

CLINICAL PRACTICE GUIDELINES

April 2007

MOH/P/PAK/126.07(GU)

MANAGEMENT OF HEART FAILURE



Ministry of Health Malaysia



Academy of Medicine Malaysia



National Heart Association of Malaysia

Statement of Intent

This clinical practice guidelines (CPG) is meant to be a guide for clinical practice, based on the best available evidence at the time of development. Adherence to these guidelines may not necessarily guarantee the best outcome in every case. Every health care provider is responsible for the management of his/her patient based on the clinical picture presented by the patient and the management options available locally.

Period of validity

This CPG was issued in April 2007 and will be reviewed in 3 years or sooner if new evidence becomes available.

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<http://www.moh.gov.my>

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<p>This is an update to the Clinical Practice Guideline on Heart Failure (published 2000). This CPG supersedes the previous CPG on Heart Failure (2000).</p>
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MESSAGE FROM THE DIRECTOR GENERAL OF HEALTH

Heart Disease is an important cause of morbidity and mortality in Malaysia. Most patients who survive a myocardial infarction or develop hypertension, will eventually develop heart failure. Thus the updating of this Clinical Practice Guidelines on Management of Heart Failure by the National Heart Association of Malaysia, Academy of Medicine and Ministry of Health is important and timely.

This Clinical Practice Guideline updates all health care providers on the latest developments in the field of Heart Failure. It uses an evidence based approach and grades each recommendation accordingly thus allowing the physician in charge to apply the latest technology, knowledge and standard of care in the management of his or her patient. It provides a choice of therapy and thus allows the healthcare provider to adapt this to the local situation wherever possible.

For this Clinical Practice Guidelines to be a success, it must be acceptable in our local setting and must be used widely.

Lastly, I would like to commend the Expert Committee for their hard work and effort in updating the guidelines for the benefit of all practicing physicians.



Y.Bhg Tan Sri Datuk Dr Hj Mohd Ismail Merican
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Rationale and Process of Guidelines Development

Cardiovascular disease is an important cause of morbidity and mortality in Malaysia. Heart Failure, the end stage of most diseases of the heart, is a common medical problem encountered in general practice and is an important cause of hospital admissions.

The 1st Clinical Practice Guidelines (CPG) in Heart Failure was published in 2000. Since then, there have been many new developments in this field. Thus the publication of this 2nd edition is timely.

This CPG was drawn up by a committee appointed by the National Heart Association of Malaysia, Ministry of Health and the Academy of Medicine. It comprises cardiologists and general physicians from the government and private sectors and the public Universities.

Objectives:

The objectives of this CPG are to assist the health care provider in:

- Preventing heart failure
- Reducing the morbidity associated with the condition and improving the quality of life of these patients
- Improving survival of patients with heart failure

Process:

Evidence was obtained by systematic review of current medical literature on Heart Failure using the usual search engines – PubMed and Ovid. International guidelines on Heart Failure were also studied. After much discussion, the draft was then drawn up by the members of the Expert Panel and submitted to the Technical Advisory Committee for Clinical Practice Guidelines, Ministry of Health Malaysia and key health personnel in the major hospitals of the Ministry of Health and the private sector for review and feedback.

The level of recommendation and the grading of evidence used in this CPG was adapted from the American Heart Association and the European Society of Cardiology (pg VII). The evidence supporting the recommendation was graded as:

- A if the data was derived from multiple randomized clinical trials involving a large number of individuals or meta-analyses.
- B if the data was derived from a single randomized clinical trial or limited to non randomized clinical trials or observational data.
- C if the recommendation was based on consensus of expert opinion or case studies only.

In certain conditions even though there are no clinical trials but where the practice is nevertheless recommended based on years of well supported clinical experience the evidence, is graded as C. An example, is anticoagulation in the presence of a large mobile left ventricular thrombus. The grades of recommendation was ranked as I, IIa, IIb or III as outlined in page VII.

Clinical Questions Addressed:

- How do you make a diagnosis of heart failure?
- How do you prevent high risk individuals from developing heart failure?
- How do you treat acute and chronic heart failure effectively using current evidence?
- How do you treat the following special groups?
 - the asymptomatic individual with impaired left ventricular function,
 - the individual with diastolic dysfunction
 - the pregnant patient with heart failure
 - infants and children with heart failure

Target Group:

This CPG is directed at all healthcare providers treating patients with heart failure – general practitioners, general and family physicians and cardiologists.

Target Population:

It is developed to treat all adults, pregnant women and children with heart failure.

Dr. Jeyamalar Rajadurai
Chairperson

GRADES OF RECOMMENDATIONS AND LEVELS OF EVIDENCE

GRADES OF RECOMMENDATION	
I	Conditions for which there is evidence and/or general agreement that a given procedure/therapy is beneficial, useful and/or effective.
II	Conditions for which there is conflicting evidence and/or divergence of opinion about the usefulness/efficacy of a procedure/therapy.
II-a	Weight of evidence/opinion is in favor of its usefulness/efficacy.
II-b	Usefulness/efficacy is less well established by evidence/opinion
III	Conditions for which there is evidence and/or general agreement that a procedure/therapy is not useful/effective and in some cases may be harmful.

LEVELS OF EVIDENCE	
A	Data derived from multiple randomized clinical trials or meta analyses
B	Data derived from a single randomized clinical trial or large non randomized studies
C	Only consensus of opinions of experts, casestudies or standard of care

Adapted from the American Heart Association and the European Society of Cardiology

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1. INTRODUCTION

Heart failure (HF) is the end stage of most diseases of the heart. The prevalence of HF varies between 3 – 20 per 1000 population, although in persons over the age of 65 years, it could be as high as 100 per 1000 population¹.

The prognosis for HF is poor, far worse than some of the common cancers². The one year mortality rate varies between 5% to 52% depending on the severity and the presence of co-morbidity^{3,4}. (Appendix 1) In a large community based study, about 40% of individuals with HF died within a year of initial diagnosis⁵. About half of all deaths are sudden and may occur at any stage of the syndrome⁶. Heart failure is an important cause of hospitalization accounting for about 10% of all medical admissions in Malaysia⁷. About 45% of patients with HF are readmitted at least once within 12 months for acute decompensation⁸. More recent epidemiological studies from the West^{9,10} seem to indicate that the prognosis has improved slightly with earlier detection of the condition and improved treatment strategies.

The aims of management are:

- Preventing the development of HF
- Reducing the morbidity associated with the condition and improving the quality of life of these patients
- Improving the survival of patients with HF

This guideline provides evidence based recommendations to help health care providers in the management of their patients with HF. Patient care should however be individualized and sound clinical judgement plays an important role in decision making.

2. DEFINITION

Heart failure is a clinical syndrome characterized by symptoms of breathlessness and fatigue, with signs of fluid retention and supported by objective evidence of cardiac dysfunction (systolic and/or diastolic). The severity of the symptoms may be graded according to the New York Heart Association (NYHA) Functional Class. (Appendix 1) These symptoms may fluctuate in severity with time and may completely disappear following therapy.

3. PATHOPHYSIOLOGY

Heart failure is due to the inability of the heart to pump blood at a rate to meet the needs of various organs of the body or its ability to do so only at high filling pressures. It may be the result of any disorder of the endocardium, myocardium, pericardium or great vessels although commonly, it is due to myocardial dysfunction. Myocardial contractility is most often reduced resulting in Left Ventricular (LV) systolic dysfunction. Occasionally, however, myocardial contractility may be preserved and LV systolic

function is normal, the HF being due to diastolic dysfunction. Commonly, LV systolic dysfunction is associated with some degree of diastolic dysfunction.

3.1 Heart Failure due to LV systolic dysfunction

In LV systolic dysfunction, cardiac output is reduced due to depressed myocardial contractility. This initiates a complex pathophysiological process which includes haemodynamic alterations and structural changes within the myocardium and vasculature. Activation of neuro- hormones such as catecholamines and the renin-angiotensin-aldosterone system play a pivotal role in this process.

3.2 Heart Failure with Preserved LV systolic function

Up to 50% of patients presenting with heart failure have normal or near normal systolic function with predominantly diastolic dysfunction¹¹. Diastolic dysfunction leads to impaired LV filling due to diminished relaxation (during early diastole) and / or reduced compliance (early to late diastole) leading to elevated filling pressures. These haemodynamic changes lead to clinical symptoms and signs similar to those of LV systolic dysfunction.

Many different classifications of HF have been used to emphasize some aspects of the condition: right vs left vs biventricular heart failure, forward vs backward failure, low output vs high output heart failure, volume overload vs pressure overload, acute vs chronic heart failure, systolic vs diastolic HF. For practical purposes, it may be sufficient to classify HF into acute heart failure (AHF) and chronic heart failure (CHF).

Acute Heart Failure is defined as rapid onset of symptoms and signs of HF due to an acute deterioration of cardiac function. Chronic Heart Failure is the chronic state when patients have stable symptoms. In these patients an acute precipitating or aggravating factor(s) may cause acute cardiac decompensation.

4. AETIOLOGY

Heart failure is not a complete diagnosis by itself. It is important to identify the underlying disease and the precipitating cause(s), if present. Although systolic and diastolic dysfunction are separate pathophysiological entities, they often share common aetiologies.

The most common underlying causes of HF in adults are:

- Coronary heart disease
- Hypertension

Slightly less common causes include:

- Idiopathic dilated cardiomyopathy
- Valvular heart disease
- Diabetic cardiomyopathy

Other causes of HF include:

- Congenital heart disease
- Cor pulmonale
- Pericardial disease: constrictive pericarditis, cardiac tamponade
- Hypertrophic cardiomyopathy
- Viral myocarditis
- Acute rheumatic fever
- Toxic: Alcohol, adriamycin, cyclophosphamide
- Endocrine and metabolic disorders: thyroid disease, acromegaly, pheochromocytoma
- Collagen vascular disease: systemic lupus erythematosus, polymyositis, polyarteritis nodosa
- Tachycardia induced cardiomyopathy
- Miscellaneous
 - severe anemia
 - peripartum cardiomyopathy
 - large A-V shunts

Patients with CHF may occasionally develop acute decompensation. Factors that can contribute to this AHF are listed in Table IV (pg 16). The more important causes are:

- Acute myocardial infarction/ myocardial ischemia
- Arrhythmias (e.g. atrial fibrillation)
- Uncontrolled Blood Pressure
- Infections (e.g pneumonia)
- Non-compliance to medications
- Excessive fluid and salt intake
- Anemia
- Development of renal failure
- Adverse effects of drug therapy (e.g. Non Steroidal Anti Inflammatory Drugs)

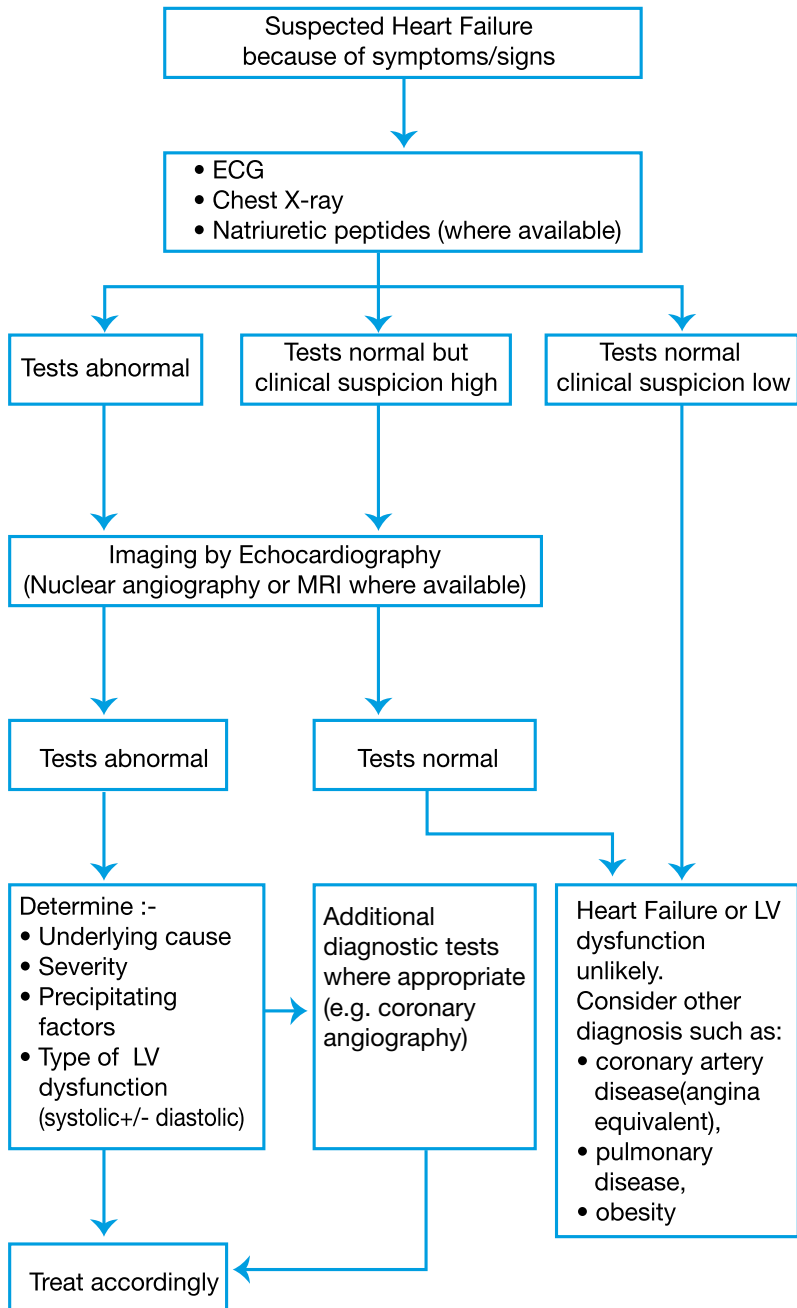
5. DIAGNOSIS

5.1 Symptoms and signs

The clinical suspicion of HF should be supported by objective evidence of cardiac dysfunction (Figure 1 - pg 4).

HF may present either as an acute medical emergency with sudden severe breathlessness (AHF) or gradually over a period of time (CHF). Breathlessness, ankle swelling, and fatigue are the characteristic symptoms of HF but may be difficult to interpret, particularly in the elderly, obese, and in women. Exercise capacity should be assessed to determine functional class (Appendix 1). Peripheral edema, elevated jugular venous pressure and hepatomegaly are the characteristic signs of congestion of systemic veins^{12,13}. Other important clinical signs of HF are

Figure 1: Algorithm for the diagnosis of Heart Failure or LV dysfunction



tachycardia, a gallop third heart sound and pulmonary crepitations. All these signs however are non-specific and may resolve following medical therapy¹³.

5.2 Investigations

Basic investigations include:

- ECG – for ischaemia/infarction, left atrial overload, LV hypertrophy and arrhythmias
- Chest X-ray – to look for cardiac size and shape, pulmonary congestion
- Blood test – FBC, renal function, liver function, glucose, lipid profile
- urinalysis – proteinuria, glycosuria

I.C

Other important investigations include:

- echocardiogram – to identify structural abnormalities and assess LV systolic and diastolic dysfunction
- natriuretic peptides or their precursors (especially BNP and NT-proBNP) – If available, this investigation is useful in the evaluation of patients presenting with acute dyspnoea in the urgent care setting in whom the clinical diagnosis of HF is uncertain¹⁴. A low-normal concentration of this marker in an untreated patient makes the diagnosis of HF unlikely¹⁵. Thus it is a useful “rule-out” test in doubtful cases.

I.C

Ila.A

Additional investigations when indicated;

- Blood tests:
 - cardiac biomarkers
 - thyroid function tests
 - C-reactive protein (to look for inflammation)
- Tests for myocardial ischemia and/or viability:
 - treadmill exercise test
 - stress echocardiography (exercise or pharmacological)
 - radionuclide studies
 - cardiac magnetic resonance imaging (CMR)
- Invasive tests:
 - coronary angiography
 - cardiac catheterization
 - endomyocardial biopsy
- Others:
 - Holter electrocardiography, loop recorders and long-time ECG recording
 - pulmonary function tests

Key Message :

- To satisfy the definition of HF, symptoms and signs and objective evidence of cardiac dysfunction must be present

6. PREVENTION

Prevention of HF should always be the primary objective of management. It is directed at individuals:

- at high risk of developing cardiac disease
- with cardiac disease but who still have normal myocardial function
- who have impaired myocardial function but who do not as yet have signs or symptoms of HF.

6.1 Individuals who are at high risk of developing HF but who do not as yet have structural heart disease. These include individuals with:

- multiple risk factors for developing coronary artery disease or who already have evidence of atherosclerotic disease (e.g. cerebral, peripheral vascular disease)
- hypertension
- diabetes
- the metabolic syndrome
- a family history of cardiomyopathy
- thyroid disorders
- renal disease

In these individuals the following measures should be taken:

- I.A • Treating hypertension to target levels. This has been shown to reduce the incidence of HF by as much as 50%¹⁶.
- I.A • Treating lipids to goal in high risk individuals to prevent cardiovascular disease^{17,18}.
- I.C • Optimizing the control of diabetes. Diabetes has been shown to increase the risk of HF¹⁹. However there has been no data as yet that controlling diabetes will prevent HF.
- I.C • Managing the metabolic syndrome.
- I.C • Detecting and treating thyroid disease early to prevent thyroid heart disease.
- I.C • Stressing the importance of a healthy life style and avoiding behaviour that could increase the risk of HF such as smoking and excessive alcohol intake. Encourage regular physical exercise and the maintenance of ideal body weight.

6.2 Individuals with cardiac disease but who do not as yet have evidence of myocardial dysfunction. Measures include:

- I.A • Early triage and treatment of the patient with myocardial infarction (MI) and/or ischemia ^{20,21}.

- Patients with coronary heart disease should be treated appropriately with antiplatelet agents^{22,23,24}, β -blockers^{25,26}, angiotensin converting inhibitors (ACEI)²⁷ and statins^{28,29}. These patients should undergo coronary revascularization as indicated. I.A
- Patients with hypertension and left ventricular hypertrophy should have their blood pressure control optimized^{30,31}. I.A
- Patients with haemodynamically significant valve disease should undergo early intervention when indicated^{32,33,34}. I.B
- Arrhythmias should be treated early and appropriately³⁵. I.B
- Patients with congenital cardiac lesions should have these corrected early whenever indicated. I.C

Both these groups of individuals should be regularly monitored looking for signs of HF, assessing LV function and progression of the underlying structural cardiac disease by clinical examination and appropriate investigations.

In addition to the measures stated above, the following have been shown to help prevent HF:

- Angiotensin- Converting Enzyme Inhibitors- ACEI (in patients with atherosclerotic vascular disease^{36,37}, diabetes and hypertension with associated cardiovascular risk factors³⁸) I.A
- Angiotensin II Receptor Blockers – ARB (in patients with atherosclerotic vascular disease, diabetes and hypertension with associated cardiovascular risk factors^{39,40}) I.C
- β -blockers (in post MI patients)^{25,26} I.A
- Statins in patients with coronary heart disease^{41,42,43} I.A

6.3. Individuals with myocardial dysfunction but who do not as yet have signs and symptoms of HF. Measures include:

- Treat the underlying cause wherever possible. I.C
- Prevent progression to HF by modulating cardiac remodeling. See section on the management of Asymptomatic Left Ventricular Dysfunction (Section 7.3.1 - pg 32)

Key Message :

- Prevention and early intervention wherever appropriate should be the primary objective of management.

7. MANAGEMENT

7.1 ACUTE HEART FAILURE (AHF)

Acute Heart Failure may present de novo or as acute decompensation of CHF. The clinical manifestations may vary from mild decompensation to Acute Cardiogenic Pulmonary Edema and Cardiogenic Shock.

Myocardial Infarction/Ischaemia is an important and common cause of AHF. The other causes are as listed in Section 4 (pg 2) and Table IV (pg 16).

I.C Patients with AHF should be hospitalized. The more ill patients should be managed in the intensive care or high dependency unit. They should have their pulse, blood pressure (BP), oxygen saturation, respiratory rate and ECG monitored continuously.

Given the urgent nature of the illness, history, examination, investigations (Table I), treatment and resuscitation should be performed simultaneously. When indicated, early access to diagnostic procedures such as echocardiography and coronary angiography is important.

Table I: Investigations in Acute Cardiogenic Pulmonary Edema

Essential Investigations:

- ECG
- Chest X-ray
- Blood Investigations : haemoglobin, serum electrolytes, urea, creatinine, serum cardiac biomarkers, arterial blood gases
- Echocardiography

Special Investigations:

- Cardiac catheterization/coronary angiography when acute intervention for acute myocardial ischaemia or infarction/valvular disease is anticipated.
- Swan Ganz catheter placement (Flowchart I - pg 12)

The principles of management are:

- Rapid recognition of the condition
- Stabilization of hemodynamics
- Improvement in clinical symptoms and signs
- Identification and treatment of the
 - underlying cause
 - precipitating / aggravating factors.

After initial clinical assessment of vital signs, treatment of AHF should be instituted as outlined in Flowchart 1 (pg 12). For grading of recommendations and levels of evidence, see Table III (pg 13).

Therapy (for dosages see Table II - pg 10)

The initial management includes a combination of the following first line therapy:

- **Oxygen** – 5 to 6 liters/minute, by mask with the aim of achieving oxygen saturation of more than 95% in order to maximize tissue oxygenation and to prevent end organ dysfunction or multi organ failure. **I.C**
Elective ventilation using non invasive positive pressure ventilation (Continuous Positive Airway Pressure [CPAP] or Bi-level Positive Airway Pressure [BiPAP]) should be considered early if necessary^{44,45}. **IIa.A**
Should the oxygen saturation be inadequate or the patient develop respiratory muscle fatigue, then endotracheal intubation and mechanical ventilation is necessary. **IIa.C**
- **Furosemide** – Intravenous (i.v.) furosemide 40 – 100mg. The dose should be individualized depending on the severity of the clinical condition⁴⁶. **I.B**
Administration of a loading dose followed by a continuous infusion has been shown to be more effective than repeated bolus injections alone^{47,48,49}. The dose should be titrated according to clinical response and renal function. **IIb.B**
- **Morphine sulphate** – i.v. 3 – 5 mg bolus (repeated if necessary, up to a total maximum of 10mg). It reduces pulmonary venous congestion and sympathetic drive⁵⁰. It is most useful in patients who are dyspnoeic and restless. Intravenous anti-emetics (metoclopramide 10mg or prochlorperazine 12.5mg) should be administered concomitantly. Care must be exercised in patients with chronic respiratory diseases. **IIb.C**
- **Nitrates** - If the BP is adequate (SBP \geq 100 mmHg), nitrates are indicated as first line therapy in AHF⁵¹. It should be administered sublingually or intravenously. The i.v. route is more effective and preferable. Patients should be closely monitored for hypotension. This commonly occurs with concomitant diuretic therapy. **I.B**
Studies have shown that the combination of i.v. nitrate and low dose furosemide is more efficacious than high dose diuretic treatment alone⁵². **I.B**
Extreme caution should be exercised in patients with aortic and mitral stenosis. Nitrates are contraindicated in severe valvular stenosis.

An attempt should be made to identify the underlying cause e.g. acute myocardial infarction/myocardial ischemia, valvular heart disease and hypertension. This would enable the appropriate treatment to be instituted early.

Table II: Drugs Commonly Used in AHF

	Route of Admin	Dosages
Diuretics Frusemide	IV Infusion	40mg – 100mg 5 – 40mg/hour (better than very high bolus doses)
Vasodilators Nitroglycerin	Infusion	5ug/min increasing at intervals of 3 – 5 min by 5ug/min increments up to 100 – 200 ug/min
Nitroprusside	Infusion	0.1 – 5ug/kg/min
Sympathomimetics Dobutamine Dopamine	Infusion Infusion	2 – 20ug/kg/min <2 ug/kg/min – renal arterial vasodilation 2 – 10ug/kg/min – inotropic doses 10 – 20ug/kg/min – peripheral vasoconstriction
Noradrenaline	Infusion	0.02 – 1ug/kg/min till desired BP is attained
Phosphodiesterase-3- Inhibitors Milrinone	Infusion	50ug/kg bolus then 0.375– 0.75ug/kg/min

Response to drug therapy should be assessed continuously. Parameters to assess during treatment include:

- Symptoms and signs
- Vital signs
 - oxygen saturation
 - heart rate
 - blood pressure
 - respiratory rate
 - urine output
 - body weight

- Investigations
 - renal function tests
- Invasive haemodynamic monitoring (if necessary)
 - pulmonary capillary wedge pressure, cardiac index

An adequate response would be reflected by an improvement in the patient's clinical condition, decrease in his heart rate and an improvement in his oxygen saturation. Generally, a SBP \geq 90mmHg would be considered adequate if the patient feels well and has good tissue perfusion as shown by the absence of giddiness, warm skin and stable renal function with good urine flow.

In most cases of mild to moderate AHF the following measures would suffice. If the patient fails to respond to the above therapy, further management would depend upon the blood pressure and tissue perfusion.

A) In the presence of an adequate blood pressure:

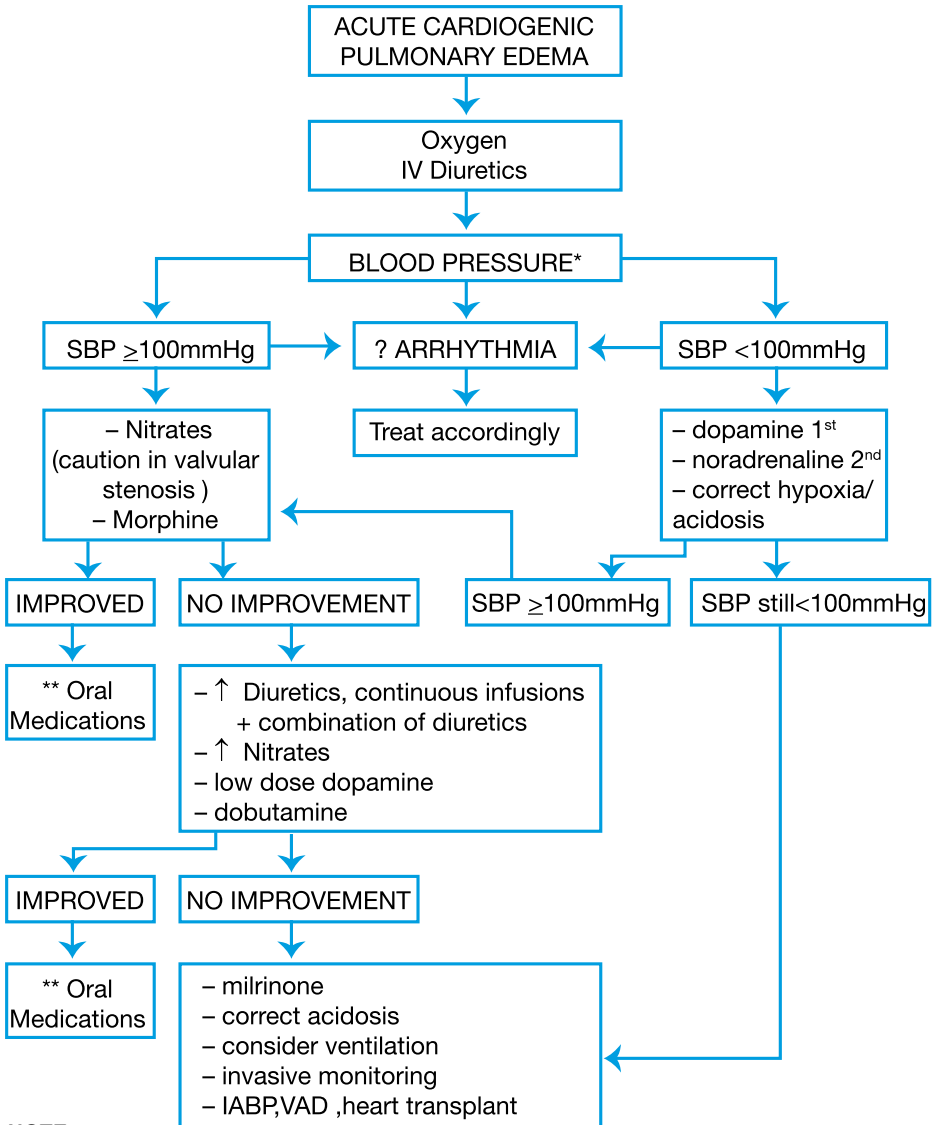
- **Furosemide:** i.v. furosemide infusion 5-40mg/hour. Combination of a loop diuretic at low doses with nitrates⁵² is superior to high dose diuretic therapy alone. **I.B**

Combination with dobutamine or dopamine⁴⁹ is also more effective than increasing the dose of diuretic alone. Alternatively one could consider adding an oral thiazide diuretic⁵³. **IIb.C**
- **Inotropes:**
 - Dopamine: Low dose at <2 ug/kg/min to improve renal flow and promote diuresis **IIb.C**
 - Dobutamine infusion : Started at 2 – 5 μ g/kg/minute and titrated by 1 – 2 μ g/kg/minute increments at 30 minute intervals until the desired clinical and haemodynamic response is attained. **IIa.C**
 - Milrinone: This agent improves symptoms and haemodynamics in AHF. **IIb.C**
- **Vasodilators:**
 - Sodium Nitroprusside would be useful in patients not responsive to nitrates. **I.C**

This drug is particularly useful in cases of uncontrolled hypertension, acute mitral or aortic regurgitation.

Continuous intra-arterial monitoring is necessary as acute changes in blood pressure with hypotension can occur. Infusion should not be continued beyond 3 days because of the danger of cyanide poisoning. Infusion should be for shorter periods in patients with hepatic and renal impairment.

Flowchart I: Management of Acute Cardiogenic Pulmonary Edema



NOTE:

* It is important to look for tissue hypoperfusion - cool peripheries, sweating, low volume pulse, decreasing urine output

** Flow Chart II

From onset, evaluate to identify correctable/reversible lesions

Special situations: Myocardial ischaemia / infarction: Treat accordingly

Hypertension: Control BP quickly

Valvular heart disease: Corrective surgery/balloon valvuloplasty

Table III: Grading of Recommendations of Therapies in the Management of AHF

Intervention	Grades of Recommendation	Level of Evidence	Comments
INITIAL MANAGEMENT CONSISTS OF :			
Oxygen	I	C	Maintain the oxygen saturation above 95%
Diuretics	I	B	Indicated for fluid retention
Nitrates	I	B	Contraindicated if SBP< 100mmHg. Use with caution in valvular stenosis.
Morphine	IIb	C	Indicated in pts who are dyspnoeic and restless
NOT RESPONSIVE TO INITIAL TREATMENT AND SBP≥100mmHg			
Diuretics	IIb	C	continuous infusion; combination with nitrates, dopamine, dobutamine or thiazide
Dobutamine	IIa	C	Indicated for peripheral hypoperfusion +/- pulmonary congestion
Dopamine (<2 µg/kg/min)	IIb	C	To improve renal perfusion and promote diuresis
Milrinone	IIb	C	Improves symptoms and hemodynamics.
Sodium Nitroprusside	I	C	Indicated in hypertensive crisis and acute valvular regurgitation
NOT RESPONSIVE TO INITIAL TREATMENT AND SBP<100mmHg			
Dopamine (>2µg/kg/min)	IIa	C	Indicated to increase the BP
Noradrenaline	IIb	C	Indicated to increase the BP
IABP	I	B	Indicated as a bridge till myocardial recovery or heart transplant
Ventricular Assist Device (VAD)	IIa	B	Indicated as a bridge till myocardial recovery or heart transplant

B) If the blood pressure is low (SBP <100mmHg) at initial presentation or drops during treatment:

- Ila.C** • Dopamine infusion
- Ilb.C** • Noradrenaline infusion or in its absence, adrenaline infusion
- I.C** • Avoid vasodilators (nitrates, nitroprusside) and morphine until the blood pressure has stabilized
- I.C** • Over diuresis or hypovolaemia - correct accordingly.

In Right Ventricular (RV) Infarction, the hypotension may respond to volume loading.

Other Measures:

- Ila.C** • **Intubation and mechanical ventilation** – Should the oxygen saturation be inadequate or the patient develops respiratory muscle fatigue, then endotracheal intubation and mechanical ventilation is necessary.
- I.C** • **Correction of acidosis**
- Ilb.C** • **Invasive haemodynamic monitoring** – where available, would be useful in patients not responsive to medical therapy and are hypotensive. This can include arterial pressure line, central venous pressure line and pulmonary artery catheter. This would allow a more accurate assessment of the fluid status of the patient and allow better titration of medications.
- I.B** • **Intra-aortic balloon counterpulsation (IABP)** – would be useful in patients who are not responding optimally to medical therapy as a bridge to definitive treatment⁵⁴. IABP would be particularly useful in patients with intractable myocardial ischaemia or acute mitral regurgitation. It is contraindicated in patients with aortic regurgitation or aortic dissection.
- Ila.B** • **Ventricular Assist Devices (VAD)** – would be useful as a bridge in patients for whom recovery from AHF is expected or for whom heart transplantation is an option⁵⁵.

Following adequate response to intravenous therapy, the patient should be converted to optimal oral medications.(Flow Chart II - pg 22) The initial dose of oral diuretics required is generally higher than the intravenous dose.

Special Situations:

- **Myocardial Ischaemia / Infarction:** Reversible myocardial ischaemia causing AHF, needs early recognition, rapid stabilization and referral for urgent coronary angiography. In acute myocardial infarction, reperfusion therapy by fibrinolytic or primary Percutaneous Coronary Intervention (PCI) may significantly improve or prevent AHF. Long term management strategies should include adequate coronary revascularization, anti platelet therapy, ACE-I and/or ARB, β -blockers and statins.
- **Hypertension:** Typically presenting as “flash pulmonary edema” with hypertensive crisis. Systolic LV function tends to be normal. The blood pressure needs to be reduced relatively quickly. It is generally suggested that the SBP be reduced by 25% over 3 to 12 hours. This is best achieved with parenteral drugs such as intravenous nitrates or nitroprusside. No attempt should be made to restore “normal” values of BP as this may cause deterioration of organ perfusion. Look for secondary causes of hypertension such as renal artery stenosis and pheochromocytoma.
- **Valvular Heart Disease:** AHF can be caused by valvular conditions such as acute mitral or aortic valve incompetence or stenosis, bacterial endocarditis, aortic dissection and prosthetic valve thrombosis. Vasodilator therapy would be beneficial in acute valvular regurgitation, but is contraindicated in severe valvular stenosis. Early access to echocardiography is crucial for the diagnosis and management. Percutaneous intervention such as mitral valve commissurotomy can be life saving in patients with severe mitral stenosis.
- **Arrhythmias:** Tachyarrhythmias particularly atrial fibrillation / atrial flutter with fast ventricular rates need to be identified and treated appropriately e.g. electrical or pharmacological cardioversion.
- **Renal Failure:** AHF and renal failure can co-exist and either may give rise to the other. Renal failure influences the response to drug therapy. In these patients with refractory fluid retention, continuous ultrafiltration may be helpful.
- **Decompensation in a Previously Stable Patient With Heart Failure:** Precipitating causes should be identified and treated appropriately. (Table IV - pg 16)

Table IV: Factors Contributing to Decompensation in a Patient with Stable HF

Patient factors

- Non compliance to medications
- Dietary indiscretion especially salt and fluid intake
- Inappropriate medications e.g. NSAIDS
- Alcohol consumption

Cardiac Causes

- Superimposed myocardial ischaemia or infarction (often asymptomatic)
- Uncontrolled hypertension
- Arrhythmias
- Pulmonary embolism
- Secondary mitral or tricuspid regurgitation

Systemic Conditions

- Superimposed infections
- Anemia
- Thyroid disease
- Electrolyte disturbances
- Worsening renal disease

Cardiogenic Shock

Cardiogenic shock carries a very high mortality rate. Features include:

- SBP<90mmHg not improved with fluid administration
- Signs of hypoperfusion-cold extremities, altered mental status, restlessness
- Reduced urine output (<20cc/hour)
- Cardiac index of <2.2 L/min/m²

It is important to establish the aetiology and institute appropriate resuscitative therapy immediately. An ECG should be obtained and continuous monitoring begun. Venous access should be secured, preferably via central venous cannulation (subclavian or internal jugular).

Important considerations are:

- **Ventricular Function:** Echocardiography would allow rapid determination of LV function and mechanical causes (e.g. acute valve regurgitation, acute septal rupture, cardiac tamponade) of cardiogenic shock. In the presence of preserved LV systolic function, other causes of shock such as sepsis and intravascular volume depletion should be considered.

- **Intra Vascular Volume Status:** An absolute or relative reduction in left ventricular filling pressures may be present. This may be due to excessive diuretic or vasodilator therapy, concomitant GI bleed or RV infarction. In the absence of signs of LV failure, fluid challenge with normal saline should be administered (usual recommended volume : 200 – 500mls). Invasive haemodynamic monitoring would be useful to guide fluid therapy.
- **Arrhythmias:** Should be identified and appropriate treatment such as cardioversion or pacing instituted. Resistant arrhythmias would require additional anti-arrhythmic drug therapy.

In the presence of cardiogenic shock or near shock (hypoperfusion with adequate blood pressure) treatment would include the following:

- **Inotropic support:** High dose dopamine and/or noradrenaline. If blood pressure is adequate in the setting of near shock, dobutamine may be used.
- **Mechanical device support:** Intra-aortic balloon pump or LV assist device.
- **Identifying correctable causes:** This includes myocardial ischaemia/infarction. Cardiogenic shock in this setting could be due to:
 - pump failure – These patients should be identified early and treated aggressively with prompt revascularization by PCI. Often they would require ventilatory support and IABP.
 - mechanical complications such as ventricular septal rupture and acute mitral regurgitation. Echocardiography will be useful in the diagnosis. Urgent surgery is beneficial but carries a high mortality.

Key Message for Management of AHF:

- Initial management consists of oxygen, frusemide, morphine and nitrates.
- The subsequent management would depend upon the response to treatment and the BP.
- Correctable/reversible underlying conditions should be identified and treated accordingly.

7.2 CHRONIC HEART FAILURE (CHF)

7.2.1 NON PHARMACOLOGICAL MEASURES

These include the following:

- a) Education
- b) Diet & Nutrition
- c) Lifestyle
- d) Exercise

a) Education

The patient and family should receive both education and counseling about the heart failure syndrome, its prognosis and drug treatments. (Appendix I)

- Counseling on the warning signs and symptoms of worsening heart failure particularly with emphasis on sudden weight gain - more than 2 kg in 3 days.
- Provide prognostic information to enable patients to make realistic decisions and plans. This is important in patients with severe HF. Chronic heart failure is a highly lethal disease, as lethal as several common malignancies.
- Educate patients on their drug regime, emphasizing the need for compliance. Patients should be made aware of the expected benefits and the potential common side effects of these drugs.
- Patients should be warned about self-medication and potential drug interactions. Refer to Appendix II.

b) Diet & Nutrition

While obese patients should be encouraged to reduce weight, it is important to maintain good nutrition. Patients should be advised on salt restriction particularly in severe HF. A good rule of thumb is to avoid adding salt and soya sauce while cooking or at the table. Refer to Appendix III on salt content of common Malaysian food. Fluid intake should be restricted to 1 – 1.5 liter/day for patients with severe HF.

c) Lifestyle

- Patients with alcoholic cardiomyopathy must abstain from alcohol. Similar abstinence is strongly encouraged in all other patients with HF.
- Smoking should be stopped.

- Patients with severe HF (NYHA Class III – IV) should be advised against pregnancy because of high maternal mortality. Recommended contraceptive methods include low-dose oestrogen and third generation progesterone. Intra-uterine contraceptive devices (IUCDs) may be used except in patients with valvular heart disease.
- In severe HF, sexual dysfunction is common and sexual practices may need to be modified to accommodate patients with impaired effort tolerance. Presently, phosphodiesterase-5-inhibitors (sildenafil, tadalafil and vardenafil) are not recommended in advanced HF. Nitrates should not be given within 24 – 48 hours of phosphodiesterase-5-inhibitor use and vice versa. Patients in NYHA class II are at intermediate risk and patients in class III – IV are at high risk of cardiac decompensation triggered by sexual activity. For use of sildenafil in patients with HF please refer to the Malaysian Consensus on the use of Sildenafil in patients with cardiac disease.

d) Exercise

Recent studies have shown that patients with compensated HF can exercise safely.

Regular dynamic exercise:

- improves psychological and physical well-being
- reduces harmful neuro-hormones
- improves muscle blood flow and function
- increases the electrical stability of the heart

Activities such as walking, cycling, swimming, golfing and bowling should be encouraged with gradual build-up to target activity levels. Specific recommendations include dynamic aerobic exercise (walking) 3 to 5 times a week for 20 to 30 min, or cycling for 20 min at 70-80% of peak heart rate 5 times a week. If the patient can physically manage to work without undue symptoms, this too can be continued.

7.2.2 PHARMACOLOGICAL MANAGEMENT

Drug therapy is the mainstay of management of CHF as outlined in Flowchart II - pg 22. For grading of recommendations and levels of evidence, see Table VII - pg 23.

a) Diuretics

Diuretics are indicated in all patients with HF in whom there are signs and symptoms of fluid retention⁵⁶. **I.C**

The dose of diuretic used is wide and dependent on individual requirements. Diuretic therapy must be used with care because overdiuresis can cause severe intravascular dehydration and deteriorating renal function. Hypokalaemia is a

common problem with diuretic use and oral potassium supplementation is usually necessary.

Thiazide diuretics may be preferred in patients with hypertensive HF and mild fluid retention. For most patients however, a loop diuretic is often required. Responsiveness to loop diuretics diminishes as HF progresses. In this situation, combination of thiazides and loop diuretics are useful as these drugs work synergistically to improve diuresis⁵³. In patients with a glomerular filtration rate below 30ml/min, thiazides are not effective alone but may be used synergistically with loop diuretics. (Table V for dosages)

Patients should be advised to record their daily weight and if there is a consistent increase in weight of more than 2kg in 3 days, they may be advised to increase their diuretic dose until “dry weight” is regained. If the weight gain and symptoms worsen, the patient should seek medical help.

TABLE V: Diuretics Used In Heart Failure

	Route of Administration	Usual Daily Dose
LOOP DIURETICS • Frusemide • Bumetanide	IV / Oral IV / Oral	20 – 80mg 0.5 – 2mg
THIAZIDES • Hydrochlorothiazide • Chlorothiazide	Oral Oral	25 – 50mg 250 – 500mg
ALDOSTERONE ANTAGONISTS • Spironolactone • Eplerenone	Oral Oral	12.5mg – 50mg 25mg – 50mg

b) Angiotensin Converting Enzyme Inhibitors (ACEI)

I.A

ACEI improve survival and quality of life in all classes of HF^{2,3}. ACEI are first-line drugs for the treatment of HF and should be given to all patients in whom there is evidence of LV systolic dysfunction as reflected by an LV ejection fraction of <40%.

In the initiation of ACEI, the following steps are recommended:

- Care should be exercised in the following patients for whom referral to a specialist may be considered.

- SBP <100mmHg
- Creatinine >250 µmol/L

- Avoid excessive diuresis before treatment. If patients are on large doses of diuretics, the blood pressure and renal function should be monitored.
- Start with a low dose. Patients should not remain on the initial low dose indefinitely. The dose should be increased gradually to the target dose (Table VI) or maximum tolerated dose.
- Monitor blood urea, creatinine and serum potassium at 7-14 days, especially in patients with impaired renal function. If the rise in serum creatinine level is >20% compared to baseline, then ACEI therapy may need to be stopped.
- Avoid potassium sparing diuretics during initiation of therapy.
- Avoid non steroidal anti-inflammatory drugs

A number of different ACEI are available. The dose should be titrated up to the maintenance level as shown in Table VI.

Table VI: Recommended doses of ACEI used in HF

ACEI	Initiating Dose	Target Dose
Captopril	6.25 mg tid	50 mg tid
Enalapril	2.5 mg bid	10 mg bid
Lisinopril	2.5 mg daily	20 mg daily
Quinapril	2.5-5 mg daily	20 mg bid
Perindopril	2 mg daily	8 mg daily
Ramipril	1.25 - 2.5 mg daily	5 mg daily
Fosinopril	10 mg daily	20 mg daily

Major adverse effects of ACEI are:

- cough
- hypotension
- renal insufficiency
- hyperkalaemia
- angioedema

Flowchart II: Optimizing Drug Therapy in CHF

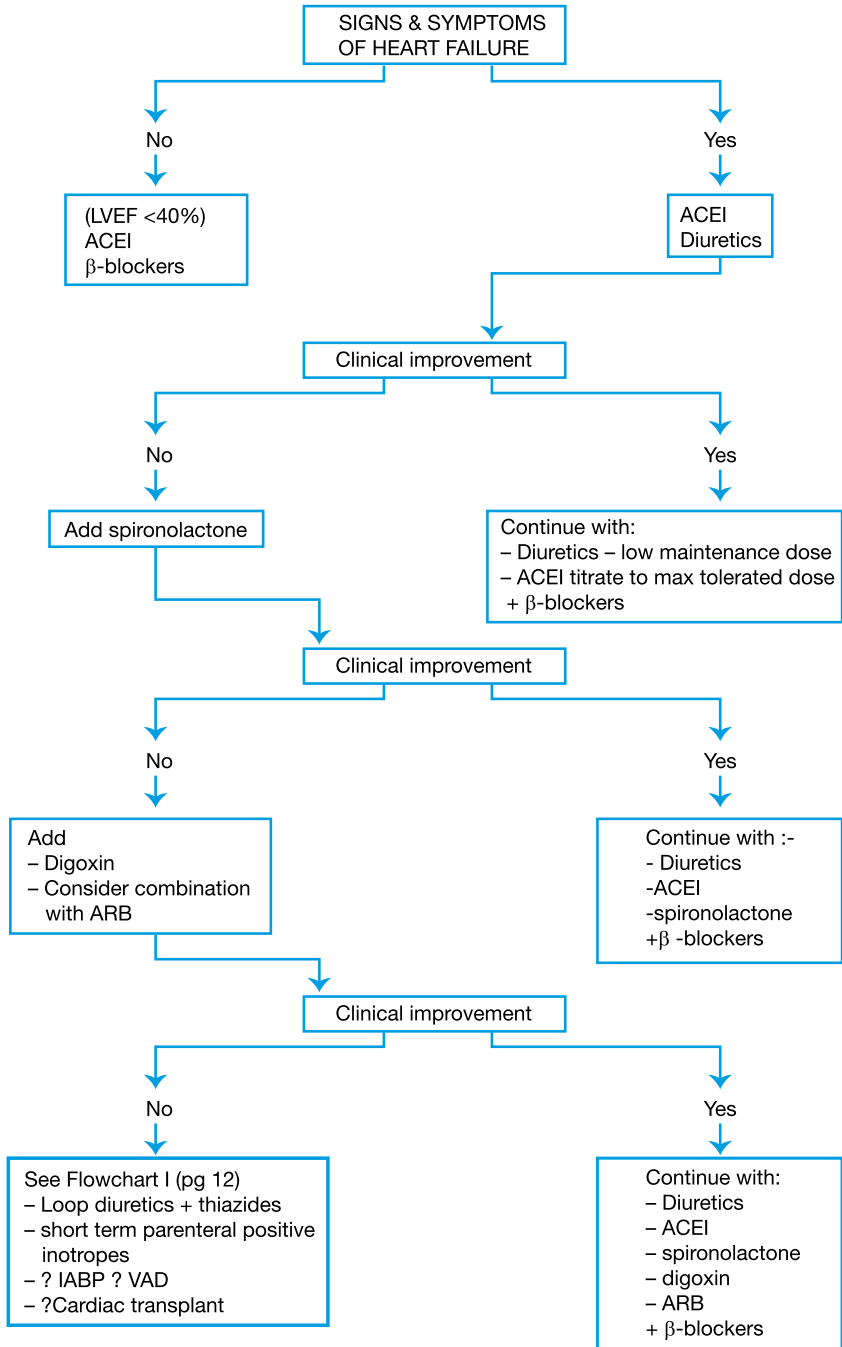


Table VII: Grading of Recommendations in the Management of CHF

Intervention	Grades of Recommendation	Level Of Evidence	Comments
INDICATED FOR FLUID RETENTION IN NYHA II – IV			
Diuretics	I	C	Not shown to improve survival.
INDICATED IN ALL PATIENTS			
ACEI	I	A	Improves survival and delays progression in all classes of HF
ARB	I	A	In ACEI intolerant patients
β-blockers	I	A	Improves survival and delays progression in all classes of HF
IN ADDITION TO THE ABOVE , THE FOLLOWING ARE INDICATED IN SELECTED PATIENTS			
ARB	I	B	In pts post MI and LVEF<40%, Valsartan shown to be comparable to captopril
Aldosterone antagonists (Spironolactone, Eplerenone)	I	B	Improves survival and reduces hospitalizations in moderate to severe HF and in post MI pts with mild HF
Digoxin	I	B	In pts with HF and AF
	IIa	B	No effect on survival. Reduces hospitalizations when added to optimal medical therapy
ACEI + ARB	IIb	B	Reduces hospitalizations when added to optimal medical therapy
ICD (implantable cardioverter defibrillator)	I	A	Improves survival in pts with resuscitated cardiac arrest, VF or sustained VT
	I	A	Improves survival in pts > 40 days post MI, LVEF ≤ 30%, on optimal medical treatment, and in NYHA II or III
	IIa	B	Improves survival in pts (no prior MI), LVEF ≤ 35%, on optimal medical treatment, and in NYHA II or III
CRT (cardiac resynchronization therapy)	I	A	Improves survival in pts on optimal medical treatment, in NYHA III, in sinus rhythm and who have cardiac dyssynchrony.

c) Angiotensin II Receptor Blockers (ARB)

- I.A In patients intolerant to ACEI, ARB should be considered^{57,58}.
- I.B In post MI patients with impaired LV function the ARB, Valsartan was found to be as effective as captopril⁵⁹. (Table VIII - pg 24)
- IIa.B In patients with severe HF the combination of ACEI and an ARB may be considered to reduce hospitalization due to HF^{58,60}.

Table VIII: Recommended doses of ARB in HF

ARB	Initiating Dose	Target Dose
Losartan	25 mg daily	50 –100 mg daily
Valsartan	40 mg daily	80 –160 mg bid
Candesartan	4 mg daily	16 – 32 mg daily

d) β -Blockers

- I.A Large clinical trials have shown that β -blockers reduce morbidity and mortality in patients with NYHA II–IV HF, of ischaemic and non-ischaemic aetiology, on standard therapy.⁶¹⁻⁶⁷
 β -blocker therapy should be initiated when pulmonary congestion is absent and the patient is clinically stable. All stable patients with current or prior symptoms of HF and reduced LV ejection fraction should be given β -blockers, unless contraindicated.
- IIb.B A recent trial indicated that initiating therapy with a β -blocker first is non-inferior to the standard approach of starting with an ACEI⁶⁴.
The benefits seen with both these drugs are additive.

In initiating β -blocker therapy the following should be considered:

- The initial dose should be low. (Table IX - pg 25)
- The dose should be slowly titrated upwards till target dose or maximum tolerated dose is achieved.
- Contraindications include the following:
 - acute HF
 - bronchial asthma or severe chronic obstructive airway disease
 - symptomatic bradycardia or hypotension
 - second or third degree heart block without a pacemaker
 - a requirement for beta agonist therapy or positive inotropic support

Patients who decompensate and are admitted in AHF may need reduction or temporary discontinuation of their β -blockers. After the patient has been stabilized and is no longer in overt HF, an attempt should be made to reinstitute β -blockers starting with low doses.

Table IX: Recommended doses of β -Blockers used in HF

β-Blockers	Initiating Dose	Target Dose
Carvedilol	3.125 mg daily	25 mg bid
Bisoprolol	1.25 mg daily	10 mg daily
Metoprolol succinate CR*	12.5 – 25 mg daily	200 mg daily

*Currently only metoprolol tartrate is available in Malaysia

e) Aldosterone Receptor Antagonists

The addition of spironolactone to ACEI, loop diuretics and digoxin in patients with severe HF reduces mortality and rehospitalization⁶⁸. Similarly, eplerenone, another aldosterone receptor antagonist, when added to β -blockers and ACEI has been shown to be beneficial when given to post MI patients with impaired LV function and mild HF⁶⁹. (Table V - pg 20)

I.B

I.B

Care should be exercised in patients with renal impairment. Serum potassium should be monitored regularly. Potassium supplements may need to be reduced or stopped. If hyperkalemia persists, then aldosterone receptor antagonists should be stopped.

f) Digoxin

Digoxin is indicated in patients with HF and atrial fibrillation⁷⁰.

I.B

Combination of digoxin and β -blockers is superior to either agent alone in patients with atrial fibrillation⁷¹.

Ila.B

In patients with HF and normal sinus rhythm, digoxin may be added if symptoms persist despite diuretics, ACEI, β -blockers and low dose spironolactone. Digoxin has no effect on mortality but reduces hospitalization^{72,73,74}.

Ila.B

No loading dose is usually required for CHF. The usual maintenance dose of digoxin is 0.125mg to 0.25mg daily. Lower doses should be used in the elderly and in patients with impaired renal function. Current data indicates that lower doses of digoxin and lower levels of serum digoxin (0.5 – 0.8 ng/ml) are efficacious and appear adequate in most patients with compensated HF^{75,76}.

g) Anti-Coagulation Therapy

Heart failure patients with the following risk factors for thromboembolism should be anti-coagulated with warfarin unless there are contraindications:

- I.A – atrial fibrillation^{77,78}
- IIa.C – intracardiac thrombus (except for organized mural thrombus)
- IIa.C – past history of thromboembolic episode(s)

h) Other Concurrent Therapies

- III.A Calcium channel blockers are not recommended for the treatment of HF due to systolic dysfunction^{79,80}.
- IIa.B Second generation dihydropyridines calcium channel blockers such as amlodipine or felodipine may be considered for the treatment of concurrent hypertension and angina^{81,82}.

i) Anti – Arrhythmic Drug Therapy

Arrhythmias are common in HF. The more common ones are:

- atrial fibrillation
- ventricular tachyarrhythmias
- bradyarrhythmias

- I.A Atrial fibrillation is a common problem among patients with HF. All patients with atrial fibrillation should be anti-coagulated with warfarin unless contraindicated^{77,78}. These patients can be managed by either rate control or rhythm control. Rate control can be achieved by using either:
 - I.B • β -blockers^{71,83} and/ or
 - I.B • digoxin⁷⁰.
- IIb.C Rhythm control can be achieved by elective cardioversion after a period of anticoagulation.
- IIa.C Sinus rhythm can be maintained by using amiodarone.

Studies show that 40 – 50% of deaths in HF are sudden^{5,84}, the risk increasing with the severity of HF. This is most often due to either sustained ventricular tachycardia (VT) or ventricular fibrillation (VF) although sometimes it may be due to a bradyarrhythmia or electromechanical dissociation^{85,86}. Occasionally rapid supraventricular tachycardias may give rise to malignant ventricular tachyarrhythmias⁸⁷.

The following medications have been shown to reduce the incidence of sudden death in addition to the other benefits discussed earlier:

- **β-blockers:** These agents were shown to reduce sudden death in the clinical trials done on post MI patients as in the HF trials^{88,89} **I.A**
- **Aldosterone antagonist, eplerenone:** In post MI patients with impaired LV function and mild HF, eplerenone reduced the incidence of sudden death⁶⁷. **I.B**
- **ACEI:** A meta-analysis of trials done following MI patients showed that ACEI reduced sudden cardiac death⁹⁰. Most of these patients had impaired LV function. **I.A**
- **Statins** in atherosclerotic heart disease: Patients with implantable cardioverter defibrillators (ICD) and on statins had fewer episodes of malignant ventricular tachyarrhythmias^{91,92}. **IIb.B**

In patients with ventricular tachyarrhythmias, the following are important:

- Identify contributing factors such as electrolyte disturbances, ischemia and drugs. **I.C**
- Implantable cardioverter defibrillator can be considered in selected patients.(section 7.2.3 - pg 28) These have been found to improve survival both as secondary prevention^{93,94} and as primary prevention^{95,96} in selected patients. **I.A**
- Anti-arrhythmic drug therapy with amiodarone can be considered as adjunctive therapy in patients with ICD to reduce the number of shocks and in patients who are not candidates for ICD. **I.C**

Patients with significant bradyarrhythmias, trifascicular blocks and high-degree AV blocks should be considered for pace-maker therapy. **I.C**

j) Refractory Cardiac Failure

Most patients will respond to the management outlined above. When increasing medication to the target dose or maximally tolerated dose, a SBP >90mmHg is generally acceptable if the patient feels well and has no giddiness. Some patients however will still be symptomatic despite optimal treatment with diuretics, ACEI and / or ARB, β-blockers, spironolactone and digoxin. When patients become refractory to therapy, hospital admission is usually indicated. Meticulous control of fluid balance is important in these patients. Aggravating causes of HF as listed in Table IV - pg 16 should be identified and treated.

The following may be considered :

- **Furosemide infusion.** These patients may require combination loop diuretics and thiazides. **IIb.C**
- **Ultrafiltration** in patients who are fluid overloaded⁹⁷. In most patients, however, the relief is temporary. **IIb.C**

IIb.C

- **Short term infusions of parenteral inotropes** – low dose dobutamine (5ug/kg/min) or milrinone. These produce symptomatic improvement but no survival benefit has been demonstrated.⁹⁸⁻¹⁰¹

The prognosis of these patients are poor. They should be referred to a HF program with expertise in the management of refractory HF to assess whether they may be potential candidates for device therapy or heart transplantation.

7.2.3 DEVICE THERAPY IN HEART FAILURE

a) Cardiac Resynchronization Therapy (CRT)

Patients who remain persistently symptomatic despite optimal medical therapy should be considered for CRT with a bi-ventricular pacemaker if there is evidence of left ventricular dyssynchrony.

Selection criteria for Biventricular Resynchronization Pacing include:

- sinus rhythm
- LV ejection fraction <35% with LV dilatation >5.5 cm
- a widened QRS interval (>120 ms) on the resting ECG

I.A Cardiac Resynchronization Therapy has been shown to improve symptoms, hospitalizations and mortality, though up to 30% of patients may not respond to this treatment¹⁰²⁻¹⁰⁶.

Documentation of mechanical dyssynchrony using the echocardiogram is likely to improve response rate to this therapy.

b) Implantable Cardioverter Defibrillator (ICD)

Sudden death due to sustained ventricular fibrillation or ventricular tachycardia can be decreased by the use of an ICD. An ICD can be implanted as secondary prevention in patients with previous cardiac arrest or documented sustained ventricular arrhythmias^{93,94}. It may also be used as primary prevention to reduce the risk of sudden cardiac death in patients with HF who are at risk of these malignant arrhythmias^{95,96}. An ICD should be considered in patients who fulfill the eligibility criteria and who otherwise have good clinical function and prognosis, to improve their survival.

Secondary prevention:

The following should be considered for implantation of ICD:

- I.A • Patients resuscitated from sudden cardiac arrest due to ventricular fibrillation or haemodynamically unstable sustained ventricular tachycardia (provided that it is not associated with acute MI or ischemia)^{93,94}. These cardiac arrest survivors have a high risk of recurrent events and implantation of an ICD has been shown to reduce mortality.

- Patients with chronic HF and a low EF who experience syncope of unclear origin have a high rate of subsequent sudden death and should also be considered for placement of an ICD. **IIb.C**

Primary prevention (prophylactic ICD implantation):

Prophylactic ICD implantation to reduce the risk of sudden death may be reasonable in patients:

- with prior MI and LVEF <30% at least one month after an MI and 3 months after revascularization by PCI or CABG, when appropriate^{95,107}. **I.A**
- with LVEF <35% and mild to moderate HF symptoms (NYHA II–III)⁹⁶. **IIa.B**

The decision regarding the balance of potential risks and benefits of ICD implantation for an individual patient remains complex.

c) Combined Biventricular Pacing with ICD Capabilities

This can be considered in patients who fulfill the criteria for biventricular pacing implant (symptomatic heart failure with LVEF <35% and ventricular dysynchrony with QRS duration >120ms) to reduce mortality and morbidity^{103,108}. **IIa.B**

7.2.4 SURGERY

Patients with HF should undergo surgery if the pathology causing the HF is amenable to surgical treatment. **I.C**

However the decision to subject a patient to surgery should take into account the functional status, prognosis and comorbid conditions of the patient.

Surgical procedures include the following:

a) Revascularization Procedures

There is no data from randomized trials to support the use of revascularization surgery for the relief of symptoms due to HF. Revascularization is not recommended as routine management of patients with coronary artery disease and HF. Operative mortality in these patients is also high¹⁰⁹. **III.C**

Coronary revascularization (by either coronary artery bypass surgery or PCI) should be considered in patients with HF and suitable coronary anatomy if they have:

- refractory angina or acute coronary syndrome, for relief of symptoms. **IIa.C**
- significant inducible ischemia and/or large areas of hibernating myocardium. **IIa.C**

Myocardial ischemia and viability should be demonstrated by tests such as dobutamine stress echocardiography, radionuclide myocardial perfusion scan or cardiac magnetic resonance imaging.

b) Valve Surgery

IIb.C Patients with HF and severe mitral regurgitation may have symptomatic improvement after mitral valve surgery (valve repair or replacement).

Patients with LV systolic dysfunction undergoing surgical coronary revascularization who also have moderate to severe mitral regurgitation secondary to ventricular dilatation may be considered for concomitant mitral valve repair or replacement.

c) LV Reduction Surgery

I.C LV aneurysmectomy is indicated in patients with a large discrete LV aneurysm who develop HF, angina pectoris, thromboembolism, and tachyarrhythmias due to the aneurysm.

IIb.C Patients with HF undergoing surgical coronary revascularization, who have areas of LV dyskinesia or akinesia may be considered for concomitant LV reduction surgery. The benefit of LV reduction surgery is being assessed in on-going trials.

d) LV Assist Devices

IIa.B Left ventricular assist devices have been used to bridge patients with HF to heart transplantation, to support patients with acute severe myocarditis with a view to recovery, and in some patients for permanent haemodynamic support ⁵⁵.

Patients awaiting heart transplantation who have become refractory to all means of medical circulatory support should be considered for a mechanical support device as a bridge to transplant.

7.2.5 HEART TRANSPLANTATION

I.C Heart transplantation is currently the only established surgical approach to the treatment of refractory HF but it is limited by the lack of donor organs.

Patients with severe HF despite optimal medical therapy, and who meet the eligibility criteria, should be considered for heart transplantation and referred for further evaluation.

Indicators of severe HF and consideration for heart transplantation include:

- Poor LVEF (<25%)
- Recurrent admissions or major limitation of the patient's daily activities
- Poor effort tolerance i.e. peak VO_2 less than 10 ml per kg per min with achievement of anaerobic metabolism
- iv inotropic dependence.

Contraindications to cardiac transplantation include any malignancy within 5 years, diabetes mellitus with widespread microvascular complications, chronic kidney, liver or lung disease, pulmonary hypertension, or other medical or psychosocial issues that would impact survival.

**Recommendations for the Management of CHF:
(Refer Flowchart II - pg 22 and Table VII - pg 23)**

	<u>Grade</u>
• Diuretics started if there are signs and symptoms of fluid retention.	I.C
• ACEI initiated and titrated to target dose or maximum tolerated dose.	I.A
• If the patient is intolerant of ACEI, consider use of ARB.	I.A
• Begin small doses of β -blockers and titrate slowly to maximal tolerated dose.	I.A
• In patients with severe HF on diuretics, ACEI and β -blockers, add spironolactone.	I.B
• Add digoxin, especially if symptoms are persistent.	IIa.B
• Alternatively an ARB may be added if symptoms are still present.	IIb.B
• For persistent signs of congestion or failure to maintain weight despite adequate dosage of loop diuretics, add a thiazide diuretic.	I.C
• Patients with persistent symptoms of HF despite the aforementioned treatments should be admitted and considered for intravenous diuretics with or without intravenous inotropic treatment.	IIb.C
• Patients with persistent symptoms despite optimal medical therapy should be considered for CRT.	I.A
• ICD should be implanted as secondary prevention in patients with resuscitated cardiac arrest and haemodynamically unstable VT.	I.A
• Heart transplantation should be considered in eligible patients who fail to respond to medical therapy.	I.C

7.3 SPECIAL GROUPS

7.3.1 Asymptomatic Left Ventricular Dysfunction

Asymptomatic patients with Left Ventricular Systolic Dysfunction (LVEF <40%) carry substantially higher risk for subsequent morbidity and mortality than the general population. The goals of treatment in these patients would be

- to slow down the progression of the disease
- prevent the development of symptoms of HF
- to improve survival

Management involves:

- Identifying patients at greatest risk of developing LV systolic dysfunction. These include patients with:
 - previous myocardial infarction
 - systolic and diastolic hypertension
 - LVH on ECG
 - diabetes mellitus and/or impaired glucose tolerance
 - metabolic syndrome
 - thyroid disorders.

Echocardiography would be helpful in assessing LV function in these high risk patients.

I.C Wherever possible, the underlying disease should be treated appropriately to prevent the development of HF.

- Drug therapy. This includes:

I.A – **ACEI**: Long term treatment with an ACEI has been shown to delay the onset of symptoms of HF and decrease the combined risk of death and hospitalization^{3,110}

I.B – **ARB**: There has been no study of the use of ARB in patients with asymptomatic left ventricular dysfunction. The ARB, Valsartan, may be an alternative in post MI patients who cannot tolerate an ACEI⁵⁹.

I.A – **β-blockers**: Controlled clinical trials of β-blockers in this subset of patients are lacking. In post MI patients and in those with coronary artery disease, β-blockers are recommended. They may be considered in all patients with LVEF<40%^{25,62,111}

III.C – **Diuretics and digoxin**: There is no role for these agents in this group of asymptomatic patients.

III.C – **Calcium Channel Blockers**: The use of calcium channel blockers with negative inotropic effects is not recommended in asymptomatic post MI patients with LVEF <40%¹¹².

- **Statins:** This has been shown to reduce coronary events in patients with coronary artery disease^{41,42,43} I.A

Key Message for the Management of Asymptomatic LV Dysfunction:

- Identify patients who are at high risk of developing LV dysfunction and treat the underlying disease appropriately
- ACEI and β -blockers (post MI) have been shown to slow down the onset of symptoms and reduce cardiac morbidity.

7.3.2 Heart Failure with Preserved Left Ventricular Systolic Function

Recent epidemiological studies suggest that as high as 35 – 45% of elderly patients hospitalized with HF have preserved LVEF^{11,113}. Commonly, these patients are women who have hypertension, diabetes mellitus, coronary artery disease and / or atrial fibrillation.

HF with preserved LVEF is commonly due to LV diastolic dysfunction. This can be demonstrated by echocardiography.

Causes of heart failure due to diastolic dysfunction includes:

- Myocardial ischemia
- Hypertension
- Myocardial hypertrophy
- Myocardial/pericardial constriction

Management of these patients includes:

- Identifying and treating the underlying cause(s) appropriately. I.C
Tachyarrhythmias should be treated and sinus rhythm restored I.C whenever possible.
- Pharmacological treatment

Limited controlled trial data exists in this group of patients. Treatment options include:

- **Diuretics:** These are necessary to control pulmonary congestion and peripheral edema but should be used cautiously so as not to lower preload excessively and thereby reduce stroke volume and cardiac output. I.C
- **β -blockers:** This could be given to lower heart rate and increase the diastolic filling period. IIa.C

Ila.C

– **Verapamil and diltiazem:** These may be used to lower the heart rate and has been shown to be beneficial in these patients¹¹⁴. Verapamil has been shown to improve functional capacity in patients with hypertrophic cardiomyopathy.¹¹⁵

Ila.B

– **ARB** have been shown to reduce hospitalization ¹¹⁶

Ilb.C

– **ACEI** may improve relaxation and cardiac distensibility directly and may have long term activity via their antihypertensive action and regression of hypertrophy and fibrosis. There is however no trial data.

Key Message for the Management of HF with preserved LV Function:

- Identify and treat the underlying cause
- Diuretics help to control pulmonary congestion and edema.
- β -blockers and calcium antagonists have also been shown to be helpful.

7.3.3 Heart Failure in Pregnancy

About 0.5 – 4% of pregnant women have cardiac disease¹¹⁷. Common causes of HF in pregnancy are hypertension, eclampsia, undetected valvular heart disease especially mitral stenosis, congenital heart disease, and occasionally peripartum cardiomyopathy. Peripartum cardiomyopathy occurs in 1:3,000 live births in Malaysia¹¹⁸.

Normal haemodynamic changes that occur in pregnancy are:

- Cardiac output increases by 30–50% during normal pregnancy.
- Cardiac output increases to 80% above baseline during labour and delivery.
- Haemodynamic changes return to baseline 2 – 4 weeks after vaginal delivery and up to 6 weeks after caesarian delivery.

In women with heart disease, these changes may have a deleterious effect on their cardiovascular system and precipitate HF. Most forms of cardiac disease can be detected by physical examination, ECG and an echocardiogram.

Maternal prognosis during pregnancy is related to functional class and type of cardiac disease. Patients with pulmonary hypertension have a very high mortality.

In the management of HF in Pregnancy, the following issues need to be

considered:

- gestational age at presentation
- clinical presentation, either as AHF or CHF
- response to medical therapy
- potential maternal and foetal risks
- timing and mode of delivery

Pregnant Women with HF should be managed by a multidisciplinary team consisting of physicians, obstetricians and paediatricians. Management involves:

- **Non pharmacological measures**

The management of patients with mild symptoms consists mainly of non-pharmacological measures such as:

- limiting strenuous exercise
- adequate rest
- maintaining a low salt diet
- treating anemia and infections early
- frequent antenatal examinations

- **Pharmacological Measures**

The following drugs may be used in the pregnant patient with HF.

- **Nitroglycerine** can be used in pregnancy for after load reduction. **IIa.C**
- **Digoxin** is safe in pregnancy and during breast feeding. **IIa.C**
- **Diuretics** may be used for preload reduction. No teratogenic effects of diuretics have been described. However diuretics impair uterine blood flow particularly placental perfusion. Thus diuretics must be used with caution. **IIa.C**
- **β-blockers** may result in intrauterine growth retardation, apnea at birth, fatal bradycardia, hypoglycaemia and hyperbilirubinemia. Thus these should be used with caution. **IIb.C**
- **ACEI and ARB** are contraindicated in pregnancy. **III.C**

7.3.4. Heart Failure in Infants and Children

Heart failure is an important condition among infants and children. The common causes are congenital heart disease, systemic diseases (such as acute rheumatic carditis and viral myocarditis), cardiomyopathy, tachyarrhythmia and post cardiac surgery. Regardless of the etiology, timely diagnosis and effective treatment are important in preventing short-term and long-term sequelae. This section will focus on the management of HF due to congenital heart disease.

Congenital heart defects leading to HF in infants and children may be due to volume or pressure overload. (Table X)

Clinical Presentation

Clinical presentation varies from mild to severe HF requiring ventilatory support. The most common congenital causes of HF can be easily classified based on age of presentation as in Table XI - pg 37. Clinical symptoms of HF include poor feeding, tachypnea, poor weight gain and failure to thrive. Older children may complain of shortness of breath on exertion. Signs of HF include respiratory distress, tachycardia, weak and thready pulse, gallop rhythm, lung crepitations and hepatomegaly.

Table X: Congenital Heart Diseases That May Cause HF in Infants And Children

Volume overload

- Ventricular septal defect
- Patent ductus arteriosus
- Atrioventricular septal defect
- Large arterio-venous fistula
- Transposition of the great arteries with ventricular septal defect
- Truncus arteriosus
- Total anomalous pulmonary venous drainage

Pressure overload

- Severe aortic stenosis
- Coarctation/interrupted aortic arch
- Critical pulmonary stenosis

Table XI : Common Causes of HF Based on Age of Presentation

1. First week of life

- Transposition of the great arteries with ventricular septal defect
- Obstructed total anomalous pulmonary venous drainage (TAPVD)
- Hypoplastic left heart syndrome
- Large systemic A-V fistulas
- PDA in premature infants
- Critical aortic stenosis

2. First one month

- Transposition of the great arteries with ventricular septal defect
- Coarctation of the aorta with associated lesions
- Critical aortic stenosis
- Large left to right shunt in premature infants (VSD, PDA)
- TAPVD, systemic A-V fistula, transposition of the great arteries

3. First 6 months

- Large left to right shunts
 - Ventricular septal defect
 - Patent ductus arteriosus
 - Atrioventricular septal defect
 - Truncus arteriosus
- Anomalous left coronary artery from the pulmonary artery (ALCAPA)

Clinical Investigations

- **ECG:** Is useful to determine the type of structural cardiac lesion but not helpful in deciding whether heart failure is present.
- **Chest X-ray:** May be pathognomonic for certain cardiac lesions. The absence of cardiomegaly almost rules out heart failure.
- **Echocardiography:** Would help to determine the structural cause of heart failure and to assess cardiac function.

Management

The management of HF consists of:

- general measures
- drug therapy
- definitive transcatheter/surgical measures

a) General measures:

These include:

- Oxygen
- Correcting acidosis, hypoglycemia, hypocalcaemia and anaemia
- Treating respiratory infections aggressively
- Nasogastric tube feeding to reduce feeding effort and prevent aspiration in neonates
- gastroesophageal reflux needs to be treated aggressively

b) Drug Therapy:

- **Loop diuretics** are the main stay of treatment in patients with volume overload conditions such as left to right shunts and/or pulmonary congestion. Diuretics should be used with caution if HF is not due to vascular congestion.
 - furosemide 1 – 4 mg/kg/day
- **Digoxin** – It is mainly used in patients with impaired ventricular function. Its role in the management of HF due to left to right shunts is unclear.
 - Digoxin 10 µg/kg/day (daily or divided doses)
- **Afterload – reducing agents** – Captopril and enalapril improve haemodynamics and HF symptoms. Use with caution in neonates, starting with low doses
 - Captopril 0.1 – 1.0mg/kg/dose (1 – 3 times per day)
 - Enalapril 0.1 – 0.5mg/kg/dose (daily dose)
- **Inotropic agents** – Norepinephrine, dopamine, dobutamine used as inotropes in the setting of acute decompensated HF. These drugs are less effective in neonates compared to infants and children because neonates have a higher level of sympathetic activity.
 - Milrinone – This has vasodilatory effects in the systemic and pulmonary vascular beds, making it ideal for the management of HF in the post operative period. It does not interact with β -blockers and thus does not cause tachycardia, increase myocardial O_2 consumption and increase after load.

c) Definitive transcatheter/surgical intervention

- Transposition of the great arteries with ventricular septal defect
 - Elective arterial switch surgery within the first 3 months of age
- Patent ductus arteriosus
 - Ventilator dependent: Surgical ligation regardless of age and body weight
 - Non ventilator dependent: Optimise antifailure therapy and elective surgical

ligation or transcatheter occlusion

- Total anomalous pulmonary venous drainage
 - Obstructed: Urgent surgical correction
 - Unobstructed: Early surgical correction
- Obstructive lesions (Aortic stenosis, pulmonary stenosis)
 - critical stenosis: Urgent relief of obstruction after stabilization
 - severe stenosis: Early relief of the obstructive lesion
- Coarctation of the aorta
 - Infants less than 3 months: Surgical correction
 - Infants more than 3 months: Balloon dilatation
- Large septal defects
 - Ventilator dependent: Surgical intervention
 - Non ventilator dependent: Optimize antifailure therapy and elective surgical closure
- Truncus arteriosus
 - Elective surgery within the first 3 months of life
- Anomalous left coronary artery from the pulmonary artery (ALCAPA)
 - Early surgery

8. CARDIOLOGY REFERRAL

Most stable patients with HF can be managed by family care physicians and GP's. We suggest referral to a cardiologist in the following situations:

- At initial presentation to confirm the diagnosis, determine the underlying cause of the HF and to advise revascularization or surgery as indicated.
- During episodes of acute decompensation.
- When symptoms are recurrent or difficult to control.
- In the presence of acute coronary syndrome to determine the need for revascularization or surgery.
- In cases of near faints, syncope, resuscitated sudden death and significant arrhythmias.
- Pregnant women with complex cardiac lesions and/or Eisenmenger's syndrome.
- Infants and children with HF.

9. CURRENT AND FUTURE DEVELOPMENT

Major studies evaluating Inhibitors of Neural Endopeptidase (NEP) and Endothelin Converting Enzyme (ECE) have been disappointing. Use of vasopressin receptor antagonists appears promising for control of fluid balance in AHF. Intermittent nesiritide and levosimendan infusions may also be useful in AHF.

Echocardiography, particularly tissue Doppler studies, may play a bigger role in helping to select patients and predicting clinical response to CRT. The effectiveness of CRT in patients with right bundle-branch block, atrial fibrillation, minor conduction abnormalities and pacemaker dependence needs to be further elucidated in future studies.

Newer devices and techniques under investigation include the use of implantable haemodynamic monitors and external counterpulsation. Mechanical assist devices are becoming smaller and the use of transcatheter energy transfer may reduce the risk of infection with these devices.

The role of cell therapy (stem cell, mesenchymal and myoblasts) in HF is being addressed in a number of on-going studies.

APPENDIX I

THE NEW YORK HEART ASSOCIATION FUNCTIONAL CLASSIFICATION

Class		1 Year Mortality
CLASS I	No limitation. Ordinary physical activity does not cause undue fatigue, dyspnoea or palpitation.	5 – 10%
CLASS II	Slight limitation of physical activity. Such patients are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnoea or angina.	10 – 15%
CLASS III	Marked limitation of physical activity. Although patients are comfortable at rest, less than ordinary activity will lead to symptoms.	15 – 20%
CLASS IV	Inability to carry on any physical activity without discomfort. Symptoms of congestive failure are present at rest. With any physical activity, increased discomfort is experienced.	20 – 50%

APPENDIX II:

IMPORTANT DRUG INTERACTIONS WITH HEART FAILURE MEDICATIONS

Non-Steroidal Anti-inflammatory Drugs (NSAID)	These cause vasoconstriction, fluid retention and renal dysfunction. The latter is more likely to occur in the presence of ACEI. NSAIDs should not be prescribed to patients in HF unless absolutely necessary.
Calcium Channel Blockers (CCB)	Short-acting nifedipine and diltiazem depress myocardial contractility.
Tricyclic Antidepressants	These may impair cardiac contractility and increase vulnerability to arrhythmias. If indicated, a selective serotonin reuptake inhibitor may be preferable.

APPENDIX III:

SALT CONTENT IN COMMON MALAYSIAN FOODS

CONTENT OF SODIUM IN FOODS			
Low Content	Moderate Content	High Content	
Fruit	Meat	Flavouring Agents	Sauces :Soya
Vegetables	Fish Egg		Tomato
Pure Oil	Milk		Barbeque
Natural Fats			Tauchloh
Sugar		Extract	Vegetable (Marmite)
Plain Flour			Meat (Bovril)
Rice		Enhancers	Monosodium Glutamate
Most Cereals			Flavouring cubes
Legumes		Rising Agents	Bicarbonate of Soda
Nuts			Baking Powder
		Dressing	Salad Cream
			Mayonnaise
		Processed Food	Tinned or Canned Food
			• Salted Crisps
			• Salted Nuts
			• Cheese
			• Packed Soup
			• Raising Agents
		Preserved Food	Salted Fish / Eggs
			Cured Meat
			Preserved Sausages
			Vegetables/Fruits
			Belacan
		Medication	Effervescent Salts
			Bicarbonate Powder

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ACKNOWLEDGEMENTS

The committee would like to thank the following for their patience, time and effort :

- Technical Advisory Committee, Clinical Practice Guidelines, Ministry of Health

- Panel of experts who reviewed the draft

DISCLOSURE STATEMENT

None of the members of the Expert Committee had any potential conflicts of interest to disclose.

SOURCES OF FUNDING

This CPG was made possible by an educational grant from Novartis, Malaysia

