and may have beneficial effects on mortality and quality of life. These conclusions were further supported by randomized trials demonstrating that predischarge education results in improved adherence to therapy, better quality of life and modest reductions in resource use (27,28). Successful transition programs are usually coordinated by an RN/ANP (29-31). Because in-hospital lengths of stay are shortening, this education should begin early during the hospitalization. Length of follow-up in a formal transition program, particularly for heart failure patients, may require up to three months (32). Understanding the physical, psychosocial and economic concerns of patients, as well as their goals and wishes, is essential to facilitate the behavioural changes necessary for self-care. Other important characteristics of transitional care include coaching patients and caregivers on managing comorbid conditions that complicate the management of heart failure, developing effective communication with their physicians and fostering collaboration among care providers (including home care services) to deliver individualized care to patients and their caregivers (31,33-37). Patient care is optimized when all health care professionals involved in the management of each patient agree on the care plan. The formal heart failure discharge

summary letter is often lacking essential information and is a missed transitional and educational opportunity (38).

Practical tips

- The goals and directions of care should be shared and openly discussed among the patient's health professionals, and it should not be assumed that all have the same perspective. Differences should be identified and a best solution agreed on.
- In appropriate cases, personal contact with the referring or primary care physician should be considered at or before the time of discharge.
- Where available, RN/APNs, with training and expertise in enhancing patient and caregiver heart failure management skills, may assess patients in hospital then follow them at home as part of a transitional care program.

Transitional care for patients with advanced heart failure

Recommendation

- As part of the transitional care process, patients with advanced heart failure and their caregivers should receive counselling for their physical, emotional, social and spiritual concerns and goals, including advance and end-of-life directives, in addition to management strategies to adequately control their symptoms (class I, level C).

The objectives of transitional care planning overlap considerably with the preferences of patients with advanced heart failure and their caregivers, and it is important to enhance patient and caregiver autonomy in symptom management (39). Discussions should address physical, emotional, social and spiritual concerns, as well as patient and caregiver goals (40-42). Patients with advanced illness and their caregivers endorse the importance of adequate discharge planning and of available resources that enable care to continue in the home (41). In advanced heart failure, patients often experience symptoms that are not typically attributed to heart failure and are less likely to be addressed by health care providers (eg, pain, falls, cognitive problems, mood and anxiety symptoms, functional decline, sleep disturbances and anorexia [43-45]). Patients with heart failure are more likely to think of death when hospitalized and, although willing to engage in discussion, they prefer that conversations be initiated by health care providers and at a time when they are still sufficiently well to be active participants (40-42,46-49). However, the timing of death for patients with advanced heart failure remains unpredictable, and palliative care (to identify and manage physical, psychosocial and spiritual problems [50]) should be considered for a substantial proportion of patients who need adequate symptom control but who may not be considered to be at the immediate end of life (51,52).

Practical tips

- Early involvement of a palliative care physician, psychiatrist or geriatrician should be considered by the patient and the caregiver, primary care physician, heart failure specialist and other key members of the heart failure team (eg, the heart failure nurse).
- In patients with advanced heart failure, despite evidence-based therapy, the goals of therapy should shift to relief of symptoms and improving quality of life.

**CARDIOMYOPATHY WITH
DIABETES MELLITUS OR OBESITY**

Diabetes mellitus and heart failure

Recommendations

- Heart failure in patients with diabetes should be treated according to current CCS national guidelines (class I, level A).
- Diabetes mellitus should be treated according to Canadian Diabetes Association national guidelines to achieve optimal control of blood glucose levels (class I, level A).

- If a thiazolidinedione is used to treat diabetes, the patient should be followed more closely for signs of fluid retention (class I, level A)
- A thiazolidinedione should be discontinued if symptomatic heart failure worsens (class I, level C).

What is it? Diabetes mellitus is a well-established risk factor for the development of coronary artery disease and for myocardial infarction. It is recognized, however, that diabetes mellitus can produce heart failure independently of coronary artery disease by causing a diabetic cardiomyopathy (53). Approximately 12% of diabetes mellitus patients have heart failure (54), and over the age of 64 years, the prevalence increases to 22% (56). In several studies, the incidence of heart failure was two- and fourfold higher in patients with diabetes mellitus than in those without (54-59). The development of heart failure in diabetes mellitus significantly increases mortality (61).

Up to 30% of heart failure patients have diabetes mellitus (55,60,62). In population and clinical trial studies (62-68), heart failure patients with diabetes mellitus have greater mortality rates than those without, and diabetes mellitus is an independent predictor of mortality in heart failure patients. Heart failure patients with diabetes mellitus have more severe heart failure symptoms and hospitalizations than those without, and diabetes mellitus is an independent predictor of heart failure hospitalization in these patients (67,68,71).

When should I suspect and diagnose it? Diabetic cardiomyopathy should be suspected in patients with both heart failure and diabetes when other causes of heart failure, such as coronary artery disease, hypertension and valvular disease do not appear to be sufficient to explain the occurrence or severity of heart failure. The diagnosis is one of exclusion in the setting of a significant history of diabetes. It is important to recognize that heart failure in the setting of diabetes may be due to diastolic dysfunction with a preserved left ventricular ejection fraction, so heart failure can be diagnosed even if the left ventricular ejection fraction is 'normal.'

How should I treat it? Although an increase in glycosylated hemoglobin in patients with diabetes mellitus is a risk factor for developing heart failure (54,61,70,71), studies have not demonstrated that glycemic control significantly reduces the incidence of heart failure (72). However, the 2003 Canadian Diabetes Association clinical practice guidelines for the prevention and management of diabetes in Canada (73) recommend that most patients with type 1 or 2 diabetes should be targeted to achieve a glycosylated hemoglobin level of 7.0% or less. Heart failure symptoms and signs should be treated according to current CCS heart failure guidelines. Blocking the renin-angiotensin-aldosterone system with an angiotensin-converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB) decreases the risk of developing diabetes mellitus in patients with heart failure (74,75). Patients with diabetes mellitus are more likely to have concomitant renal dysfunction and, although ACE inhibitors, ARBs and spironolactone are recommended and used in diabetes patients, renal function and serum electrolytes should be followed more closely. Also, thiazolidinediones are known to produce fluid retention and may cause or exacerbate heart failure; thus, patients on this therapy should be monitored more closely for signs of fluid retention, which may be associated with worsening heart failure.

When should I refer the patient? Because the prognosis is worse for patients with both heart failure and diabetes, most patients should be referred to a diabetes clinic and a heart failure clinic, where available, for optimization of management plans.

Practical tips

- The sodium and water content of a diabetic diet should be evaluated in patients with symptomatic heart failure and diabetes.

- In patients with both heart failure and diabetes, close collaboration is important between the staff of the two clinics with regard to drug and dietary recommendations.

Obesity and heart failure

Recommendations

- Heart failure in obese patients should be treated according to CCS national guidelines (class I, level A).
- Health professionals caring for overweight or obese individuals should educate them about the increased risk of heart failure (class IIa, level C).
- Obese heart failure patients should be educated about appropriate dietary changes (class IIb, level C).

What is it? Statistics Canada reported in 2004 (76) that 36% of Canadians 18 years of age or older have a body mass index (BMI) of 25 kg/m² or greater (overweight), and 23% have a BMI of 30 kg/m² or greater (obese). Overweight and obesity have been identified as independent risk factors for the development of heart failure (58,77-80). For each one-unit increase in BMI, the risk of heart failure increases 5% for men and 7% for women, with a continuous gradient and no evidence of a threshold (81). In individuals with underlying coronary artery disease, obesity is independently related to the development of heart failure (82,83). Obesity is associated with an increase in total blood volume and cardiac output because of the high metabolic activity of adipose tissue. In moderate to severe obesity, this may lead to left ventricular dilation, increased left ventricular wall stress, compensatory (eccentric) left ventricular hypertrophy and left ventricular diastolic dysfunction (81). Left ventricular systolic dysfunction may occur if wall stress remains high because of inadequate hypertrophy (84). There may be excessive lipid accumulation within the myocardium, which is directly cardiotoxic and causes left ventricular remodelling and a dilated cardiomyopathy (85).

When should I suspect it? Obesity-related cardiomyopathy should be suspected in heart failure patients who weigh 75% or more than their ideal body weight, whose BMI is 40 kg/m² or greater, and especially in those who have been obese for 10 years or longer (81,84-86).

How do I diagnose it? The diagnosis is one of exclusion of other principal causes of heart failure in patients with significant obesity. Elevated levels of plasma BNP/NT-proBNP may be helpful if clinical uncertainty exists about the cause of symptoms that can mimic with heart failure (eg, shortness of breath and fatigue).

How should I treat it? The heart failure should be treated according to current national heart failure guidelines (5,6). Once the patient presents with heart failure, actual obesity may not adversely affect the patient's outcome. Indeed, among heart failure patients, subjects with a higher BMI are at decreased risk of death and hospitalization compared with those with a lower BMI (the obesity paradox). However, weight loss in obese heart failure patients has been associated with decreases in left ventricular mass, along with improvements in left ventricular systolic function, diastolic function and symptoms (81,87-91). Because of the accepted broad-based benefits of weight loss, most obese heart failure patients should be educated about appropriate dietary changes (81).

When should I refer the patient? These cases are usually complex, and once the diagnosis of heart failure has been made, the patient should be referred to an obesity clinic and a heart failure clinic to optimize the management plans.

Practical tips

- Obstructive sleep apnea should initially be assessed with screening questions (snoring, daytime sleepiness, poor quality sleep – best obtained from bed partner, if available), followed by a sleep study, if indicated, and treated with continuous positive airway pressure if the diagnosis is confirmed.

- Bariatric surgery may be considered in some patients with severe obesity and mild cardiac dysfunction.
- The use of weight loss medications to prevent heart failure cannot be recommended at this time.

HYPERTROPHIC CARDIOMYOPATHY

Recommendations

- Hypertrophic cardiomyopathy (HCM) should be suspected in a heart failure patient with unexplained ventricular hypertrophy, pathological heart murmurs (from dynamic outflow obstruction), abnormal electrocardiogram (ECG) patterns (pseudoinfarction, giant negative T waves), unexplained syncope (particularly in young athletes) or a positive family history (class I, level C).
- Transthoracic echocardiography should be performed in all patients suspected to have HCM, and cardiac magnetic resonance (CMR) imaging may be used when echocardiographic imaging (including contrast echocardiography) is nondiagnostic (class I, level C).
- Patients with HCM should be treated to manage symptoms and prevent sudden cardiac death (class I, level B).
- Beta-blockers are recommended as first-line drug therapy to control symptoms (class I, level B).
- Patients with HCM who survive a cardiac arrest should be offered an implantable cardioverter defibrillator (ICD) (class I, level B).
- Patients with HCM who have sustained ventricular tachycardia should be considered for an ICD (class IIa, level B).
- Patients with HCM and multiple high-risk factors for sudden cardiac death should be considered for an ICD (class I, level B).
- All first-degree relatives of patients with HCM should be screened for the disease with an ECG and echocardiography (class I, level C).
- Athletes with HCM should avoid strenuous competitive activities to reduce the risk of sudden cardiac death (class I, level C).

What is it? HCM is a disease of the myocardium characterized by pathological and disproportionate hypertrophy of the left ventricle and, sometimes, the right ventricle. It is most often diagnosed as an inherited condition with an autosomal dominant pattern but variable penetrance. The prevalence of HCM is estimated to be 1:500 in the general adult population (92). The genetic, morphological and clinical heterogeneity of HCM explains the diverse nomenclature used historically to describe this disease, such as hypertrophic obstructive cardiomyopathy, idiopathic hypertrophic subaortic stenosis, muscular subaortic stenosis, asymmetrical septal hypertrophy, apical asymmetrical hypertrophy and familial HCM. The predominant genotype in HCM is a mutation in the genes that encode proteins of the cardiac sarcomere. More than 430 mutations in 12 genes (beta-myosin heavy chain being the most common) have been identified to date (93). Nonsarcomeric mutations, such as those of lysosomal-associated membrane protein 2 and AMP-activated protein kinase gamma 2 (94), also give rise to phenotypes that mimic HCM. The pathology of HCM is characterized by myocyte disarray, cellular hypertrophy and interstitial fibrosis.

The onset of HCM can occur in both early and late adulthood (95), and there is a well-defined risk of sudden death, often at a young age. The majority of patients with HCM are asymptomatic (96). Symptoms may include chest pain, dyspnea, palpitations or syncope. Symptoms can arise as a consequence of left ventricular outflow tract obstruction (with secondary mitral regurgitation), tachyarrhythmia

(especially ventricular tachycardia and atrial fibrillation), myocardial ischemia (chest pain is common, even in the absence of coronary artery disease) (97), impaired diastolic function or systolic dysfunction. In approximately 5% to 10% of cases, the disease progresses to a burnt-out phase, with the development of severe systolic dysfunction that resembles dilated cardiomyopathy (97,98). HCM increases the risk of heart failure approximately fivefold (99).

When should I suspect it? HCM should be suspected in any individual who presents with unexplained ventricular hypertrophy, pathological heart murmurs (from dynamic outflow obstruction), abnormal ECG patterns (pseudoinfarction, giant negative T waves), unexplained syncope (particularly in young athletes) or a positive family history. A number of hereditary syndromes (including Friedreich's ataxia [100], or Noonan and LEOPARD syndromes [101]) have also been linked to HCM. Approximately 30% of the cases are diagnosed de novo in elderly patients (102).

How should I diagnose it? Transthoracic echocardiography (with or without contrast) is the imaging modality of choice, and may include a provocative test for dynamic outflow left ventricular outflow tract obstruction. CMR imaging may be used if initial imaging results are non-diagnostic (103). Tissue Doppler imaging may aid in early diagnosis (104). Localized hypertrophy of the interventricular septum is the most common pattern of hypertrophy, but other patterns are also possible. Dynamic left ventricular outflow obstruction occurs in approximately 30% to 50% of cases and may be latent (105). Differentiation must be made from other pathologies that mimic HCM in appearance, including concentric hypertrophy due to systemic hypertension, physiological hypertrophy seen in trained athletes and discrete/disproportionate upper septal hypertrophy in elderly patients. Cardiac biopsy is rarely necessary.

How should I treat it? There is no cure for this disorder. Management includes treatment of symptoms and prevention of sudden cardiac death. There are no randomized clinical trials to guide therapy, so recommendations are based on small clinical studies, clinical observational studies and expert consensus opinions. There is no consensus regarding medical therapy for asymptomatic individuals. To relieve symptoms (exertional dyspnea and/or chest pain), drug therapy with beta-blockers is first-line therapy (95,105-109). Verapamil has been used in patients who do not respond to, or are intolerant of, beta-blockers (110), but should be used with caution in patients with severe symptoms and evidence of pulmonary hypertension because they may have serious adverse reactions, including death (111). Disopyramide has negative inotropic effects and has been used to relieve symptoms due to outflow tract obstruction (112), but its pro-arrhythmic effects limit its use to patients with symptoms not responding to other therapies. Other associated conditions should be treated appropriately, such as anticoagulation for atrial fibrillation.

Patients with severe symptoms (NYHA class III or IV) refractory to drug therapy may benefit from mechanical relief of persisting outflow tract obstruction by surgery (myectomy) or alcohol ablation (107). Operative mortality in experienced centres is 1% to 2%. Alcohol septal ablation is a newer technique, and procedural success rates and mortality from several centres appear to be equal to surgical rates, although a high-grade atrioventricular block requiring a permanent pacemaker is reported in 5% to 30% of patients (113,114). The long-term risk of malignant ventricular arrhythmias and sudden death related to the scar created by the ablation is unknown. Dual-chamber pacing was initially considered to be an alternative therapy to reduce outflow tract gradients and relieve symptoms, but several randomized controlled studies have failed to demonstrate a reduction in outflow gradient, or improvement of symptoms or quality of life (115). Approximately 5% of patients with HCM develop systolic left ventricular dysfunction and heart failure. These patients should be treated according to recommendations for management of heart failure caused by left ventricular systolic dysfunction (5,6).

All patients with HCM should be assessed for risk of sudden cardiac death because it is a well-recognized complication, at approximately 1% per year. Clinical risk factors for sudden death include prior

cardiac arrest, history of sudden death in close relatives (particularly at a young age), a history of unexplained syncope, nonsustained ventricular tachycardia on Holter monitoring, blunted blood pressure response to exercise, and left ventricular wall thickness greater than 30 mm (116). It is important to recognize that risk factors identify populations at higher risk, but risk assessment in an individual is less certain because of heterogeneity of the expression and complexity of the disease, low prevalence in the population and variable external factors. There are some data showing that intense physical activity is causally related to sudden death (117). In addition, there is some circumstantial evidence showing that avoidance of competitive sporting activity reduces the risk of sudden death in individuals with HCM. Therefore, the expert consensus is that athletes with HCM should avoid strenuous, competitive activities (118). Immediate family members of individuals with HCM should be screened periodically to update their risk assessment and participation in competitive sports.

There is no evidence that drug therapy reduces the risk of sudden death, even in high-risk patients. An ICD is indicated for patients with HCM who survive a cardiac arrest or have had sustained ventricular tachycardia. There are no clinical trials to guide therapy for primary prevention in individuals with high-risk factors, but there is a consensus that consideration should be given to implantation of an ICD in those patients with multiple high-risk factors (107). Patients with a single high-risk factor, such as a family history of sudden death at a young age, should be individually assessed for ICD implantation, including a discussion of the level of risk acceptable to the individual and potential adverse effects with an ICD, such as inappropriate ICD discharges, lead complications and infection.

When should I refer the patient? All patients diagnosed with HCM should be referred for a specialist cardiac assessment, which should include an assessment of risk of sudden death. HCM is often an inherited disorder, and as such, all first-degree relatives of the identified proband should undergo initial screening with ECG (119) and echocardiography for HCM. For adult relatives, periodic screening with echocardiography should continue indefinitely every five years (107,108). It is important to recognize that the phenotypic expression of the disease may be late-onset, so first-degree relatives should be evaluated periodically. Presently, genetic testing for the diagnosis of sporadic cases remains investigational because a negative test does not reliably exclude the disease (pick-up rate is approximately 60% to 65%) (120,121).

Practical tips

- Heart failure symptoms in patients with HCM may be due to diastolic function (most common), outflow tract obstruction (less common), rhythm disturbance, or concomitant valvular or ischemic heart disease.
- Consider referral to specialized centres with expertise in the evaluation and management of HCM, including genetic testing, provocative testing during echocardiographic evaluation, and the use of alcohol septal ablation and/or septal myectomy.
- Patients with HCM, reduced systolic function and disproportionate heart failure symptoms may have developed a restrictive type of cardiomyopathy, which is less responsive to usual heart failure medication. If symptoms are advanced, referral to a cardiac transplantation centre should be considered in appropriate patients.
- All first-degree relatives of patients with HCM may be considered for repeat screening at five-year intervals.

RESTRICTIVE CARDIOMYOPATHY

Recommendations

- Restrictive cardiomyopathy (RCM) should be considered when severe heart failure occurs with Kussmaul's sign on examination, as well as normal or small ventricles, large atria and thickened ventricular walls (class I, level C).

TABLE 2
Classification of types of restrictive cardiomyopathies according to cause

Myocardial	
Noninfiltrative	Idiopathic*, familial, hypertrophic or diabetic cardiomyopathy, scleroderma, pseudoxanthoma elasticum
Infiltrative	Amyloidosis*, sarcoidosis*, fatty infiltration, Gaucher's or Hurler's disease
Storage disease	Hemochromatosis, Fabry's or glycogen storage disease
Endomyocardial	Endomyocardial fibrosis*, hypereosinophilic syndrome, carcinoid heart disease, metastatic cancers, radiation*, toxic effects of anthracycline*, drugs causing fibrous endocarditis (serotonin, methysergide, ergotamine, mercurial agents, busulfan)

*These conditions are more likely to be encountered in clinical practice. Adapted from reference 123

- Echocardiography, CMR imaging and cardiac catheterization should be considered to help in diagnosis (class I, level C).
- Therapy for patients with RCM should address any identified cause, but should generally focus on symptom control, with careful use of standard heart failure treatments (class I, level C).

What is it? Among cardiomyopathies, RCM is the least common category found in the western world (122,123). It is characterized by myocardium with markedly stiff ventricular walls, restrictive ventricular filling and reduced diastolic volume of either or both ventricles, and normal or near-normal systolic function (123,124). Myocardial fibrosis, infiltration or endomyocardial scarring is generally responsible for the typical features of diastolic dysfunction (123,125). Consequently, RCM shares similar functional characteristics with constrictive pericarditis, and differentiation between the two is difficult but imperative because surgery may potentially cure the latter (122). Many specific diseases may result in RCM, but the underlying cause most often remains unidentified. Amyloid myocardial deposition (with or without coexistent multiple myeloma) is a frequent cause, but many other situations may also result in RCM (Table 2). Rare hereditary forms of RCM have been described, such as troponin I gene mutations or in association with skeletal muscle disease (123,126). The prognosis of patients with RCM varies greatly, but it is generally one of inevitable downward symptomatic progression with a high mortality rate (124,127).

When should I suspect it? Patients usually exhibit typical symptoms and signs of heart failure, including Kussmaul's sign that may be disproportionate to the degree of systolic or valvular dysfunction. A third or fourth heart sound or both may be present on cardiac auscultation, together with a systolic murmur caused by atrioventricular valvular insufficiency. Hepatomegaly, ascites and, in more advanced cases, anasarca, may be present. Notably, the apex beat is usually palpable in RCM, but not in constrictive pericarditis (123). The ECG is frequently abnormal with decreased voltage, bundle branch block or intraventricular conduction delay, or poor R wave progression mimicking myocardial infarction (128). The ECG can be normal despite significant conduction system involvement. Atrioventricular conduction abnormalities may be found and can be associated with a poorer prognosis. Sinus node disease is frequent, and typical characteristics of the sick sinus syndrome are encountered (129). Arrhythmias, mostly atrial fibrillation, are frequent and are thought to be caused by amyloid deposition (130).

How should I diagnose it? A positive Kussmaul's sign is very common, especially in the setting of ongoing heart failure. The chest x-ray may show a normal heart size, although cardiomegaly may occur if systolic dysfunction is present. Echocardiography may be normal early in the disease process, but small ventricular chambers with increased wall thickness, very large atria, and thickening of valvular apparatus and

interatrial septum are often seen. Left ventricular systolic function is usually normal, but may be reduced in advanced disease. Pericardial effusion is common, but rarely results in tamponade (131). The sparkling appearance of the thickened walls, presumably related to amyloid deposition, was previously believed to be typical on two-dimensional echocardiography, but is less reliable than recent technology (eg, harmonic imaging [132]). Doppler echocardiography is useful for the diagnosis of diastolic function abnormalities and has prognostic value (133), with a restrictive pattern carrying a worse prognosis. In addition, Doppler evaluation is helpful in discriminating between constrictive and restrictive physiology. Tissue Doppler imaging of early diastolic mitral annular velocity and colour M-mode flow propagation are also useful in distinguishing between constrictive pericarditis and RCM (134,135).

CMR can precisely image functional and morphological changes (136), including quantification of left and right ventricular function, hypertrophy, volumes and regional wall motion abnormalities, and may provide early insight into the disease process and etiology. Myocardial tissue differentiation such as fibrosis (137), inflammation (138) or infiltration may be obtained with the use of contrast medium (gadolinium-diethylenetriamine penta-acetic acid) in T1-weighted sequences. One of the major advances with CMR is the description of an early unusual contrast washout in amyloidosis (139), with subendocardial contrast enhancement associated with nonsuppressible signal of remote myocardium, which may have important therapeutic implications. CMR may increase the sensitivity of myocardial biopsy (140,141) to diagnose the presence or absence of sarcoidosis in the myocardium (142), can further describe the nature of myocardial damage (fibrosis or inflammation) and may help to direct treatment (143). CMR may be helpful in distinguishing between active myocardial disease and clinical remission in systemic lupus erythematosus (144), suspecting the presence of cardiac fibrosis in Churg-Strauss syndrome (a rare form of systemic vasculitis) (145), and detecting early indications of cardiac iron overload in thalassemia patients (146).

Abnormalities in serum protein electrophoresis suggest amyloidosis, while a high plasma level of ferritin, in combination with increased transferrin saturation, suggests hemochromatosis. Specific morphological features (especially musculoskeletal) in the setting of renal disease and a family history of metabolic abnormalities suggest the presence of an infiltrative disorder, such as Fabry's disease. Fabry's disease is a rare X-linked disorder that can present with neuropathy, renal failure and heart failure in affected men and hemizygous women. Genetic testing can determine the exact gene defect, but elevated urinary globotriaosylceramide, reduced plasma alpha-galactosidase activity are diagnostic (147). These disorders usually require tissue diagnosis, either from cardiac tissue or other affected organs, such as the kidneys. An abdominal fat aspirate is safe and may assist in the diagnosis of amyloidosis. If the result of an abdominal fat aspirate is negative (128), endomyocardial biopsy may help if cardiac amyloidosis is suspected, and kidney biopsy may also be useful if the estimated glomerular filtration rate is low, suggesting renal involvement. Immunohistochemical staining should be performed because it helps to differentiate between systemic senile, familial and primary forms of amyloidosis, and clarifies prognosis and management, which differ in the various forms. Unsuspected hereditary amyloidosis may be present in nearly 10% of patients thought to have the primary (AL) form (148). The absence of concomitant symptoms and signs of systemic illness, nonspecific laboratory findings and negative endomyocardial biopsy strongly suggest idiopathic RCM. Scintigraphy with technetium-99m pyrophosphate, as well as with other agents that bind to calcium, is frequently positive, with extensive amyloid infiltration. Scanning with specialized agents may also identify sympathetic denervation in patients with cardiac amyloidosis (149). Ventricular arrhythmias may be a forerunner for sudden death, and a signal-averaged ECG has been suggested to help in identifying patients at risk (150).

Differentiating between RCM and constrictive pericarditis may be difficult. The characteristic hemodynamic feature of both on cardiac

catheterization is a marked and rapid early decrease in ventricular pressure at the beginning of diastole, with a rapid increase to a plateau in early diastole (this latter finding may be absent in RCM) – the ‘dip and plateau’ or ‘square root’ sign. Both systemic and pulmonary venous pressures are elevated (frequently higher than 50 mmHg in RCM, although lower in constrictive pericarditis), and patients with RCM typically have left ventricular filling pressure that exceeds right ventricular filling pressure by more than 5 mmHg (this difference can be revealed by exercise, fluid challenge or the Valsalva manoeuvre). In constrictive pericarditis, filling pressures are similar in both ventricles, and the plateau of the right ventricular diastolic pressure is usually at least one-third of the peak right ventricular systolic pressure, but frequently lower in RCM. In the setting of rapid early diastolic ventricular filling, an increase in right ventricular peak systolic pressure during inspiration may occur with a reduction of left ventricular peak systolic pressure. Endomyocardial biopsy (scarring or infiltration) and computed tomography (pericardium thickening) may also be useful for differential diagnosis; however, in rare cases, open biopsy may be required (122).

How should I treat it? Treatment depends on the underlying etiology and is usually supportive (ie, control of volume, blood pressure, heart rate and other factors that may aggravate heart failure). However, some patients with secondary forms may receive disease-specific treatment (eg, the cardiomyopathy related to iron overload, which is improved by removal of the iron, and Fabry’s disease, in which enzyme replacement therapy has demonstrated efficacy) (151,152). Vasodilators and diuretics may be necessary for symptom alleviation, but hypotension and a low output state with hypoperfusion may occur, and these medications should be used carefully (123). Digitalis glycosides should also be used very carefully, because patients with cardiac amyloidosis appear to be very sensitive to this agent (153), although digitalis may be helpful for additional rate control in atrial fibrillation. Some negative inotropic calcium channel blockers should also be used with caution. Permanent pacemaker implantation may be necessary in patients with advanced conducting system abnormalities (154). Patients with a plasma cell dyscrasia and RCM caused by light-chain deposition sometimes, but rarely, improve with chemotherapy (155).

The treatment of cardiac amyloidosis is usually disappointing, with a median survival of less than one year, even though some improvement in symptoms and survival have been demonstrated with alkylating agents used in primary (AL) amyloidosis (156). The treatment is mostly symptomatic, as has been recommended in previous guidelines (6). Autologous bone marrow transplantation is being increasingly used for primary (AL) amyloidosis treatment; however, patients with advanced cardiac amyloidosis or multiorgan involvement do not seem to benefit (157). Cardiac transplantation for amyloidosis is usually not an option, with disappointing long-term results (30% to 40% survival at four to five years) because of progressive disease in other organs or reappearance in the grafted heart. A few centres are investigating heart transplantation followed by stem cell transplantation. Survival in senile amyloidosis is much better than for the primary form (60 versus six months for patients with heart failure).

When should I refer the patient? All patients with a known or suspected RCM should be referred early to a cardiologist for consideration of additional testing or treatments, as well as education of the patients and their families about the expected prognosis. Other profiles of patients to refer include symptoms and signs of heart failure and normal ejection fraction but without an ‘obvious’ cause; no response to standard heart failure therapy; and if additional investigations are needed to define the diagnosis.

Practical tips

- Referral to a specialist is necessary to distinguish RCM from constrictive pericarditis.
- Digitalis, vasodilators, calcium channel blockers and nitrates are not very effective, are associated with increased side effects and, if used, should be monitored closely.

- Treatment focus should be on control of volume overload and of factors known to aggravate heart failure, such as rhythm disturbance (including tachycardia), hypertension, ischemia, and concomitant disease (especially renal).

TACHYCARDIA-INDUCED CARDIOMYOPATHY

Recommendations

- Tachycardia-induced cardiomyopathy should be suspected when left ventricular dysfunction, with or without typical heart failure signs or symptoms, occurs with a persistent inappropriate tachycardia or tachyarrhythmia without another identified cause for the heart dysfunction (class I, level C).
- Patients with tachycardia-induced cardiomyopathy should be treated to a resting target heart rate below 80 beats/min (class IIa, level C).
- Beta-blockers are the preferred drug for most patients with tachycardia-induced cardiomyopathy (class IIa, level C).
- Amiodarone, digoxin and rate-limiting calcium channel blockers may be considered in selected patients if beta-blockers do not achieve target heart rates (class IIb, level C).
- Patients with persistent tachyarrhythmias and heart failure signs or symptoms despite optimal medical therapy should be referred to an electrophysiologist for consideration of ablation of the arrhythmia (class IIa, level C).

What is it? Tachycardia-induced cardiomyopathy is caused by persistent supraventricular or ventricular arrhythmias. The most common arrhythmias are atrial fibrillation (158), atrial flutter (159), atrial tachycardia, junctional tachycardia (160) and ventricular tachycardia (161). Tachycardia-induced cardiomyopathy should be suspected when new-onset heart failure signs or symptoms occur together with the following three major features: abnormal systolic function (ejection fraction less than 50%); prolonged periods of atrial or ventricular arrhythmia with a high heart rate (ie, higher than 100 beats/min); and no other principal etiology identified (eg, myocarditis, coronary artery disease, hypertension). Although the true incidence is not known, it is generally accepted as being uncommon. It may occur at any age – from intrauterine through adult life – and has been associated with other concomitant conditions, including postheart transplantation (162).

When should I suspect it? While sinus tachycardia is a common physiological response to heart failure, persistent sinus tachycardia or a tachyarrhythmia is not. If heart failure symptoms and signs are mild or absent, any tachycardia may be considered inappropriate. In that circumstance, if a cardiomyopathy is detected without another identified cause, the tachycardia should be considered to be possibly causative. It can be a more difficult differential diagnosis if the patient presents late and has clear clinical evidence of heart failure with a tachycardia. In this scenario, the heart failure should be treated aggressively first with standard acute heart failure therapy. If the heart failure symptoms clear but the tachycardia persists, the diagnosis may be considered. In clinical practice, many patients with tachycardia-induced cardiomyopathy present with atrial fibrillation and very rapid ventricular response rates (eg, more than 120 beats/min at rest) but no awareness of palpitations or the rapid rate itself. Atrial fibrillation can occur as both a cause and a consequence of a cardiomyopathy or heart failure.

How do I diagnose it? In most cases, it is a diagnosis of exclusion. It is important to exclude persistent and inadequately treated heart failure. It is also important to exclude hyperthyroidism, anemia, pheochromocytoma and other conditions that can produce a tachycardia. If these are excluded and if ventricular dysfunction or heart failure persist with a tachycardia or tachyarrhythmia, a tachycardia-induced cardiomyopathy should be considered. The final diagnosis often requires a cause-and-effect response – an improvement in cardiac function following a reduction in heart rate.

TABLE 3
Endocrine, toxin and nutritional causes of heart failure

Endocrine	Toxin	Nutritional
Acromegaly	Alcohol	Anorexia nervosa
Adrenocortical insufficiency	Chemotherapy: anthracyclines (doxorubicin, daunorubicin), cyclophosphamide, cytostatic agents, interferons, interleukin-2, trastuzumab, imatinib, cetuximab	Carnitine deficiency
Cushing's disease		Protein deficiency (kwashiorkor)
Hyperthyroidism	Drugs: corticosteroids, cocaine, metamphetamine, anabolic steroids,	Selenium deficiency
Hypothyroidism	bleomycin, doxorubicin, phenothiazines, antidepressants	Thiamine deficiency (beriberi)
Pheochromocytoma	Heavy metals (cobalt, mercury, phosphorus)	Vitamin D excess
	Herbal products	
	Radiation (radiotherapy)	

How should I treat it? It is considered to be a potentially reversible cause of heart failure. With appropriate heart rate and/or rhythm control, clinical, hemodynamic and structural parameters may normalize in as early as four weeks (160,162-165). Treatment of heart failure should follow the CCS heart failure guidelines (5), with additional emphasis on correcting and controlling the underlying causative rhythm. Medical therapy consists principally of beta blockade to reduce ventricular rate to less than 80 beats/min, and considering digoxin and amiodarone in resistant cases. Rate-limiting calcium channel blockers may be considered, but should be used with caution if systolic function is significantly impaired. In atrial fibrillation, rhythm control may require antiarrhythmic drugs or interventions, recognizing that these patients have not been studied extensively in clinical trials. Electrical control and/or electrophysiological ablation may be necessary for resistant tachyarrhythmias (163,164). Clinicians should be aware that future episodes of tachycardia may result in more rapid deterioration in systolic function and that, although infrequent, sudden cardiac death has been reported (165).

When should I refer the patient? These patients should be referred early to centres with expertise in heart failure management and the availability of electrophysiology interventions.

Practical tip

- If a persistent tachycardia is present in a patient with heart failure or a cardiomyopathy, an underlying cause should always be sought.

OTHER CARDIOMYOPATHIES

There are many causes of cardiomyopathy, some of which are more prevalent in countries other than Canada. However, with our growing population and increased travel and movement from country to country, it is important to be aware of potential causes before attaching the description 'idiopathic'. A high index of suspicion and early intervention are important because some causes are correctable. The scope of the present paper does not allow a detailed review of each cause, but a broad summary is given in Table 3. A breakdown of more specific symptoms, signs, diagnostic steps and some treatments is given in Tables 4 to 6. In the following text, more focus is paid to three selected cardiomyopathies associated with alcohol, chemotherapy and cocaine. A careful and detailed history and physical examination are important and should cover the following areas: family history; alcohol use; nutrition; nonprescription drugs/medications; prior malignancy requiring radiation or chemotherapy; exposure to chemicals and heavy metals; and symptoms and signs of hypo- or hyperthyroidism, pheochromocytoma and acromegaly. Any toxins should be removed and deficiencies should be corrected. In most cases, usual heart failure care and medications are appropriate (6).

Recommendations

- In a patient suspected of having a cardiomyopathy, the initial history should include questions about family history, concomitant illnesses, prior malignancy requiring radiation or chemotherapy, symptoms of hypo- or hyperthyroidism, pheochromocytoma, acromegaly, previous travel, occupational exposure to chemicals or heavy metals, nutritional status,

alternative medicine/naturopathic agents, illicit drug use and exposure to HIV (class I, level C).

- In rare cases in which a clearly defined and reversible cause of the cardiomyopathy has been corrected and the heart function has normalized, heart failure medications may be withdrawn by a specialist. However, in most cases, heart failure drugs such as ACE inhibitors, ARBs and beta-blockers are continued indefinitely. Other discretionary drugs, such as digoxin and diuretics, may be discontinued and the patient's stability should be followed closely (class I, level C).

Practical tip

- It is important to recognize that a cardiomyopathy can develop without a reduction in left ventricular ejection fraction (ie, diastolic dysfunction or heart failure with a preserved ejection fraction).

Alcohol-induced cardiomyopathy

Recommendation

- Permanent abstinence from alcohol must be recommended and reinforced in patients diagnosed with an alcohol-related cardiomyopathy (class I, level C).

What is it? Alcohol consumption has been long-recognized as one of the major risk factor for developing dilated cardiomyopathy (166). Alcohol has been shown to have the many negative effects on myocardial function: myocytolysis and fibrosis (167), impaired sarcoplasmic reticular uptake of calcium (168), inhibition of myosin ATPase (169), reduction in myocardial high-energy phosphates (170) and impairment in diastolic function (171). Although heavy intake of alcohol that is regular and of prolonged duration is associated with dilated cardiomyopathy, light to moderate alcohol intake may actually protect the heart from developing heart failure (172).

When should I suspect and diagnose it? Excessive alcohol consumption will likely have been present for at least 10 years before the symptoms of heart failure develop (166,173). When an alcohol-induced cardiomyopathy is suspected, and before attributing it to excessive alcohol consumption, it is important to rule out other causes, although some patients may have a mixed etiology. Many patients with alcoholic heart disease also have atrial fibrillation, often with fast ventricular response rates.

How do I treat it? Abstinence is critical and must be maintained in the long-term. Patients with alcohol-induced cardiomyopathy who stop using alcohol may have an improved ejection fraction over the course of three years (174). Education about the alcohol consumption causing the cardiomyopathy and its serious prognosis may be sufficient in some patients to lead to abstinence. However, simple advice is often insufficient, and most patients should receive more intense professional counselling. Standard heart failure therapy is used with low-dose diuretics, ACE inhibitors plus a beta-blocker, as detailed in previous CCS guidelines (5).

When should I refer the patient? Refer to a heart failure clinic and specialist if the heart failure does not respond to standard therapy, and refer to a counselling program to help deal with alcohol addiction if abstinence is not achieved quickly.

TABLE 4
Endocrine disorders associated with cardiomyopathies

Syndrome (reference)	Causes	Symptoms and signs	Diagnosis	Treatment
Acromegaly (183)	Growth hormone and insulin-like growth factor 1 excess	Tachycardia and hypertension, diabetes, rhythm disturbances. Biventricular hypertrophy and diastolic dysfunction	Nonsuppressibility of serum growth hormone levels following glucose loading	Surgery or pharmacotherapy may improve cardiovascular morbidity
Adrenal insufficiency (Addison's disease) (184)	Lack of ACTH	Hypotension, hypokalemia, syncope, bradycardia, prolonged QT, low voltage and heart failure	Decrease response of the adrenal cortex to ACTH	Replacement of the deficient steroid hydrocortisone
Cushing's disease (185)	Excess production of glucocorticoids and androgens	Hypertension, central obesity, proximal muscle weakness, myocardial infarction, stroke and cardiomyopathy	Lack of appropriate suppression of cortisol secretion by dexamethasone	Treat specific cause
Hypothyroidism (myxoedema) (186)	Low production of T3 and T4	Cardiac dilation, bradycardia, weak arterial pulses, angina, hypotension, distant heart sounds, low voltage and peripheral edema	TSH, free T4	Hormone replacement
Hyperthyroidism (187)	Excess production of T3 and T4	Tachycardia, wide pulse pressure, hyperkinetic cardiac apex, high CO heart failure	TSH, free T4	Treat thyroid disease. Be careful with the use of beta-blockers
Pheochromocytoma (188)	Catecholamine-producing tumour	Hypertension 'paroxysmal', sweating, acute pulmonary edema, tachycardia, LVH, short PR interval, ST abnormalities, heart failure, myocarditis	Increase of plasma metanephrine levels	Phenoxybenzamine hydrochloride, beta-blockers and surgery

ACTH Adrenocorticotrophic hormone; CO Cardiac output; LVH Left ventricular hypertrophy; T3 Triiodothyronine; T4 Thyroxine; TSH Thyroid-stimulating hormone

Chemotherapy-induced heart failure

Recommendations

- Patients receiving known cardiotoxic agents for their cancer should be carefully monitored during and after therapy with assessments of left ventricular function. If left ventricular function deteriorates, patients should be treated aggressively with beta-blockers and other standard heart failure therapies (class IIa, level B).
- Patients with a history of chemotherapy-induced cardiomyopathy or heart failure should generally not receive the same agent as was given previously, and other cancer treatment options should be considered (class IIa, level B).

What is it? This form of cardiomyopathy can occur with a variety of chemotherapeutic drugs (Table 5), but is more common and severe with anthracyclines and herceptin. With these latter agents, it may affect up to 20% of patients receiving them (175), and it is dose-related (176). The cardiotoxic effects are secondary to oxygen free radicals, lipid peroxidation and drug metabolite action on the calcium pump (177-179). The clinical manifestations of cardiomyopathy secondary to anthracycline toxicity are similar to dilated cardiomyopathy. It has been reported as early as one week following the last dose of doxorubicin, but can present years after chemotherapy. Even with a normal left ventricular ejection fraction, once the total dose of doxorubicin exceeds 450 mg/m², histological monitoring by endomyocardial biopsy is warranted before an additional drug is administered (179). Patients with a known pre-existing low left ventricular ejection fraction should receive anthracyclines only as a last resort.

When should I suspect it? Clearly, the patient must have had previous exposure to culprit chemotherapeutic agents. The dose regimens and any estimates of left ventricular function before chemotherapy should be checked.

How do I diagnose it? It is reasonable to attribute the heart failure to chemotherapy if systolic function was known to be normal before chemotherapy, if potentially cardiotoxic drugs and doses were received and if no other major causes of heart failure are identified.

Endomyocardial biopsy is the most sensitive test, if required, to confirm the diagnosis (178).

How should I treat it? Primary prevention is important. Baseline and periodic post-treatment left ventricular ejection fraction measurements should be carefully monitored. While it is not uncommon for transient left ventricular dysfunction to occur following the administration of cardiotoxic agents, the development of the full heart failure syndrome is much less common, with occurrence in well under 5% of cases. The total dose of anthracycline should not exceed 450 mg/m². Weekly smaller infusions or daily continuous intravenous administration should be considered (179). Trastuzumab-induced cardiomyopathy is reversible with discontinuation of therapy (180). The cancer specialist should be informed of a diagnosis of cardiomyopathy or heart failure related to chemotherapy. Patients should generally not have cardiotoxic chemotherapy in the future because the cardiomyopathy will recur with repeat exposure. Alternative chemotherapeutic agents must be considered if the cancer relapses. Standard heart failure therapy is used with low-dose diuretics, ACE inhibitors plus a beta-blocker, as detailed in previous CCS guidelines (5).

When should I refer the patient? All patients with chemotherapy-induced cardiomyopathy should be referred to a heart failure specialist at the time of diagnosis. The patient's treating oncologist should be informed of the diagnosis, if they were unaware, and the patient may be re-referred.

Cocaine-induced cardiomyopathy

Recommendation

- Permanent abstinence from cocaine must be recommended and reinforced in patients diagnosed with a cocaine-induced cardiomyopathy (class I, level B).

What is it? In addition to the known effect on coronary atherosclerosis and vasospasm, long-term cocaine use may cause dilated cardiomyopathy secondary to direct toxicity to the myocardium or a hypersensitivity myocarditis (181,186). Focal myocyte necrosis, focal myocarditis, sarcoplasmic vacuolization and myofibrillar loss have been variably demonstrated in myocardial biopsy specimens obtained in the setting of acute cocaine toxicity (180). Acute myocardial

TABLE 5
Toxins associated with cardiomyopathies

Toxin (references)	Causes	Symptoms and signs	Diagnosis	Treatment
Alcohol (172,174,189,190)	Excessive alcohol use. Heavy drinking: for women more than 1 drink per day and for men more than 2 drinks per day. Binge drinking: for women more than 3 drinks and for men more than 4 drinks	Symptoms and signs of heart failure. Symptoms and signs of chronic liver disease	Good history, blood level	Abstaining form alcohol; usual heart failure medications
Illicit drugs and medications	History of drug or chemotherapy use. May be related to the dose and duration	Symptoms and signs of heart failure. Symptoms, signs or history of underlying disease.	Careful history taking of present or previous use of prescribed and over-the-counter medications	Discontinue the drug-supportive measures. Usual heart failure medications.
Cocaine (178,179,191) Metamphetamine, antidepressants, corticosteroids, anabolic steroids, phenothiazines		Cocaine may cause thrombosis, coronary spasm, chest pain and myocardial infraction. May also cause endocarditis and aortic dissection	Prior or recent history of cocaine use	Calcium channel blockers may be useful in cocaine-induced chest pain or coronary spasm
Chemotherapy Anthracycline (176,181, 182,192) (doxorubicin, daunorubicin), bleomycin, adriamycin; cyclophosphamide; cytostatic agents; interferons, interleukin-2 Trastuzumab (180)	Cardiotoxic drugs used to treat cancer	Symptoms and signs of heart failure. Symptoms, signs or history of malignancy	Prior history of malignancies with chemotherapy. May need myocardial biopsy.	Standard heart failure treatment may reverse the abnormalities. Avoid using these agents again
Heavy metals (195) (cobalt, mercury phosphorus)	Outbreaks of cardiomyopathy occurred among heavy consumers of cobalt-fortified beer. It is likely that poor nutrition and ethanol had played a synergistic role		The two main target organs are the skin and the respiratory tract. Cobalt itself may cause allergic dermatitis, rhinitis and asthma	Avoid exposure. Usual heart failure treatment
Herbal (194)	Chinese herbal mixture, blue cohosh	Symptoms and signs of heart failure	History of herbal product use	Standard heart failure treatment
Radiation (195)	Radiation may cause microcirculatory damage and interstitial fibrosis	Symptoms and signs of diastolic heart failure	History of radiation	Standard heart failure treatment. Avoid further radiation

depression may also manifest as left ventricular apical ballooning syndrome or Tako-tsubo cardiomyopathy, an entity associated with high circulating levels of catecholamines, myocyte injury and microvascular dysfunction, with close histopathological resemblances to cocaine-mediated cardiotoxicity (180). Hypertension and myocardial ischemia, including focal coronary artery stenosis, may also be present (179).

When should I suspect it? A physician should have a high level of suspicion in appropriate patients, although a history of cocaine use may not be admitted by the patient.

How should I diagnose it? There must be evidence of repeated cocaine use (by history or toxicology screen), and other causes of cardiomyopathy should be excluded.

How should I treat it? Abstinence from further cocaine use is critical. Treatment with beta-blockers is questionable and requires further investigation. Other standard heart failure therapies should be used (5). Patients with typical coronary stenosis should be treated according to ischemic heart disease guidelines.

When should I refer the patient? Because many such patients are addicted to cocaine, they should be referred early to a drug addiction rehabilitation program and a heart failure specialist.

Practical tip

- For patients at risk of future cocaine use, a beta-blocker with combined alpha-blocking properties (eg carvedilol) may be preferred.

TESTS THAT ASSIST IN EVALUATION AND DIAGNOSIS OF CARDIOMYOPATHY

Recommendations

- When the cause of a cardiomyopathy is unknown, further testing should be performed based on the suspected cause (class I, level C).
- The choice of test(s) should first be informed by careful history and physical examinations, and when clinical evidence suggests a possible cause and the planned test(s) result would be reasonably expected to lead to a change in clinical care, the test(s) should be performed (class I, level C).
- Patients with atherosclerotic risk factors should be evaluated for coronary artery disease as a cause of their cardiomyopathy (class I, level C).

TABLE 6
Nutritional disorders associated with cardiomyopathies

Syndrome (reference)	Causes	Symptoms and signs	Diagnosis	Treatment
Carnitine deficiency (196)	Low carnitine intake	Symptoms of heart failure. May see signs of malnutrition	Blood level. Endomyocardial biopsy	Exogenous carnitine administration
Hypervitaminosis D and other causes of severe hypophosphatemia (197)	Inadequate endogenous production of vitamin D3. Poor diet or malabsorption	Rickets in children, osteomalacia in adults	Good history and physical. Ca, Mg; low 1,25(OH)2D; hypophosphatemia	Treat underlying cause. Endocrine consultation. May need supplement
Selenium deficiency (198)	Selenium deficiency is associated with heart failure in geographic areas where dietary selenium is low	Symptoms of heart failure	History and physical	Selenium supplement
Protein intake insufficient (kwashiorkor) (198,199)	The heart failure is most likely secondary to selenium deficit. In infants and young children	Symptoms of heart failure. Hypothermia, hypotension, tachycardia, edema, low pulse volume, dermatitis and others	History and physical	Correction of fluid and electrolytes. Management of associated problems
Thiamine deficiency (beriberi) (200)	At least 3 months of a diet deficient in thiamine (eg, 'polished rice'); alcohol	Edema. High CO heart failure. Peripheral neuritis. Mid-systolic murmur, third heart sound	History and physical. Decreased serum thiamine level	Thiamine replacement
Anorexia nervosa (201)	Malnutrition, poor diet	Sinus bradycardia, prolonged QT, arrhythmias, cardiomegaly	History, physical, BMI, electrolytes, blood urea nitrogen, creatinine, echo, electrocardiogram	Supportive. Good nutrition. Psychological support. Monitor serum electrolytes

BMI Body mass index; Ca Calcium; CO Cardiac output; Echo Echocardiography; Mg Magnesium; 1,25(OH)2D 1,25-dihydroxyvitamin D

Patients with a cardiomyopathy for which the cause has not yet been identified should normally have a measurement of baseline complete blood count, serum electrolytes and creatinine, liver function tests and thyroid-stimulating hormone, although these only rarely identify the cause. Although natriuretic peptides are increasingly used in patients with suspected heart failure to confirm the diagnosis when there is uncertainty, they cannot identify or differentiate among different causes of cardiomyopathy. When the cause of cardiomyopathy or heart failure remains unknown, further testing to diagnose the cause should be performed based on the suspected cause of cardiomyopathy. Rare causes of cardiomyopathy include hemochromatosis, amyloidosis, progressive systemic sclerosis, endomyocardial fibrosis and sarcoidosis, to name just a few. These and others can be screened for with the tests below. Because heart failure is common and the conditions referred to below are very uncommon, the specific tests outlined below should only be performed when clinical evidence suggests the possibility of the disorder in question. The test result would then reasonably be expected to lead to a change in clinical care.

Genetic testing may be obtained in selected individuals through the Canadian College of Medical Geneticists or a local academic department of genetics. These tests are usually not covered by provincial medical insurance and can be costly. Information is available at the following Web site: ccmg.medical.org/policy.html. Genetic testing in heart failure patients occurs most frequently as part of research activity, for the diagnosis or prognosis of possible cardiomyopathy in known or suspected families with cardiomyopathy (especially HCM), or for identification of hemochromatosis. Thus, genetic testing should only be performed in the setting of a consultation by a trained geneticist and in a clinical scenario that supports the use for genetic testing.

Practical tips

- Plasma BNP/NT-proBNP levels are not helpful in identifying the cause of a cardiomyopathy.
- Magnetic resonance imaging is more sensitive for iron deposits than a computed tomographic scan. Computed tomography should be performed if magnetic resonance imaging is not available.

Blood tests

- Hemochromatosis: elevated ferritin greater than 200 µg/L in premenopausal women and 300 µg/L in men and postmenopausal women, fasting transferrin saturation of greater than 45% to 50% (values greater than 60% in men and 50% in women are highly specific).
- Progressive systemic sclerosis: positive antibody – extractable nuclear antigen, hypergammaglobulinemia, microangiopathic hemolytic anemia.
- Pheochromocytoma: plasma metanephrine testing has the highest sensitivity (96%) for detecting a pheochromocytoma and a specificity of 85%.
- HIV: HIV test.
- Hypereosinophilic syndrome: eosinophilic count greater than 1500 cells/µL, anemia of chronic disease in approximately 50% of patients, platelet count often normal, but may be high or low.
- Fabry's disease: reduced plasma alpha-galactosidase activity.

24 h urine collection

- Pheochromocytoma: urinary metanephrines.
- Amyloid RCM: amyloid protein.
- Fabry's disease: elevated urinary globotriaosylceramide.

ECG

- Ischemic cardiomyopathy: Q wave or non-Q wave infarction.
- RCMs: low voltage, first-degree atrioventricular block, right bundle branch block, left atrial enlargement, poor R wave progression mimicking myocardial infarction.
- HCM: diffuse or focal giant T wave inversion, left ventricular hypertrophy without significant hypertension, nonspecific intraventricular conduction delay, septal Q waves.

- Fabry's disease: sinus bradycardia, nonspecific ST segment changes, T wave inversion, short PR interval.

Chest x-ray

- Sarcoidosis: bilateral hilar lymphadenopathy.
- Systemic sclerosis: fibrosis of the basal parts of the lungs, diffuse ground-glass and honeycomb lung patterns.

Ophthalmic examination

- Sarcoidosis: uveitis.
- Fabry's disease: slit-lamp microscopy to identify typical specific changes in the cornea, lens, retina and conjunctiva.

Echocardiography

- Ischemic cardiomyopathy: regional wall motion abnormalities in coronary artery disease distributions.
- Hypertensive cardiomyopathy: concentric left ventricular hypertrophy, significant left ventricular diastolic dysfunction.
- Valvular cardiomyopathy: moderate to severe structural valve abnormalities.
- RCMs: restrictive filling pattern, small ventricular chambers with increased wall thickness, very large atria, thickening of valve structures and interatrial septum.
- Amyloid cardiomyopathy: sparkling appearance or hyperechogenicity of the thickened walls, especially the septum.
- Endomyocardial fibrosis: fibrosis and thickening of the inferior and basal left ventricular wall, apical obliteration, thrombi adherent to endocardial surface.
- Carcinoid heart: fibrosis of the endocardium usually involving the right side of the heart, frequently involving the ventricular aspect of the tricuspid valve and associated chordae.
- HCM: asymmetric septal hypertrophy, ventricular hypertrophy, left ventricular outflow obstruction may be present.
- Fabry's disease: progressive concentric left ventricular hypertrophy, septal thickening and diastolic dysfunction in advanced stages, mitral valve prolapse and thickening may also be observed.
- Hypereosinophilic syndrome: intracardiac thrombi, fibrosis as areas of increased echogenicity or posterior mitral valve leaflet thickening, mitral and tricuspid valve dysfunction.

Cardiac nuclear imaging

- Ischemic cardiomyopathy: regional wall motion abnormalities with poor perfusion or viability.
- Amyloidosis: scintigraphy with technetium-99m pyrophosphate and other agents that bind to calcium is frequently positive with extensive amyloid infiltration.

Cardiac catheterization or angiography

- Ischemic cardiomyopathy: hemodynamically significant, major coronary artery disease.
- Valvular cardiomyopathy: hemodynamically significant structural valve disease.
- RCMs: pressure tracings diagnostic of a restrictive filling pattern.
- Endomyocardial fibrosis: left and right ventriculography exhibits distortion of chamber morphology by fibrosis and obliteration, and variable degrees of mitral and tricuspid regurgitation.
- Endomyocardial fibrosis or Chagas' disease: mushroom sign describes shape of the affected ventricle when the apex is obliterated completely by fibrosis.

Endomyocardial biopsy

- Myocarditis: inflammatory infiltrate and associated myocyte necrosis.
- Giant cell myocarditis: inflammatory infiltrates with giant cells.
- Amyloidosis: Congo red-binding and immunostaining.
- Sarcoidosis: patchy; biopsy usually not needed for diagnosis. If performed, biopsy can show noncaseating granulomas, but they are easily missed.
- Endomyocardial fibrosis: patchy; biopsy usually not needed for diagnosis. If performed, biopsy can show reactive fibrosis associated with a selective increase in type I collagen deposition, subendocardial infarction and fibrosis, and thrombus formation.
- Hypereosinophilic syndrome: high levels of eosinophils in the tissue biopsy.

Cardiac computed tomography

- Endomyocardial fibrosis: a fibrotic process delineated as a band of low attenuation within the endocardium, with possible obliteration of the apex and inflow tract.

CMR imaging

- RCM: fibrosis, inflammation or infiltration may be differentiated from healthy myocardium using a contrast medium (gadolinium-diethylenetriamine penta-acetic acid) in T1-weighted sequences.
- Amyloid cardiomyopathy: early unusual contrast washout with subendocardial contrast enhancement associated with noncompressible signal of remote myocardium.
- Ischemic cardiomyopathy: subendocardial scar tissue with gadolinium, as above.
- Endomyocardial fibrosis: oblitative changes in the ventricles, atrial dilation.
- Left ventricular noncompaction: marked trabeculation of muscle with more thickness of noncompacted than compacted myocardium.

Abdominal computed tomography

- Hemochromatosis: iron deposition.
- Pheochromocytoma: adrenal masses detected with an accuracy of 85% to 90% and with a spatial resolution of 1 cm or greater.

Abdominal magnetic resonance imaging

- Hemochromatosis: more sensitive for iron deposition than computed tomography.

Tissue biopsy

- Liver biopsy: hemochromatosis – iron deposition.
- Rectal, fat pad, stomach, salivary glands or bone marrow biopsy: amyloid deposition.
- Skin biopsy: Fabry's and Gaucher's diseases – alpha-galactosidase A activity.

Genetic testing

- Primary hemochromatosis (hereditary hemochromatosis gene mutation).
- Familial sarcoidosis.

- Carcinoid heart (mutation of multiple endocrine neoplasia type 1 gene).
- HCM (can identify patients with poor prognosis). The dominant genotype in HCM is a mutation in the genes that encode proteins of the cardiac sarcomere. More than 430 mutations in 12 genes (beta-myosin heavy chain being the most common) have now been identified.
- Pheochromocytoma.
- Amyloidosis: hereditary amyloidosis may be present in nearly 10% of patients thought to have the primary (AL) form.
- Fabry's disease: DNA isolated from blood or biopsy specimens can be used for analysis of the galactosidase A gene sequence to identify the disease-causing mutation. DNA testing is the preferred method for identifying and confirming the carrier status of women in whom enzyme activity is within or near the reference range.

CONCLUSIONS

A heart failure patient's journey is fraught with many challenges for the patient, their family and friends, their primary care providers, their specialist and other health care providers, and their local/regional health care facilities. The journey begins best with a prompt and accurate diagnosis of heart failure, followed by early intervention with evidence-based therapy and close follow-up to anticipate and prevent complications. Many patients may fall through some cracks but do surprisingly well, while others stabilize but succumb to a sudden fatal arrhythmia. Coordination of care and collaboration in follow-up is critical to success.

The present guideline paper represents the commitment of the CCS to recognize heart failure as a major health care challenge, and to provide advice and resources to help meet that challenge. Previous guidelines have addressed the best therapies and solutions to common challenges such as intercurrent illnesses. The present publication has addressed important issues for which fewer clinical trials have been published, but for which many clinical trials are needed. Some material could not be included in the present manuscript, and

additional information, resources and tools will be published on the CCS Heart Failure guideline Web site (www.hfcc.ca). The goal of the CCS is to see a measurable change in heart failure care and outcomes in Canada.

ACKNOWLEDGEMENTS: This Consensus Conference was supported by the Canadian Cardiovascular Society. The authors are indebted to Marie-Josée Martin, Jody McCombe and Kim Harrison for their logistic and administrative support.

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CONFLICTS OF INTEREST: The panelists had complete editorial independence in the development and writing of this manuscript, and have completed conflict of interest disclosure statements, which are available at www.hfcc.ca or www.ccs.ca. A full description of the planning of this Consensus Conference and the ongoing process (including the needs assessment, the methods of searching for and selecting the evidence for review) are also available on these Web sites.

APPENDIX

Suggested template for transition of care plan from a specialist to the primary care practitioner (PCP)

Clinical status

- Record diagnoses
- Identify current problems and condition at discharge
- List recommendations from subspecialty consultants, if applicable
- List medications
 - Current drugs and doses
 - Drugs requiring dose titration (advise when to titrate, what to watch for, target dose)
- Provide current laboratory results (advise when to repeat, what to watch for, how to respond)
- Identify follow-up plan/tests (give timeframe to return, to see PCP, to see other providers)
- Identify resuscitation and other end-of-life issues discussed in hospital

Education

- Who was educated (ie, patient, family or caregiver)
 - What was taught:
 - Fluids – eg, 2 L/day
 - Salt – eg, <2 g/day sodium diet, foods to avoid, how to read food labels, recipe suggestions given
 - Weight – eg, daily morning weight, keep a record, call the clinic if gain/loss of >3 lb in 1–2 days or 5 lb in one week
 - Symptoms – eg, important to recognize worsening heart failure symptoms, instructed on what to do (see PCP if mild, contact heart failure clinic if moderate, go to emergency department if severe)
 - Medications – eg, take regularly, do not stop or change dose without consulting PCP or heart failure clinic, notify PCP or clinic if side effects, avoid over-the-counter anti-inflammatory medications
 - Activity – eg, walk daily, avoid heavy lifting, pace activities as tolerated, referred (yes/no) to exercise program
 - When to see PCP and return to specialist
-

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