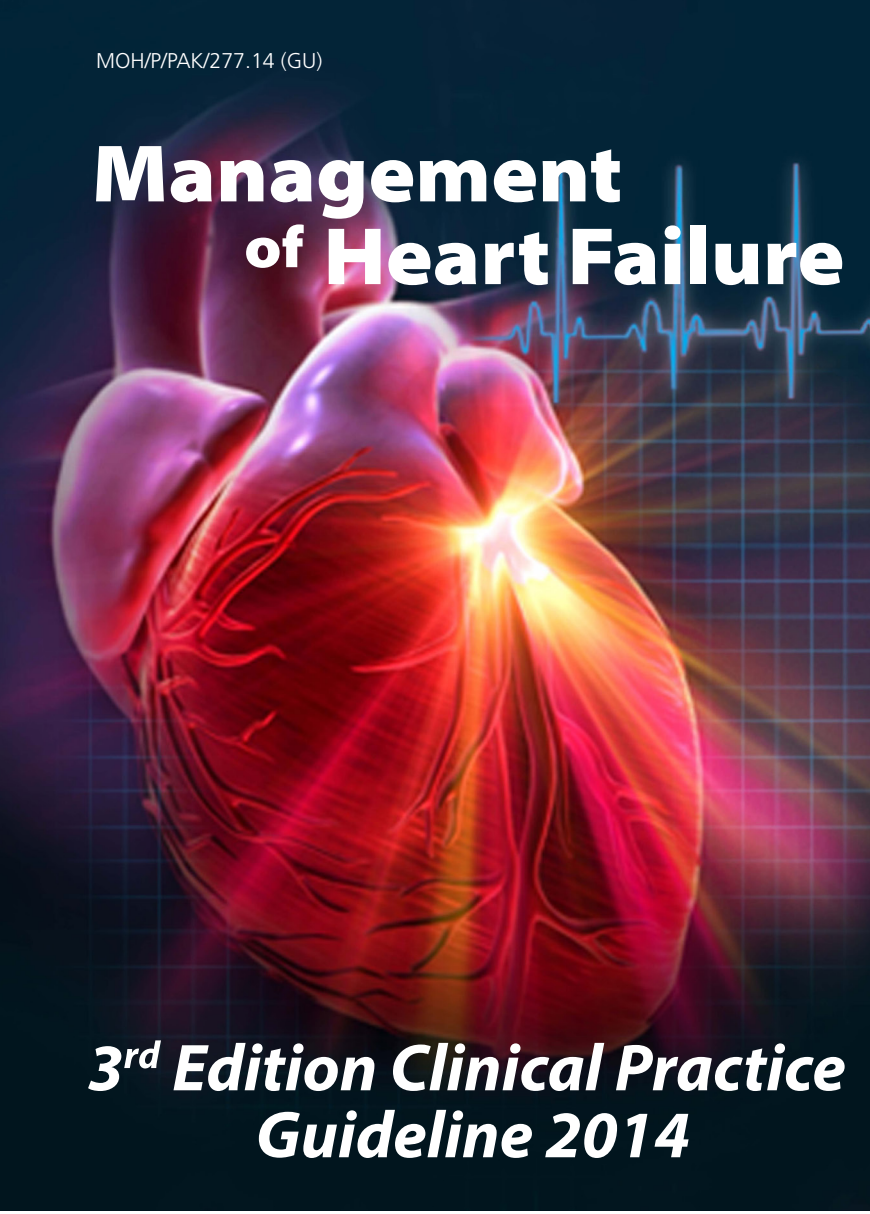
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Management of Heart Failure



3rd Edition Clinical Practice Guideline 2014

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 2014 and will be reviewed in 5 years or sooner if new evidence becomes available.

CPG Secretariat
c/o Health Technology Assessment Unit
Medical Development Division
Ministry of Health Malaysia
4th Floor, Block E1, Parcel E
62590, Putrajaya.

Electronic version available on the following website:
http://www.moh.gov.my http://wwtttamed.org.my

This is an update to the Clinical Practice Guidelines on Heart Failure (published 2000 and 2007). This CPG supersedes the previous CPG's on Heart Failure (2000,2007).

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. With ageing of the population, the prevalence of heart failure is expected to increase. Thus the publication of this Clinical Practice Guidelines on Heart Failure by the National Heart Association of Malaysia, Academy of Medicine and Ministry of Health is important and timely.

This Guidelines updates all health care providers on the latest developments in the field of Heart failure. This is the 3rd edition of the Clinical Practice Guidelines. As in previous editions, 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 to 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.

Datuk Dr. Noor Hisham Abdullah
(Director General of Health Malaysia)

Members Of The Expert Panel

Chairperson:

Dr. Jeyamalar Rajadurai — *Consultant Cardiologist, Subang Jaya Medical Center*

Members
(in alphabetical order)

Dr. David Chew — *Consultant Cardiologist, Institute Jantung Negara*

Dr. Hasri Samion — *Consultant Paediatric Cardiologist, Institute Jantung Negara*

Dr. Kannan Pasamanickam — *Consultant Cardiologist, Subang Jaya Medical Center*

Dr. Mohd Rahal Yusof — *Specialist in Internal Medicine, Hospital Kuala Lumpur*

Dr. Nik Mazlina binti Mohammad — *Family Medicine Specialist, Klinik Kesihatan Kajang*

Dr. Robaayah Zambahari — *Senior Consultant Cardiologist, Institute Jantung Negara*

Dr. Sim Kui Hian — *Consultant Cardiologist, Pusat Jantung Hospital Umum Sarawak*

Dr. Sree Raman — *Senior Consultant Physician, Tuanku Ja'afar Hospital Seremban*

Dr. Wan Azman Wan Ahmad — *Consultant Cardiologist, Pusat Perubatan Universiti Malaya*

List Of External Reviewers
(in alphabetical order)

Dr. Aris Chandran *Senior Consultant Physician, Hospital Raja Permaisuri Bainun Perak*

Dr. Alan Fong *Consultant Cardiologist, Pusat Jantung Hospital Umum Sarawak*

Dr. Nik Sherina *Famliy Medicine Specialist, Rawatan Utama Pusat Perubatan Universiti Malaya*

Dr. Mimi Omar *Family Medicine Specialist, Klinik Kesihatan Kelana Jaya Kuala Lumpur*

Dr. Wong Kai Fatt *General Practitioner, Klinik Tan Kuala Lumpur*

Dr. Santha Kumari *Senior Consultant Physician, Hospital Tengku Ampuan Rahimah Selangor*

Dr. Liew Houng Bang *Consultant Cardiologist, Hospital Queen Elizabeth II Sabah*

Dr.Mohd Nizam Mat Bah *Consultant Paediatric Cardiologist, Hospital Sultanah Aminah Johor*

Dr. Hung Liang Choo *Consultant Paediatrician & Paediatric Cardiologist Paediatric Institute Hospital Kuala Lumpur*

Rationale and Process of Guidelines Development

Cardiovascular disease is an important cause of morbidity and mortality in Malaysia. Heart Failure (HF), 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. With aging of the population the prevalence of HF is expected to increase.

The 1st Clinical Practice Guidelines (CPG) in HF was published in 2000 with the 2nd edition in 2007. This current document is an update of the last edition. Since then, there have been many new developments in this field. Thus the publication of this 3rd edition is timely.

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

Objectives:

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

- the prevention of HF
- the diagnosis and treatment of HF
- reducing the morbidity associated with the condition and improving the quality of life of these patients
- improving survival of patients with HF

Process:

The previous CPG published in 2007 was used as a base. In addition to the previous clinical questions that needed to be updated, the Expert Panel formulated new questions that needed to be addressed. These clinical questions were then divided into sections and each member was assigned one or more topics.

A review of current medical literature on HF from 2007 (the date of the last CPG) till 30thSeptember 2013 was performed. Literature search was carried out using the following electronic databases – PubMed and Cochrane Database of Systemic Reviews.The following MeSH terms or free text terms were used either singly or in combination:

"Heart Failure", "Congestive cardiac failure", "Acute Heart Failure, "Chronic Heart Failure" "Right heart failure", "left heart failure", [MeSH], "Heart Failure Reduced Left Ventricular Function" , Heart Failure Preserved Left Ventricular Function"[MeSH]

The search was filtered to clinical trials and reviews, involving humans and published in the English language. The relevant articles were carefully selected from this huge list. In addition, the reference lists of all relevant articles retrieved were searched to identify further studies.Experts in the field were also contacted to obtain further information. International guidelines on HF-the American Heart Association/American College of Cardiology and European Society of Cardiology - were also studied. All literature retrieved were appraised by members of the Expert Panel and all statements and recommendations made were collectively agreed by the group. The grading of evidence and the level of recommendation used in this CPG was adapted from the American College of Cardiology/ American Heart Association and the European Society of Cardiology (pg 6).

After much discussion, the draft was then drawn up 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.

Clinical Questions Addressed:

- How do you make a diagnosis of HF?
- Who are individuals at high risk of developing HF and how do you prevent them from developing HF?
- How do you treat acute and chronic HF effectively using current knowledge and available resources?
- How do you prevent recurrent admissions for acute decompensated HF
- How do you treat the following special groups?
  - the asymptomatic individual with reduced left ventricular (LV) function.
  - the individual with HF due to preserved LV function
  - the pregnant patient with HF
  - infants and children with HF
  - the individual with refractory and terminal HF

Target Group:

This CPG is directed at all healthcare providers treating patients with HF - general practitioners, general and family physicians, both adult and paediatric cardiologists and obstreticians.

Target Population:

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

Dr. Jeyamalar Rajadurai
Chairperson

Levels of Evidence and Grades of Recommendations

Grades Of Recommendation	
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, case studies or standard of care

Levels Of Evidence	
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.

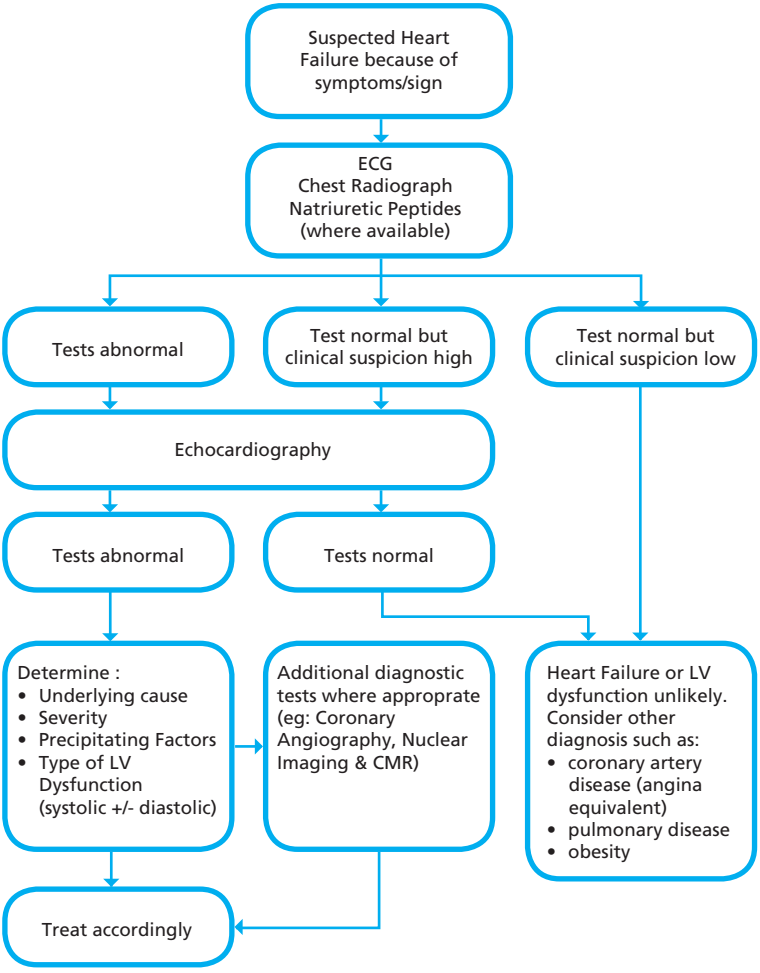
Adapted from the American Heart Association and the European Society of Cardiology

(Available at: http://assets.cardiosource.com/Methodology_Manual_for_ACC_AHA_Writing-_Committees and at http://www.escardio.org/guidelines-surveys/escguidelines/about/Pages/rules-writing.aspx).

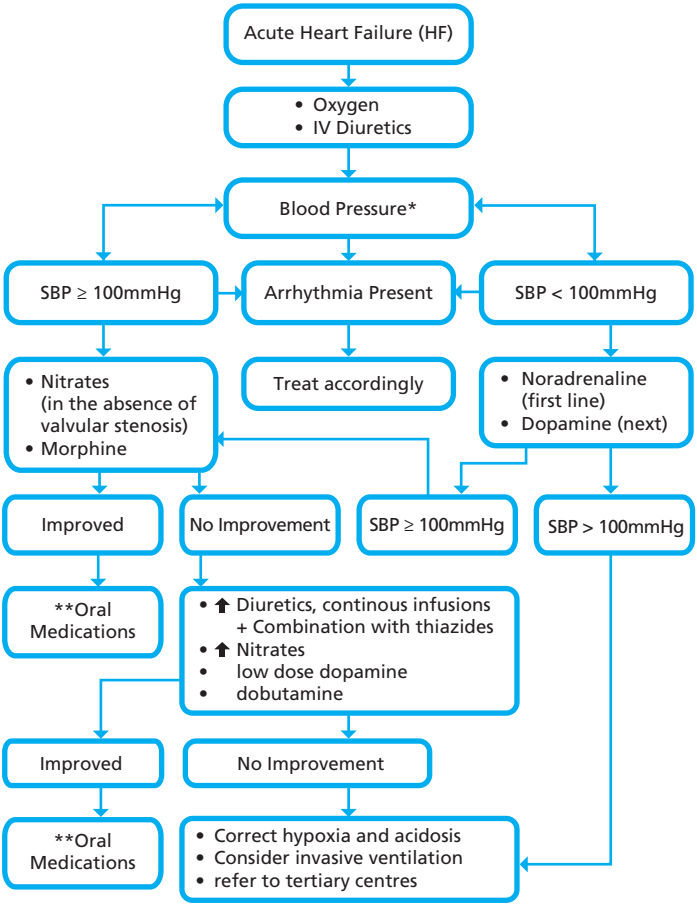
Summary

- Heart Failure (HF) is a clinical diagnosis. To satisfy the definition of HF, symptoms, signs and/or objective evidence of cardiac dysfunction must be present. (see Fig 1, pg 9)
- HF may occur in the presence of reduced left ventricular (LV) function, the left ventricular ejection fraction (LVEF) ≤ 40% (HF*r*EF) or with normal LV function, the LVEF ≥ 50% (HF*p*EF). If the LVEF is 41% - 49% it is called HF*p*EF, borderline.
- It may be classified as Acute HF or chronic HF depending on the acuteness of the clinical presentation.
- It is important to determine and treat the underlying etiology. Common causes are coronary artery disease and hypertension.
- Prevention and early intervention wherever appropriate, should be the primary objective of management.
- For the management of Acute HF and Chronic HF and grades of recommendations, see Flow Chart I, pg 10 and Table 1, pg 11 and Flow chart II, pg 12 and Table 2, pg 13 respectively
- Non pharmacological measures involves counseling the patient and family about the disease, diet and fluid intake, regular exercise and appropriate lifestyle changes such as smoking cessation and abstinence from alcohol.
- Performance measures should be instituted to assess quality of care.

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



Flowchart I : Management of Acute HF



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

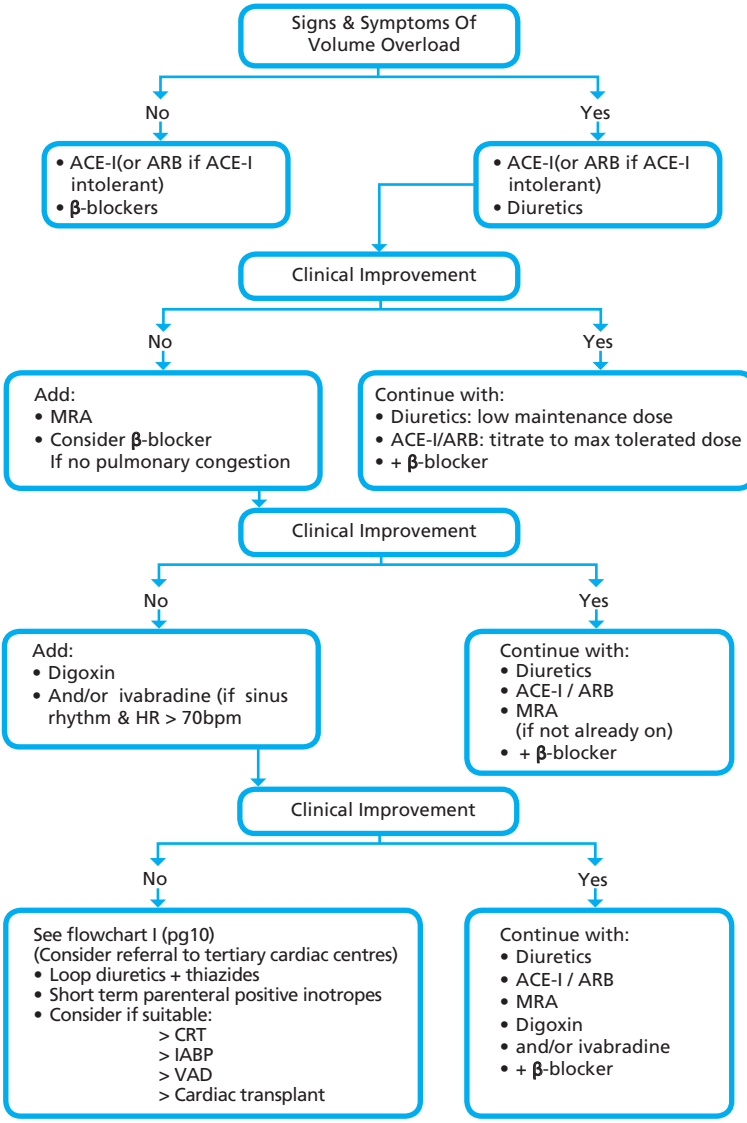
Refer :

- *section 7.1 for drug details and table V for dosages*
- *section 8.2 for guidelines for referral to tertiary cardiac centres*

Table I : Grading of Recommendations in the Management of Acute HF

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	B	Indicated in pts who are dyspnoeic and restless
Not Responsive To Initial Treatment And Sbp≥100mmHg			
Diuretics	IIa	B	Continuous infusion; combination with nitrates, dopamine, dobutamine or thiazide
Dopamine (<2-3µg/kg/min)	IIa	B	To improve renal perfusion and promote diuresis
Dobutamine	IIa	B	Indicated for peripheral hypoperfusion +/- pulmonary congestion
Not Responsive To Initial Treatment And Sbp<100mmHg			
Noradrenaline	IIa	B	Indicated to increase the BP
Dopamine (>5µg/kg/min)	IIb	B	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

Flowchart II: Optimizing Drug Therapy in Chronic HF



Refer :

- *section 7.2.2 for drug details and table S VI-IX for dosages*
- *section 8.2 for guidelines for referral to tertiary cardiac centres*

Table II: Grading of Recommendations in the Management of Chronic HF

Intervention	Grades of Recommendation	Levels of Evidence	Comments
Indicated For Fluid Retention In NYHA II - IV			
Diuretics	I	B	Not shown to improve survival.
Indicated In All Patients			
ACE-I	I	A	Improves survival and delays progression in all classes of HF
ARB	I	A	In ACE-I 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
Mineralocorticoid receptor 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
Ivabradine	IIa	B	Reduces hospitalizations when added to optimal medical therapy in patients in sinus rhythm and heart rate > 70bpm
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.

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1. Introduction

Heart failure (HF) is a clinical syndrome and represents the end stage of most heart diseases. 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 population[1].

Coronary Artery Disease (CAD) and Hypertension (HTN) are the main causes of HF among adults in Malaysia accounting for almost 70% of all cases.[2] This is similar to that noted in Western countries.[3] The prognosis for HF remains poor. The one year mortality rate varies between 5% to 52% depending on the severity and the presence of co-morbidity.[4,5] In a large community based study, about 40% of individuals with HF died within a year of initial diagnosis.[6] HF is an important cause of hospitalization accounting for about 6% - 10% of all acute medical admissions in Malaysia.[2,7] It is also an important cause of hospital re-admissions. About 25% of patients with HF are readmitted within 30 days for acute decompensation.[8,9] Therefore HF poses a major health and economic burden.

This guidelines 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

HF is an abnormality of cardiac structure or function leading to an impairment of ventricular filling or ejection of blood. It is a clinical syndrome in which patients have typical symptoms (e.g. breathlessness, ankle swelling and fatigue) and signs (e.g. elevated jugular venous pressure, ankle edema, pulmonary crackles, and displaced apex beat). Occasionally some patients may present without signs or symptoms of volume overload.

3. Pathophysiology

HF 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 often reduced resulting in heart failure with reduced ejection function (HF*r*EF). Occasionally, myocardial contractility may be preserved and left ventricular ejection fraction (LVEF) is normal, the symptoms being due to diastolic dysfunction ie heart failure with preserved ejection fraction (HF*p*EF).Often patients with a reduced LVEF have features of diastolic dysfunction as well. (Table III,pg 16)

3.1 HF*r*EF

In HF*r*EF, 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 the neurohumoral systems such as the sympathetic nervous system and the renin-angiotensin-aldosterone system, play a pivotal role in this process.

3.2 HF*p*EF

Up to 50% of patients presenting with HF have normal systolic function (LVEF≥50%) with predominantly diastolic dysfunction.[10,11,12] Diastolic dysfunction leads to impaired left ventricular (LV) filling due to decreased 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 HF*r*EF.

Many different classifications of HF have been used to emphasize some aspect of the condition. For practical purposes, it may be sufficient to classify HF into:

- Acute heart failure (Acute HF)
- Chronic heart failure (Chronic HF)

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

Older terms such as congestive cardiac failure may be used if patients present with both right and left ventricular fluid overload.

Table III : Pathophysiological Classification of Heart Failure (HF)

Classification	LVEF(%)
I. Heart Failure with Reduced Ejection Fraction (HF*r*EF)	≤40%
II. Heart Failure with Preserved Ejection Fraction (HF*p*EF),borderline	41-49%
III Heart Failure with Preserved Ejection Fraction (HF*p*EF)	≥50%

4. Aetiology

Heart failure is not a complete diagnosis. 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 artery disease
- Hypertension

Slightly less common causes include:
- Dilated cardiomyopathy-idiopathic, familial
- 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, phaechromocytoma
- Collagen vascular disease: systemic lupus erythematosis, polymyositis, polyarteritis nodosa
- Tachycardia induced cardiomyopathy
- Miscellaneous
  - severe anemia
  - peripartum cardiomyopathy
  - large A-V shunts
  - stress (Takotsubo) cardiomyopathy

Patients with Chronic HF may occasionally develop acute decompensation. Factors that can contribute to this Acute HF are listed in Table IV,pg 23. 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 *(See Figure 1, pg 9)*

There is no single diagnostic test for HF because it is a clinical diagnosis based on a careful history and physical examination.

The clinical suspicion of HF should be supported by objective evidence of cardiac dysfunction. Breathlessness with orthopnoea, paroxysmal nocturnal dyspnoea (PND), reduced exercise tolerance and ankle swelling are the characteristic symptoms of HF.

Signs which are more specific for HF are an elevated jugular venous pulse (JVP), third heart sound, laterally displaced apical impulse in the presence of a cardiac murmur. Other supportive signs include peripheral edema, tachycardia, narrow pulse pressure, pulmonary crepitations, hepatomegaly and ascites. The presence of jugular venous distension and a third heart sound are associated with adverse outcomes.[13] A fourth heart sound is more frequent in patients with HF*p*EF.

These symptoms and signs are sometimes difficult to interpret in the elderly, the obese and in patients with chronic lung disease. The clinical signs may resolve completely following medical therapy, making the findings at presentation essential for the diagnosis.[14] Occasionally symptoms and signs of volume overload may be absent and the patient may present with fatigue only.

Exercise capacity is assessed by the New York Heart Association (NYHA) functional classification. (Appendix I,pg 58)

Once the diagnosis of HF has been made, it is important to establish the aetiology of the syndrome (see section 4,pg 17)

The diagnosis of HF*r*EF requires these conditions to be satisfied:

- Symptoms and signs typical of HF
- Objective evidence of reduced LVEF

In the diagnosis of HF*p*EF the requirements are:[15,16]

- Symptoms and signs typical of HF
- Objective evidence of a normal, non-dilated LV and/or evidence of diastolic dysfunction
- Relevant structural heart disease (LV hypertrophy/LA enlargement)

Investigations

Basic investigations include:

- **12 lead ECG** - to identify heart rate, heart rhythm, QRS morphology, QRS duration, QRS voltage, evidence of ischaemia, LV hypertrophy and arrhythmias
- **Chest radiograph** - to identify pulmonary congestion, cardiac size and shape, and presence of other underlying lung pathology. Patients with HF*p*EF may have a normal cardiac size.
- **Blood tests** - FBC, renal function, liver function, serum glucose, lipid profile
- **Urinalysis** - evidence of proteinuria, glycosuria

Other important investigations include:

- **Echocardiography** : This will allow assessment of :
  - LV chamber size, volumes and systolic function
  - LV wall thickness, evidence of scarring and wall motion abnormality
  - Diastolic function of the heart
  - Valvular structure and function
  - Congenital cardiac defects
  - LV mechanical dyssynchrony
- **Natriuretic peptides** (Brain natriuretic peptide (BNP) or N-terminal pro BNP (NTproBNP)

BNP or NTproBNP are a family of hormones secreted by the ventricles in response to wall stress. They are useful in 2 situations :

- In the emergency setting, it is a useful "rule out" test for patients presenting with acute dyspnea. A level of <100pg/ml for BNP and <300pg/ml for NTproBNP makes the diagnosis of acute HF unlikely.[17,18,19] Levels of natriuretic peptides increase with age, but is reduced in obesity.
- A high level supports the diagnosis of acute HF and very high levels correlate with the severity of HF and adverse outcomes.

Additional investigations when indicated;

- **Blood tests**:
  - serum cardiac biomarkers (troponins, creatine kinase (CK), creatine kinase-myoglobin band (CKMB) - to look for myocardial necrosis)
  - 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, signs and/or 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/CAD but who do not as yet have structural heart disease. These include individuals with:
- multiple risk factors for developing CAD or who already have evidence of atherosclerotic disease in other vascular beds (e.g. cerebral, peripheral vascular disease)
- hypertension
- diabetes
- the metabolic syndrome
- severe hyperlipidemia
- a family history of cardiomyopathy
- thyroid disorders
- renal disease
- cardiotoxins – excessive alcohol consumption, chemotherapeutic agents
- sleep-disordered breathing especially obstructive sleep apnoea

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%.[20] The elderly have an absolute risk reduction of 1.5-2.5% in the incidence of HF over a period of 2-4 years and in those over the age of 80 years, there is a 64 % reduction in new onset HF.[21-24]

I, B
- Smoking cessation-Current smokers have a higher risk of HF compared to non-smokers and ex-smokers.[25] Quitting smoking appears to have a substantial and early effect (within two years) on decreasing morbidity and mortality in patients with left ventricular dysfunction, which is at least as large as proven drug treatments recommended in patients with left ventricular dysfunction.[26]

- Treating lipids to goal in all individuals to prevent cardiovascular disease. Even low risk individuals benefit from statin therapy although the use of pharmacotherapy for primary prevention should be individualized.[27,28] (See 4th Ed. Malaysian CPG on Dyslipidemia, 2011) *I, A*
- Optimizing the control of diabetes- Diabetes, especially in the presence of poor glycemic control, has been shown to increase the risk of HF independent of co-existing hypertension and/or CAD.[29-31] However there has been no evidence that intensive diabetic control will prevent HF. *I, B*
- Managing the metabolic syndrome appropriately with treatment of risk factors to target goals. *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 behavior that could increase the risk of HF such as excessive alcohol intake. *I, C*
- Regular physical exercise and maintenance of ideal body weight. *I, B*
- Reducing salt intake to<5gm/day[32] *I, B*
- Studies on the prevention of HF by n-3 fatty acids have been mixed.[33,34] A recent study in patients with multiple cardiovascular risk factors or atherosclerotic vascular disease who had no previous MI, showed that n-3 fatty acids did not reduce cardiovascular mortality and morbidity.[35] *IIa, B*
- When administering potentially cardiotoxic chemotherapy, monitor regularly for deteriorating LV function. *IIa, C*
  Small studies with β-blockers and angiotensin converting enzyme inhibitors (ACE-I) or angiotensin receptor blockers (ARB) have been shown to prevent cardiotoxic cardiomyopathy.[36,37] Treatment currently has to be individualized. *IIb, B*
- Obstructive sleep apnoea has been associated with HF although the use of Continuous Positive Airway Pressure (CPAP) has not been shown to reduce the incidence of HF.[38,39] *IIb, B*

6.2 Individuals with cardiac disease but who do not as yet have evidence of myocardial dysfunction. In addition to that mentioned in section 6.1, other strategies include:

- Early triage and appropriate treatment of patients with acute coronary syndrome.[40-42] *I, A*
- Patients with CAD should be treated appropriately with antiplatelet agents,[43-47] β-blockers,[48,49] ACE-I[50] and statins.[51,52] These patients should undergo coronary revascularization as indicated. *I, A*
- Patients with hypertension and left ventricular hypertrophy (LVH) should have their blood pressure control optimized. Regression of LVH has been shown to be associated with a lower incidence of new onset HF.[53] *I, B*

I, B • Patients with haemodynamically significant valve disease should undergo early intervention as indicated.[54]

I, C • Arrhythmias should be treated early and appropriately.[55]

I, C • Patients with congenital cardiac lesions should have these corrected early whenever indicated.

These individuals should be regularly monitored 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:

I, A • ACE-I - have been shown to reduce the incidence of HF by 23% in individuals with CAD and normal LV systolic function.[20] These medications also reduce new onset HF in patients with atherosclerotic vascular disease [56,57], diabetes and hypertension with associated cardiovascular risk factors.[58]

IIa, A • ARB - in patients with atherosclerotic vascular disease, diabetes and hypertension with associated cardiovascular risk factors ARBs have been shown to reduce cardiac events.[59-62] These agents are non-inferior to ACE-I and should be considered in ACE-I intolerant patients.[63]

I, A • β-blockers - in patients post myocardial infarction (MI)[64,65]

I, A • Statins in patients with CAD[27,51,66]

6.3 Individuals with myocardial dysfunction but who do not as yet have signs and symptoms of HF. (Asymptomatic Left Ventricular Dysfunction) Measures include:

I, C • Treat the underlying cause wherever possible.

• Prevent progression to HF by modulating cardiac remodeling. See section on the management of Asymptomatic Left Ventricular Dysfunction (Section 7.3.1)

Key Message:

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

7.1 Acute Heart Failure

Acute heart failure (Acute HF) is described as the rapid onset, or rapid worsening of the symptoms and signs of HF. The "rapidness" of the deterioration in symptoms can be within hours to several days depending on the cause of the Acute HF. It may present de novo (first presentation) or more commonly, as a result of deterioration of a previously diagnosed stable patient with HF.

The spectrum of clinical findings may range from worsening of peripheral oedema to life threatening pulmonary oedema or cardiogenic shock.

Myocardial Infarction/Ischaemia is an important and common cause of Acute HF. The other causes and factors contributing to decompensation in patients with stable HF are as listed in Table IV.

Most patients with Acute HF would require hospitalization. The more ill patients should be managed in the Coronary Care Unit or High Dependency Unit with continuous hemodynamic monitoring. *I, C*

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 and COX-2 inhibitors
• 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

Essential Investigations in Acute HF include:

- ECG
- Chest Radiograph
- Blood Investigations: hemoglobin, serum electrolytes, urea, creatinine, cardiac biomarkers (troponin, CKMB, Natriuretic Peptides)
- Blood gases may be considered
- Echocardiography

Assessment and management must be made promptly and simultaneously.

The principles of management are:

- Rapid recognition of the condition
- Identification and stabilization of life threatening hemodynamics
- Identification and treatment of the underlying cause and precipitating/ aggravating factors
- Relief of clinical symptoms and signs

After initial clinical assessment of vital signs, treatment of Acute HF should be instituted as outlined in Flowchart I,pg 10. For grading of recommendations and levels of evidence, see Table I,pg 11.

Therapy (for dosages see Table V,pg 25)

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

I, C

- **Oxygen** - Aim to achieve oxygen saturation of more than 95% in order to maximize tissue oxygenation and to prevent end organ dysfunction or multi organ failure.

  Elective ventilation using non invasive positive pressure ventilation (CPAP or Bi-level Positive Airway Pressure [BiPAP]) should be considered early if necessary.[67-70]

IIa, C

  Should the oxygen saturation be inadequate or the patient develops respiratory muscle fatigue, then endotracheal intubation and mechanical ventilation is necessary.

I, B

- **Frusemide** – Intravenous (i.v.) frusemide 40 - 100mg. The dose should be individualized depending on the severity of the clinical condition.[71]

IIa, B

  Administration of a loading dose followed by a continuous infusion has been shown to be more effective than repeated bolus injections alone in producing greater diuresis and weight reduction.[72-75] The dose should be titrated according to clinical response and renal function. There is a lack of data on short term mortality at present.[75]

I, B

- **Nitrates** - If the BP is adequate (SBP > 100 mmHg), nitrates should be considered.[76-78] It should be administered intravenously. Patients should be closely monitored for hypotension. This commonly occurs with concomitant diuretic therapy.

Studies have shown that the combination of i.v. nitrate and low dose frusemide is more efficacious than high dose diuretic treatment alone.[78] *I, B*

Extreme caution should be exercised in patients with aortic and mitral stenosis. Nitrates are contraindicated in severe valvular stenosis.

- **Morphine sulphate** - i.v. 1- 3 mg bolus (repeated if necessary, up to a maximum of 10mg). It reduces pulmonary venous congestion although its effect on venodilation has actually been shown to be minimal.[79] It reduces anxiety and is most useful in patients who are dyspnoeic and restless. Intravenous anti-emetics (metoclopramide 10mg or prochlorperazine 12.5mg) should be administered concomitantly. *IIb, B*

  Morphine should be used with caution as some recent data seem to indicate that it may actually do more harm.[80,81] Care must be exercised in patients with chronic respiratory disease.

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

Table V: Drugs Commonly Used in Acute HF

	Route of Admin	Dosages
Diuretics		
Frusemide	IV Infusion	40mg-100mg 5-20mg/hour (better than intermittent very high bolus doses)
Vasodilators		
Nitroglycerin	Infusion	5 – 200mcg/min
Isosorbide dinitrate	Infusion	1 – 10mg/hr
Nitroprusside	Infusion	0.1 – 5mcg/kg/min
Sympathomimetics		
Dobutamine	Infusion	2 – 20mcg/kg/min
Dopamine	Infusion	<2 – 3mcg/kg/min - renal arterial vasodilation 2 – 5mcg/kg/min - inotropic doses 5 – 15mcg/kg/min - peripheral vasoconstriction
Noradrenaline	Infusion	0.02 – 1mcg/kg/min till desired blood pressure is attained

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
  - Serum potassium, sodium and magnesium
  - 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, an improvement in his oxygen saturation and urine output. Generally, a SBP ≥ 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 Acute HF 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 :-

I, B • **Frusemide:** i.v. frusemide infusion 5-20mg/hour. Combination of a loop diuretic at low doses with nitrates is superior to high dose diuretic therapy alone.[78]

IIa, B Combination with:

IIa, C
- dopamine[82]
- dobutamine

are also more effective than increasing the dose of diuretic alone.

IIa, B Alternatively one could consider adding an oral thiazide diuretic[72,83,84]

An attenuated diuretic response has been shown to be associated with poor prognosis and increased risk of death.[85]

- **Inotropes:**

IIa, B
- Dopamine : Low dose at <2-3mcg/kg/min to improve renal flow and promote diuresis[86]

IIb, B
- Dobutamine infusion : Started at 2 – 5mcg/kg/minute and titrated by 1- 2mcg/kg/minute increments at 30 minute intervals until the desired clinical and haemodynamic response is attained.

Dobutamine improved cardiac output but did not reduce pulmonary capillary wedge pressure or hospital stay. It was associated with significant ventricular tachyarrhythmias.[87,88,89]

- **Vasodilators:**
  - Sodium Nitroprusside would be useful in patients not responsive to nitrates.[90] This drug is particularly useful in cases of uncontrolled hypertension, acute mitral or aortic regurgitation *IIa, B*

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.

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

- Noradrenaline infusion. The use of noradrenaline was associated with less adverse events compared to dopamine in the treatment of shock.[91] A small study showed that the combination of noradrenaline and dobutamine was a more reliable and safer strategy that using an adrenaline infusion.[92] *IIa, B*
- Dopamine infusion[91] *IIb, B*
- Avoid vasodilators (nitrates, nitroprusside) and morphine until the blood pressure has stabilized *I, C*
- Over diuresis or hypovolaemia - correct accordingly. *I, C*

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

Other Measures

- **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. *IIa, C*
- **Correction of acidosis** *I,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.[93-95] *IIb, B*
- **Intra-aortic balloon counterpulsation (IABP)** - would be useful in patients who are not responding optimally to medical therapy as a bridge to definitive treatment. IABP would be particularly useful in patients with intractable myocardial ischaemia or acute mitral regurgitation.[96,97] *IIa, B*

In acute MI complicated by cardiogenic shock, IABP has been found to be effective in patients undergoing reperfusion by fibrinolytic therapy. In those undergoing primary PCI, IABP has not been shown to reduce mortality.[98,99]

IABP is contraindicated in patients with aortic regurgitation or aortic dissection.

IIa, B

- **Ventricular Assist Devices (VAD)** - would be useful as a bridge in patients for whom recovery from Acute HF is expected or for whom heart transplantation is an option.[100-102]

Following adequate response to intravenous therapy, the patient should be converted to optimal oral medications. (see Flow Chart II, pg 12) The initial dose of oral diuretics required is generally higher than the intravenous dose.

There are other agents such as tolvapton, levosimendan and nesiritide have shown symptomatic improvement in Acute HF but have been associated with either neutral or an increase in adverse events.[103-106]

Special Situations

- **Myocardial Ischaemia / Infarction:** Reversible myocardial ischaemia causing Acute HF, needs early recognition, rapid stabilization and referral for urgent coronary angiography. In acute MI, reperfusion therapy by fibrinolytic or primary Percutaneous Coronary Intervention (PCI) may significantly improve or prevent Acute HF. Long term management strategy 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 12hours. 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 phaeochromocytoma.

- **Valvular Heart Disease:** Acute HF 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:** Acute HF and renal failure can co-exist and either may give rise to the other. Renal failure influences the response to drug therapy.[107] In these patients with refractory fluid retention, continuous ultrafiltration may be considered.[108]

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 < 1.8 L/min/m^2 without support or 2.2 L/min/m^2 with support

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 LV filling pressures may be present. This may be due to excessive diuretic or vasodilator therapy, concomitant gastro-intestinal 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-arrhythymic drug therapy.

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

- **Inotropic support:** Noradrenaline and/or dopamine. 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.

7.2 CHRONIC HEART FAILURE

7.2.1 NON PHARMACOLOGICAL MEASURES

These include the following :-

a) Education
b) Diet & Nutrition
c) Lifestyle
d) Exercise
e) Sleep Disorders
f) Social Support

A) Education

I, B

- The patient and family should receive both education and counseling about the HF syndrome, its prognosis and drug treatments.[109-112]
- Counseling on the warning signs and symptoms of worsening HF 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 HF is a highly lethal disease, as lethal as several common malignancies (Appendix I,pg 58)
- 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. (Appendix II,pg 58)

B) Diet & Nutrition

I, B It is important to maintain good nutrition.[113] Obese patients should be encouraged to reduce weight. Excessive weight loss and leanness however, are important predictors of poor prognosis in Chronic HF.[114]

IIa, B Patients should be advised on salt restriction particularly in severe HF.[115-119] A good rule of thumb is to avoid adding salt and soya sauce while cooking or at the table. Refer to Appendix III,pg 58 on salt content of common Malaysian food.

I, C Fluid intake should be restricted to 1-1.5 liter/day if HF symptoms are still not well controlled with medications.[116,117]

C) Lifestyle

- Patients with alcoholic cardiomyopathy must abstain from alcohol. Similar abstinence is strongly encouraged in all other patients with HF.[120]
- Smoking should be stopped.[121] *I, B*
- Patients with severe HF (NYHA Class III-IV) should be advised against pregnancy because of high maternal mortality.[122,123] *IIa, C*
- 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.[122]

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, tadanafil 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.[124]

D) Exercise

Recent studies have shown that patients with compensated HF can exercise safely.[125-127] Regular dynamic exercise : *I, A*

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

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.

E) Sleep Disorders

Causes of sleep disturbances in HF include pulmonary congestion, nocturnal diuresis due to diuretics and anxiety.

Up to 53% of adults with HF have been shown to have either central or obstructive sleep apnea.[128-130] Adverse effects of obstructive sleep apnoea include hypoxemia, hypercapnia and increased afterload. Treatment will include weight loss and CPAP. In patients with sleep apnea and HF, CPAP can increase LVEF and improve quality of life. To date, there is no conclusive evidence that CPAP improves prognosis in HF patients.[130-134] *IIa, B*

F) Social support
This reduces stress and helps in maintaining a healthy lifestyle and compliance to treatment. Absence of social support has been associated with higher hospitalization rates.[135-137]

7.2.2 PHARMACOLOGICAL MANAGEMENT

Drug therapy is the mainstay of management of Chronic HF as outlined in Flowchart II,pg 12. For grading of recommendations and levels of evidence, see Table II,pg 13.

A) Diuretics

I, C

Diuretics are indicated in all patients with HF in whom there are signs and symptoms of fluid retention.[138]

The dose of diuretic used is variable and dependent on individual requirements. In the presence of severe congestive HF, oral diuretic therapy may be ineffective. Intravenous therapy may be preferred.

Adequate doses of diuretic should be used. However, these patients should be monitored closely as overdiuresis can cause intravascular volume depletion leading to hypotension and deterioration of 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 diuresis.[83] In patients with a glomerular filtration rate below 30ml/min, thiazides are not effective alone but may be used synergistically with loop diuretics. (Table VI 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 VI: Diuretics Used In Heart Failure

	Route of Administration	Usual Daily Dose
LOOP DIURETICS		
• Frusemide	IV / Oral	20 - 80mg
• Bumetanide	IV / Oral	0.5 - 2mg (up to 10 mg max)
THIAZIDES		
• Hydrochlorothiazide	Oral	25 - 50mg
• Chlorothiazide	Oral	250 - 500mg
MINERALOCORTICOID ANTAGONISTS		
• Spironolactone	Oral	12.5mg – 50mg
• Eplerenone	Oral	25mg - 50mg

B) Angiotensin Converting Enzyme Inhibitors (ACE-I)

ACE-I improve survival and quality of life in all classes of HF.[139-141] ACE-I are the 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 LVEF of <40%. *I, A*

The available data suggest that there are no differences among available ACE-I in their effects on symptoms or survival.[141]

In the initiation of ACE-I, 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 VII) or the 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 ACE-I therapy may need to be stopped temporarily.
- Avoid non steroidal anti-inflammatory drugs

A number of different ACE-I are available. The dose should be titrated up to the target level as shown in Table VII.

Table VII: Recommended doses of ACE-I 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 ACE-I are :-

- cough
- hypotension
- renal insufficiency
- hyperkalaemia
- Angioedema

C) β-Blockers

I, A Large clinical trials have shown that β-blockers reduce morbidity and mortality in patients with NYHA II-IV HF, of both ischaemic and non-ischaemic aetiology, on top of standard therapy.[142-150]

β-blockers 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 LVEF should be given β-blockers unless contraindicated.

IIa, B Initiating therapy with a β-blocker first is non-inferior to the standard approach of starting with an ACE-I.[145]

The benefits seen with both these drugs are additive.

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

- The initial dose should be small. (Table VIII)
- The dose should be slowly titrated upwards till target dose or maximum tolerated dose is achieved.
- Contraindications include the following :
  - 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 Acute HF should be maintained on the same dose of β-blockers unless the clinical condition (hypotension or significant bradycardia) warrants a temporary reduction in the dose. After the patient has been stabilized and is no longer in overt HF, an attempt should be made to up-titrate to the target or maximum tolerated dose of β-blockers.

Table VIII: 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
Nebivolol***	1.25 mg	10 mg daily

* *Only the above mentioned β-blockers have been shown to improve CV outcomes.*
** *Currently only metoprolol tartrate is available in Malaysia*
*** *one study showed reduction in composite endpoint of death or CV hospitalization with no reduction in mortality*[150]

D) Mineralocorticoid Receptor Antagonists (MRA)

The addition of spironolactone to ACE-I, loop diuretics and digoxin in patients with severe HF reduces mortality and rehospitalization.[151] Similarly, eplerenone, another MRA, when added to β-blockers and ACE-I in patients post MI with impaired LV function and mild HF, has been shown to be beneficial.[152,153] (Table VI,pg 33) *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 the dose of MRA should be reduced or stopped.

Spironolactone can cause breast enlargement and discomfort in men ; this is infrequent with eplerenone.

E) Angiotensin II Receptor Blockers (ARB)

In patients intolerant to ACE-I, ARB should be considered.[154-158] *I, A*

In patients post MI with impaired LV function the ARB, Valsartan, was found to be as effective as captopril.[159] (Table IX) *I, B*

In patients who are still symptomatic despite being on ACE-I and β-blockers and in whom a MRA is not tolerated, the addition of an ARB may be considered to reduce hospitalization due to HF.[154,160,161] *IIb, B*

Table IX: Recommended doses of ARB in HF

ARB	Initiating Dose	Target Dose
Losartan	25 mg daily	150 mg daily
Valsartan	40 mg daily	160 mg bid
Candesartan	4 mg daily	32 mg daily

F) Ivabradine

IIa, B Ivabradine slows the heart rate in sinus rhythm but has no effect on the ventricular rate in atrial fibrillation. In patients on optimal medical therapy with diuretics, ACE-I and β-blockers and a resting heart rate of >70/min, the addition of Ivabradine resulted in a reduction in hospitalization, improvement in LV function and quality of life without an effect on mortality.[162,163] It would be useful in patients who have contraindications to β-blockers.

Ivabradine can cause symptomatic bradycardia and visual disturbances.

G) Digoxin

In the past digoxin was used as first line therapy in patients with HF and atrial fibrillation.[164,165] However at present, β-blockers are an integral component of HF management. Digoxin may be considered in patients with HF and AF in the following situations:

IIa, C • rate control is inadequate on β-blockers alone.

IIa, C • β-blockers are contra indicated.

IIa, C • rapid control of the ventricular rate with parenteral drugs is required

IIa, B Combination of digoxin and β-blockers is superior to either agent alone in patients with atrial fibrillation.[166,167]

IIb, B In patients with HF and normal sinus rhythm, digoxin may be added if symptoms persist despite diuretics, ACE-I, β-blockers and low dose MRA. Digoxin has no effect on mortality but reduces hospitalization.[168-170]

No loading dose is required for Chronic HF. 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.[171,172]

H) Anti-Coagulation Therapy

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

I, A - atrial fibrillation [173,174]

Atrial fibrillation is a common problem among patients with HF. All patients with atrial fibrillation should be anti-coagulated with warfarin unless contraindicated.[175]

IIa, B New anticoagulant drugs – oral direct thrombin inhibitors (dabigatran) or factor Xa inhibitors (rivaroxaban, apixaban) may be used in place of warfarin. Care has to be exercised with these agents in renal impairment. Disadvantages include absence of antidotes in the event of bleeding and significantly increased costs compared to warfarin. [176,177,178]

IIa, C - intracardiac thrombus (except for organized mural thrombus)

IIa, C - past history of thromboembolic episode(s)

I) Other Concurrent Therapies

Calcium channel blockers are not recommended for the treatment of HF due to systolic dysfunction.[179-181] *III, A*

Second generation dihydropyridine calcium channel blockers such as amlodipine or felodipine may be considered for the treatment of concurrent hypertension and angina.[182,183] *IIa, B*

Nitrates have many theoretical benefits when used in HF.These effects are however short lived due to the development of tolerance and pseudotolerance. Almost all the large clinical trials have been with the hydralazine- nitrate combination which seem to be most benefial in black patients.[184] *IIb.C*

J) Anti – Arrhythmic Drug Therapy

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

- atrial fibrillation
- ventricular tachyarrhythmias
- bradyarrhythmias

J.1) Atrial Fibrillation

These patients can be managed by either rate control or rhythm control.

- Rate control.

This can be achieved by using either:

- β-blockers[165,166,174,185] and/ or *I, A*
- digoxin[174] *IIb, B*

β-blockers are preferred over digoxin as it provides rate control during exercise and improves morbidity and mortality in patients with HF. Rate control is better when digoxin and β-blockers are used in combination rather than with each drug individually.[166,167]

- Rhythm control

This is indicated in patients intolerant of AF even after rate control. It can be achieved either by pharmacological cardioversion with amiodarone or by elective electrical cardioversion after a period of anticoagulation.[174] *IIb, B*

Sinus rhythm can be maintained by using amiodarone.[174] *IIa, B*

J.2 Ventricular Arrhythmias

Studies show that 40-50% of deaths in HF are sudden, the risk increasing with the severity of HF.[186,187] 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.[188,189] Occasionally rapid supraventricular tachycardias may give rise to malignant ventricular tachyarrhythmias.[190]

The following medications have been shown to reduce the incidence of sudden cardiac death (SCD) :

I, A
- **β-blockers:-** These agents were shown to reduce SCD in the clinical trials done on patients post MI as well as in the HF trials[190-193]

I, B
- **Mineralocortocoid antagonist** have been shown to reduce the incidence of SCD[193,194,195]

I, A
- **ACE-I:** Analysis of trials done following myocardial infarction showed that ACE-I reduced SCD.[193,196-198]

IIb, B
- **Statins:-** have a modest beneficial effect on SCD[199]

In addition to the above, in patients with ventricular tachyarrhythmias, the following are important:

I, C
- Identify contributing factors such as electrolyte disturbances, ischemia and drugs.

I, A
- Implantable cardioverter defibrillator (ICD) (section 7.2.3) These have been found to improve survival in both
  - secondary prevention [200,201,202]

IIa,A
  - primary prevention[203,204] in selected patients.

IIa, B
- Anti-arrhythymic 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.[205]

I, A
Patients with significant bradyarrhythmias, trifascicular blocks and high-degree AV blocks should be considered for pace-maker therapy.[206]

Prior to implanting a conventional pacemaker, the need for an ICD or Cardiac Resynchronisation Therapy (CRT) device should be considered.

7.2.3 DEVICE THERAPY IN HEART FAILURE

A) Cardiac Resynchronization Therapy (CRT)
Patients who remain persistently symptomatic (NYHA class II - III) 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 CRT include all of the following:
- sinus rhythm
- LVEF <35%
- a widened QRS interval (>120 ms) on the resting ECG

CRT has been shown to improve symptoms, hospitalizations and mortality, though up to 30% of patients may be non-responders.[207-211] *I, A*

Patients with milder symptoms and in NYHA class II are more likely to benefit if their QRS>150ms and they have a left bundle branch block (LBBB) pattern in their resting ECG.[212-215]

Patients with permanent atrial fibrillation are less likely to respond unless they have atrio-ventricular block, which would allow continuous ventricular pacing.[216,217]

Regular monitoring is recommended after device implantation to adjust medical therapies and reprogram the device as necessary.

B) Implantable Cardioverter Defibrillator (ICD)
SCD 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 sudden cardiac arrest or documented sustained ventricular arrhythmias.[200,201,202]

It may also be used as primary prevention to reduce the risk of SCD in patients with HF who are at risk.[203,204, 218-220] 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:
- Patients resuscitated from SCD due to ventricular fibrillation or hemodynamically unstable sustained ventricular tachycardia (provided that it is not associated with acute MI or ischemia).[200,201,202] These cardiac arrest survivors have a high risk of recurrent events and implantation of an ICD has been shown to reduce mortality. *I, A*
- Patients with chronic HF and a low EF who experience syncope of unclear origin have a high rate of subsequent SCD 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 SCD may be reasonable in patients with:

IIa, A
- prior MI and LVEF<30% at least one month after an MI and 3 months after revascularization by PCI or CABG, when appropriate.[203,218,219]

IIa, B
- LVEF <35% and mild to moderate HF symptoms (NYHA II–III).[204,220] 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

IIa, B
This should be considered in patients who have malignant ventricular arrhythmias and also 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.[221,222]

7.2.4 SURGERY FOR HEART FAILURE

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

I, C
Patients with CAD and HF may benefit from revascularization by either PCI or coronary artery bypass surgery (CABG), particularly if they have angina and anatomy that is suitable for revascularization (left main stem or triple vessel disease).The benefit of revascularization is likely to be more in patients with mild left ventricular dysfunction, severe CAD with angina, viable myocardium and reversible ischemia.

IIa, B
The STICH trial found no difference in total mortality between CABG or medical therapy in patients with severe heart failure (LVEF < 35%) and significant CAD, but patients who underwent CABG had reduced combined risk of cardiovascular (CV) death and CV hospitalizations.[223]

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

IIa, C
- refractory angina or acute coronary syndrome, for relief of symptoms.

IIa, C
- significant inducible ischemia and/or large areas of hibernating myocardium.

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

Patients with HF and severe mitral regurgitation, non ischemic in origin, may have symptomatic improvement after mitral valve surgery. If the LVEF <30%, mitral valve repair is preferred as mitral valve replacement is associated with poorer outcomes.[224] *IIb, C*

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.[225,226] A recent small studied observed no significant difference in left ventricular reverse remodeling or survival at 12 months between patients who underwent mitral-valve repair and those who underwent mitral-valve replacement for ischemic mitral reguritation.[227] *IIa, B*

C) LV Reduction Surgery

LV aneurysmectomy is indicated in patients with a large discrete LV aneurysm who develop HF, angina pectoris, thromboembolism, and tachyarrhythmias due to the aneurysm.[228] *I, C*

Patients with HF undergoing surgical coronary revascularization, who have areas of LV dyskinesia or akinesia do not benefit from concomitant LV reduction surgery.[229] *IIb, B*

D) LV Assist Devices

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 is increasingly being used for long term haemodynamic support in eligible patients (destination therapy).[230-232] *IIa, B*

Patients awaiting heart transplantation who have become refractory to medical therapy and require inotropic support should be considered for a mechanical support device as a bridge to transplant.

7.2.5 HEART TRANSPLANTATION

Heart transplantation is an established treatment of refractory end stage HF but it is limited by the lack of donor organs.[233,234] *IIa, C*

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 VO2 less than 10 ml per kg per min
- 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.

7.3.1 ASYMPTOMATIC LEFT VENTRICULAR DYSFUNCTION

The prevalence of Asymptomatic LV Systolic Dysfunction (ASLVSD) varies with the diagnostic LVEF criteria that is used as a cutoff as well as the population studied. About 0.9-2.1% in the general population have asymptomatic LVEF<40%.[235,236]

Patients with ASLVD (LVEF <40%) carry substantially higher risk for subsequent morbidity and mortality than the general population. The rate of progression to symptomatic HF was estimated to be 9.7% per year and the risk of death or HF hospitalization was 8%.[237,238] Outcomes are worse if effective therapy is initiated after patients develop overt HF.[239]

Asymptomatic moderate to severe LV diastolic dysfunction is also common (5.6%) and associated with an adverse prognosis.[236]

Screening may be done by: [240]

- **Resting ECG -** not very specific or sensitive
- **Echocardiography -** this is the most specific test
- **BNP levels -** may be used to identify individuals who may need an echocardiogram.

These screening tests are more cost effective and of greater value when used to screen high risk individuals.[240-242] These include patients with:

- coronary artery disease
- hypertension
- diabetes mellitus
- peripheral arterial or cerebrovascular disease
- excessive alcohol intake
- family history of cardiomyopathy
- abnormal resting ECG
- cardiomegaly on the CXR

The goals of treatment in these patients are to:

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

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

Drug therapy. This includes:

I, A
- **ACE-I:** Long term treatment with an ACE-I has been shown to delay the onset of symptoms of HF and decrease the combined risk of death and hospitalization.[237,238,243,244]
- **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 ACE-I.[159]

I, A
- **β-blockers:** In post MI patients and in those with CAD, **β**-blockers are recommended. They may be considered in all patients with LVEF<40%.[245,246]

- **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%.[247] *III, C*

Key Message:

- Identify patients who are at high risk of developing LV dysfunction and treat the underlying disease appropriately.
- ACE-I 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 FUNCTION

The prevalence of HF with preserved LV systolic function (HF*p*EF) varies between 40-71% depending on the LVEF criteria used as cut off.[248,249] HF*p*EF constitutes more than half of HF in older adults and the prevalence is increasing over time.[247,248] Commonly, these patients are older women who have hypertension. Significant co morbid conditions such as diabetes mellitus, CAD, obesity and / or atrial fibrillation are also often present.[248- 250] The presence of diabetes, a lower systolic BP, hemoglobin and estimated Glomerular Filtration Rate (eGFR) were associated with a poorer outcome.[250]

HF*p*EF is a clinical diagnosis and largely one of excluding mitral valve disease, fluid overload, cor pulmonale and other potential non cardiac causes of dyspnea.

Criteria that have been proposed to diagnose HF*p*EF include:[15,16]

- clinical signs or symptoms of HF such as exertional dyspnea, orthopnea, atrial gallop sounds, and pulmonary rales combined with a suggestive chest X-ray and a favorable response to diuretics,
- evidence of preserved or normal LVEF (>50% or more within 72 hours of the event) and LV end diastolic volume index (LVEDVI)< 97mL/m^2
- evidence of abnormal LV diastolic dysfunction that can be determined by Doppler echocardiography or cardiac catheterization. Invasive hemodynamic measurements complemented, where necessary, by additional exercise testing with assessment of LV volumes and pressures to detect exercise-induced elevation of filling pressures is the gold standard for diagnosing diastolic dysfunction. However, echocardiography with tissue doppler is obtained more easily and several criteria have been proposed to diagnose diastolic dysfunction.[15]

Hypertension remains the most important cause of HF*p*EF, with a prevalence of 60% to 89% from large controlled trials, epidemiological studies, and HF registries.[251] Diastolic dysfunction may be due to myocardial or pericardial disease. (see Table X,pg 45)

The management of these patients remains empiric, since trial data are limited. It includes:

I, C • Identifying and treating the underlying cause(s) appropriately.

I, A - Hypertension should be treated to target goals.[252,253] Improved BP control has been shown to reduce hospitalization for HF.[252]

I, C - CAD is common in patients with HF*p*EF and this should be treated appropriately.

I, C • Tachyarrhythmias should be treated and sinus rhythm restored whenever possible. If the patient remains in persistent atrial fibrillation, **β**-blockers or calcium channel blockers alone or in combination are the usual first line agents used for rate control.

I, A Patients with paroxysmal or persistent atrial fibrillation should be anticoagulated.[173,174]

• Pharmacological treatment
Treatment options include:

I, C - **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.

IIa, C - **β-blockers:** This could be given to lower heart rate and increase the diastolic filling period. At present, however, there is no good demonstration that **β**-blockers is beneficial in the treatment of HF*p*EF.[150,254]

IIa, C - **Calcium Channel Blockers (Verapamil and diltiazem):** These may be used to lower the heart rate and has been shown to be beneficial.[255]

IIa, B - Verapamil has been shown to improve functional capacity in patients with hypertrophic cardiomyopathy.[256]

IIb, B - **ARB** trials have shown mixed results. One large trial showed a reduction in hospitalization while another large trial was neutral.[257,258]

IIb, B - **ACE-I** may improve relaxation and cardiac distensibility directly and may have long term activity via their antihypertensive action and regression of hypertrophy and fibrosis. One small study showed an almost significant trend toward reduction in the primary end point of combined all-cause mortality and unexpected hospitalization for HF while another trial was neutral.[259,260]

IIb, B - **MRA:** Recent studies showed that spironolactone improved diastolic function and reduced hospitalization but did not result in improvement in symptoms, exercise capacity or quality of life.[261-263] Hyperkalemia was more common in those on MRA.

• **Exercise training:** This is safe and improves exercise capacity and quality of life.[264] It should consist of dynamic isotonic and not static exercise.

Key Message:

- HF*p*EF is a common cause of HF in the elderly.
- Hypertension is an important cause and should be treated according to guidelines.
- Management remains empiric since trial data are limited.

Table X: Causes of Diastolic Dysfunction

Myocardial disorders	
Myocardial diseases	
Infiltrative	Amyloidosis
	Sarcoidosis
	Fatty infiltration
Noninfiltrative	Ischemic cardiomyopathy
	Idiopathic cardiomyopathy
	Diabetic cardiomyopathy
	Hypertrophic cardiomyopathy
Endomyocardial diseases	Endomyocardial fibrosis
	Hypereosinophilic syndrome
Storage disease	Hemochromatosis
	Glycogen storage disease
Pericardial disorders	
Pericardial constriction	Constrictive pericarditis
	Effusive constrictive pericarditis
Pericardial effusions	Pericardial effusion with cardiac compression
	Glycogen storage disease

Adapted from: *van Kraaij DJ, van Pol PE, Ruiters AW, de Swart JB, Lips DJ, Lencer N, et al. Diagnosing diastolic heart failure. Eur J Heart Failure 2002;4:419-430.*

7.3.3 HEART FAILURE IN PREGNANCY

About 0.5 – 4% of pregnant women have cardiac disease.[265] Common causes of HF in pregnancy are hypertension, eclampsia, undetected valvular heart disease especially mitral stenosis, congenital heart disease, and occasionally peripartum cardiomyopathy. The prevalence of peripartum cardiomyopathy (PPCM) in Malaysia is estimated at 34 per 100,000 life birth.[266] The prevalence of PPCM in other parts of the world varies from 0.88 per 100,000 live births in USA to 250 per 100,000 live birth in Haiti.[267]

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. The periods of greatest risk for cardiac events during pregnancy are early third trimester, at delivery and in the immediate post-partum period.

Most forms of cardiac disease can be detected by physical examination, ECG and echocardiography.

Predictors of maternal risk for cardiac complication include.[122,267]

- History of HF before pregnancy
- Prior arrhythmia (symptomatic sustained tachyarrhythmia or bradyarrhythmia requiring treatment)
- NYHA class > 2
- Valvular stenosis (aortic or mitral valve area < 1.5 cm2) and LV outflow tract obstruction (peak gradient > 30mmHg)
- Myocardial dysfunction (LVEF < 40%)
- Pulmonary hypertension

Pregnancy is contra-indicated in:[122,267]

- severe pulmonary hypertension (pulmonary artery pressure > ¾ systemic pressure)
- Eisenmengers' syndrome
- Cardiomyopathy with class III or IV HF
- Severe obstructive lesions (aortic stenosis [valve area <0.7cm^2], mitral stenosis [valve area < 1.0cm^2], coarctation [systolic gradient > 20mmHg], hypertrophic obstructive cardiomyopathy [outflow tract gradients of more than 30-50mmHg at rest and 75-100mmHg after provocation)
- Marfan's syndrome with aortic root ≥40mm
- Severe maternal cyanosis(oxygen saturation<85%)
- Past history of peripartum cardiomyopathy with persistent LV dysfunction and/or HF

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

- gestational age at presentation
- clinical presentation, either as Acute HF or Chronic HF
- 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 during pregnancy 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 fetal bradycardia, hypoglycaemia and hyperbilirubinemia. Selective β-blockers such as atenolol or metoprolol are generally preferred. *IIb, C*
  - ACE-I and ARB are contraindicated in pregnancy. ACE-I can be used in the post partum period but not in breast-feeding mothers. *III, C*

- Other treatment considerations in the pregnant patient:
  - Patients with atrial fibrillation who are hemodynamically unstable should be promptly electrically cardioverted. This is safe in pregnancy.
  - Anticoagulation is indicated in the presence of atrial fibrillation, dilated Left atrium or mechanical prosthetic heart valve
  - Patients with valvular lesions who remain symptomatic despite optimal medical treatment may be considered for percutaneous valve Intervention or surgery
  - Commonly recommended antihyperthensive drugs include methyldopa, labetalol,calcium channel blockers and hydralazine[268,269,270]

Management during delivery involves: [122,267]

- Vaginal delivery with epidural anaesthesia is the preferred mode of delivery in most cases. Caesarian section is indicated:
  - for obstetric reasons
  - in patients on warfarin
  - in patients with severe pulmonary hypertension
- It is beneficial to shorten the second stage of labour by forceps or vacuum assisted delivery
- Left lateral decubitus position is preferred to attenuate the hemodynamic effects in the supine position
- Oxytoxic drugs are best avoided unless blood loss become excessive
- Routine antibiotic prophylaxis is not recommended in patients with valvular heart disease undergoing uncomplicated vaginal delivery or caesarian section.

Post partum care and follow up:

- After delivery, careful monitoring of hemodynamics is important for at least 24 hour or longer in high risk patients
- Patients with severe cardiac lesions should remain hospitalized for a longer period because the hemodynamics may remain abnormal for up to 10 days after delivery
- After the postpartum period, a full cardiac assessment should be performed and appropriate contraception should be advised

7.3.4. HEART FAILURE IN INFANTS AND CHILDREN

HF in infants and children is an important clinical condition and has diverse etiologies and clinical presentations. The common causes are;[271]

- congenital heart disease,
- acquired diseases such as rheumatic carditis, endocarditis and viral myocarditis,
- cardiomyopathy,
- tachyarrhythmia,
- post cardiac surgery.

Regardless of the etiology, timely diagnosis and effective treatment are important in preventing short-term and long-term sequelae.

The largest HF burden comes from infants and children born with congenital heart disease.[271] Among cardiac malformations, left to right systolic shunts are the most common causes of HF as shown in table XI, pg 49. In this situation, a volume overload on the left side of the heart causes preload stress and ineffective pulmonary re-circulation.

Valvular regurgitation lesions, either acquired or congenital, also cause volume overload to the heart. The most common are mitral and aortic regurgitation due to rheumatic valve disease. Severe prolapse of the aortic valve cusp in the setting of neglected doubly-committed sub-aortic ventricular defect may also cause aortic regurgitation.

Right sided volume overload presenting with HF rarely occurs in large atrial septal defect and anomalous pulmonary venous drainage. The latter will present in the neonatal period when there is an associated obstructive lesion. Generally, the highly compliant right ventricle can cope with volume overload and only fails after many years.

Severe obstructive lesions (critical aortic stenosis, critical pulmonary stenosis or neonatal coarctation) often present with HF in the early neonatal period, when the ductus arteriosus closes.

HF in an anatomically normal heart is less common in infants and children. It is either due to a primarily cardiac pathology or part of a systemic illness as illustrated in table XII,pg 50.

Table XI: Structural Heart Diseases That May Cause HF in Infants And Children

Shunt Lesions
• Ventricular septal defect
• Patent ductusarteriosus
• Aortopulmonary window
• Atrioventricularseptal defect
• Single ventricle without pulmonary stenosis
• Atrial septal defect (rare)
Valvular Regurgitation
• Mitral regurgitation
• Aortic regurgitation
Inflow Obstruction
• Cortriatriatum
• Pulmonary vein stenosis
• Mitral stenosis
Outflow Obstruction
• Aortic stenosis (valve/sub-valve/supravalvular)
• Pulmonary stenosis
• Aortic coarctation
Total/Partial Anomalous Pulmonary Venous Connection

Cardiomyopathy is a genetically related disease that occur approximately 1.13 in 100,000 children.[273] In these cases, HF symptoms are due to an enlarged ventricle with poor ventricular systolic function. They may also present with cardiac arrhythmias.

Clinical Presentation
Clinical presentation varies from mild to severe HF requiring ventilator support. The most common congenital causes of HF can be easily classified based on age of presentation as in Table XIII,pg 51. 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.[274]

Clinical Investigations
- **Pulse oximetry -** is helpful in identifying infants with HF with underlying congenital cyanotic heart disease.
- **ECG -** is useful to determine the type of structural cardiac lesion but not helpful in deciding whether HF is present or not. ECG is essential in looking for arrhythmias.

- **Chest X-ray -** May be pathognomonic for certain cardiac lesions. It has a high specificity but low sensitivity for detecting cardiac enlargement. The absence of cardiomegaly almost rules out HF.[275]
- **Echocardiography -** Not useful for the diagnosis of HF but it is essential to determine the structural cause of HF and to assess cardiac function.
- **Cardiac biomarkers -** These have been used extensively in assessing the severity and also predicting the course of the disease in adults. Its clinical use in infants and children is however limited.[276]

Table XII : Etiology of HF in infants and Children with Structurally Normal Heart

Primary Cardiac Pathology
• Cardiomyopathy
• Myocarditis
• Myocardial infarction
• Acquired valve disorders
• Hypertension
• Kawasaki syndrome
• Arrhythmia (bradycardia or tachycardia)
Non-cardiac Pathology
• Anemia
• Sepsis
• Hypoglycemia
• Diabetic ketoacidosis
• Hypothyroidism
• Other endocrinopathies
• Arteriovenous fistula
• Renal failure
• Muscular dystrophies

Management

In treating HF in infants and children it is important to determine the underlying etiology. Prompt diagnosis as well as timely referral for treatment either by surgical correction or an interventional procedure can prevent or ameliorate HF.

The principle of managing HF in infants and children includes supportive measures, anti-failure medications and definitive structural relief/correction as outlined below:[271]

Principles of managing heart failure

a) General measures:
These include:
- Oxygen therapy
- Correcting acidosis, hypoglycemia, hypocalcaemia and anaemia
- Treating respiratory infections aggressively
- Nasogastric tube feeding to reduce feeding effort and prevent aspiration in neonates
- Treating gastroesophageal reflux aggressively

Table XIII :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
- Neonatal coarctation

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)

b) Anti-failure medication: Generally, this is guided by information derived from studies in adults. Given the many causes of HF in this group, it is likely that they will respond differently to these medications.

- **Loop diuretics** - are the mainstay 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.[277]
- **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.[278]
- **Afterload–reducing agents** - Captopril and enalapril improve haemodynamics and HF symptoms. Use with caution in neonates, starting with a low dose.[279,280]
  - Captopril 0.1 mcg/kg/dose (1 - 3 times per day)
  - Enalapril 0.1-0.5 mcg/kg/dose (daily dose)
  - 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 oxygen consumption or increase after load.
- **Inotropic agents** - Norepinephrine, dopamine and dobutamine are 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.

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: Optimize anti-failure medication 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 o fthe obstructive lesion
- Coarctation of the aorta
  - Infants less than 3 months: Surgical correction
  - Infants more than 3 months: Balloon dilatation
- Large septal defects
  - Ventilatordependent: Surgical intervention
  - Non-ventilator dependent: Optimize anti-failure therapy and elective surgical closure

- Truncus arteriosus
  - Surgery within the first 3 months of life
- Anomalous left coronary artery from the pulmonary artery (ALCAPA)
  - Surgery at diagnosis

The ultimate therapy for HF that is unresponsive to treatment is cardiac transplantation. The decision is institutional preference and generally based on the availability of specialized clinical support unit, anticipated quality of life and donor availability.

Prognosis
The outcome of infants and children with HF depends largely on its etiology. When non-anatomical disorders are the cause, the success is related to the treatment of the underlying cause.

For many structural congenital defects (volume load conditions), surgery and interventional treatment can be curative. In some patients, it may only be palliative with improvement in clinical symptoms.

7.3.5. REFRACTORY HEART FAILURE

These are patients with severe symptoms despite maximal medical therapy. When patients become refractory to therapy, hospital admission is usually indicated. Meticulous control of fluid balance is important. Aggravating causes of HF as listed in Table IV,pg 23 should be identified and treated.

These patients may need specialized treatment such as continuous inotrope infusion, ventricular assist devices and consideration for cardiac transplantation.

The following may be required :-

- **Frusemide infusions.** These patients may require combination loop diuretics and thiazides. *IIb, C*
- **Ultrafiltration** in patients who are fluid overloaded.[108] In most patients, however, the relief is temporary. *IIb, B*
- **Short term infusions of parenteral inotropes** - low dose dobutamine (5mcg/kg/min) or milrinone. These produce symptomatic improvement but no survival benefit has been demonstrated.[281-283] *IIb, B*

The prognosis of these patients is poor. They should be referred to HF specialists to assess whether they may be potential candidates for device therapy or heart transplantation.

7.3.6 END OF LIFE CARE

It is important to recognize patients who appear to be approaching the terminal phase of their illness. These patients have:

- no identifiable reversible cause
- been on optimum tolerated conventional drugs
- worsening renal function
- fail to respond to appropriate changes in diuretic and vasodilator drugs
- sustained hypotension

In these patients it is important to :[284-286]

- explore their wishes in terms of options for care and place of care.
- provide symptom relief. Medications that may be useful include analgesics, antiemetics, anxiolytics, opioids and diuretics etc.
- discuss with patient and family when it would be appropriate to switch off devices such as ICD or CRT
- avoid inappropriate invasive procedures
- discuss issues of "Allow Natural Death (Do Not Resuscitate)" with patient and family.
- provide physical, psychological, social and spiritual support of patient and family support

7.3.7 TERMINAL HEART FAILURE –the last few days of life

As death approaches agitation, terminal restlessness, delirium and death rattles are common. In these patients, it is important to manage issues such as urinary retention, constipation, pain and uncomfortable position in bed. Once patient is semi-conscious, nursing in coma position will be most useful for drainage of retained secretions.[285,286]

8. ORGANIZATION OF CARE & MULTI DISCIPLINARY APPROACH

8.1 Monitoring and follow-up

All patients with chronic HF require monitoring which includes:

- clinical assessment of functional capacity – NYHA functional class or 6 min walk test
- fluid status and body weight
- blood pressure, heart rate and rhythm
- examination of cardiovascular and respiratory system
- cognitive status and nutritional status
- review of medications, including compliance, adjustment of doses, need for up-titration and possible side effects including erectile dysfunction
- serum urea, electrolytes, creatinine and eGFR as necessary

More detailed monitoring will be required if the patient has significant comorbidity such as diabetes mellitus, Chronic Kidney Disease (CKD) or if their condition has deteriorated since the previous review.

The frequency of monitoring should depend on the clinical status and stability of the patient. The monitoring interval should be short (days to 2 weeks) if the clinical condition or medication has been changed. It is required at least 6-monthly for stable patients with previously documented episode(s) of HF.

Patients who wish to be involved in monitoring of their condition should be provided with sufficient education and support from their healthcare professional to do this, with clear guidelines as to what to do in the event of deterioration (e.g. increasing dose of diuretics if the weight increases by > 2 kg in 3 days).

HF is characterised by recurrent hospitalisations. Recent studies on prevention of re-hospitalisation have focused on:

- home telemonitoring (the patient's status is assessed in the patient's own home)
- natriuretic peptide-guided therapy- use of serum natriuretic peptide levels to guide uptitration of drugs compared with 'usual' care.[287]
- formal follow-up by a HF team

8.2 Cardiology Referral

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

1. At initial presentation to confirm the diagnosis, determine the underlying cause of the HF and to advice on appropriate intervention if indicated.
2. During episodes of acute decompensation.
3. Known HF not responding to treatment ie when symptoms are recurrent or difficult to control
4. Known HF with symptomatic hypotension or excessive bradycardia
5. In the presence of acute coronary syndrome to determine the need for revascularization by PCI or CABG.
6. In cases of near faints, syncope, resuscitated sudden death and significant arrhythmias.
7. In any patient with significant valve disease not previously assessed or with worsening valve disease.
8. Women with significant structural heart disease and past history of HF or LV dysfunction who intent to get pregnant. This is for pre conception counselling.
9. Pregnant women with complex cardiac lesions and/or Eisenmenger's syndrome.
10. Infants and children with HF

8.3 Heart Failure Clinics

HF clinics enable focussed delivery of care by medical staff familiar with the problems and needs of such patients.

The out patient management of patients with HF requires a multi-disciplinary approach to provide patient education, optimization of medical treatment, psychosocial support, consideration for more advanced therapy including devices and heart transplantation, cardiac rehabilitation and palliative care.This would involve medical experts with interest and competence in the management of HF, supported by HF nurses, pharmacists, dieticians, physiotherapists, primary care providers, and social workers.

High risk and/or persistently symptomatic HF patients benefit from these clinics. Such set ups can improve outcomes through structured follow-up and better access to care.

9. FUTURE DEVELOPMENT

Future developments may focus on:

- novel pharmacological therapies (e.g. serelaxin, LCZ 696)
  A recent large trial compared an angiotensin receptor neprilysin inhibitor (LCZ 696) with the ACE-I enalapril on top of other standard therapy in patients with HF and reduced LV function. LCZ 696 was found to be superior to enalapril, with a significant reduction in death and in hospitalizations for HF.[288]
- Genetic and molecular research may provide further insight into diagnosis, classification and treatment of HF.
- Cell-based therapies to repair or restore the myocardium. To date, these have demonstrated modest benefit and phase III trials are on-going.[289]
- Advances in device therapy that can support the patient until the heart recovers.
- Effective programs to prevent new onset HF and re-hospitalisations eg usage of natriuretic peptide-guided treatment of HF.[287]

10. PERFORMANCE MEASURES

Performance measures should be used with the goal of improving quality of care for HF.[290,291]

Process performance measures focus on the aspects of care that are delivered to a patient, while outcome measures focus on the end-points such as mortality or hospitalisation.

Process Performance indicators includes:

- % of patients who had documentation of NYHA Functional Class
- % of patients who had LVEF measurement
- % of patients discharged with ACE-I/ARB
- % of patients discharged on **β**-blockers
- % of patients given a post discharge appointment

Outcome Measures indicators include:

- In hospital mortality

Refer to Appendix IV for calculation of these measures.

11. IMPLEMENTING THE GUIDELINES AND RESOURCE IMPLICATIONS

Both acute and chronic HF are common problems encountered at all levels of healthcare, both in district and general hospitals and in family medicine clinics. To ensure that patients receive good evidence-based care, the information in this CPG must be successfully disseminated. This can be done by ensuring:

– Continuous medical education via regular seminars, lectures and roadshows particularly at the district hospital and family medicine clinics. There is generally a lack of knowledge of evidenced based therapy of HF. Thus education and training is the most important aspect of the implementation of this CPG.

– Availability of the drugs mentioned in this CPG. Most of these are already easily available in the Ministry Of Health Drug formulary. Healthcare personnel need however, to be educated on their appropriate and timely usage.

– Coordinated linkages between primary healthcare personnel and tertiary cardiac centres to allow easy and appropriate referrals. Guidelines for referral are in section 8.2.

– Widespread availability of this CPG to healthcare providers via printed copies, electronic websites, etc.

Appendix

Appendix I

The New York Heart Association Functional Classification

Class		1 Years Mortality
CLASS I	No limitation.Ordinary physical activity does not cause undue fatique,dyspnoea or palpitation.	5 - 10%
CLASS II	Slight limitation of physical activity. Such patients are comfortable at rest. Ordinary physical activity results in fatique, 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 is 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 Vegetables Pure Oil Natural Fats Sugar Plain Flour Rice Most Cereals Legumes Rice	Meat Fish Egg Milk	Flavouring Agents	Sauces : Soya Tomato Barbeque Tauchioh
		Extract	Vegetable (Marmite) Meat (Bovril)
		Enhancers	Monosodium Glutamate Flavouring cubes
		Rising Agents	Bicarbonate of Soda Baking Powder
		Dressing	Salad Cream Moyonnaise
		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	EffervescentsSalts Bicarbonate Powder

Appendix IV

Calculation Of Performance And Outcome Measures

% of patients who had documentation of NYHA Functional Class	=	Number of patients who had documentation of **NYHA Functional Class** Number of HF patients who were seen during that time period	X 100
% of patients who had LVEF measurement	=	Number of patients who **had LVEF measurement** Number of HF patients who were seen during that time period	X 100
% of patients discharged with ACE-I / ARB	=	Number of patients who were on ACE-I/ **ARB at discharge** Number of HF patients who were seen during that time period	X 100
% of patients of discharged on **β**-blockers	=	Number of patients who were on **β**-blockers at **discharge** Number of HF patients who were seen during that time period	X 100
% of patients given a post discharge appointment	=	Number of patients who were given a post **discharge appointment** Number of HF patients who were seen during that time period	X 100

HEART FAILURE FOLLOW – UP FLOWCHART

Name:_____ RN_____

Age:_____ Sex:_____

Date of Diagnosis/First Visit:_____

Ht:_____ Wt:_____

Underlying Cause:

Ischemic Heart Disease:	☐	Hypertension:	☐
Diabetes:	☐	Cardiomyopathy:	☐
Valve Disease:	☐	Others:	☐

LVEF and date measured :_____

FOLLOW UP CHART

	Date of Visit				
1	NYHA				
2	Edema				
3	Heart rate				
4	BP				
5	Weight				
6	Frusemide	Y / N	Y / N	Y / N	Y / N
	Dose				
7	ACE-I/ARB	Y / N	Y / N	Y / N	Y / N
	Name of drug:				
	Present dose				
8	β-blockers	Y / N	Y / N	Y / N	Y / N
	Name of drug				
	Present dose				
9	Spironolactone	Y / N	Y / N	Y / N	Y / N
	Present dose				

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