Society Guidelines

The 2012 Canadian Cardiovascular Society Heart Failure Management Guidelines Update: Focus on Acute and Chronic Heart Failure

Primary Panel Authors: Robert S. McKelvie, MD, PhD, FRCPC (Chair),a Gordon W. Moe, MD, FRCPC (Co-chair),b Justin A. Ezekowitz, MB, BCh, MSc, FRCPC,c George A. Heckman, MD, MSc, FRCPC,d,e Jeannine Costigan, RN, MScN, APNd,e Anique Ducharme, MD, FRCPC,f Estrellita Estrella-Holder, RN, BN, MScA, CCN(C),g Nadia Giannetti, MD, FRCPC,h Adam Grzeslo, MD, CCFP, FCFP,ai Karen Harkness, RN, BScN, CCNC, PhD,a Jonathan G. Howlett, MD, FRCPC,i Simon Kouz, MD, FRCPC, FACC, k Kori Leblanc, BScPhm, ACPR PharmD,l Elizabeth Mann, MD, FRCPC, FACP, m Anil Nigam, MD, MSc, FRCPC,f Eileen O’Meara, MD, FRCPC,f Miroslaw Rajda, MD, FRCPC,m Brian Steinhart, MD, FRCPC,b Elizabeth Swiggum, MD, FRCPC,n Vy Van Le, MD, FRCPC,f and Shelley Zierothe, MD, FRCPC° Secondary Panel Authors: J. Malcolm O. Arnold, MD, FRCPC,p Tom Ashton, MD, FRCPC,q Michel D’Astous, MD, FRCPC,r Paul Dorian, MD, FRCPC,1 Haissam Haddad, MD, FRCPC, s Debra L. Isaac, MD, FRCPC,i Marie-Hélène Leblanc, MD, FRCPC,1 Peter Liu, MD, FRCPC,1 Vivek Rao, MD, PhD, FRCPSc,1
Heather J. Ross, MD, FRCPC,1 and Bruce Sussex, MD, FRCPCa

a Hamilton Health Sciences, McMaster University, Hamilton, Ontario, Canada; b St Michael’s Hospital, Toronto, Ontario, Canada; c University of Alberta, Edmonton, Alberta, Canada; d University of Waterloo, Waterloo, Ontario, Canada; e St Mary’s General Hospital, Kitchener, Ontario, Canada; f Institut de Cardiologie de Montréal, Montreal, Québec, Canada; g St Boniface General Hospital, Cardiac Sciences Program, Winnipeg, Manitoba, Canada; h McGill University, Montreal, Québec, Canada; i Joseph Brant Memorial Hospital, Burlington, Ontario, Canada; j University of Calgary, Calgary, Alberta, Canada; k Centre Hospitalier Régional de Lanaudière, Joliette, Québec and Université Laval, Québec, Canada; l University of Toronto, Toronto, Ontario, Canada; m QE II Health Sciences Centre, Dalhousie University, Halifax, Nova Scotia, Canada; n Royal Jubilee Hospital, Victoria, British Columbia, Canada; o Cardiac Sciences Program, St Boniface General Hospital, Winnipeg, Manitoba, Canada; p Western Ontario, London, Ontario, Canada; q Penticton, British Columbia, Canada; r Université de Moncton, Moncton, New Brunswick, Canada; s Ottawa Heart Institute, Ottawa, Ontario, Canada; t Hôpital Laval, Sainte-Foy, Québec, Canada; u Health Sciences Centre, St John’s, Newfoundland, Canada

Received for publication September 14, 2012. Accepted October 4, 2012.

Corresponding author: Dr Robert S. McKelvie, Hamilton Health Sciences, DBCVSRI, 237 Barton St East, Hamilton, Ontario L8L 2X2, Canada. Tel.: +1-905-572-7155.
E-mail: Robert.McKelvie@phi.ca

The disclosure information of the authors and reviewers is available from the CCS on the following websites: www.ccs.ca and/or www.ccsguidelineprograms.ca.

This statement was developed following a thorough consideration of medical literature and the best available evidence and clinical experience. It represents the consensus of a Canadian panel comprised of multidisciplinary experts on this topic with a mandate to formulate disease-specific recommendations. These recommendations are aimed to provide a reasonable and practical approach to care for specialists and allied health professionals obliged with the duty of bestowing optimal care to patients and families, and can be subject to change as scientific knowledge and technology advance and as practice patterns evolve. The statement is not intended to be a substitute for physicians using their individual judgment in managing clinical care in consultation with the patient, with appropriate regard to all the individual circumstances of the patient, diagnostic and treatment options available and available resources. Adherence to these recommendations will not necessarily produce successful outcomes in every case.

Canadian Journal of Cardiology 29 (2013) 168 –181

0828-282X/$ – see front matter © 2013 Canadian Cardiovascular Society. Published by Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.cjca.2012.10.007
The Canadian Cardiovascular Society (CCS) has published heart failure (HF) guidelines since 2006 and implemented the National HF Workshop Initiative; a series of workshops initiated to discuss Guideline implementation and identify challenges facing health care providers in HF management. The annual updates have produced a series of evidence-based reports with recommendations and practical tips outlining HF management.

The constitution and roles of the primary and secondary panels, systematic review strategy, and methods for formulating the recommendations are described in detail on the CCS HF Consensus Web site (www.ccsguidelineprograms.ca).

The 2012 CCS HF Consensus Update objectives are to provide an overall review of HF management and recommendations. The Guidelines deal with the areas of (1) acute HF (AHF) and (2) chronic stable HF.

The recommendations follow the Grading of Recommendations Assessment, Development, and Evaluation (GRADE). The GRADE system classifies the quality of evidence as High (further research very unlikely to change confidence in the estimate of effect), Moderate (further research likely to have an important impact on confidence in the estimate of effect and may change the estimate), Low (further research very likely to have an important impact on confidence in the estimate of effect and likely to change the estimate), and Very Low (estimate of the effect very uncertain). The GRADE system offers 2 grades of recommendations: “Strong” (desirable effects clearly outweigh undesirable effects or clearly do not) and “Weak.” When trade-offs are less certain, either because of low-quality evidence or because evidence suggests desirable and undesirable effects are closely balanced, weak recommendations become mandatory. Also new this year is the inclusion of values and preferences that complement the GRADE system of recommendations.

### Acute Heart Failure

**Diagnosis, evaluations, and investigation**

The diagnosis of AHF is based on a constellation of symptoms (eg, orthopnea and shortness of breath on exertion) and signs (eg, edema and respiratory crackles). Physical examination evaluates systemic perfusion and presence of congestion (cold or warm, wet or dry; Supplemental Figure S1). Laboratory testing, electrocardiogram (ECG), chest x-ray, and echocardiogram are all important to obtain.

A slight mild elevation of cardiac troponin is not infrequently observed in acute decompensation and not necessarily indicative of myocardial infarction (MI). The utility of natriuretic peptide (NP) to exclude (“rule out”) or confirm (“rule in”) the diagnosis in the appropriate clinical scenario is well established. NPs are best used when the diagnosis is uncertain; their clinical utility and relevant cut points have been well established. Several clinical scoring systems have been derived and validated and combine commonly used clinical features with NP values to improve diagnosis and decision-making. The most commonly used clinical scoring system (Table 1) was developed by Baggish et al. Prospective trials are under way, testing variations of these systems.

**RECOMMENDATION**

1. We recommend a thorough clinical evaluation of the patient to assess their clinical hemodynamic profile (Strong Recommendation, Low-Quality Evidence).
2. We recommend the use of a validated diagnostic scoring system for patients in whom the diagnosis of AHF is being considered (Strong Recommendation, Moderate-Quality Evidence).
3. We recommend that in the clinical scenario in which the clinical diagnosis of AHF is of intermediate pretest probability, NP level be obtained to rule out (brain NP [BNP] < 100 pg/mL; N-terminal [NT]-proBNP < 300 pg/mL) or rule in (BNP > 500 pg/mL; NT-proBNP > 900 pg/mL if age 50–75 years, NT-proBNP > 1800 if age > 75 years) AHF as the cause for the presenting symptoms suspicious of AHF (Strong Recommendation, Moderate-Quality Evidence).

**Values and preferences.** This recommendation places a relatively high value on evaluating the constellation of clinical findings in a patient with suspected AHF and less value on an individual physical examination finding, presenting symptom, or investigation.

**Practical tip.** A precipitating cause for AHF should be sought.
An ECG and a chest x-ray should be performed within 2 hours of initial presentation.

Initial blood tests should include: complete blood count, creatinine, blood urea nitrogen, glucose, sodium, potassium, and troponin.

A transthoracic echocardiogram should be performed within 72 hours of presentation. For patients with a previous echocardiogram, another is not required unless there has been a significant change in clinical status requiring investigation, a lack of clinical response to appropriate therapy, and/or it is greater than 12 months since the previous echocardiogram.

Measurement of BNP or NT-proBNP measurements might be considered even with an already established diagnosis of HF in order to obtain prognostic information.

**Treatment, monitoring, and disposition**

Oxygen should be used cautiously in normoxic patients because of concerns of increasing systemic vascular resistance and reducing cardiac output. Bilevel positive airway pressure (BiPAP) or continuous positive airway pressure (CPAP) should be considered for patients with a high respiratory rate (eg, > 25 breaths per minute) and persistent systemic arterial hypoxemia despite high flow oxygen administration. However, routine use of noninvasive ventilation (NIV) is not advisable. In the Three Interventions in Cardiogenic Pulmonary Edema (3CPO) trial, patients with acute pulmonary edema were randomized to standard oxygen therapy, CPAP, or NIV, and followed to the primary end point of 7-day mortality. There was no difference between the 3 arms on 7-day mortality rate and 30-day mortality rate, intubation rates, or admission to an intensive care unit. Therefore NIV should be used only in patients with acute respiratory distress unresponsive to medical therapy. NIV carries the risk of worsening right HF, hypercapnia, aspiration, and pneumothorax. Endotracheal intubation may be used if less invasive modes of oxygen delivery fail or if the patient is in cardiogenic shock. There is a paucity of evidence to support the use of intravenous morphine to treat dyspnea, however some data suggest there might be adverse effects.

Oral and intravenous diuretics remain the mainstay of early therapy directed toward AHF (Supplemental Table S2). Intravenous diuretics increase urine output by excretion of sodium and water, leading to a decrease in extracellular fluid volume, total body water, and sodium. Reduction in cardiac filling pressures, peripheral congestion, and pulmonary edema usually follow. Intravenous loop diuretics also cause an early decrease in right atrial and pulmonary capillary wedge pressure through a vasodilatory effect. When using high intravenous doses reflex vasodilatation might occur. In AHF, by normalizing loading conditions, these high doses might reduce neurohormonal activation in the short-term. Patients presenting with AHF and congestion should receive intravenous loop diuretics. Therapy may be initiated in the ambulance, or in-hospital. Combining loop diuretics with thiazides or spironolactone has been proposed and seems to be effective, with fewer side effects than a higher dose of a loop diuretic. In patients with severe edema, oral loop diuretics might not be adequately absorbed and might be of little use.

**Table 1. A clinical scoring system for diagnosis of AHF**

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Possible score</th>
<th>Your patient’s score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt; 75 y</td>
<td>1</td>
<td>0-5</td>
</tr>
<tr>
<td>Orthopnea present</td>
<td>2</td>
<td>Intermediate 6-8</td>
</tr>
<tr>
<td>Lack of cough</td>
<td>3</td>
<td>High 9-14</td>
</tr>
<tr>
<td>Current loop diuretic use</td>
<td>1</td>
<td>14 Total =</td>
</tr>
<tr>
<td>(before presentation)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rales on lung exam</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Lack of fever</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Elevated NT-proBNP*</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Interstitial edema on chest x-ray</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

AHF, acute heart failure; NT-proBNP, N-terminal pro brain natriuretic peptide.

* Elevated NT-proBNP was defined as > 450 pg/mL if age < 50 years and > 900 pg/mL if age > 50 years.

Vasodilators have not been shown to reduce mortality. Intravenous isosorbide dinitrate (in conjunction with low dose furosemide) was tested against low dose nitrates with high dose diuretics. This prehospital trial of 110 patients showed that the strategy of early and high dose nitroglycerin (compared with high dose intravenous diuretics) reduced mechanical ventilation rates, and improved oxygen saturation. Another trial compared nesiritide, nitroglycerin, or placebo added to standard therapy for 3 hours, followed by nesiritide or nitroglycerin added to standard treatment for 24 hours in AHF. The primary end points of changes in pulmonary capillary wedge pressure and patient self-evaluation of dyspnea at 3 hours were improved with nesiritide vs placebo. However, nitroglycerin improved early, short-term dyspnea assessment compared with placebo.

The Acute Study of Clinical Effectiveness of Nesiritide in Decompensated Heart Failure (ASCEND-HF) trial tested nesiritide vs placebo in 7007 patients with AHF enrolled within 24 hours of first intravenous medication. Nesiritide did not reduce mortality, rehospitalization, or the composite of these end points at 30 days. The use of nitroprusside in AHF has not been supported by any randomized controlled trial (RCT). However, observational studies support its use in advanced HF by clinicians with experience and expertise in managing low-output acute or sub-acute HF.

Inotropic agents have not been shown to improve patient outcomes. The Outcomes of a Prospective Trial of Intravenous Milrinone for Exacerbations of Chronic Heart Fail-
Angiotensin-converting enzyme (ACE) inhibitors should not be used early in the management of AHF. Though calcium channel blockers (CCBs) are also not advised, patients with HF with preserved ejection fraction (HF-PEF) and atrial fibrillation, a rate-limiting CCB may be used to control rapid ventricular rate. Continuation of β-blocker upon admission for AHF is safe. In an RCT of 169 patients with AHF, patients either discontinued β-blockade for 3 days or continued the medication unchanged. The trial showed that continuing the β-blocker was noninferior for the primary end point of dyspnea and well-being and was associated with a higher rate of β-blocker prescription at 3 months.

Venovenous ultrafiltration may be of benefit in relieving congestion particularly in diuretic-resistant patients. However, a recent study suggests this technology may be no more effective than pharmacologic therapy in most patients. Vasoressin receptor antagonists (eg, tolvaptan) can rapidly and effectively reduce body weight and restore serum sodium in hypotensive patients with circulatory congestion, and a nonsignificant increase in the number of deaths in-hospital and after 60 days was seen in the milrinone group. A post hoc analysis demonstrated a higher incidence of death or rehospitalization in patients with underlying ischemic HF aetiology.

Values and preferences. This recommendation places relatively higher value on the physiologic studies demonstrating potential harm with the use of excess oxygen in normoxic patients and less value on long-term clinical usage of supplemental oxygen without supportive data.

2. We recommend CPAP or BIPAP not be used routinely (Strong Recommendation, Moderate-Quality Evidence).

Values and preferences. This recommendation places high weight on RCT data with a demonstrated lack of efficacy and with safety concerns in routine use. Treatment with BIPAP/CPAP might be appropriate for patients with persistent hypoxia and pulmonary edema.

3. We recommend intravenous diuretics be given as first-line therapy for patients with congestion (Strong Recommendation, Moderate-Quality Evidence).

4. We recommend for patients requiring intravenous diuretic therapy, furosemide may be dosed intermittently (eg, twice daily) or as a continuous infusion (Strong Recommendation, Moderate-Quality Evidence).

5. We recommend the following intravenous vasodilators, titrated to systolic BP (SBP) > 100 mm Hg, for relief of dyspnea in hemodynamically stable patients (SBP > 100 mm Hg):
   i. Nitroglycerin (Strong Recommendation, Moderate-Quality Evidence);
   ii. Nesiritide (Weak Recommendation, High-Quality Evidence);
   iii. Nitroprusside (Weak Recommendation, Low-Quality Evidence).

Values and preferences. This recommendation places a high value on the relief of the symptom of dyspnea and less value on the lack of efficacy of vasodilators or diuretics to reduce hospitalization or mortality.

6. We recommend hemodynamically stable patients do not routinely receive inotropes like dobutamine, dopamine, or milrinone (Strong Recommendation, High-Quality Evidence).

Values and preferences. This recommendation for inotropes place high value on the potential harm demonstrated when systematically studied in clinical trials and less value on potential short term hemodynamic effects of inotropes.

7. We recommend continuation of chronic β-blocker therapy with AHF, unless the patient is symptomatic from hypotension or bradycardia (Strong Recommendation, Moderate-Quality Evidence).
Values and preferences. This recommendation places higher value on the RCT evidence of efficacy and safety to continue β-blockers, the ability of clinicians to use clinical judgement and lesser value on observational evidence for patients with AHF.

8. We recommend tolvaptan be considered for patients with symptomatic or non-hyponatraemic (< 130 mmol/L) and persistent congestion despite standard therapy, to correct hyponatraemia and the related symptoms (Weak Recommendation, Moderate-Quality Evidence).

Values and preferences. This recommendation places higher value on the correction of symptoms and complications related to hyponatraemia and lesser value on the lack of efficacy of vasopressin antagonists to reduce HF-related hospitalizations or mortality.

Practical tip. In patients at risk or with a previous history of CO₂ retention (eg, chronic obstructive lung disease) permissive hypervolemia might be necessary and can be evaluated with arterial blood gas measurement.

In situations in which intravenous nitroglycerin is not appropriate or available, repeated sublingual nitroglycerin, a nitroglycerin patch, or oral isosorbide dinitrate might be useful for dyspnea relief in patients with a SBP > 100 mm Hg.

Intravenous vasoconstrictor agents (eg, phenylephrine, norepinephrine) should generally be avoided for AHF management except for patients hypotensive with SBP < 90 mm Hg, associated signs or symptoms, and significant change from baseline.

In patients with low SBP (< 90 mm Hg), low cardiac output and either euvoeemia or hypervolemia, inotropes may be used for stabilization.

Patients with persistent congestion despite diuretic therapy, with or without impaired renal function, may, under experienced supervision, receive continuous venovenous ultrafiltration.

An ACE inhibitor should not be started in the acute setting (eg, the first 8-12 hours) unless elevated BP is present, and should be initiated after the acute event (eg, > 24 hours), and be continued particularly if the patient is already being treated with chronic ACE inhibitor therapy.

CCBs should be avoided as treatment in the setting of reduced ejection fraction (REF) < 40%.

Chronic Heart Failure

Diagnosis, evaluation, and investigation

The diagnosis of HF is made when symptoms and physical signs of congestion and reduced tissue perfusion are documented in the setting of abnormal systolic and/or diastolic cardiac function. Making a diagnosis of HF can be difficult because the cardinal triad of edema, fatigue, and dyspnea are neither sensitive nor specific manifestations and atypical presentations should be recognized particularly when evaluating women, obese patients, and the elderly. A history and physical examination should be performed in all patients; initial investigations should confirm or exclude HF and identify systemic disorders (eg, thyroid dysfunction) that can be etiologic or potentially affect disease progression. Measurements of NPs are useful when the initial diagnosis or diagnosis of decompensation is uncertain. Echocardiography is useful to assess systolic and diastolic function, cardiac anatomy (eg, volume, geometry, and left ventricular mass), and pericardial disease. Radionuclide angiography is useful to assess cardiac function and volumes where echocardiographic images are suboptimal (eg, obese patients, patients with emphysema). Coronary angiography should also be considered in patients who have angina or positive noninvasive tests and might be potential candidates for revascularization. Cardiac magnetic resonance might be useful in identifying inflammatory and infiltrative disorders and provide prognostic information. Functional capacity should be assessed and the New York Heart Association (NYHA) functional classification is a simple, validated measure of HF clinical severity (Fig. 1).

RECOMMENDATION

1. We recommend conducting a thorough medical history and physical examination when making a diagnosis of HF. Diseases that can cause HF or contribute to its progression should be screened. These include: family history of cardiomyopathy or sudden death, alcohol abuse, homocystinemia, sarcoidosis, amyloidosis, HIV infection, neuroendocrinopathies (eg, pheochromocytoma, hypothroidism), rheumatologic diseases (eg, collagen vascular diseases), nutritional deficiencies (eg, thiamine), and sleep apnea (Strong Recommendation, Low-Quality Evidence).

2. We recommend that a 12-lead ECG be performed to determine heart rhythm, heart rate, QRS duration, and morphology, and to detect possible aetiologies (Strong Recommendation, Low-Quality Evidence).

3. We recommend, if available, the measurement of NP (BNP and NT-proBNP) to rule in or rule out a diagnosis of HF and to obtain prognostic information (Strong Recommendation, High-Quality Evidence).

4. We recommend that echocardiography be performed in all patients with suspected HF to assess cardiac structure and function, to quantify systolic function for planning and monitoring of treatment, and for prognostic stratification (Strong Recommendation, Moderate-Quality of Evidence).

5. We recommend coronary angiography be performed in patients with angina pectoris who are deemed suitable candidates for coronary revascularization to document coronary anatomy (Strong Recommendation, Low-Quality of Evidence).

6. We recommend a validated measure of severity of symptoms and physical activity, such as the NYHA classification to document coronary anatomy (Strong Recommendation, High-Quality Evidence).

Values and preferences. These recommendations place greater value on basic evaluations that are widely available and less value on more advanced tests (eg, cardiac magnetic resonance) that should be reserved for selected patients.

Heart failure with preserved ejection fraction

Approximately 50% of HF patients seen in clinics have HF-PEF. HF-PEF is more prevalent in the elderly,
women, and in patients with a history of hypertension. In practice, HF-PEF is diagnosed when typical clinical HF findings are accompanied by PEF and the absence of significant valvular abnormalities. The reported mortality rate for HF-PEF is less than found for HF with REF (HF-REF), although it is unacceptably high; however, the studies have generally shown that morbidity, especially in HF hospitalizations, is similar to HF-REF. There are still very limited evidence-based outcome-modifying therapies for HF-PEF, with most RCTs evaluating ACE inhibitors and angiotensin receptor blockers (ARBs) showing neutral or marginal benefits. The main approach therefore is to control the risk factors potentially etiologic for the syndrome such as hypertension and myocardial ischemia. Diuretics are typically used to control symptoms of congestion, and β-blockers and rate-lowering CCBs to control heart rate, if required. ACE inhibitors and ARBs may be used if there are other non-HF indications for their use.

**RECOMMENDATION**

1. We recommend systolic/diastolic hypertension be controlled according to the hypertension guidelines to prevent and treat HF-PEF (Strong Recommendation, High-Quality Evidence).
2. We recommend diuretics be used to control symptoms from pulmonary congestion and peripheral edema (Strong Recommendation, High-Quality Evidence).

---

**Figure 1.** Algorithm for diagnosis of heart failure. CBC, complete blood count; CT, computed tomography. *Normal ejection fraction does not rule out heart failure with preserved ejection fraction. Adapted with permission from Arnold et al.*
**Mineralocorticoid receptor antagonists (MRAs) greatly improve mortality/morbidity in patients with MI complicated by left ventricular dysfunction and HF, and patients with HF-REF with mild to moderate symptoms accompanied by high risk features, and patients with advanced HF. There is, however, limited trial experience with the combined use of ACE inhibitors, ARBs, and MRAs.**

β-Blockers such as bisoprolol, metoprolol CR/XL, and carvedilol reduce mortality in patients with HF-REF on ACE inhibitors. However, bucindolol did not reduce mortality. β-Blocker should be initiated in stable patients although it can also be initiated with caution in patients with recent decompensation.

Diuretics relieve dyspnea and edema effectively. Although there are no large trials of diuretic therapy, a meta-analysis suggests they reduce the risk of worsening HF, death, and improve exercise capacity.

Digoxin reduced HF hospitalization in patients with REF in sinus rhythm in 1 RCT and systematic review of small trials suggested some benefits in symptoms and worsening HF. These trials were performed before the widespread use of β-blockers.

An early RCT performed before the recognition of the benefits of ACE inhibitors and β-blockers demonstrated marginal mortality and symptom benefit from a combination of hydralazine and isosorbide dinitrate. The African-American Heart Failure Trial (A-HeFT) showed that adding a fixed-dose combination of isosorbide dinitrate plus hydralazine to a contemporary standard therapy reduced mortality, first hospitalization for HF, and improved quality of life among African-American patients with HF-REF.

A recent study in patients with NYHA class II-IV symptoms and ejection fraction (EF) ≤40% has demonstrated that the use of omega-3 polyunsaturated fatty acids (1 g daily) results in a modest reduction in cardiovascular (CV) mortality and hospitalization.

Resting heart rate independently predicts CV events, including HF hospitalization. Iverapill, a drug that inhibits the I_f channel, when approved might be considered in patients who remain symptomatic with a heart rate > 70 beats per minute despite optimal medical therapy including β-blockers, to reduce hospitalizations and deaths because of HF.

An RCT in patients with HF-REF has demonstrated that patients randomized to receive aspirin 300 mg daily have increased risk of HF hospitalization. Antiplatelet agents such as aspirin should therefore be administered only to patients with HF who have a documented history of coronary artery disease and stroke or who are deemed high risk for CV events. A recent RCT has demonstrated that in patients with REF who are in sinus rhythm, there is no significant difference between treatment with warfarin and aspirin in the risk of stroke.

Commonly used medications such as the thiazolidinediones, nonsteroidal anti-inflammatory agents and cyclooxygenase-2 inhibitors have been implicated in the exacerbation of HF and should be avoided if possible.

A list of evidence-based HF pharmacologic agents and the doses in the management of HF-REF is shown in Supplemental Table S3.
**RECOMMENDATION**

**ACE inhibitor**

1. We recommend an ACE inhibitor be used in all patients as soon as safely possible after a MI and be continued indefinitely if EF < 40% or if HF complicates a MI (Strong Recommendation, High-Quality Evidence).

2. We recommend ACE inhibitors be used in all asymptomatic patients with an EF < 35% (Strong Recommendation, Moderate-Quality Evidence).

3. We recommend ACE inhibitors be used in all asymptomatic HF patients and EF < 40%. (Strong Recommendation, High-Quality Evidence).

**ARB**

4. We recommend an ARB be used in patients who cannot tolerate an ACE inhibitor (Strong Recommendation, High-Quality Evidence).

5. We recommend an ARB be added to an ACE inhibitor for patients with NYHA class II-IV HF and EF ≤ 40% deemed at increased risk of HF events despite optimal treatment with an ACE inhibitor and β-blocker as tolerated (Strong Recommendation, Moderate-Quality Evidence).

6. We recommend an ARB be considered instead of an ACE inhibitor for patients with acute MI with HF or an EF < 40% who cannot tolerate an ACE inhibitor (Strong Recommendation, Moderate-Quality Evidence).

7. We recommend ARBs be considered as adjunctive therapy to ACE inhibitors when β-blockers are either contraindicated or not tolerated after careful attempts at initiation (Weak Recommendation, Low-Quality Evidence).

8. We recommend routine combination of an ACE inhibitor, ARB, and MRA not be used for patients with current or previous symptoms of HF and REF (Strong Recommendation, Low-Quality Evidence).

**MRA**

9. We recommend an MRA such as eplerenone be considered for patients > 55 years with mild to moderate HF during standard HF treatments with EF ≤ 30% (or ≤ 35% if QRS duration > 130 ms) and recent (6 months) hospitalization for CV disease or with elevated BNP or NT-proBNP levels (Strong Recommendation, High-Quality Evidence).

10. We recommend an MRA such as eplerenone be considered in patients after an MI with EF ≤ 30% and HF or EF ≤ 30% alone in the presence of diabetes (Strong Recommendation, High-Quality Evidence).

11. We recommend an MRA such as spironolactone be considered for patients with an EF < 30% and severe chronic HF (NYHA III-IV) despite optimization of other recommended treatments (Strong Recommendation, High-Quality Evidence).

**Values and preferences.** The above recommendations place a high value on an understanding that among a given drug class, only drugs proven to be beneficial in large trials can be used because their effective target doses capable of modifying clinical outcome are known, and less value on individual response. If a drug with proven mortality or morbidity benefits is not tolerated by the patient, other concomitant drugs with less proven benefit can be carefully re-evaluated to determine whether their dose can be reduced or the drug discontinued to allow for better tolerance of the drug with proven benefit. These values and preferences also apply to the recommendations of other classes of drugs discussed below. Furthermore, because there are still no data on outcome-modifying pharmacologic treatment in HF-PEF, the above recommendations apply predominantly to patients with HF-REF.

**Practical tip.** Consider reducing the dose of diuretic if the patient is otherwise stable, and reassess the need and the dose of other vasodilators, such as long-acting nitrate, if no longer clinically needed.

An increase in serum creatinine of up to 30% is not unexpected in many HF patients when an ACE inhibitor or ARB is introduced; if the increase stabilizes at 30% or less, there is no immediate need to decrease the drug dose but closer long-term monitoring might be required.

MRAs can increase serum potassium, especially during an acute dehydrating illness in which renal dysfunction can worsen, and close monitoring of serum creatinine and potassium is required.

Combining an ARB with an ACE inhibitor increases the risk of hypotension, hyperkalemia, and renal dysfunction, and it should be used with caution.

**RECOMMENDATION**

**β-Blocker**

1. We recommend all HF patients with an EF ≤ 40% receive a β-blocker proven to be beneficial in clinical trials (Strong Recommendation, High-Quality Evidence).

2. We recommend NYHA class IV patients be stabilized before initiation of a β-blocker (Strong Recommendation, High-Quality Evidence).

3. We recommend therapy be initiated at a low dose and titrated to the target dose used in large trials or the maximum tolerated dose if less than the target dose (Strong Recommendation, Moderate-Quality Evidence).

4. We recommend a β-blocker not be generally introduced to patients with symptomatic hypotension despite adjustment of other therapies, patients with severe reactive airways disease, symptomatic bradycardia, or with significant atrioventricular block without a permanent pacemaker; stable chronic obstructive pulmonary disease is not a contraindication for use of β blockade (Strong Recommendation, Moderate-Quality Evidence).

**Values and preferences.** These recommendations place a very high value on the understanding that only β-blockers that have been shown to improve clinical outcomes should be used.

**Practical tip.** Objective improvement in cardiac function might not be apparent for 6-12 months after initiation.
Major reduction in dose or abrupt withdrawal should be avoided in the case of worsening HF. If the patient is hypotensive, consider reducing the dose of other medications before reducing the β-blocker dosage. Temporary discontinuation might occasionally be necessary in patients with shock. Whenever possible, reinstitution of treatment should be attempted before hospital discharge.

RECOMMENDATION

Diuretics

1. We recommend a loop diuretic, such as furosemide, for most patients with HF and congestive symptoms. When acute congestion is cleared, the lowest dose should be used that is compatible with stable signs and symptoms (Strong Recommendation, Low-Quality Evidence).

2. We recommend that for patients with persistent volume overload despite optimal medical therapy and increases in loop diuretics, cautious addition of a second diuretic (a thiazide or low dose metolazone) may be considered as long as it is possible to closely monitor morning weight, renal function, and serum potassium (Weak Recommendation, Moderate-Quality Evidence).

Values and preferences. These recommendations place a high value on the understanding that diuretics have not been shown to improve survival like the ACE inhibitors and β-blockers but are frequently required to relieve congestion.

Digoxin

3. We recommend digoxin in patients in sinus rhythm who continue to have moderate to severe symptoms, despite optimized HF therapy to relieve symptoms and reduce hospitalizations (Strong Recommendation, Moderate-Quality Evidence).

4. We recommend digoxin in patients with chronic atrial fibrillation (AF) and poor control of ventricular rate despite optimal β-blocker therapy, or when β-blockers cannot be used (Strong Recommendation, Low-Quality Evidence).

Values and preferences. These recommendations place a high value on the understanding that the use of cardiac glycosides in chronic HF remains controversial. Digoxin can cause atrial and ventricular arrhythmias particularly in the presence of hypokalemia. Not all glycosides and not all preparations have been studied in terms of efficacy and safety.

Isosorbide dinitrate and hydralazine

5. We recommend the combination of isosorbide dinitrate and hydralazine be considered in addition to standard therapy for black Canadians with HF-REF (Strong Recommendation, Moderate-Quality Evidence) and may be considered for others including non-black HF patients unable to tolerate an ACE inhibitor or ARB because of intolerance, hyperkalemia, or renal dysfunction (Strong Recommendation, Low-Quality Evidence).

Values and preferences. Adverse effects such as headache, nausea, dizziness, and hypotension are common and frequently require a reduction in dose or discontinuation.

Omega-3 polyunsaturated fatty acids

6. We recommend omega-3 polyunsaturated fatty acid therapy at a dose of 1 g daily be considered for reduction in morbidity and CV mortality in patients with mild to severe HF and reduced EF (Strong Recommendation, Moderate-Quality Evidence).

Practical tip. In presence of significant renal dysfunction, higher doses or combination diuretic agents might be needed; blood work needs to be closely followed.

In patients with recurrent fluid retention who are able to follow instructions can be taught to adjust their diuretic dose based on symptoms and changes in daily body weight.

In patients receiving digoxin, serum potassium and creatinine should be measured with increases in digoxin or diuretic dose, addition or discontinuation of an interacting drug, or during a dehydrating illness, to reduce the risk of digoxin toxicity. Patients with reduced or fluctuating renal function, the elderly, those with low body weight, and women are at increased risk of digoxin toxicity and might require more frequent monitoring including digoxin levels.

Nitrates alone can be useful to relieve dyspnea or angina but continuous use should generally be avoided because of the risk of development of tolerance.

RECOMMENDATION

Platelet inhibition and anticoagulation

1. We recommend aspirin at a dose of between 81 and 325 mg be considered only in HF patients with clear indications for secondary prevention of CV events (Strong Recommendation, High-Quality Evidence).

2. We recommend anticoagulation not be used routinely for HF patients who are in sinus rhythm (Strong Recommendation, High-Quality Evidence).

3. We recommend anticoagulation be considered for patients with demonstrated intracardiac thrombus, previous systemic embolism, or after a large anterior MI (Weak Recommendation, Low-Quality Evidence).

Implantable cardioverter-defibrillator

The evidence for the recommendations for implantable cardioverter-defibrillator (ICD) therapy in HF management has been discussed extensively in the 2009 CCS HF Guidelines. In brief, primary ICD therapy improves survival in patients with NYHA II-III ischemic and nonischemic HF with EF ≤ 35% and in patients with a previous MI with EF ≤ 30%. In contrast, ICD therapy does not provide any survival benefit early after an MI.
RECOMMENDATION

1. We recommend an ICD be implanted in patients with HF-REF with a history of hemodynamically significant or sustained ventricular arrhythmia (secondary prevention) (Strong Recommendation, High-Quality Evidence).

2. We recommend consideration of primary ICD therapy in patients with:
   i. Ischemic cardiomyopathy, NYHA class II-III, EF \( \leq 35\% \), measured at least 1 month post MI, and at least 3 months post coronary revascularization procedure (Strong Recommendation, High-Quality Evidence);
   ii. Ischemic cardiomyopathy, NYHA class I, and an EF \( \leq 30\% \) at least 1 month post MI, and at least 3 months post coronary revascularization procedure (Strong Recommendation, High-Quality Evidence);
   iii. Nonischemic cardiomyopathy, NYHA class II-III, EF \( \leq 35\% \), measured at least 9 months after optimal medical therapy (Strong Recommendation, High-Quality Evidence).

3. We recommend an ICD not be implanted in NYHA class IV HF patients who are not expected to improve with any further therapy and who are not candidates for cardiac transplant or mechanical circulatory support (Strong Recommendation, Moderate-Quality Evidence).

Values and preferences. These recommendations place a very high value on the recognition that patients and family members should be carefully counselled as to the purpose of an ICD and the associated complications. If HF progresses to terminal stage, deactivation of the ICD can be considered after careful discussion.

Cardiac resynchronization therapy

Since the previously published CCS HF guideline recommendations on cardiac resynchronization therapy (CRT)\(^4,89\) which were based on earlier landmark RCTs conducted in patients with more severe symptoms,\(^94,95\) additional trials and analyses have been published mandating the revision of the previous recommendations to include patients with mild HF symptoms and to place more emphasis on QRS morphology and duration, and the importance of sinus rhythm in the selection of patients.\(^96-102\) These broad recommendations are in principal in general agreement with the more comprehensive recommendations discussed in the CCS CRT guidelines.

RECOMMENDATION

1. We recommend CRT in patients with NYHA III and ambulatory NYHA IV HF despite optimal medical therapy, in sinus rhythm with QRS duration \( \geq 130\) ms and left bundle branch block (LBBB) QRS morphology and EF \( \leq 35\% \) (Strong Recommendation, High-Quality Evidence).

2. We recommend CRT with an ICD in NYHA II HF patients despite optimal medical therapy, in sinus rhythm with a QRS duration \( \geq 130\) ms with LBBB QRS morphology and EF \( \leq 30\% \) (Strong Recommendation, High-Quality Evidence).

3. We recommend that CRT be considered in NYHA class II, NYHA class III, and ambulatory NYHA class IV HF patients, in sinus rhythm, EF \( \leq 35\% \), and QRS duration \( \geq 150\) ms with non-LBBB QRS morphology (Weak Recommendation, Low-Quality Evidence).

4. We recommend the addition of ICD therapy be considered for patients referred for CRT who meet primary ICD requirements (Strong Recommendation, High-Quality Evidence).

Values and preferences. These recommendations place a significant value on the derived benefit of CRT in patient groups specifically included in the landmark RCTs, and less value on post hoc subgroup analyses and systematic analyses. Based on these trials, there is insufficient evidence to recommend CRT in patients with NYHA class I status or in hospitalized NYHA class IV patients, or those in AF. Patients with a QRS duration \( \geq 150\) ms are universally more likely to benefit from CRT than patients with less prolongation. CRT pacemaker therapy should also be considered in patients who are not candidates for ICD therapy such as those with a limited life expectancy because of significant comorbidities, and in patients who decline to receive an ICD.

Atrial fibrillation

AF is a common arrhythmia in HF, and is associated with higher rates of adverse clinical events\(^103\) and increased risk of thromboembolism including stroke.\(^104\) AF should be managed and classified according to current AF guidelines.\(^105\) The general approach is to control rate.\(^106,107\) There are limited data to support a specific upper heart rate target; however, the current CCS AF guidelines recommend the target rate be \( < 100\) beats per minute.\(^107\) β-Blockers are preferred over digoxin for rate control.\(^107\) Rate-lowering CCBs are acceptable alternatives in patients with HF-PEF.\(^108\) The combination of β-blocker and digoxin is more effective than β-blocker alone in controlling ventricular response.\(^109\) A rhythm control strategy has not been demonstrated to be superior to a rate-control strategy in reducing mortality or morbidity in patients with HF.\(^110\) When rhythm control is required because of symptoms, amiodarone is preferred over class I agents and dronedarone.\(^111,112\) Unless contraindicated, oral anticoagulants should be initiated in patients deemed high risk for stroke as per current AF guidelines.\(^105\)

RECOMMENDATION

1. We recommend in patients with HF and AF that the ventricular rate be controlled at rest and during exercise (Strong Recommendation, Moderate-Quality Evidence).
2. We recommend that restoration and maintenance of sinus rhythm not be performed routinely (Strong Recommendation, High-Quality Evidence).

3. We recommend β-blockers for rate control particularly in those with HF-REF (Strong Recommendation, Moderate-Quality Evidence).

4. We recommend β-blockers combined with digoxin for uncontrolled ventricular rates on β-blocker therapy at optimal dose alone (Strong Recommendation, Moderate-Quality Evidence).

5. We recommend rate-limiting CCBs be considered for rate control in HF-PEF (Weak Recommendation, Low-Quality Evidence).

6. We recommend the use of antiarrhythmic therapy to achieve and maintain sinus rhythm, if rhythm control is indicated, be restricted to amiodarone (Strong Recommendation, Moderate-Quality Evidence).

7. We recommend oral anticoagulation for AF in HF patients deemed high risk for stroke unless contraindicated as per current AF guidelines, and not to coadminister with antiplatelet agents unless the latter are needed for other indications (Strong Recommendation, High-Quality Evidence).

Values and preferences. These recommendations are based on an understanding that the management of HF patients with AF should be individualized with respect to the need to identify precipitating factors, to assess the risk of therapy such as the development of bradycardia and proarrrhythmia with antiarrhythmic agents, and the bleeding risk of systemic anticoagulation.

Practical tip. Nondihydropyridine CCBs should not be used to control heart rate in patients with HF-REF because they can depress cardiac function and worsen HF. Dronedarone should not be used in patients with an EF < 35% and/or with recent decompensated HF because of increased risk of mortality. Agents such as sotalol, flecainide, and propafenone should also be avoided.

Acknowledgements

The present consensus conference was supported by the CCS. The authors are indebted to Marie-Josée Martin and Mirela Lukac for logistic and administrative support.

References


52. Meta-analysis Global Group in Chronic Heart Failure (MAGGIC). The survival of patients with heart failure with preserved or reduced left ventricular ejection fraction: an individual patient data meta-analysis. Eur Heart J 2011;33:1750-7.


Supplementary Material

To access the supplementary material accompanying this article, visit the online version of the Canadian Journal of Cardiology at www.onlinecjc.ca and at http://dx.doi.org/10.1016/j.cjca.2012.10.007.