Heart-Failure Management: Focus on Heart-Failure Practice Guidelines

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Introduction

Heart failure (HF) is associated with a high burden of mortality and morbidity, reduced quality of life, and increasing healthcare costs [1, 2]. HF is largely a disease of old age, and it is becoming increasingly prevalent with the gradual aging of the global population [3]. HF is a complex syndrome in which abnormal heart function results in, or increases the subsequent risk of clinical symptoms and signs of low cardiac output and/or pulmonary and systemic congestion [4].

Because most evidence-based recommendations for HF management derive from clinical trials involving patients with significant left ventricular systolic dysfunction, the term "heart failure" in various guideline documents has been used to refer to predominant left ventricular systolic dysfunction, unless otherwise reported [5–7]. The increasing recognition of the existence of clinical HF in patients with normal ejection fraction (EF) has led to heightened awareness of the limitations of evidence-based therapy for this important group of patients. A better understanding of the underlying pathophysiological mechanism, combined with the many new treatments developed over the last 20 years, has greatly improved the prognosis of patients with HF, and many patients can now hope for long periods of stable improved symptoms and improved heart function. Nonetheless, an inexorable course of HF can also occur, while many new approaches to treatment continue to develop. Advances in multidisciplinary care, heart failure clinics, polypharmacy, device therapy, and surgical approaches have greatly helped in improving the care of patients with HF [6].

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Heart failure is major and growing public health problem. In the USA, approximately 5 million patients have HF, and more than 550,000 patients are diagnosed with first-time HF each year. HF is the primary reason for 12–15 million office visits and 6.5 million hospital days each year [6]. Over one million patients are hospitalized annually for HF as the primary diagnosis [6]. HF treatment also causes a major economic burden on healthcare expenditures. In the USA, in 2005, the estimated total direct and indirect cost of HF was approximately $27.9 billion [6].

The European society of Cardiology (ESC) represents European countries with a population of over 900 million and these countries have at least 10 million patients with HF [7]. There are also patients with myocardial systolic dysfunction without symptoms of HF who also constitute approximately a similar prevalence [8]. The prognosis of HF is uniformly poor if the underlying problem cannot be rectified. Half of patients carrying a diagnosis of HF die within 4 years; in patients with severe heart failure, more than 50% die within 1 year [9].

Management of Heart Failure

Management of HF begins with an accurate diagnosis and requires a rational combination-drug therapy; individualization of care for each patient based on their symptoms, clinical presentation, and disease severity; appropriate mechanical interventions, including revascularization and devices; collaborative efforts among healthcare professionals; and education and cooperation of the patient and their immediate caregivers. Managing patients with HF can be challenging, and practice guidelines provide a great help in caring for such patients. These published guidelines and consensus recommendations provide an evidence-based roadmap to translate knowledge into practice and allow healthcare practitioners to reach the best clinical judgment and decisions for their individual patients.

Presently, three main guidelines for the diagnosis and management of chronic HF in adults are followed internationally. These are: (1) ACC/AHA 2005 guideline update for the diagnosis and management of chronic heart failure in adults: a report of the American College of Cardiology /American Heart Association task force on practice guidelines: Developed in collaboration with the American College of Chest Physicians and the International Society for Heart and Lung Transplantation: endorsed by the Heart Rhythm Society [6]; (2) ESC Guidelines: guidelines for the diagnosis and treatment of chronic heart failure (Update 2005). The task force for the diagnosis and treatment of chronic heart failure of the European Society of Cardiology [7];

and (3) Canadian Cardiovascular Society Consensus Conference Recommendations on heart failure 2006: diagnosis and management [5].

All three guidelines are in agreement in defining the class of recommendation and the grade of evidence for any diagnostic procedure or treatment.

- 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 favor 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-analysis.
- Level of evidence B: Data derive from a single randomized clinical trial or nonrandomized studies.
- Level of evidence C: Consensus of opinion of experts and/or small studies.

Management of HF in general constitutes nonpharmacological methods, pharmacotherapy, device therapy, and surgical procedures. This article compares the recommendations made by different practice guidelines for the management of patients with chronic HF.

Nonpharmacological Interventions

In patients with HF in the presence of systolic left ventricular (LV) dysfunction (LVEF ≤ 40%), all symptomatic patients should be advised about exercise training, salt and fluid restriction, and weight management. Aggressive risk factor reduction should be attempted and lifestyle modification should be advised.

All the guidelines recommend dietary salt restriction (class I, level C). The CCS and ESC guidelines recommend exercise training in HF patients (class I, level C). The ACC/AHA guidelines recommend exercise training in patients with HF as class I, level B indication. The CCS guidelines stress daily weight measurements (class I, level C) while ACC/AHA guidelines advise that the healthcare provider should record the body weight of the patient at each visit. Avoidance of smoking, excessive use of alcohol, and use of illicit drugs is stressed in ACC/AHA and ESC guidelines. Recommendations made in different practice guidelines for nonpharmacological interventions in HF are shown in Table 1.

Table 1. Non-pharmacological management of heart failure (HF): comparison of different practice guidelines

Indication	ACC/AHA guideline (2005)	ESC guideline (2005)	CCS consensus conference on HF recommendations (2006)
Exercise training	Class I, level B	Class I, level C	Class II a, level B
Dietary salt restriction	Class I, level C	Class I, level C	Class I, level C
Daily morning weight monitoring			Class I, level C
Daily fluid restriction		Class I, level C	Class I, level C
Avoid: smoking, excessive alcohol use, and illicit drug use	Class I, level C	Class I, level C	

Pharmacotherapy

There have been many landmark clinical trials and meta-analysis of the use of angiotensin-converting enzyme inhibitors (ACEI) [10] and beta-blockers (BB) [11] in HF, such that these types of drugs have become standard therapy and should be considered in all patients diagnosed with HF. The timing of introduction should be individualized to maximize tolerability and long-term persistence with therapy. In general, acute symptoms should be relieved, but an ACEI or a BB should be introduced as early as the patient's condition allows. All of the practice guidelines are in agreement for strongly recommending (class I, level A) the use of ACEI and BB in patients with HF unless contraindications exist. Tables 2 and 3 list the practice guideline recommendations for the use of ACEIs and BBs in HF patients.

In patients who are already on a combination of ACEI and BB but continue to have heart failure symptoms or hospitalizations, an angiotensin-II-receptor blockers (ARB) should be added [12]. Aldosterone antagonists (spironolactone, eplerenone) are effective in patients with severe post-myocardial-infarction HF or in long-term follow-up, especially in those patients recently hospitalized for HF [13]. Recommendations of practice guidelines is shown in Table 2.

Table 2. Pharmacotherapy of heart failure: comparison of different practice guidelines

Drugs	ACC/AHA guideline (2005)	ESC guideline (2005)	CCS consensus conference on HF recommendations (2006)
ACE inhibitors			
HT and LVH, no symptom of HF	Class IIa, level B		Class IIa, level B
Asymptomatic patients, LVEF ≤ 35%	Class I, level A	Class I, level A	Class I, level A
HF symptoms, LVEF ≤ 40%	Class I, level A	Class I, level A	Class I, level A
Post-AMI, LVEF ≤ 40%, AHF post AMI	Class I, level A	Class I, level A	Class I, level A
ARBs			
Patients who cannot tolerate ACEI; low EF, no symptom of HF	Class I, level A		Class I, level A
ARBs instead of ACEI in AHF with AMI or HF symptoms with LVEF ≤ 40%	Class IIa, level A	Class I, level B	Class I, level B
ARBs added to ACEI for persistent HF symptoms	Class IIb, level B	Class IIa, level B	Class I, level A
ARBs with ACEI when beta-blockers are contraindicated or not tolerated			Class IIa, level B
Aldosterone antagonists			
Severe HF symptoms, LVEF ≤ 30%, and optimized drug therapy	Class I, level B	Class I, level B	Class I, level B
AHF with LVEF ≤ 30% following AMI		Class I, level B	Class IIa, level B

ACEI, Angiotensin-converting-enzyme inhibitors; *ARBs*, angiotensin II receptor blockers; *HF*, heart failure; *LVEF*, left ventricular ejection fraction; *AHF*, acute heart failure; *AMI*, acute myocardial infarction; LVH, left ventricular hypertrophy

Angiotensin-Converting-Enzyme Inhibitors

- ACEI should be used in all patients as soon as safely possible after acute myocardial infarction, and should be continued indefinitely if LVEF is < 40% or if acute HF complicated the myocardial infarction (class I, level A).
- ACEI should be used in all asymptomatic patients with an LVEF < 35% (class I, level A).
- ACEI should be used in all patients with symptoms of HF and an LVEF < 40% (class I, level A).

Angiotensin-Receptor Blockers

- ARBs should be used in patients who cannot tolerate ACEIs, although renal dysfunction and hyperkalemia may recur (class I, level A).
- ARBs should be added to an ACEI for patients with persistent HF symptoms who are assessed to be at increased risk of HF hospitalization, despite optimal treatment with other recommended drugs (class I, level A).
- ARBs may be considered instead of an ACEI for patients with acute MI with acute HF or LVEF < 40% (class I, level B).
- ARBs may also be considered as adjunctive therapy to ACEI when BB are either contraindicated or not tolerated after careful attempt at initiation (class IIa, level B).

Beta-blockers

- All HF patients with an LVEF ≤ 40% should receive a BB proven to be beneficial in large-scale clinical trials (carvedilol, bisoprolol, metoprolol CR/XL) (class I, level A).
- Patients with NYHA class IV symptoms should be stabilized before initiation of a BB (class I, level C).
- Therapy should be initiated at a low dose and titrated to the target dose used in large-scale clinical trials or the maximum tolerated dose if less than the target dose (class I, level B).
- Beta-blockers should not normally be introduced in patients with symptomatic hypotension despite adjustment of other therapies, severe reactive airway disease, symptomatic bradycardia, or significant AV block without a permanent pacemaker. Stable chronic obstructive pulmonary disease is not a contraindication (class I, level B).

Aldosterone Antagonists

- Aldosterone antagonism with spironolactone or eplerenone should be considered for patients with an LVEF < 30% and severe symptomatic chronic HF despite optimization of other recommended treatments (class I, level B), or acute HF with an LVEF < 30% following myocardial infarction (class IIa, level B), if serum creatinine is < 200 μmol/l and potassium is < 5.2 mmol/l.

Vasodilators

- The combination of isosorbide dinitrate and hydralazine should be considered in addition to standard therapy for African-Americans with systolic dysfunction (class IIa, level B), and may be considered for other HF patients unable to tolerate other recommended standard therapy (class IIb, level B). Practice guideline recommendations for the use of vasodilators are given in Table 3.

Diuretics

- A loop diuretic, such as furosemide, is recommended for most patients with HF and congestive symptoms. Once acute congestion is cleared, the lowest minimal dose should be used that is comparable with stable signs and symptoms (class I, level C).
- For patients with persistent volume overload despite optimal, other medical therapy and an increase in loop diuretics, cautious addition of a second diuretic (for example, a thiazide or low-dose metolazone) may be considered as long as it is possible to closely monitor morning daily weight, renal function, and serum potassium (class IIb, level B).

Digoxin

- In patients in sinus rhythm who continue to have moderate to severe persistent symptoms despite optimized HF medical therapy, digoxin is recommended to relieve symptoms and reduce hospitalizations (class I, level A).
- In patients with chronic atrial fibrillation and poor control of ventricular rate despite BB therapy, or when BBs cannot be used, digoxin should be considered (class IIa, level B).

Table 3. Pharmacotherapy of heart failure: comparison of different practice guidelines

Drugs	ACC/AHA guideline (2005)	ESC guideline (2005)	CCS consensus conference on HF recommendations (2006)
Beta-blockers			
All recent or remote MI, regardless of LVEF or HF	Class I, level A	Class I, level A	
Reduced LVEF, no HF Sx	Class I, level C		
HF with LVEF ≤ 4 0%	Class I, level A		Class I, level A
Digoxin			
Current or prior Sx of HF, reduced LVEF, optimized medical therapy	Class IIa, level B	Class IIa, level B	Class I, level A
Any degree of HF with AF		Class I, level B	Class IIa, level B
Vasodilators (nitrates, hydralazine)			
Reduced LVEF, persistent HF Sx on ACEI and BB	Class IIa, level A		Class IIb, level B Afro-Americans: Class IIa, level A
Reduced LVEF, HF Sx, intolerant to ACEI or ARBs	Class IIb, level C	Class IIa, level B	

ACEI, Angiotensin-converting-enzyme inhibitors; *ARBs*, angiotensin II receptor blockers; *BB*, beta-blockers; *HF*, heart failure; *LVEF*, left ventricular ejection fraction; *MI,* myocardial infarction; *Sx,* symptom

CCS guidelines [5] recommend the use of digoxin as a class I indication to reduce hospitalization in patients with sinus rhythm and moderate to severe HF symptoms despite optimized HF medical therapy, while ESC guidelines [7] recommend the use of digoxin as a class I indication for patients with atrial fibrillation (AF) and HF.

Drugs To Be Avoided in Heart-Failure Patients

It is also important to recognize that certain classes of drugs can exacerbate the syndrome of HF and thus should be avoided in most patients [6]. These are:

- Anti-arrhythmic agents: Only amiodarone and dofetilide have been shown not to adversely affect survival.
- Calcium-channel blockers (CCB): only vasoselective CCBs have been shown not to adversely effect survival.
- Nonsteroidal anti-inflammatory drugs.

Focus on Specialized Heart-Failure Clinics

Despite the clear survival benefits supporting the use of pharmacological therapies in the management of HF patients, prognosis associated with recurrent and prolonged hospitalization remains poor. Strategies incorporating post-discharge follow-up by a multidisciplinary team of specially trained staff and/or access to specialized HF clinics reduce mortality and all-cause hospitalizations. A recent review found a significant reduction in all-cause mortality when such multidisciplinary teams were used [14].

Multidisciplinary outpatient management of HF and disease management programs staffed by physicians, nurses, pharmacists, and other healthcare professionals with expertise in HF management should be developed and used for assessment and management of high -risk patients with HF. Multidisciplinary care should include close clinical follow-up, patient and caregiver education, telemanagement or telemonitoring, and home visits by specialized HF healthcare professionals, where resources are available. CCS consensus conference recommendations have stressed the role of multidisciplinary outpatient HF management and disease management programs [5].

Implantation of an ICD To Prevent Sudden Cardiac Death in Patients with Heart Failure

In patients with documented sustained ventricular tachycardia (VT) or ventricular fibrillation (VF), the implantable cardioverter defibrillator (ICD) is highly effective in treating recurrences of these arrhythmias, either by antitachycardia pacing or cardioversion/defibrillation. Implantation of an ICD has been shown to reduce mortality in cardiac-arrest survivors. An ICD is indicated for “secondary prevention” of sudden cardiac death (SCD) due to ventricular tachyarrhythmia in patients with otherwise good clinical func-

tion and prognosis, for which the prolongation of survival is the goal. All the three guidelines are in agreement about ICD implantation in such patients (Table 4). ACC/AHA and ESC guidelines have considered this as a class I, level A recommendation. The CCS guidelines have mentioned that ICDs are the therapy of choice for prevention of SCD and all-cause mortality in patients with a history of sustained VT or VF, cardiac arrest, or unexplained syncope in the presence of left ventricular dysfunction.

Table 4. Implantable cardioverter defibrillator implantation: comparison of different heart-failure practice guidelines

Indication	ACC/AHA guideline (2005)	ESC guideline (2005)	CCS consensus conference on HF recommendations (2006)
Implantable cardioverter defibrillator (ICD)			
CAD, LVEF ≤ 30%, 1 month post-MI, 3 months post-coronary revascularization procedure	Class I, level A	Class I, level A (LVEF < 30–35%)	Class I, level A
NIDCM present for at least 9 months, NYHA class II–III, LVEF ≤ 30%	Class I, level B		Class II a, level B
NIDCM present for at least 9 months, NYHA class II–III, LVEF 31–35%	Class IIa, level B		Class II b, level C
CAD, prior MI, 3 months post-revascularization, LVEF 31–35%, inducible VT/VF on EPS			Class IIa, level B
CAD, prior MI, 3 months post-revascularization, LVEF 31–35% without EPS			Class IIb, level C
HF, reduced LVEF, with history of cardiac arrest, VF or hemodynamically destabilizing VT	Class I, level A		

CAD, Coronary artery disease; *MI*, myocardial infarction; *LVEF*, left ventricular ejection fraction; *NIDCM*, nonischemic dilated cardiomyopathy; *NYHA*, New York Heart Association; *EPS*, electrophysiological study; *VT*, ventricular tachycardia; *VF*, ventricular fibrillation

All of the multicenter trials aimed at the primary prevention of SCD that assessed the usefulness of ICD implantation to reduce all-cause mortality selected patients with low LVEF. The most common LVEF cutoff was 35%, although the MADIT II study had a cutoff of 30% [15]. Most studies did not specifically select patients with symptomatic congestive heart failure (CHF), although the largest study, *Sudden Cardiac Death and Heart Failure Trial* (SCD-HeF Trial), did select patients with current HF symptoms, NYHA class II or III, and a history of HF for more than 3 months [16]. In the SCD-HeF Trial, 2,521 patients with HF and LVEF ≤ 35% were randomized to placebo, amiodarone, or single-lead ICD implantation. After a median follow-up of 45.5 months, there was a significant reduction in mortality in patients with ICD therapy. There was no difference between placebo and amiodarone on survival [16].

All three practice guidelines for HF management are in agreement and have recommended ICD implantation for primary prevention to reduce total mortality by a reduction of SCD in patients with LV dysfunction due to prior myocardial infarction (MI) who are at least 40 days post-MI, have an LVEF ≤ 30–40%, are NYHA functional class II or III, are receiving chronic optimal medical therapy, and who have reasonable expectation of survival with a good functional status for more than 1 year. A class I, level of evidence A recommendation has been given to this patient subset (Table 4). The ACC/AHA and CCS consensus conference HF guidelines also give separate recommendations for patients with nonischemic dilated cardiomyopathy (Table 4). The ECS HF guidelines do not mention nonischemic cardiomyopathy recommendations separately.

While ICDs are highly effective in preventing death due to ventricular tachyarrhythmia, frequent shocks from the ICD can lead to a reduced quality of life. For symptoms from recurrent discharges triggered by ventricular arrhythmias or AF, anti-arrhythmic therapy, most often amiodarone, may be added [6]. For recurrent ICD discharges from VT despite anti-arrhythmic therapy, catheter ablation may be effective (ACC/AHA guidelines). It is important to note that ICDs have the potential to aggravate HF and have been associated with an increase in HF hospitalizations (ACC/AHA guidelines).

Cardiac Resynchronization Therapy

Patients with HF and LV dysfunction commonly have intra- and interventricular conduction delays that are associated with cardiac mechanical dyssynchrony. These compromise ventricular function and are frequently asso-

ciated with severe symptoms and poor prognosis. CRT uses biventricular pacing to attempt to synchronize the activation of the septum and the LV free wall, and to improve overall LV function [17].

CRT, when added to optimal medical therapy in persistently symptomatic patients, has resulted in significant improvements in quality of life, functional class, exercise capacity, exercise tolerance, EF, and survival in patients randomized to such therapy [17]. Two major trials (COMPANION and CARE-HF) assessed the role of CRT in patients with NYHA class III–IV symptoms on optimal medical therapy, QRS duration ≥ 120 ms, and an LVEF ≤ 35% [18, 19].The CRT group, compared with the medical therapy group, had significantly fewer deaths from any cause and fewer unplanned hospitalization for a major cardiovascular event. As well, the CRT group had better improvement in EF, overall symptoms, and quality of life scores than the medical-therapy-only group [18, 19].

All three guidelines are in agreement with recommending CRT for patients with symptomatic (NYHA III or IV) HF despite optimal medical therapy, who are in normal sinus rhythm and a QRS duration ≥ 120 ms, and a LVEF ≤ 35% (class I, level A) (Table 5).

Table 5. Cardiac resynchronization therapy: comparison of different heart-failure practice guidelines

Indication	ACC/AHA guideline (2005)	ESC guideline (2005)	CCS consensus conference on HF recommendations (2006)
Cardiac resynchronization therapy (CRT)			
HF, NYHA class III-IV despite optimal medical therapy, NSR, QRS ≥ 120 ms, LVEF ≤ 35%	Class I, level A	Class I, level A	Class I, level A
ICD + CRT for patients meeting requirement criteria for ICD		Class IIa, level B	Class IIa, level B

HF, Heart failure; *NYHA*, New York Heart Association; *NSR*, normal sinus rhythm; *ICD*, implantable cardioverter defibrillator

ICD therapy combined with biventricular pacing can be effective for primary prevention to reduce total mortality by a reduction in SCD in patients with NYHA functional class III or IV, who are receiving optimal medical therapy, in sinus rhythm with a QRS complex of ≥ 120 ms, and who have reasonable expectation of survival with a good functional status for more than 1 year. According to the ESC and CCS guidelines, this is a class II A, level B recommendation (Table 5).

Future Directions

The understanding of HF has grown exponentially over the past 20 years and has fuelled many landmark clinical trials that have given definitive answers. The recommendations made in the present guidelines are based on clinical trials that have already been published. There are many trials that are in progress and planning, and these will no doubt provide new information and evidence to guide future recommendations and guidelines [20].

Some of these new and ongoing HF trials are:

- HF-ACTION: Heart Failure - A controlled trial investigating outcomes of exercise training
- AF-CHF: Atrial fibrillation in congestive heart failure
- WARCEF: Warfarin versus aspirin in reduced cardiac ejection fraction
- RED-HF: Reduction of events with darbepoetin alpha in heart failure
- I-PRESERVE: Irbesartanin heart failure with preserved systolic function
- UNLOAD: Use of nitroprusside in left ventricular dysfunction and obstructive aortic valve disease
- STICH: Surgical treatment for ischemic heart failure
- RAFT: Resynchronization /defibrillation for advanced heart failure trial
- REVERSE: Resynchronization reverses remodeling in systolic left ventricular dysfunction
- MADIT-CRT: Multicentre automatic defibrillator implantation cardiac resynchronization therapy trial

Conclusions

The provision of optimal care to patients with HF presents many challenges to the patient, their family or caregivers, the physician, other healthcare providers, and healthcare systems. Practicing guidelines provide support for physicians and other healthcare professionals concerned with the management of HF patients. They also provide advice on how to manage these

patients. Documented and published evidence on diagnosis, efficacy, and safety is the main basis of these guidelines. An organized system of specialist HF care improves symptoms and reduces hospitalization and mortality. Multidisciplinary disease-management programs for patients at high risk for hospital admission or clinical deterioration are recommended to facilitate the implementation of practice guidelines [7].

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