GHA Pocket Guidelines
Committee for Practice Guidelines to improve the quality of clinical practice and patient care in the GCC countries
Management of Patients with Heart Failure
2011
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List of Abbreviations

- ACEI ACE Inhibitors
- ARB Angiotensin Receptor Antagonists
- BB Beta-Blockers
- BMI Body Mass Index
- BP Blood Pressure
- CA Calcium Antagonists
- CHD Coronary Heart Disease
- CVD Cardiovascular Disease
- DBP Diastolic Blood Pressure
- DM Diabetes Mellitus
- ECG Electrocardiography
- HTN Hypertension
- LVH Left Ventricular Hypertrophy
- MS Metabolic Syndrome
- SBP Systolic Blood Pressure
<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
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<tbody>
<tr>
<td>CRT</td>
<td>Cardiac resynchronization therapy</td>
</tr>
<tr>
<td>ECHO</td>
<td>Echocardiography</td>
</tr>
<tr>
<td>AHF</td>
<td>Acute heart failure</td>
</tr>
<tr>
<td>DOE</td>
<td>Dyspnea on exertion</td>
</tr>
<tr>
<td>RAAS</td>
<td>Renin angiotensin aldosterone system</td>
</tr>
<tr>
<td>AADs</td>
<td>Antiarrhythmic drugs</td>
</tr>
<tr>
<td>PDE I</td>
<td>Phosphodiesterase inhibitor</td>
</tr>
<tr>
<td>PAC</td>
<td>Pulmonary artery catheter</td>
</tr>
<tr>
<td>JVP</td>
<td>Jugular Venous Pressure</td>
</tr>
<tr>
<td>EF</td>
<td>Ejection Fraction</td>
</tr>
<tr>
<td>RV</td>
<td>Right Ventricular</td>
</tr>
<tr>
<td>PND</td>
<td>Paroxysmal Nocturnal Dyspnea</td>
</tr>
<tr>
<td>HR</td>
<td>Heart Rate</td>
</tr>
<tr>
<td>CBC</td>
<td>Complete Blood Count</td>
</tr>
<tr>
<td>LFTs</td>
<td>Liver Function Tests</td>
</tr>
<tr>
<td>TSH</td>
<td>Thyroid Stimulating Hormone</td>
</tr>
<tr>
<td>UA</td>
<td>Urinalysis</td>
</tr>
<tr>
<td>HbA1C</td>
<td>Hemoglobin A1 C</td>
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<tr>
<td>BNP</td>
<td>B-type Natriuretic Peptide</td>
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<tr>
<td>NT-proBNP</td>
<td>N-terminal pro BNP</td>
</tr>
<tr>
<td>MI</td>
<td>Myocardial Infarction</td>
</tr>
<tr>
<td>LBBB</td>
<td>Left Bundle Block</td>
</tr>
<tr>
<td>HIV</td>
<td>Human Immunodeficiency Virus</td>
</tr>
<tr>
<td>MRI</td>
<td>Magnetic Resonance Imaging</td>
</tr>
<tr>
<td>AVP</td>
<td>Arginine Vasopressin</td>
</tr>
<tr>
<td>CAD</td>
<td>Coronary Artery Disease</td>
</tr>
<tr>
<td>AIDS</td>
<td>Acquired Immuno Deficiency Syndrome</td>
</tr>
<tr>
<td>ANA</td>
<td>Antineutrophil Antibodies</td>
</tr>
<tr>
<td>QOL</td>
<td>Quality of Life</td>
</tr>
<tr>
<td>ICD</td>
<td>Implantable Cardiac Device</td>
</tr>
<tr>
<td>AVR</td>
<td>Aortic Valve Regurgitation</td>
</tr>
<tr>
<td>AR</td>
<td>Aortic Regurgitation</td>
</tr>
<tr>
<td>MVR</td>
<td>Mitral Valve Regurgitation</td>
</tr>
</tbody>
</table>
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PREFACE

The purpose of the 2011 Gulf Heart Association (GHA) Guideline for the Management of heart failure is to provide adequate review of the current clinical evidences in relation to classification, diagnoses, and management of heart failure and to make these evidences available for both primary care and specialist physicians in the Arabian Gulf Countries.

It is important to note that the contents of these guidelines, a significant amount of which are exerts from international guidelines, are meant to serve as general guideline and should therefore be used in conjunction with appropriate diagnoses and treatment approaches for heart failure.

The GHA task force for heart failure understands that the judgment of the treating clinician in diagnosis, treatment, and follow up of patients remains the single most important approach for an effective management of heart failure.

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Gulf Heart Association

Definition

- Heart failure (HF) is a heterogeneous syndrome in which abnormalities of cardiac function are responsible for the inability of the heart to pump blood at an output sufficient to meet the requirements of metabolizing tissues or the ability to do so only at abnormally elevated diastolic pressures or volumes.
- Acute heart failure (AHF) is defined as a rapid onset or change in the signs and symptoms of HF, resulting in a pressing need for urgent intervention. AHF may be related to ischaemia, arrhythmias, valvular dysfunction, pericardial disease, increased filling pressures or elevated systemic resistance.

Heart failure is characterized by signs and symptoms of:
- Intravascular and interstitial volume overload (shortness of breath, rales, elevated jugular venous pressure, and edema) and/or manifestations of inadequate tissue perfusion (impaired exercise tolerance, fatigue, signs of hypoperfusion, renal dysfunction.)
Pathophysiology of Heart Failure

Managing Heart Failure

- Poor ventricular function/myocardial damage (e.g., post myocardial infarction, dilated cardiomyopathy)
  - Heart failure
    - Decreased stroke volume and cardiac output
      - Neurohormonal response
        - Activation of sympathetic system
        - Renin angiotensin aldosterone system
          - Vasoconstriction: increased sympathetic tone, angiotensin II, endothelins, impaired nitric oxide release
          - Sodium and fluid retention: increased vasopressin and aldosterone
            - Further stress on ventricular wall and dilatation (remodelling) leading to worsening of ventricular function
              - Further heart failure

Clinical evaluation

Managing Heart Failure

- CHF?
  - Yes
    - Low EF?
      - Yes
        - Precipitant of decompensation (if old dx)
      - No
        - No
          - No
            - No
              - “Heart failure with preserved ejection fraction”
        - No
          - Yes
            - Etiology (if new dx)
              - Treatment

Severe Valve disease?

Severe renal dysfunction?
### Key features of the clinical history of patients with HF

**Symptoms**
- Breathlessness,
- Fatigue angina,
- Palpitation, Syncope.

**Cardiovascular events**
- Coronary artery disease
- Myocardial infarction
- Cardiac surgery
- Stroke or peripheral vascular disease
- Valvular disease or dysfunction.

**Risk profile**
- Family history,
- Smoking, Dyslipidemia,
- Hypertension, Diabetes.

**Orthopnea, paroxysmal nocturnal Dyspnea**
- (Tiredness, Exhaustion)

**Thrombolysis**
- Percutaneous coronary intervention
- Coronary artery bypass graft

### Key features of the clinical examination of patients with HF

**Appearance**
- Alertness, nutritional status, weight.

**Pulse**
- Rate, Rhythm and Character

**Blood pressure**
- Systolic, diastolic, pulse pressure

**Fluid overload**
- JVP, Peripheral oedema (ankle and sacrum), Hepatomegaly and ascitis

**Lung**
- Respiratory rate
- Rales
- Pleural effusion

**Heart**
- Apex displacement
- Gallop rhythm
- Murmur suggesting valvular lesion
Common clinical manifestations of HF

<table>
<thead>
<tr>
<th>Dominant clinical features</th>
<th>Symptoms</th>
<th>Signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral congestion</td>
<td>Tiredness, fatigue, anorexia. Severe breathlessness at rest, Confusion, weakness, cold peripheries.</td>
<td>Peripheral oedema</td>
</tr>
<tr>
<td>Pulmonary Oedema</td>
<td></td>
<td>Raised JVP</td>
</tr>
<tr>
<td>Cardiogenic Shock; (Low output syndromes)</td>
<td></td>
<td>Pulmonary oedema</td>
</tr>
<tr>
<td>High blood pressure (Hypertensive HF)</td>
<td></td>
<td>Heptomegaly, ascitis</td>
</tr>
<tr>
<td>Right HF, ascits</td>
<td></td>
<td>Fluid overload (congestion)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cachexia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Crackles or rales over the lung, pleural effusion, Tachycardia, Tachypnea</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Poor peripheral perfusion, Systolic BP&lt;90mmHg</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Anuria or oliguria.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Usually raised BP, LVH, preserved EF.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Evidence of RV dysfunction, Raised JVP, peripheral oedema, hepatomegaly, gut congestion</td>
</tr>
</tbody>
</table>

Framingham Criteria: very helpful in diagnosis of heart failure as illustrated in the table:

<table>
<thead>
<tr>
<th>Framingham Criteria for Clinical Diagnosis of Congestive Heart Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major Criteria</td>
</tr>
<tr>
<td>PND</td>
</tr>
<tr>
<td>Orthopnea</td>
</tr>
<tr>
<td>Elevated JVP</td>
</tr>
<tr>
<td>Rales</td>
</tr>
<tr>
<td>S3</td>
</tr>
<tr>
<td>CXR cardiomegaly</td>
</tr>
<tr>
<td>CXR pulmonary oedema</td>
</tr>
</tbody>
</table>
Clinical Classification of heart failure severity by NYHA functional class and ACC/AHA HF stage and how they can be linked

<table>
<thead>
<tr>
<th>Classification of HF severity</th>
<th>ACC/AHA HF stage¹</th>
<th>NYHA Functional Class²</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>At high risk for heart failure but without structural heart disease or symptoms of heart failure (eg, patients with hypertension or coronary artery disease)</td>
<td>None</td>
</tr>
<tr>
<td>B</td>
<td>Structural heart disease but without symptoms of failure</td>
<td>I</td>
</tr>
</tbody>
</table>
| C | Structural heart disease with prior or current symptoms of heart failure | II | Symptomatic with moderate exertion.  
III | Symptomatic with minimal exertion |
| D | Refractory heart failure requiring specialized interventions | IV | Symptomatic at rest |

Diagnostic Evaluation

Routine investigations
- Routine Chemistry, renal function, CBC, LFTs, TSH, UA. Hb A1C, lipids, BNP, NT-proBNP (lia-high negative pred.value)
- Chest radiography (cardiomegaly, pulmonary venous congestion)
- Electrocardiogram: Old MI or recent MI, Arrhythmia, LVH, some forms of Cardiomyopathy are tachycardia related, LBBB
- Echocardiogram: Etiology, severity, treatment, prognosis

Other labs
- Iron studies, HIV, protein electrophersis, autoimmune serologies & inflammatory markers, endocrine/metabolic
- Cardiopulmonary Exercise testing
- Evaluation for sleep disordered breathing
- Stress imaging-lack or specificity
- Cardiac MRI can be useful to evaluate myocardial, pericardial and infiltrative diseases
### Common Laboratory test abnormalities in heart failure

<table>
<thead>
<tr>
<th>Abnormality</th>
<th>Cause</th>
<th>Clinical implication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased serum creatinine (&gt;150micmol/l)</td>
<td>Renal disease, ACEI/ARB, aldosterone blockade</td>
<td>Calculate GFR, consider reducing ACEI/ARB or aldosterone blockade dose Check potassium and BUN</td>
</tr>
<tr>
<td>Anaemia (13g/dl in men, 12 in women)</td>
<td>Chronic HF, hemodilution, iron loss or poor utilization, renal failure, chronic disease.</td>
<td>Diagnostic work up Consider treatment</td>
</tr>
<tr>
<td>Hyponatremia (&lt;135mmol/l)</td>
<td>Chronic HF, haemodilution, AVP release, diuretics</td>
<td>Consider water restriction, reducing diuretics dosage Ultra filtration, vasopressin antagonist</td>
</tr>
<tr>
<td>Hypokalemia (&lt;3.5mmol/l)</td>
<td>Diuretics, secondary hyperaldosteronism</td>
<td>Risk of arrhythmia Consider potassium supplement, ACEI/ARB, aldosterone blockers</td>
</tr>
<tr>
<td>Hyperkalemia (&gt;5.5 mmol/l)</td>
<td>Renal failure, potassium supplement, renin-antagonist-aldosteron system blockers</td>
<td>Stop potassium sparing treatment (ACEI/ARB, aldosterone blockers) Assess renal function and PH Risk of bradycardia</td>
</tr>
<tr>
<td>Hyperuricemia (&gt;500Mic mol/l)</td>
<td>Diuretics treatment, gout, malignancy</td>
<td>Allopurinol</td>
</tr>
<tr>
<td>BNP &gt;400 pg/ml, NT-proBNP&gt;2000 pg/ml</td>
<td>Increased ventricular wall stress</td>
<td>HF likely Indication for echo Consider treatment</td>
</tr>
</tbody>
</table>

### Natriuretic Peptides (NP’s) (BNP and NT proBNP)

NP levels increase with increased intracardiac pressures
- Degree of increase reflects degree of cardiac dysfunction
- Don’t distinguish systolic from diastolic heart failure
- Don’t distinguish left from right heart failure
- NP higher than expected in women, elderly and patients with renal failure
- NP elevated is expected in obesity, constrictive pericarditis, acute heart failure and heart failure due to mitral stenosis
- Most useful in patients without prior diagnosis or treatment for heart failure
- Difficulty interpreting immediately elevated levels in patients
already receiving treatment for ventricular dysfunction of heart failure

Concentrations of B-type natriuretic peptide (BNP) or N-terminal pro-B-type natriuretic peptide (NT-proBNP) should be measured in patients being evaluated for dyspnea in which the contribution of HF is not known. Final diagnosis requires interpreting these results in the context of all available clinical data and should not to be considered a stand alone test.

Flow chart for the diagnosis of HF in untreated patients with symptoms suggestive of HF using Natriuretic peptides
Role of echocardiography in heart failure
Echocardiography is essential to:

- Characterize the anatomical and functional abnormalities in patients suspected of having heart failure, and with symptomatic heart failure.
- Provide prognostic information and assist in the management of patients with acute, chronic and end-stage HF.
- Determine chamber dimensions and left ventricular ejection fraction (LVEF). The LVEF can be measured by volumetric method (Simpson) or by eye-ball method.
- Differentiate between systolic and diastolic (preserved systolic function) heart failure.

Common Factors that precipitate Hospitalization for Heart Failure

- Noncompliance with medical regimen, Sodium and/or fluid restriction
- Acute myocardial ischemia
- Uncorrected high blood pressure
- Atrial fibrillation and other arrhythmias

Recent addition of negative inotropic drugs (e.g., verapamil, nifedipine, diltiazem, beta blockers)
- Pulmonary embolus
- Nonsteroidal anti-inflammatory drugs
- Excessive alcohol or illicit drug use
- Endocrine abnormalities (e.g., diabetes mellitus, hyperthyroidism, hypothyroidism)
- Concurrent infections (e.g., pneumonia, viral illnesses)

Causes of Dilated Cardiomyopathy (low EF)

Common clinically:

- CAD
- Hypertension
- Idiopathic (family history in 20-30%)

Less common clinically:

- Chronic severe valvular regurgitation
Alcohol
Myocarditis
Tachycardia- Induced
Thyroid disorder
AIDS
Infiltrative disease(sarcoid and hemochromatosis)
Pheochromocytoma

Need to understand the pathophysiology of reduced ejection fraction in order to appreciate treatment rational:

I. Effect of afterload – in heart failure, increase in afterload (blood pressure, aortic valve resistance and ventricular mass) decreases stroke volume.

II. Frank Staling law - in heart failure, the relationship between preload (filling left ventricular pressure) and stroke volume will be shifted to the right and downward, so for any given preload the stroke volume will be low. In acute heart failure, aim to optimize filling pressure and in chronic to improve myocardial function.

III. Natural history - after an index event, the heart gets dilated and the ejection fraction gets reduced over time, hence heart failure moves from asymptomatic state to symptomatic state.
IV. Neurohormonal activation

a. RAAS
b. Sympathetic nervous system

- Certain therapies only recommended for higher NYHA class

**Determine ventricular size and function**
- Guides treatment decisions, prognostic value

**Establish Volume status**
- Determine need for diuretics

**Goals of ongoing evaluation**

- **Determine symptoms, functional class, volume status**
- **Determine medications tolerance:**
  - Symptoms of hypertension
  - Check orthostatic vital signs
  - Electrolyte and renal function for RAA inhibitors
  - Role out iatrogenic (new AADs, CCB, d/c HF medication)

**Lifestyle compliance and education**
- Ensure taking meds as prescribed
- Diet and sodium restriction
- Avoids NSAIDs, excessive alcohol
- Role out triggers for decompensation (Arrhythmia, infection, pulmonary process, thyroid, renal injury, anemia)

**Goals in initial evaluation**

- **Determine etiology:**
  - Treat reversible causes (eg ischemia, tachycardia)
  - Prognostic significance
- **Determine functional class**
  - History
  - Cardiopulmonary Exercise test or 6 minute walk
Nonpharmacologic Management in Patients With Chronic Heart Failure

Diet and Nutrition

Sodium intake
Dietary sodium restriction (2-3 g daily) is recommended for patients with HF and preserved or depressed left ventricular ejection fraction (LVEF). Further restriction (< 2 g daily) may be considered in moderate to severe HF.

Fluid intake
Restriction of daily fluid intake to < 2 L is recommended in patients with severe hyponatremia (serum sodium < 130 mEq/L) and should be considered for all patients demonstrating fluid retention that is difficult to control despite high doses of diuretic and sodium restriction.

Weight management
Weight reduction in obese [body mass index (BMI) >30 kg/m2] persons with HF should be considered in order to prevent the progression of HF, decrease symptoms, and improve well-being. In moderate to severe HF, weight reduction should not routinely be recommended since unintentional weight loss and anorexia are common problems. Patients should weigh themselves on a regular basis to monitor weight change, preferably as part of a regular daily routine. In the case of a sudden unexpected weight gain of >2 kg in 3 days, patients may increase their diuretic dose and should alert the healthcare team.

Exercise Training
Exercise training appears to have therapeutic benefits for patients with CHF. Regular, moderate daily activity is recommended for all patients with heart failure.

Sleep Disorders
Patients with symptomatic HF frequently have sleep-related breathing disorders (central or obstructive sleep apnoea). These conditions may be associated with increased morbidity and mortality. Treatment with a continuous positive airway pressure (CPAP) should be considered in obstructive sleep apnoea documented by polysomnography.
Psychological Support
Depression has been recognized as a common and adverse feature of CHF. Pharmacologic or nonpharmacologic treatment of depression might improve the quality of life of HF patients.

Sexual Activity
Sexual problems related to cardiovascular disease, medical treatment or psychological factors such as fatigue and depression are common in patients with HF. The use of phosphodiesterase-5 inhibitors such as sildenafil may be considered for use for sexual dysfunction in patients with chronic stable HF. These agents are not recommended in patients taking nitrate preparations.

Pregnancy and Contraception
Pregnancy may lead to deterioration of HF due to the rise in blood volume and increase in cardiac output, as well as the substantial increase in extravascular fluid. Importantly, many medications used in HF treatment are contraindicated during pregnancy. The risk of pregnancy is considered greater than the risks linked to contraceptive use. It is recommended that women with heart failure discuss contraceptives and planned pregnancy with a physician in order to take an informed decision based on assessment of potential risks.

Smoking
Smoking is a known risk factor for cardiovascular disease. It is recommended that patients receive support and advice and be motivated to stop smoking.

Immunization
Pneumococcal vaccination and annual influenza vaccination should be considered in patients with symptomatic HF without known contraindications.

Nonsteroidal Anti-Inflammatory Drugs
Nonsteroidal anti-inflammatory drugs, including cyclooxygenase-2 inhibitors, are not recommended in patients with chronic HF. The risk of renal failure and fluid retention is markedly increased in the setting of reduced renal function or ACE inhibitor therapy.

Treatment of Asymptomatic left ventricular dysfunction:
- Treat hypertension, hyperlipidemia
- Smoking cessation
- Encourage regular exercise
- Discourage alcohol, illicit drug use
- ACE-I, beta blockers
Treatment of Symptomatic left ventricular dysfunction:

- ACE-inhibitors
- Beta blockers
- Diuretics (volume overload)
- Digoxin (NYHA class II-IV)
- Aldosterone antagonists (selected NYHA class III-IV)

**Pharmacological Therapy**

**Goals of heart failure treatment**

(1) improving symptoms and quality of life,
(2) slowing the progression or reversing cardiac and peripheral dysfunction, and
(3) reducing mortality.

**Drugs reducing mortality**

(1) Beta blockers
(2) Angiotensinconverting enzyme (ACE) inhibitors
(3) Angiotensin receptor blockers (ARBs)
(4) Aldosterone antagonists
(5) The combination of hydralazine and an oral nitrate

**Angiotensin-converting enzyme inhibitors (ACEIs)**

**Recommendations**

ACE inhibitors are recommended for routine administration to symptomatic and asymptomatic patients with LVEF ≤ 40%.

ACE inhibitors should be titrated to doses used in clinical trials, as tolerated during concomitant uptitration of beta blockers.

**ACE Inhibitors Side effects and practical Tips:**

**Hypotension** - adjust dose, treat the patient and not the number

**Hyperkalemia** - Adjust dose, accept some increase but monitor carefully

**Azotemia** - adjust dose, accept some increase in createnine and check within a week

**Cough** - remember not all cough =ACE inhibitor

**Angioedema** - contraindication to ACE-I
Moderate renal insufficiency should not be considered a contraindication to the use of ACE inhibitors, although careful attention to serum potassium and creatinine levels is imperative.

The major symptomatic side effect is a dry cough that usually does not require discontinuation of the drug. If the cough impairs the patient’s quality of life, alternative therapy, such as an ARB, is recommended.

### Angiotensin Receptor Blockers (ARBs)

**Recommendation**

An ARB is recommended as an alternative in patients intolerant of an ACEI. In these patients, an ARB reduces the risk of death from a cardiovascular cause or hospital admission for worsening HF.

Unless contraindicated or not tolerated, an ARB is recommended in patients with HF and an LVEF ≤ 40% who remain symptomatic despite optimal treatment with an ACEI and b-blocker, unless also taking an aldosterone antagonist. Treatment with an ARB improves ventricular function and patient well-being, and reduces hospital admission for worsening HF.

**β-Blockers**

**Recommendations**

Unless contraindicated or not tolerated, a β-blocker should be used in all asymptomatic and symptomatic patients with HF and an LVEF ≤ 40%.

The marked beneficial effects of beta blockade has been well demonstrated in large-scale clinical trials of symptomatic patients with NYHA class II-IV HF and reduced LVEF using carvedilol, bisoprolol, and metoprolol succinate.

Beta blocker therapy is recommended even if there is concomitant diabetes, chronic obstructive lung disease, or peripheral vascular disease.

Beta blocker therapy should be used with caution in patients with diabetes with recurrent hypoglycemia, with asthma, or with resting limb ischemia. Considerable caution should be used if beta blockers are initiated in patients with marked bradycardia (<55 beats/min) or marked hypotension (systolic blood pressure<80mmHg).

Beta blockers are contraindicated in patients with asthma and active bronchospasm.
It is recommended that beta blockade be initiated at low doses and uptitrated gradually, typically at 2-week intervals in patients with reduced LVEF, and after 3-10 day intervals in patients with reduced LVEF following newly diagnosed MI.

It is recommended that beta blocker therapy be continued in most patients experiencing a symptomatic exacerbation of HF during chronic maintenance treatment, unless they develop cardiogenic shock, refractory volume overload, or symptomatic bradycardia.

A temporary reduction of dose (generally by one half) in this setting may be considered. Abrupt discontinuation in patients with symptomatic exacerbation should be avoided, unless the situation is life-threatening. If discontinued or reduced, beta blockers should be reinstated before the patient is discharged. In general, doses should be up titrated to the previous well-tolerated dose as soon as safely possible.

Table 7.1. ACE-inhibitor, Angiotensin Receptor Blocker, and Beta-Blocker Therapy in HF with Low LVEF

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Trade Name</th>
<th>Initial Daily Dose</th>
<th>Target Dose</th>
<th>Mean Dose Achieved in Clinical Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ACE-inhibitors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Captopril</td>
<td>Capoten</td>
<td>6.25 mg tid</td>
<td>500 mg tid</td>
<td>127.7 mg/day</td>
</tr>
<tr>
<td>Enalapril</td>
<td>Vasotec</td>
<td>2.5 mg bid</td>
<td>10 mg tid</td>
<td>16.6 mg/day</td>
</tr>
<tr>
<td>Fosinopril</td>
<td>Monopril</td>
<td>5 – 10 mg qd</td>
<td>80 mg tid</td>
<td>n/a</td>
</tr>
<tr>
<td>Lisinopril</td>
<td>Zestril, Prinivil</td>
<td>2.5 – 5 mg qd</td>
<td>20 mg tid</td>
<td>*4.5 mg/day (low dose ATLAS) 33.2 MG/DAY (high dose ATLAS)</td>
</tr>
<tr>
<td>Quinapril</td>
<td>Accupril</td>
<td>5 mg bid</td>
<td>80 mg qd</td>
<td>n/a</td>
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<tr>
<td>Ramipril</td>
<td>Altace</td>
<td>1.25-2.5 mg qd</td>
<td>10 mg qd</td>
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<td>Trandolapril</td>
<td>Mavik</td>
<td>1 mg qd</td>
<td>4 mg qd</td>
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<tr>
<td><strong>Angiotensin Receptor Blockers</strong></td>
<td></td>
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<tr>
<td>Candesartan</td>
<td>Atacand</td>
<td>4-8 mg qd</td>
<td>32 mg qd</td>
<td>24 mg/day</td>
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<tr>
<td>Losartan</td>
<td>Cozaar</td>
<td>12.5-25 mg qd</td>
<td>150 mg qd</td>
<td>129 mg/day</td>
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<tr>
<td>Valsartan</td>
<td>Diovan</td>
<td>40 mg bid</td>
<td>160 mg bid</td>
<td>254 mg/day</td>
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<tr>
<td><strong>Beta-blockers</strong></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

39
### Aldosterone Antagonists

**Recommendations**

Administration of an aldosterone antagonist is recommended for patients with NYHA class IV (or class III, previously class IV) HF from reduced LVEF (< 35%) while receiving standard therapy, including diuretics.

Administration of an aldosterone antagonist should be considered in patients following an acute MI, with clinical HF signs and symptoms or history of diabetes mellitus, and an LVEF < 40%. Patients should be on standard therapy, including an ACE inhibitor (or ARB) and a beta blocker.

Aldosterone antagonists are not recommended when creatinine is > 2.5 mg/dL (or creatinine clearance is < 30 ml/min) or serum potassium is >5.0 mmol/L or in conjunction with other potassium-sparing diuretics.

Serum potassium concentration should be monitored frequently following initiation or change in an aldosterone antagonist. In the absence of persistent hypokalemia (> 4.0 mmol/L), supplemental potassium is not recommended in patients taking an aldosterone antagonist.

| Aldosterone Antagonists          | Recommendation | Administration of an aldosterone antagonist is recommended for patients with NYHA class IV (or class III, previously class IV) HF from reduced LVEF (< 35%) while receiving standard therapy, including diuretics. Administration of an aldosterone antagonist should be considered in patients following an acute MI, with clinical HF signs and symptoms or history of diabetes mellitus, and an LVEF < 40%. Patients should be on standard therapy, including an ACE inhibitor (or ARB) and a beta blocker. Aldosterone antagonists are not recommended when creatinine is > 2.5 mg/dL (or creatinine clearance is < 30 ml/min) or serum potassium is >5.0 mmol/L or in conjunction with other potassium-sparing diuretics. Serum potassium concentration should be monitored frequently following initiation or change in an aldosterone antagonist. In the absence of persistent hypokalemia (> 4.0 mmol/L), supplemental potassium is not recommended in patients taking an aldosterone antagonist. |

| Bisoprolol | Zebeta | 1.25 mg qd | 10 mg qd | 8.6 mg/day |
| Carvedilol | Coreq | 3.125 mg bid | 25 mg bid | 37 mg/day |
| Carvedilol | Coreq CR | 10 mg qd | 80 mg qd |
| Metoprolol succinate CR/XL | Toprol XL | 12.5-25 mg qd | 200 mg qd | 159 mg/day |

| Aldosterone Antagonists          | Recommendation | Administration of an aldosterone antagonist is recommended for patients with NYHA class IV (or class III, previously class IV) HF from reduced LVEF (< 35%) while receiving standard therapy, including diuretics. Administration of an aldosterone antagonist should be considered in patients following an acute MI, with clinical HF signs and symptoms or history of diabetes mellitus, and an LVEF < 40%. Patients should be on standard therapy, including an ACE inhibitor (or ARB) and a beta blocker. Aldosterone antagonists are not recommended when creatinine is > 2.5 mg/dL (or creatinine clearance is < 30 ml/min) or serum potassium is >5.0 mmol/L or in conjunction with other potassium-sparing diuretics. Serum potassium concentration should be monitored frequently following initiation or change in an aldosterone antagonist. In the absence of persistent hypokalemia (> 4.0 mmol/L), supplemental potassium is not recommended in patients taking an aldosterone antagonist. |

| Spironolactone | Aldactone | 12.5 to 25 mg qd | 25 mg qd | 26 mg/day |
| Eplerenone | Inspra | 25 mg qd | 50 mg qd | 42.6 mg/day |

| Other Vasodilators          | Recommendation | Administration of an aldosterone antagonist is recommended for patients with NYHA class IV (or class III, previously class IV) HF from reduced LVEF (< 35%) while receiving standard therapy, including diuretics. Administration of an aldosterone antagonist should be considered in patients following an acute MI, with clinical HF signs and symptoms or history of diabetes mellitus, and an LVEF < 40%. Patients should be on standard therapy, including an ACE inhibitor (or ARB) and a beta blocker. Aldosterone antagonists are not recommended when creatinine is > 2.5 mg/dL (or creatinine clearance is < 30 ml/min) or serum potassium is >5.0 mmol/L or in conjunction with other potassium-sparing diuretics. Serum potassium concentration should be monitored frequently following initiation or change in an aldosterone antagonist. In the absence of persistent hypokalemia (> 4.0 mmol/L), supplemental potassium is not recommended in patients taking an aldosterone antagonist. |

| Fixed dose Hydralazine/Isosorbide clinitrate | BiDil | 37.5 mg hydralazine/20 mg Isosorbide dinitrate tid | 75 mg hydralazine/40 mg Isosorbide dinitrate tid | 142.5 mg hydralazine/76 mg Isosorbide dinitrate/day |
| Hydralazine | Apresoline | 37.5 mg qid | 75 mg qid | 270 mg/day |
| Isosorbide dinitrate | Isontil | 20 mg qid | 40 mg qid | 136 mg/day |

*No difference in mortality between high and low dose groups but 12% lower risk of death or hospitalization in high dose group vs. low dose group.*
Spironolactone should be used in conjunction with standard therapy, including ACE inhibitors, digoxin, diuretics, and beta blockers. It should be initiated at a dose of 12.5 to 25 mg per day. Spironolactone can be titrated to 37.5 mg or 50 mg with careful monitoring in patients with refractory HF or persistent hypokalemia. Serum potassium and creatinine should be monitored closely in the first few weeks of therapy. If the serum potassium exceeds 5.0 mmol/L, then the dose of spironolactone should be decreased to 25 mg every other day and medications that could contribute to hyperkalemia should be adjusted.

The risk of hyperkalemia with aldosterone antagonism is increased in patients with older age, diabetes, higher serum creatinine levels, and higher ACE inhibitor doses. In community settings the risk is far higher than documented during careful monitoring in trial settings, and may be as high as 20%.

Hydralazine and Isosorbide Dinitrate (H-ISDN)

Recommendations

In symptomatic patients with an LVEF ≤ 40%, the combination of H-ISDN may be used as an alternative if there is intolerance to both an ACEI and an ARB.

Adding the combination of H-ISDN should be considered in patients with persistent symptoms despite treatment with an ACEI, b-blocker, and an ARB or aldosterone antagonist.

Starting dose: hydralazine 10-25 mg and ISDN 20 mg t.i.d. Consider dose up-titration after 2–4 weeks. Do not increase dose with symptomatic hypotension. If tolerated, aim for evidence-based target dose—hydralazine 75 mg and ISDN 40 mg t.i.d.—or maximum tolerated dose.

Potential adverse effects

Symptomatic hypotension (e.g. dizziness)—often improves with time; consider reducing dose of other hypotensive agents (except ACEI/ARB/b-blocker/aldosterone antagonist). Asymptomatic hypotension does not require intervention. Arthralgia/muscle aches, joint pain or swelling, pericarditis/pleuritis, rash or fever—consider drug-induced lupus-like syndrome; check ANA, discontinue H-ISDN.
Diuretics

**Recommendations**

Diuretic therapy is recommended to restore and maintain normal volume status in patients with clinical evidence of fluid overload. Loop diuretics rather than thiazide-type diuretics are typically necessary to restore normal volume status in patients with HF.

The initial dose of diuretic may be increased as necessary to relieve congestion. Restoration of normal volume status may require multiple adjustments over many days and occasionally weeks in patients with severe fluid overload evidenced by massive edema or ascites. After a diuretic effect is achieved with short-acting loop diuretics, increasing administration frequency to twice or even 3 times per day will provide more diuresis with less physiologic perturbation than larger single doses.

Addition of chlorothiazides or metolazone, once or twice daily, to loop diuretics should be considered in patients with persistent fluid retention despite high dose loop diuretic therapy. But chronic daily use, especially of metolazone, should be avoided if possible because of the potential for electrolyte shifts and volume depletion.

In all patients hospitalized with HF, both with preserved and low ejection fraction, transition should be made from intravenous to oral diuretic therapy with careful attention to oral diuretic dosing and monitoring of electrolytes. With all medication changes, the patient should be monitored for supine and upright hypotension and worsening renal function and HF signs/symptoms.

<table>
<thead>
<tr>
<th>Diuretic dosages</th>
<th>Initial dose (mg)</th>
<th>Usual daily dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Loop diuretics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* furosemide</td>
<td>20 - 40</td>
<td>40 - 240</td>
</tr>
<tr>
<td>* bumetanide</td>
<td>0.5 - 1.0</td>
<td>1 - 5</td>
</tr>
<tr>
<td>* torasemide</td>
<td>5 - 10</td>
<td>10 - 20</td>
</tr>
<tr>
<td><strong>Thiazides</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>bendroflumethiazide</td>
<td>2.5</td>
<td>2.5 - 10</td>
</tr>
<tr>
<td>hydrochlorothiazide</td>
<td>25</td>
<td>12.5 - 100</td>
</tr>
<tr>
<td>metolazone</td>
<td>2.5</td>
<td>2.5 - 5</td>
</tr>
</tbody>
</table>
**Potassium-sparing diuretics***

<table>
<thead>
<tr>
<th></th>
<th>+ ACEI/ARB</th>
<th>-ACEI/ARB</th>
<th>+ACEI/ARB</th>
<th>-ACEI/ARB</th>
</tr>
</thead>
<tbody>
<tr>
<td>spironolactone/</td>
<td>12.5 – 25</td>
<td>50</td>
<td>50</td>
<td>100 – 200</td>
</tr>
<tr>
<td>eplerenone</td>
<td>2.5</td>
<td>5</td>
<td>20</td>
<td>40</td>
</tr>
<tr>
<td>amiloride</td>
<td>25</td>
<td>50</td>
<td>100</td>
<td>200</td>
</tr>
<tr>
<td>triamterene</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* This agent also has vasodilator properties.
** In hypotensive patients (SBP < 100mmHg) initiation of therapy without a bolus is recommended.
*** Aldosterone antagonists should always be preferred to other potassium sparing diuretics.

---

**Digoxin**

**Recommendation**

Digoxin should be considered for achieving adequate control of the ventricular response to atrial fibrillation in patients with HF.

Digoxin may be considered to improve symptoms in patients with reduced LVEF (LVEF ≤40%) who have signs or symptoms of HF while receiving standard therapy, including ACE inhibitors and beta blockers.

Although little controversy exists as to the benefit of digoxin in patients with symptomatic HF with reduced LVEF and concomitant atrial fibrillation, the debate continues over its current role in similar patients with normal sinus rhythm.

It is recommended that the dose of digoxin, which should be based on lean body mass, renal function, and concomitant medications, should be 125 microgram daily in the majority of patients and the serum digoxin level should be < 1.0 ng/mL, generally 0.7-0.9 ng/mL. High doses of digoxin (maintenance dose > 0.25 mg daily) for the purpose of rate control are not recommended.

**Ivabradine**

Ivabradine may be considered in patients with HF and an LVEF ≤ 35 % and resting HR >70 bpm who remain symptomatic despite optimal treatment with ACE inhibitors or ARBs, beta blockers, and aldosterone antagonists.

**Anticoagulation** (warfarin) only in
- Atrial fibrillation
- History of embolic episodes
- Left ventricular apical thrombus
When to hospitalize?
Persistent NYHA class IV symptoms
Persistent volume overload
Unexplained symptomatic hypotension
Worsening renal failure
Altered mentation
Hemodynamic significant arrhythmias

Device Therapy for Heart Failure

A. Dilated cardiomyopathy and ICD
- Refer to electrophysiologisy for ICD if:
  - Idiopathic or ischemic cardiomyopathy (EF ≤ 35%) and NYHA class II-III
  - Must not have:
    - CABG or PCI in past 3 months
    - Acute MI within 40 days
    - Other disease with <1 year survival
- Do not treat with antiarrhythmics

B. Dilated cardiomyopathy and Biventricular Pacing
- Cardiac asynchrony:
  - Impairs systolic and diastolic function
  - Cause Mitral regurgitation
- Resynchronization therapy:
  - Subjective: improve quality of life and NYHA class
  - Objective: improve 6 minute walk, ejection fraction and survival
  - NYHA class III-IV heart failure
  - Optimized, stable medical regimen
  - QRS duration ≥ 120msec
  - EF ≤ 35%

Biventricular Pacing for Dilated Cardiomyopathy
- Cardiac asynchrony is bad
  - Impairs systolic and diastolic functions
  - Mitral regurgitation
  - Prognosis
- Resynchronization therapy
  - Subjective: QOL, NYHA class
  - Objective: 6 minute walk, EF, survival

Approximately 30 percent of patients with cardiomyopathy have wide QRS complex such as left or right bundle-branch block,
leading to loss of coordination of ventricular contraction. This dyssynchronous pattern of ventricular contraction is believed to contribute to the pathophysiology of heart failure, reducing the already diminished contractile reserve of the heart. Pacing modalities that utilize biventricular (BiV) or left ventricular (LV) stimulation to optimize cardiac pump function through synchronization of ventricular contraction are referred to as cardiac resynchronization therapy (CRT). Resynchronization therapies can be present in a single device, in a device equipped with bradycardia pacing support with an ICD (CRT-D) or without an ICD (CRT-P).

**Hemodynamic effects of ventricular dyssynchrony:**

1. **Mitral valve abnormalities:**
   - delayed mitral valve opening
   - distorted mitral valve annulus
   - mitral regurgitation

2. **Aortic valve abnormalities:**
   - delayed aortic valve opening and closing

3. **Left ventricular (LV) abnormalities:**
   - abnormal septal motion

   - reduced duration of LV filling
   - decreased cardiac output, ejection fraction and mean arterial pressure
   - increased end systolic volume

**Positive effects of CRT:**

1. **Clinical benefits:**
   - improvement of NYHA class
   - improvement of quality of life
   - reduction of hospitalization for heart failure
   - improvement of VO2 max
   - reduction in mortality

2. **Hemodynamic benefits:**
   - improvement of diastolic LV filling
   - improvement of ejection fraction, cardiac output and dP/dT
   - reduction of mitral regurgitation
   - reversal of LV remodeling
   - improvement of neurohormonal balance
   - restoration of autonomic imbalance
When to refer to electrophysiologist?

Patients with heart failure and the following clinical profile should be referred to the electrophysiologist for consideration of CRT device. For detailed recommendations see the next section.

1. Symptomatic patients in NYHA class III or IV despite optimal medical therapy
2. LVEF ≤ 35%
3. QRS duration ≥ 120 ms

Indications of CRT-D/CRT-P implant in various clinical scenarios:

(1) Recommendation in patients with heart failure in NYHA class III/IV

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Patient Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRT-P/CRT-D is recommended to reduce morbidity and mortality&lt;sup&gt;d&lt;/sup&gt;</td>
<td>NYHA function class III/IV LVEF ≤35%, QRS ≥120 ms, SR Optimal medical therapy Class IV patients should be ambulatory</td>
</tr>
</tbody>
</table>

(2) Recommendation in patients with heart failure NYHA class II

<table>
<thead>
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<th>Patient Population</th>
</tr>
</thead>
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<tr>
<td>CRT preferentially by CRT-D is recommended to reduce morbidity or to prevent disease progression&lt;sup&gt;d&lt;/sup&gt;</td>
<td>NYHA function class II LVEF ≤35%, QRS ≥150 ms, SR Optimal medical therapy</td>
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</table>

(3) Recommendations in patients with heart failure and permanent atrial fibrillation

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Patient Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRT-P/CRT-D&lt;sup&gt;d&lt;/sup&gt; should be considered to reduce morbidity</td>
<td>NYHA function class III/IV LVEF ≤35%, QRS ≥130 ms Pacemaker dependency induced By AV nodal ablation</td>
</tr>
<tr>
<td>CRT-P/CRT-D&lt;sup&gt;d&lt;/sup&gt; should be considered to reduce morbidity</td>
<td>NYHA function class III/IV LVEF ≤35%, QRS ≥130 ms Slow ventricular rate and frequent pacing</td>
</tr>
</tbody>
</table>
(4) Recommendations in patients with heart failure and concomitant class I PPM indication

<table>
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<th>Recommendations</th>
<th>Patient Population</th>
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<tr>
<td>CRT-P/CRT-D&lt;sup&gt;d&lt;/sup&gt; is recommended to reduce morbidity</td>
<td>NYHA function class III/IV LVEF ≤35%, QRS ≥120 ms</td>
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<tr>
<td>CRT-P/CRT-D&lt;sup&gt;d&lt;/sup&gt; should be considered to reduce morbidity</td>
<td>NYHA function class III/IV LVEF ≤35%, QRS ≥120 ms</td>
</tr>
<tr>
<td>CRT-P/CRT-D&lt;sup&gt;d&lt;/sup&gt; may be considered to reduce morbidity</td>
<td>NYHA function class II LVEF ≤35%, QRS ≥120 ms</td>
</tr>
</tbody>
</table>

**Key points**

- LV dilatation no longer required in the recommendation.
- Class IV patients should be ambulatory.
- Reasonable expectation of survival with good functional status for 1 year for CRT-D.
- Evidence is strongest for patients with typical LBBB.
- Similar level of evidence for CRT-P and CRT-D
- In patients with mild heart failure improvement was primarily seen in patients with QRS 150 ms and/or typical LBBB and women with LBBB demonstrated a particularly favourable response.
- NYHA class III/IV symptoms and an LVEF of 35% are well established indications for ICD

- Frequent pacing is defined as 95% pacemaker dependency
- Chronic RV pacing in patients with LV dysfunction should be avoided.
- CRT may permit adequate up-titration of b-blocker treatment
- Cardiac resynchronization therapy (CRT) and ICD (CRT-D) in select patients with HF believed to be “end stage” may be considered on the grounds that CRT-D may, in itself, improve their prognosis

**Surgical therapy for heart failure in dilated cardiomyopathy**

**Revascularization**

**Ventricular remodeling surgery**

**Mitral surgery**

**Ventricular assist devices**

**Transplantation**

**Coronary Revascularization in the Patient with Severe Left Ventricular Dysfunction**

In the absence of confirmatory randomized data, it is generally accepted that in the presence of documented contractile reserve...
(myocardial viability) and graftable targets with good runoff, and in the absence of significant right ventricular dysfunction, pulmonary hypertension, and marked left ventricular dilation, patients with coronary artery disease and left ventricular dysfunction should be strongly considered for coronary revascularization.

What is the optimum role of percutaneous coronary intervention (PCI) in the revascularization of patients with ischemic cardiomyopathy (ICM)?

Most revascularization studies have involved revascularization via coronary artery bypass surgery (CABG) for the overwhelming majority of patients with ICM. Even with the use of coronary stenting, all comparative trials of surgery versus PCI have documented less consistent revascularization with PCI.

On the other hand, PCI has shown to have been effective at least over the short-term, for some high risk patient subsets. The importance of complete revascularization for a patient with ICM has also been a deterrent to the routine use of PCI for these patients. For patients with coronary vascular anatomy suitable for stenting, second generation (drug-coated) stents may provide more consistent and long lasting revascularization than previous PCT technologies.

Valve Surgery for Patients with Left Ventricular Dysfunction

Aortic Stenosis And Severe Left Ventricular Dysfunction
In patients with AS and severe left ventricular dysfunction in whom contractile reserve can be documented, AVR (1) can be performed with an acceptable operative mortality, (2) leads to symptomatic improvement in most survivors, and (3) confers a short- and long term survival benefit in comparison to medical therapy.

Aortic Regurgitation And Severe Left Ventricular Dysfunction
The consensus from the available literature is that for patients with severe left ventricular dysfunction and chronic AR, even those with markedly dilated left ventricles, AVR can be performed with an acceptable operative mortality of approximately 8–15%. Long-term survival approaches 70% at 5 years, which is better than with no treatment or medical treatment alone, as inferred from natural history studies. However, no studies that directly compare medical therapy to AVR in this subgroup exist, and probably will not exist, as the prognosis of medical treatment alone for dilated cardiomyopathy secondary to AR is extremely poor.
Mitral Valve Surgery in Severe Left Ventricular Dysfunction

Mitral valve surgery for patients with severe LV dysfunction and MR historically was high risk and with only limited effectiveness. The outcomes and hence that reputation, however, are changing. Several centers are now reporting mitral valve repair in these patients with acceptable mortality. Late improvements in ventricular function and volumes, improved quality of life for the patient, and improved NYHA class. Three- and five-year survival appear to be quite good compared to patients with MR, severe LV dysfunction, and only medical therapy. In general, repair is preferable to valve replacement.

Summary Of Dilated Cardiomyopathy Management

<table>
<thead>
<tr>
<th>Referral</th>
<th>Treatment</th>
<th>Evaluate</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV inotrops</td>
<td>ACE-I</td>
<td>Etiology</td>
</tr>
<tr>
<td>Rhythm issues</td>
<td>Beta Blockers</td>
<td>Ischemic</td>
</tr>
<tr>
<td>Bi-V PM</td>
<td>Diuretics, Digoxin,</td>
<td>Reversible</td>
</tr>
<tr>
<td>CABG, MVR</td>
<td>Spironolactone PRN symptoms</td>
<td>Precipitants</td>
</tr>
<tr>
<td>Transplantation</td>
<td></td>
<td>Avoid</td>
</tr>
<tr>
<td>VAD</td>
<td></td>
<td>unnecessary testing</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Holter, biopsy,</td>
</tr>
</tbody>
</table>
Flow chart management of heart failure with low EF

**At Risk for Heart Failure**

**Stage A**
- At high risk for HF but without structural heart disease or symptoms of HF
- e.g.: Patients with:
  - Hypertension
  - Atherosclerotic disease
  - Diabetes
  - Metabolic syndrome or patients
  - Using cardiotoxins
  - With HFx CM

**Stage B**
- Structural heart disease but without symptoms of HF.
- e.g.: Patients with:
  - Previous MI
  - LV remodeling including LVH and low EF
  - Asymptomatic valvular disease

**Stage C**
- Structural heart disease with prior of current symptoms of HF
- e.g.: Patients with:
  - Known structural heart disease
  - Shortness of breath and fatigue, reduced exercise tolerance

**Heart Failure**

**Stage D**
- Refractory HF requiring specialized interventions
- e.g.: Patients who have marked symptoms at rest despite maximal medical therapy (e.g., those who are recurrently hospitalized or cannot be safely discharged from the hospital without specialized interventions)

**Therapy Goals**

**Stage A**
- Treat hypertension
- Encourage smoking cessation
- Treat lipid disorders
- Encourage regular exercise
- Discourage alcohol intake, illicit drug use
- Control metabolic syndrome
- Drugs
  - ACEI or ARB in appropriate patients
  - Beta-blockers in appropriate patients
  - Devices in selected patients
  - Implantable defibrillators

**Stage B**
- All measures under stage A
  - Drugs
  - ACEI or ARB in appropriate patients
  - Beta-blockers in appropriate patients
  - Implantable defibrillators

**Stage C**
- All measures under stage A and B
  - Dietary salt restriction Drugs for routine use
  - Diuretic for fluid retention
  - ACEI
  - Beta-blockers
  - Drugs in selected patients
  - Aldosterone antagonist
  - ARBs
  - Digoxin
  - Hydralazine/nitrates
  - Devices in selected patients
  - Biventricular pacing
  - Implantable defibrillators

**Stage D**
- Appropriate measures under stages A, B, C
- Decision re: appropriate level of care Options
- Compassionate end-of-life care/hospice
- Extraordinary measures
  - Heart transplant
  - Chronic oxygen therapy
  - Mechanical support
  - Experimental surgery or drugs
Advanced or refractory Heart Failure
Fluid status management: may require renal replacement therapy
May not tolerate RAAS or SNS agonism
Referral to heart failure centre transplant, VAD ventricular assisted device
Continuous infusion of positive inotropic agent for palliation
Discuss end of life care options, advanced directives

Heart failure with Preserved Ejection Fraction-Causes and management

Cardiomyopathies
- Hypertrophic
- Asymptomatic
  - Avoid heavy exertion, strenuous exercise
  - Screen relatives
  - Avoid positive inotropes (digoxin)
  - Avoid preload/afterload reduction
  - Judicious use of diuretics for volume overload
  - ? beta blockers
- Symptomatic
  - Same as asymptomatic patients. Plus…
  - Negative inotropes to decrease obstruction
  - Beta blockers, verapamil, disopyramide
  - Septal reduction therapy
- Surgical vs. alcohol ablation
- SCD. Symptomatic VT. Or family history of SCD for ICD
- Dual chamber pacing

- Restrictive
  - Idiopathic muscular diastolic dysfunction
  - Rare
  - Dyspnea, atrial arrhythmias
  - Elevated venous pressures, rapid jugular venous descent
  - Pleural effusions, edema, ascites
  - Echo: normal ventricle, atria very large
  - Treatment: cautious diuresis, manage ischemia PRN and avoid digoxin, transplantation

- Infiltrative Amyloid
  - Systemic illness-constitutional symptoms, GI, neurological, cardiac, bruising
  - Low voltage ECG, pseudoinfarct pattern
  - Echocardiography
  - Thick LV walls (sparkling myocardial appearance)
  - Constrictive pericarditis

- Biventricular heart failure, edema/ascites often predominate
- Hx of pericarditis, CV surgery, radiation or CTD
- Mimics cirrhosis
- Elevated JVP

Other (see table below)
Common clinical scenarios

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Common clinical scenarios</th>
</tr>
</thead>
</table>
| No standard therapeutic approach (mainly symptomatic) | Elderly  
Women > men  
Hypertension  
CAD  
Atrial fibrillation and other heart rate issues  
Volume overload (indiscriminate sodium use) |
| Tailor to individual patient’s needs           |                                                        |
| Optimize heart rate                            |                                                        |
| Treat volume overload                          |                                                        |
| BP and ischemia control                        |                                                        |

**Acute Heart failure**

**Definition and Etiology**

Acute heart failure (AHF) a rapid onset of symptoms and signs, secondary to abnormal cardiac function. Cardiac dysfunction can be related to systolic or diastolic dysfunction, to abnormalities in cardiac rhythm or to preload and afterload mismatch. It is often life threatening and requires urgent treatment.

**Causes of decompensation in heart failure:**
- Noncompliance
- Ischemia
- Inadequate pretreatment
- Arrhythmia
- Miscellaneous
- Hypertension

Rapid Assessment of Hemodynamic Status and Management

**Congestion at Rest**

<table>
<thead>
<tr>
<th></th>
<th>Warm &amp; Dry</th>
<th>Warm &amp; Wet (67%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NO</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Low Perfusion</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>at Rest</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Cold &amp; Dry(5%)</strong></td>
<td>(inotrops, mechanical</td>
<td></td>
</tr>
<tr>
<td></td>
<td>circulatory support)</td>
<td></td>
</tr>
<tr>
<td><strong>Cold &amp; Wet</strong></td>
<td>(diurese, inotrops,</td>
<td></td>
</tr>
<tr>
<td></td>
<td>vasodilat)</td>
<td></td>
</tr>
<tr>
<td><strong>Yes</strong></td>
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</tr>
</tbody>
</table>

**Initial management of acute heart failure**

- Correct hypoxia and increase cardiac output, renal perfusion, sodium excretion and urinary output
- Ultimately ultrafiltration or dialysis may be required
- Devices may be indicated such as intraaortic balloon pump, assisted ventilation, or a circulatory assist device as temporary measure or as temporary measure or as bridge for heart transplantation.
- Oxygen by face mask or CPAP (SpO2 target >95%)
- IV morphine (2.5-5mg prn)
- IV loop diuretic therapy
- Vasodilatation by nitrate or niproprusside
- Inotropic support with severe AHF or hypotension
- IV fluids if low filling pressure
- Concomitant metabolic condition treated according to the diagnostic work up and laboratory status

**Monitoring fluid intake and measuring output**

Effect of HF treatment should be monitored with careful measurement of fluid intake and output; vital signs; body weight, determined at the same time each day; clinical signs (supine and standing) and symptoms of systemic perfusion and congestion. Daily serum electrolytes, urea nitrogen, and creatinine concentrations should be measured during the use of intravenous diuretics or active titration of HF medications (Class I C).

When diuresis is inadequate to relieve congestion, as evidence by clinical evaluation, the diuretic regimen should be intensified using either:

a. higher doses of loop diuretics;

b. addition of a second diuretic (such as metolazone, spironolactone or intravenous chlorthiazide) or

c. Continuous infusion of a loop diuretic (Class I C).

**Preserving End-Organ Performance**

In patients with clinical evidence of hypotension associated with hypoperfusion and obvious evidence of elevated cardiac filling pressures (e.g., elevated jugular venous pressure; elevated pulmonary artery wedge pressure), intravenous inotropic or vasopressor drugs should be administered to maintain systemic perfusion and preserve end-organ performance while more definitive therapy is considered.

Invasive hemodynamic monitoring should be performed to guide therapy in patients who are in respiratory distress or with clinical evidence of impaired perfusion in whom the adequacy or excess of intracardiac filling pressures cannot be determined from clinical assessment.

**Reconciling and Adjusting Medications**

Medications should be reconciled in every patient and adjusted as appropriate on admission to and discharge from the hospital. In patients with reduced ejection fraction experiencing a symptomatic exacerbation of HF requiring hospitalization during chronic maintenance treatment with oral therapies known to improve outcomes, particularly ACE inhibitors or ARBs and beta-blocker therapy, it is recommended that these therapies be continued in most patients in the absence of hemodynamic instability or contraindications.

In patients hospitalized with HF with reduced ejection fraction not treated with oral therapies known to improve outcomes, particularly
ACE inhibitors or ARBs and beta-blocker therapy, initiation of these therapies is recommended in stable patients prior to hospital discharge. Initiation of beta-blocker therapy is recommended after optimization of volume status and successful discontinuation of intravenous diuretics, vasodilators, and inotropic agents. Beta-blocker therapy should be initiated at a low dose and only in stable patients. Particular caution should be used when initiating beta-blockers in patients who have required inotropes during their hospital course.

**Urgent Cardiac Catheterization and Revascularization**

When patients present with acute HF and known or suspected acute myocardial ischemia due to occlusive coronary disease, especially when there are signs and symptoms of inadequate systemic perfusion, urgent cardiac catheterization and revascularization is reasonable where it is likely to prolong meaningful survival.

**Invasive Hemodynamic Monitoring**

Invasive hemodynamic monitoring can be useful for carefully selected patients with acute HF who have persistent symptoms despite empiric adjustment of standard therapies, and

a. whose fluid status, perfusion, or systemic or pulmonary vascular resistances are uncertain;
b. whose systolic pressure remains low, pr is associated with symptoms, despite initial therapy;
c. whose renal function is worsening with therapy;
d. who require parenteral vasoactive agents; or
e. who may need consideration for advanced device therapy or transplantation.

**Ultrafiltration and Intravenous Inotropic Drugs**

Ultrafiltration is reasonable for patients with refractory congestion not responding to medical therapy. Intravenous inotropic drugs such as dopamine, dobutamine or milrinone might be reasonable for those patients presenting with documented severe systolic dysfunction, low blood pressure and evidence of low cardiac output, with or without congestion, to maintain systemic perfusion and preserve end-organ performance.
### Oxygen/NIV Loop diuretic +/- vasodilator

**Clinical evaluation**

<table>
<thead>
<tr>
<th>SBP &gt; 100 mmHg</th>
<th>SBP 90-100 mmHg</th>
<th>SBP &lt; 90 mmHg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vasodilator (NTG, nitroprusside Nesiritide, levosimendan)</td>
<td>Vasodilator and/or Inotrope (clobutamine, PDEI, Levosimendan)</td>
<td>Consider preload Correction with fluids Inotrope (dopamine)</td>
</tr>
</tbody>
</table>

**Good response**

Stabilise and initiate Diuretic, ACEI/ARB, beta-blocker

**Poor response**

Inotrope Vasopressor Mechanical support

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### Fluid retention

<table>
<thead>
<tr>
<th>Fluid retention</th>
<th>Diuretic</th>
<th>Daily Dose (mg)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate</td>
<td>Furosemide or bumetanide or torasemide</td>
<td>20 – 40</td>
<td>Oral or i.v. according to clinical symptoms</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.5 – 1</td>
<td>Titrate dose according to clinical response – Monitor K, Na, creatinine, blood pressure</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10 – 20</td>
<td>– Monitor K, Na, creatinine, blood pressure</td>
</tr>
</tbody>
</table>

| Severe          | Furosemide Furosemide infusion Bumetanide Torasemide | 40 – 100 (5 – 40 mg/h) | i.v. Increase dose. Better than very high bolus doses oral or i.v. Oral |
|                 |          | 1 – 4          | Oral |
|                 |          | 20 – 100       | Oral |

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### To do list prior to hospital discharge in CHF

Discontinuation of inotrops 48h prior to discharge 24hr stabilization with oral diuretics, electrolyte supplementation and vasodilator drugs Patient and family education regarding diet and medications Follow up visit with cardiologist in 7-10 days Telephone or visiting nurse contact within 3 days

<table>
<thead>
<tr>
<th>With alkalosis</th>
<th>Acetazolamide</th>
<th>0.5mg</th>
<th>i.v.</th>
</tr>
</thead>
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<tr>
<td>Refractory to loop diuretics</td>
<td>Add dopamine (renal vasodilation) or dobutamine</td>
<td>50 – 100</td>
<td>Consider ultrafiltration or haemodialysis if coexisting renal failure</td>
</tr>
<tr>
<td>Refractory to loop diuretics and thiazides</td>
<td>Add hydrochlorothiazide or metolazone Or spironolactone</td>
<td>2.5 – 10</td>
<td>Spironolactone best choice if no renal failure and normal or low serum potassium</td>
</tr>
<tr>
<td>Refractory to loop diuretics and thiazides</td>
<td>Add spironolactone</td>
<td>25 – 50</td>
<td>MTZ(Metolazone) more potent: if creatinine clr &lt; 30ml/ min</td>
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<tr>
<td>Vasodilator</td>
<td>Indications</td>
</tr>
<tr>
<td>------------------</td>
<td>----------------------------------</td>
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<tr>
<td>Nitroglycerine</td>
<td>Pulmonary congestion/oedema</td>
</tr>
<tr>
<td>Isosorbide Dinitrate</td>
<td>Pulmonary congestion/oedema</td>
</tr>
<tr>
<td>Nitroprusside</td>
<td>Hypertensive HF congestion/oedema</td>
</tr>
<tr>
<td>Nesiritide*</td>
<td>Pulmonary congestion/oedema</td>
</tr>
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### Treatment Summary

<table>
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<tr>
<th>Drug</th>
<th>Bolus</th>
<th>Infusion rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dobutamine</td>
<td>No</td>
<td>2 to 20 μg/kg/min (β+)</td>
</tr>
<tr>
<td>Dopamine</td>
<td>No</td>
<td>&lt;3 μg/kg/min; inotropic (δ+) 3 – 5 μg/kg/min: inotropic (β+) &gt; 5 μg/kg/min: (β+), vasopressor (α+)</td>
</tr>
<tr>
<td>Milrinone</td>
<td>25 – 75 μg/kg over 10 – 20 min</td>
<td>0.375 – 0.75 μg/kg/min</td>
</tr>
<tr>
<td>Enoximone</td>
<td>0.25 – 0.75 mg/kg</td>
<td>1.25 – 7.5 μg/kg/min</td>
</tr>
<tr>
<td>Levosimendan*</td>
<td>12 μg/kg over 10 min (optional)**</td>
<td>0.1 μg/kg/min which can be decreased to 0.05 or increased to 0.2 μg/kg/min</td>
</tr>
<tr>
<td>Norepinephrine</td>
<td>No</td>
<td>0.2 – 1.0 μg/kg/min</td>
</tr>
<tr>
<td>Epinephrine</td>
<td>Bolus: 1 mg can be given i.v. during resuscitation, repeated every 3 – 5 min</td>
<td>0.05 – 0.5 μg/kg/min</td>
</tr>
</tbody>
</table>

* This agent also has vasodilator properties.

** In hypotensive patients. (SBP < 100mmHg) initiation of therapy without a bolus is recommended.

A. For all
   - Prevention. Control of risk factors
     - Life style
     - Treat etiologic cause/aggravating factors
     - Drug therapy
     - Personal care. Team work

B. Selected patients
   a. Revascularization if ischemia causes HF
   b. ICD (Implantable cardiac defibrillator)
   c. Ventricular resynchronization
   d. Ventricular assist devices
   e. Heart transplant
   f. Transplantation