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CLINICAL PRACTICE GUIDELINES

MANAGEMENT OF HEART FAILURE 2019

4th Edition

Ministry of Health Malaysia
Academy of Medicine Malaysia
National Heart Association of Malaysia

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MANAGEMENT OF HEART FAILURE 2019

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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 healthcare 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 2019 and will be reviewed in 5 years or sooner if new evidence becomes available.

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This is an update to the Clinical Practice Guidelines on Heart Failure (published 2000, 2007 and 2014). It supersedes the previous CPGs on Heart Failure (2000, 2007, 2014).

MESSAGE FROM THE DIRECTOR GENERAL OF HEALTH

It gives me great pleasure to write a message for another Clinical Practice Guideline (CPG) on the Management of Heart Failure (HF), which is now in its fourth edition. The first CPG in HF was published in 2000 with revisions in 2007 and 2014.

Cardiovascular disease is an important cause of morbidity and mortality in Malaysia. HF, the end stage of most diseases of the heart, is a common medical problem encountered in clinical practice and is an important cause of hospital admissions and readmissions. It is also an important cause of hospital expenditure.

Since the last CPG in 2014 the treatment modalities for the management of HF has expanded extensively. There have been many significant developments in the use of drugs and devices. These guideline-changing data have been incorporated into this CPG, taking into account our local health resources.

A CPG is only successful if it is accepted and implemented. I encourage all healthcare providers involved in the management of HF in children and adults to adopt these recommendations in your practice.

Finally, I would like to congratulate the Chairman and members of the Expert Committee for developing such a comprehensive CPG. Thanks to you, as well as the External Reviewers, for your time and effort.

Datuk Dr Noor Hisham Abdullah
Director-General of Health Malaysia

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RATIONALE AND PROCESS OF GUIDELINES DEVELOPMENT

Cardiovascular disease (CVD) 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 and readmissions. It is also an important cause of hospital expenditure. As the population ages, the prevalence of HF is expected to increase.

The 1st Clinical Practice Guidelines (CPG) in HF was published in 2000 with revisions in 2007 and 2014. Since then, there have been many new developments in this field. Thus the publication of this 4th edition is timely. This CPG proposes a structured multidisciplinary strategy for the seamless care of patients with HF between hospital and community care.

This CPG was drawn up by a committee appointed by the National Heart Association of Malaysia and Ministry of Health. It consists of a multidisciplinary team of cardiologists, nephrologists, family medicine specialists, general physicians and pharmacists from the government, private sectors and the public Universities. The external reviewers were also made up of a multidisciplinary team. Members of the public - patients and carers - however, were not included.

Objectives:

The objectives of this CPG are to:

- Update the current management of HF based on recent evidence with respect to:
  - Prevention
  - Diagnosis
  - Treatment – pharmacotherapy, device and surgical therapy
  - Rehabilitation
  - End of life and palliative care
- Recognise and manage HF in special populations:
  - Adult congenital heart disease
  - Geriatric population
  - Pregnant women
- Develop a structured multidisciplinary strategy for the management of patients with HF both in the primary and secondary care setting.

Process

The last CPG published in 2014 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 1st October 2013 (the date of the last CPG) till 31st August 2018 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], Acute decompensated heart failure, tachycardia-induced cardiomyopathy, heart failure mid-range, refractory heart failure, terminal heart failure, end stage heart failure, cardio-oncology.

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 (Table 1, Page 12).

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:

There were several topics and subtopics that were formulated addressing the diagnosis and management of HF.

For ***diagnosis:*** In a person presenting with shortness of breath:

- What features in the history and clinical examination would make one suspect this patient is having a HF?
- What diagnostic tests help confirm the clinical suspicion of HF with reasonable sensitivity and specificity?
  - ECG
  - Chest X-ray
  - Natriuretic peptides
  - Echocardiogram

For ***therapy***, the topics and subtopics were formulated using the PICO method as follows:

P: Population - Persons with confirmed HF and:

- Reduced left ventricular (LV) function (LVEF < 40%) - Heart failure with reduced ejection fraction (HF*r*EF) and:
  - Congested (Volume overload)
  - Hypotensive (Cold)
  - Combination of congestion and hypotension
    - Coronary artery disease (CAD)
    - Atrial fibrillation
    - Older persons
    - Persons with diabetes
    - Women
    - Chronic kidney disease
      - Not on renal replacement therapy
      - On renal replacement therapy

- Preserved LV function (LVEF > 50%) Heart failure with preserved ejection fraction (HF*p*EF)

- Mid range LV function (LVEF: 40-50%) Heart failure with mid-range LVEF (HF*mr*EF)

I: Intervention:

- Non-pharmacological therapy
- Pharmacological therapy:
  - Diuretics
  - Angiotensin Converting Enzyme Inhibitors (ACE-I)
  - Angiotensin Receptor Blockers (ARB)
  - β-blockers
  - Mineralocorticoid Antagonists (MRA)
  - Statins
  - Etc
- Surgery :
  - Valve surgery
  - Coronary artery bypass surgery
- Device therapy
  - Cardiac resynchronisation therapy
  - Catheter ablation
  - Pacemaker therapy

C: Comparison:

- Non-pharmacological therapy vs no non-pharmacological therapy
- Diuretics vs no diuretics
- ACE-I vs no ACE-I
- Etc

O: Outcome:

- Improvement in symptoms
- Reduce hospital readmissions for HF
- Reduction in Major Cardiovascular Disease Event Rate (myocardial infarction (MI), stroke, cardiovascular (CV) death)
- Reduction in all-cause mortality

Type of Question - Involves:

- Therapy drug therapy, surgery, device therapy
- Harm -
  - Worsening of symptoms and readmission rate
  - Increase in cardiovascular event rate (MI, HF, CV death)
  - Increase in bleeding risk and stroke rate
  - Adverse effects due to pharmacotherapy
- Prognosis - reduction in MI, HF, CV death and improvement in all-cause mortality

Type of Study

- Systematic review and meta-analysis
- Randomised controlled studies
- Cohort studies

Thus, there were numerous clinical questions formulated.
Example of some of these Clinical Questions:

- In a person with HF*r*EF and congested (volume overload) will the use of diuretics lead to an improvement in symptoms, hospital readmission, cardiac event rate and/or all-cause mortality?
- In a person with HF*r*EF and not congested (volume overload) will the use of diuretics lead to an improvement in symptoms, hospital readmission, cardiac event rate and/or all-cause mortality?
- In a person with HF*r*EF and congested (volume overload) will the use of ACE-I lead to an improvement in symptoms, hospital readmission, cardiac event rate and/or all-cause mortality?
- In a person with HF*r*EF and CAD, will coronary artery bypass surgery lead to an improvement in symptoms, hospital readmission, cardiac event rate and/or all-cause mortality?
- In a person with HF*p*EF and congested (volume overload) will the use of ACE-I lead to an improvement in symptoms, hospital readmission, cardiac event rate and/or all-cause mortality?

Target Group:

This guideline is directed at all healthcare providers involved in the management of HF in children and adults.

Target Population:

It is developed to treat all individuals with and at risk of HF.

Period of Validity of the Guidelines:

These guidelines need to be revised at least every 5 years to keep abreast with recent developments and knowledge that is being learnt.

Applicability of the Guidelines and Resource Implications:

This guideline was developed taking into account our local health resources. Blood investigations, chest radiographs, ECGs and echocardiograms are common in almost all public health facilities. The drugs used to treat HF - diuretics, ACE-I, β-blockers have been approved for use in Malaysia and available in public hospitals as generics.

This guideline aims to educate health care professionals on strategies to optimise existing resources in the timely management of patients with HF.

Facilitators and Barriers:

The main barrier for successful implementation of this CPG is the lack of knowledge of healthcare providers in the:

- Diagnosis of HF.
- Management of HF - initial treatment and long term follow-up.
- Optimisation of therapy and when to refer to tertiary centres.

Implementation of the Guidelines:

The implementation of the recommendations of a CPG is part of good clinical governance. To ensure successful implementation of this CPG we suggest:

- Increasing public awareness of CVD and HF in general and educating them on the importance of seeking early medical attention.
- Continuous medical education and training of healthcare providers on the importance of appropriate management of patients with HF. This can be done by road shows, electronic media, and in-house training sessions.

Clinical audit by individual hospitals and units to ensure compliance using the suggested performance measures in Section 12, Page 115 and Appendix VI, pg 121.

Dr. Jeyamalar Rajadurai
Chairperson

Table 1: GRADES OF RECOMMENDATIONS AND LEVELS OF EVIDENCE

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

LEVELS OF EVIDENCE	
A	Data derived from multiple randomised clinical trials or meta analyses.
B	Data derived from a single randomised clinical trial or large non-randomised studies.
C	Only consensus of opinions of experts, case studies or standard of Care.

Adapted from the American College of Cardiology Foundation / 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).

TABLE OF CONTENTS

GLOSSARY

Abbreviation	Description
ACE-I	Angiotensin Converting Enzyme Inhibitors
ACHD	Adult Congenital Heart Disease
AF	Atrial Fibrillation
AHF	Acute Heart Failure
ARB	Angiotensin Receptor Blockers
ARNI	Angiotensin-Receptor Blocker- Neprilysin Inhibitor
ASD	Atrial Septal Defects
ASLVSD	Asymptomatic Lv Systolic Dysfunction
AV	Atrial Ventricular
BNP	Brain Natriuretic Peptide
CABG	Coronary Artery Bypass Surgery
CAD	Coronary Artery Disease
CKD	Chronic Kidney Disease
CKMB	Creatine Kinase-Muscle/Brain Band
CMRI	Cardiac Magnetic Resonance Imaging
CV	Cardiovascular
CVD	Cardiovascular Disease
CPAP	Continous Positive Airway Pressure
CPG	Clinical Practice Guideline
CRS	Cardiorenal Syndrome
CRT	Cardiac Resynchronisation Therapy
CSA	Central Sleep Apnoea
DBP	Diastolic Blood Pressure
DOAC	Direct Oral Anticoagulants
DPP-4i	Dipeptidyl Peptidase 4 Inhibitors

Abbreviation	Description
DVT	Deep Vein Thrombosis
ECG	Electrocardiogram
EF	Ejection Fractions
eGFR	Estimated Glomerular Filtration Rate
GGT	Gamma-Glutamyl Transferase
GLP-1	Glucagon Like Peptide-1
HF	Heart Failure
HFC	Heart Failure Clinic
HFNC	High Flow Nasal Cannula
HfmrEF	Heart Failure With Mid-Range LVEF
Hf*r*EF	Heart Failure With Reduced Ejection Fraction
Hf*p*EF	Heart Failure With Preserved Ejection Fraction
HRQoL	Health Related Quality Of Life
IABP	Intra-Aortic Balloon Counterpulsation
ICD	Implantable Cardioverter Defibrillator
JVP	Jugular Venous Pulse
LBBB	Left Bundle Branch Block
LV	Left Ventricular
LVAD	Left Ventricular Assist Device
LVEF	Left Ventricular Ejection Fraction
LVH	Left Ventricular Hypertrophy
MI	Myocardial Infarction
MRA	Mineralocortocoid Receptor Antagonist
NP	Natriuretic Peptide
NSAIDs	Non-Steroidal Anti-Inflammatory Drugs

Abbreviation	Description
NTproBNP	N-Terminal Pro BNP
NYHA	New York Heart Association
OMT	Optimal Medical Treatment
OSA	Obstructive Sleep Apnoea
PCI	Percutaneous Coronary Intervention
PND	Paroxysmal Nocturnal Dyspnoea
PP	Pulse Pressure
PS	Pulmonary Stenosis
PSG	Polysomnography
RAS	Renin Angiotensin System
RCT	Randomise Control Trial
RV	Right Ventricular
SBP	Systolic Blood Pressure
SCD	Sudden Cardiac Death
SDB	Sleep Disordered Breathing
SGLT2i	Sodium-Glucose Cotransport-2 Inhibitors
VAD	Ventricular Assist Device
VF	Ventricular Fibrillation
VSD	Ventricular Septal Defect
VT	Ventricular Tachycardia

WHAT'S NEW IN THE GUIDELINES

	3rd Ed CPG Heart Failure (Old)	4th Ed CPG Heart Failure (New)
Acute Heart Failure	Acute Cardiogenic Pulmonary Oedema	Concept of classification according to clinical presentation: ➢ Warm and wet - adequate perfusion but congested (lungs and/or periphery) ➢ Cold and dry - hypoperfusion and dehydrated/not congested ➢ Cold and wet - hypoperfusion and congested (lungs and/or periphery) ➢ Warm and dry - adequate perfusion and dehydrated/not congested. These patients have either mild HF or are in the compensated stage of HF.
Oxygen Therapy	-	High flow nasal cannula (HFNC) seems more effective than conventional oxygen therapy and non-inferior to non-invasive positive pressure ventilation in most studies. **(IIa, B)**
Pharmacotherapy of HF*r*EF	-	ARNI should be considered as a replacement to ACE-I/ARB in patients with HF*r*EF who remain symptomatic to decrease CV death, HF hospitalisations, and symptoms. **(I,B)**
Surgical Management of HF*r*EF	No mention of mitraclip	In patients with moderate to severe MR and who are not surgical candidates, the use of mitralclip has shown mixed results. **(IIb,B)**
		8.5.1. Diabetes and Heart Failure 8.5.3. Heart Failure in Adult Congenital Heart Disease 8.5.4. Arrhythymia induced Heart Failure 8.5.5. Cardio-oncology and Heart Failure 8.5.6. Heart Failure and Kidney Dysfunction 9. Organisation of Care 14. Heart Failure in the Paediatric population

PART 1

Management of Heart Failure in Adults

SUMMARY

Key Message 1:

- Heart Failure (HF) is an important cause of hospitalisation accounting for about 6%-10% of all acute medical admissions and an important cause of hospital readmissions in Malaysia.
- HF costs was estimated to account for approximately 1.8% of total health expenditure.

Key message 2: Definition and Classfication

- HF is a clinical syndrome due to any structural or physiological abnormality of the heart resulting in its inability to meet the metabolic demands of the body or its ability to do so only at higher than normal filling pressures.
- HF can also be classified according to the clinical presentation into:
  - Acute heart failure (Acute HF)
  - Chronic heart failure (Chronic HF).
- In the setting of Left Ventricular (LV) myocardial dysfunction, left ventricular ejection fraction (LVEF) may be:
  - Reduced (LVEF ≤ 40%) - Heart failure with reduced ejection function (HF*r*EF).
  - Preserved (LVEF ≥ 50%) - Heart failure with preserved ejection fraction (HF*p*EF)
  - Mid-range (LVEF 41%-49%) - Heart failure with the LVEF being in the mid range (HF*mr*EF).

Key message 3: Diagnosis

- The clinical suspicion of HF should be supported by objective clinical evidence of cardiac dysfunction. (Flow Chart I, Page 28)
- Exercise capacity in a patient with heart disease is assessed by the New York Heart Association (NYHA) functional classification.
- Relevant investigations help to confirm the diagnosis and determine the type of HF and the aetiology.

Key message 4: Prevention

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

Key message 5: Acute Heart Failure (AHF)

- AHF may present as:
  - Pulmonary and/or peripheral oedema ("wet" - volume overload)
  - Low output state - shock ("dry" - usually due to pump failure)
  - Combination of pulmonary oedema and a low output state
- The principles of management are:
  - Rapid recognition of the condition.
  - Identification and stabilisation of life threatening haemodynamics.
  - Maintaining oxygenation and perfusion of the vital organs.
  - Relieving clinical symptoms and signs.
  - Identification and treatment of the underlying cause and precipitating/ aggravating factors.
- After initial clinical assessment, management should be instituted as in Flow Chart II, Page 29.
- For grading of recommendations and levels of evidence, see Table 2, Page 30.

Key message 6: Heart Failure with Reduced Left Ventricular Function (HF*r*EF)

- Non-pharmacological measures - These include:
  - Education of the patient and family about the disease, treatment options and prognosis.
  - Encouraging lifestyle measures such as:
    - Regular exercise
    - Avoid adding salt and flavouring sauces such as soya sauce, tomato ketchup and chilli sauce while cooking or at the table.
    - Fluid intake should be individualised. - A general recommendation is 1-1.5 litres per day in patients with normal renal function.
    - Smoking cessation and avoiding alcohol.
  - Advice regarding sexual activities and pregnancy.
- Pharmacological management:
  - After initial clinical assessment, management should be instituted as in Flow Chart III, Page 31.
  - For grading of recommendations and levels of evidence, see Table 3, Page 33.
  - Medications that have been shown to improve survival in HF*r*EF include:
    - Angiotensin converting Enzyme Inhibitors (ACE-I)/ Angiotensin II Receptor Blockers (ARB) if ACE-I intolerant
    - Angiotensin receptor-neprilysin inhibitor (ARNI)
    - β-blockers
    - Mineralcorticoid receptor antagonist (MRA)

- Device therapy:
  - Cardiac resynchronisation therapy (CRT) can be considered in patients with all of the following criteria:
    - Sinus rhythm
    - LVEF ≤ 35%
    - Left Bundle Branch Block (LBBB)
    - QRS duration > 150ms
  - An implantable cardioverter defibrillator (ICD) is indicated for secondary prevention in:
    - Patients resuscitated from sudden cardian death (SCD) due to ventricular fibrillation or haemodynamically unstable sustained ventricular tachycardia.
    - Prior MI and LVEF ≤ 40% with non-sustained VT AND inducible sustained VT or VF during an an electrophysiology (EP) study.
    - Patients with chronic HF and LVEF ≤ 35% who experience syncope of unclear origin.
- Surgery For HF
  - Coronary revascularisation (by either coronary artery bypass graft (CABG) or percutaneous coronary intervention (PCI)) should be considered in patients with HF and suitable coronary anatomy.

Key message 7: Asymptomatic LV Dysfunction

- 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.

Key message 8:Heart Failure with Preserved LV Function (HF*p*EF)

- 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.
- Treat volume overload with diuretics and manage comorbidities.

Key message 9: HFrEF in Special Groups

- **Diabetes**
  - Persons with diabetes are managed in the same manner as persons without diabetes.
  - When managing diabetes in patients with HF:
    - The sodium-glucose cotransport-2 inhibitors (SGLT2i) have been shown to reduce CV mortality and HF hospitalisations.
    - Saxagliptin, a dipeptidyl peptidase 4 inhibitors (DPP-4i) and thiazolidinediones are best avoided because of a trend towards harm.
    - Sulphonylureas, biguanides like metformin and alpha-glucosidase inhibitors like acarbose are generally safe.
- **Pregnancy**
  - The management of HF in pregnancy is more difficult than in the non-pregnant state and should be managed by a multidisciplinary team consisting of physicians, obstetricians and paediatricians.
  - Patients with LVEF < 30% and those in NYHA Class III and IV should be strongly advised not to get pregnant. They should be refered to the pre-pregnancy clinic for advise on the modes of contraception. If pregnant, termination should be considered.
  - HF that develops during pregnancy can be managed with the judicious use of diuretics, digoxin, nitrates, β-blockers and/or hydralazine.
- **Arrhythmias**
  - Arrhythmia-induced HF (also known as Tachycardia-induced cardiomyopathy) is a reversible cause of HF.
  - Successful treatment of the arrhythmia by drug therapy or catheter ablation can result in normalisation of LV function.
- **Cardio-oncology**
  - Chemotherapy-induced cardiomyopathy is not common; clinical HF occurs in 1-5%.
  - Close collaboration between the oncologist and the cardiologist is important.
  - Patients undergoing chemotherapy should have a careful clinical evaluation and assessment and treatment of CV risk factors.
- **Chronic Kidney Disease**
  - Cardiac and kidney disease frequently co-exist and this increases the complexity and costs of care, and may interact to worsen prognosis.
  - Management includes the use of intravenous diuretics, careful use of Renin Angiotensin System (RAS) blockers, β-blockers and occasionally ultrafiltration and haemodialysis.

Key message 10: Advanced Heart Failure

Patients with advanced HF should be referred to assess whether they may be potential candidates for mechanical circulatory support (e.g. Left Ventricular Assist Device - LVAD) and consideration for heart transplant.

Patients with refractory symptoms despite guideline-directed medical therapy, should be considered for palliative and end of life care.

Key message 11: Organisation of Care

Heart Failure clinics will serve as an intermediary between in-patient hospital care and community primary care.

Key Recommendations

Key Recommendation # 1:

- In making a diagnosis of Heart failure, a detailed history and a thorough physical examination are important.
- The clinical suspicion of HF should be supported by objective clinical evidence of cardiac dysfunction. (Flow Chart I, Page 28)
- The exercise capacity in a patient with heart disease should be assessed by the New York Heart Association (NYHA) functional classification. (Table 6, Page 40)

Key Recommendation # 2:

- To confirm the diagnosis and determine the type of HF and the aetiology, the following should be performed:
  - Basic investigations such as ECG, Chest Radiography, blood and urine tests.
  - An echocardiogram to help determine the type of HF (HF*r*EF, HF*mr*EF or HF*p*EF) and identify structural cardiac defects.

Key Recommendation # 3:

- The underlying disease and the precipitating cause(s), if present, need to be identified so that disease-specific treatment can be initiated early.

Key Recommendation # 4:

- The primary objective of management should be prevention of HF and early intervention, wherever appropriate.

Key Recommendation # 5:

- In Acute HF, it is important to:
  - Rapidly recognise the condition.
  - Identify and stabilise haemodynamics.
  - Maintain oxygenation and perfusion of the vital organs.
  - Relieve clinical symptoms and signs.
  - Identify and treat the underlying cause and precipitating/aggravating factors.
- After initial clinical assessment, management should be instituted as in Flow Chart II, Page 29.

Key Recommendation # 6:

- In Chronic HF, non-pharmacological measures play an important role and it is important to :
  - Educate patient and family about the disease, treatment options and prognosis.
  - Encourage lifestyle measures.
  - Individualise fluid intake - A general recommendation is 1-1.5 litres per day in patients with normal renal function.
  - Provide advice regarding sexual activities and pregnancy.

Key Recommendation # 7:

Management of chronic HF due to HF*r*EF is as in Flow Chart III, Page 31.

- Pharmacological Agents that should be administered are those that have been shown to improve survival in HF*r*EF and these include:
  - ACE-I/ARB if ACE-I intolerant
  - ARNI
  - β-blockers
  - MRA
- The doses of these medications should be slowly up-titrated to the maximal tolerated doses. (Tables 10-13, Pages 68, 70-72)

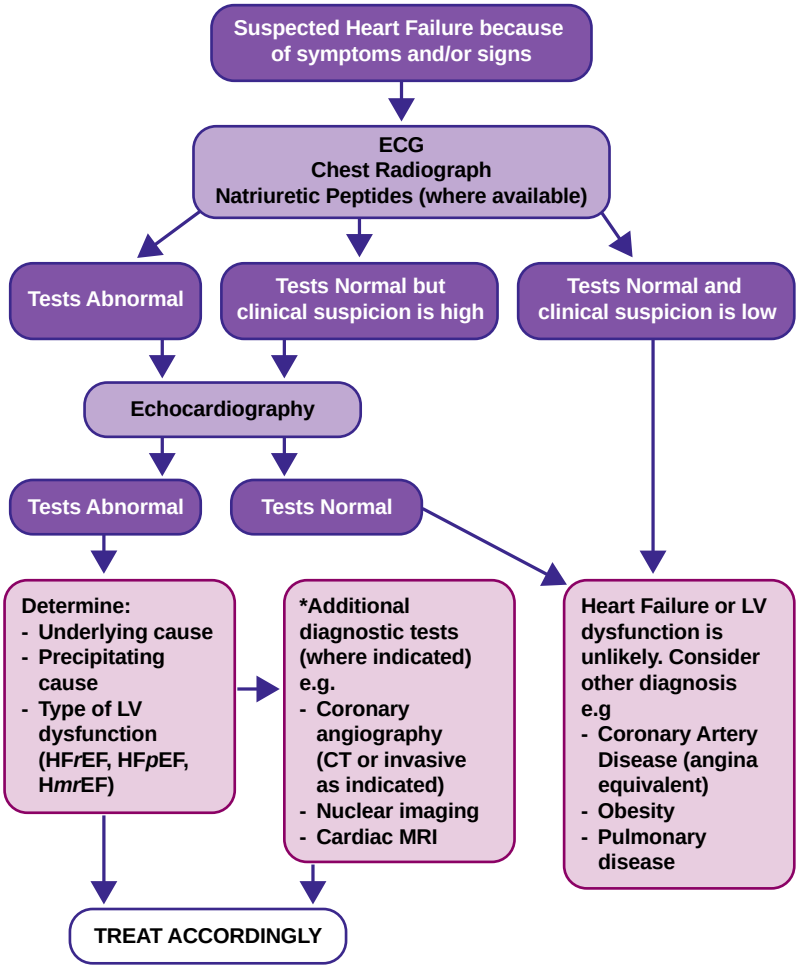
Key Recommendation # 8:
In patients with HF*r*EF, Device therapy should be considered in patients who fulfil the eligibility criteria, who otherwise have good clinical function and prognosis (life expectancy of more than 1 year) to improve their survival.

- CRT can be considered in patients with all of the following criteria:
  - Sinus rhythm
  - LVEF ≤ 35%
  - LBBB
  - QRS duration > 150ms
- An ICD is indicated for secondary prevention in:
  - Patients resuscitated from SCD due to ventricular fibrillation or haemodynamically unstable sustained ventricular tachycardia.
  - Patients with chronic HF and LVEF ≤ 35% who experience syncope of unclear origin.
  - Prior MI and LVEF ≤ 40% with non-sustained VT AND inducible sustained VT or VF during an EP study.

Key Recommendation # 9:
- In patients with HF*r*EF, coronary revascularisation (by either CABG or PCI) should be considered in patients with HF and suitable coronary anatomy.

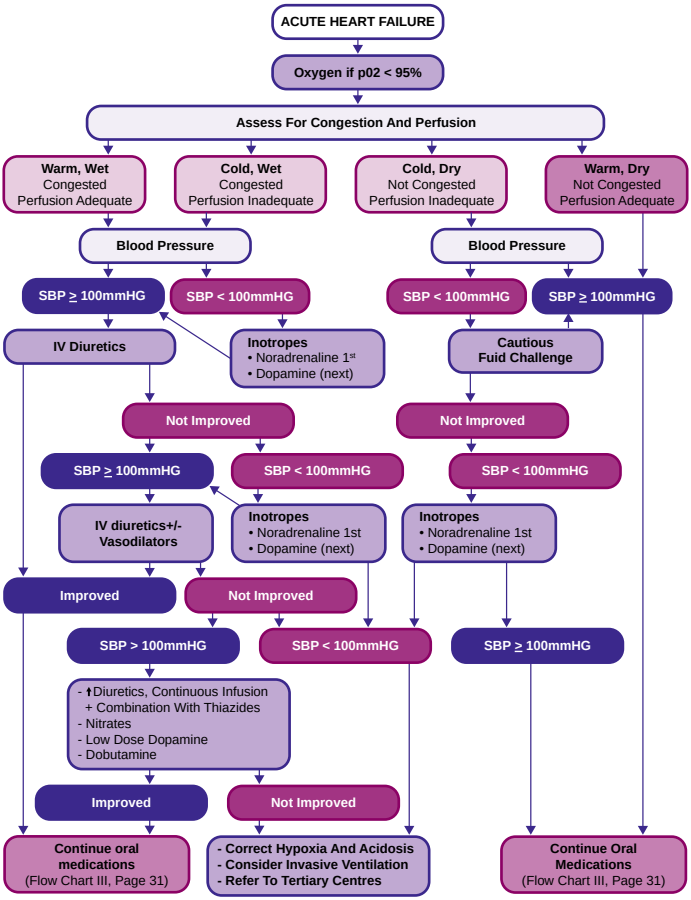
Key Recommendation # 10:
- In managing patients with HF*p*EF:
  - Hypertension is an important cause and should be treated according to guidelines.
  - Treat volume overload with diuretics
  - Manage comorbidities.

Flow Chart I: Algorithm for the Diagnosis of Heart Failure or LV Dysfunction



* Section 6, Page 39

Flow Chart II: Management of Acute Heart Failure



*__Hypoperfusion:__ *cold peripheries, capillary refill time more than 2 seconds, diaphoresis, oliguria, dizziness, confusion, narrow pulse pressure, hypotension.*

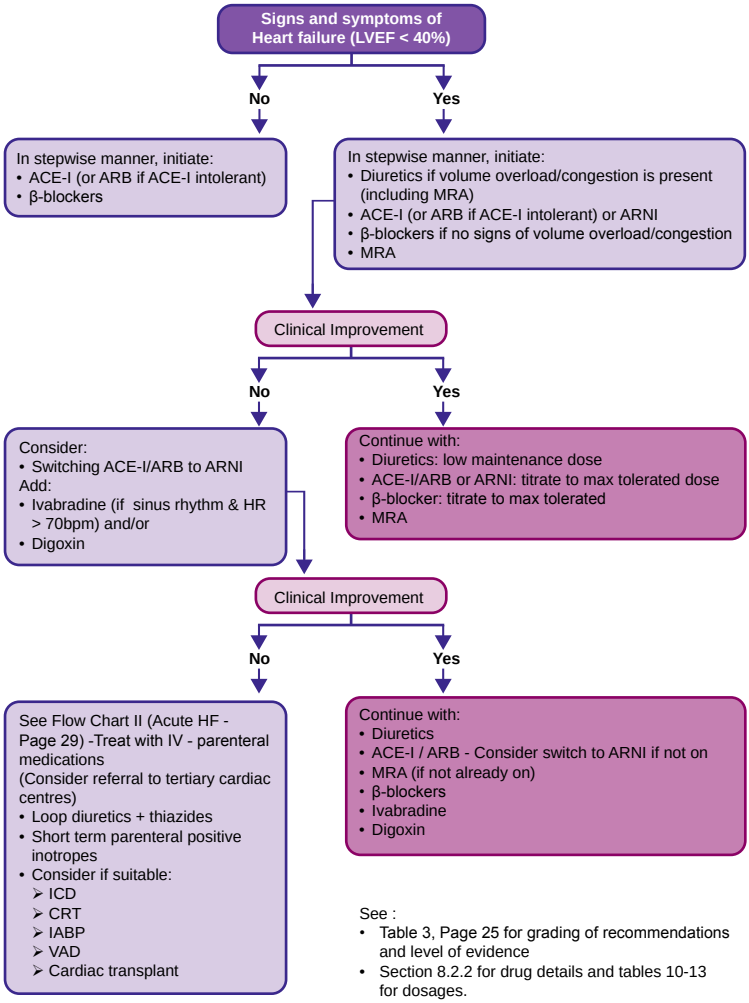
**__Congestion:__ *peripheral oedema, orthopnoea, paroxysmal nocturnal dyspnoea, lung crepitations, jugular venous dilatation, hepatojugular reflux, congested hepatomegaly, gut congestion, ascites.*

From onset, evaluate to identify correctable/reversible lesions-arrhythmias, hypertension, myocardial ischaemia/infarction, valvular heart disease.

Table 2: Grading of Recommendations in the Management of Acute HF

Intervention	Grades of Recommendation	Levels 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 patients 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 (<2-3ug/kg/min)	IIb	B	To improve renal perfusion and promote diuresis
Dobutamine	IIb	B	Indicated for peripheral hypoperfusion +/- pulmonary congestion
NOT RESPONSIVE TO INITIAL TREATMENT AND SBP < 100mmHg			
Noradrenaline	IIa	B	Indicated to increase the BP
Dopamine (> 5ug/kg/min)	IIb	B	Indicated to increase the BP
IABP	IIa	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

Flow Chart III: Optimising Drug Therapy In Chronic HF*r*EF



See :
- Table 3, Page 25 for grading of recommendations and level of evidence
- Section 8.2.2 for drug details and tables 10-13 for dosages.

Table 3: Grading of Recommendations in the Management of Chronic HF*r*EF

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			
Mineralocorticoid receptor antagonists (Spironolactone, Eplerenone)	I	A	Improves survival and reduces hospitalisations in moderate to severe HF and in post MI patients with mild HF.
ARB (in place of ACE-I)	I	B	In patients post MI and LVEF < 40%, Valsartan shown to be comparable to captopril.
ARNI (in place of ACE-I/ARB)	I	B	In patients with HF*r*EF who remain symptomatic to decrease CV death, HF hospitalisations, and symptoms.
Digoxin	I	B	In patients with HF and AF.
	IIa	B	No effect on survival. Reduces hospitalisations when added to optimal medical therapy.
Ivabradine	IIa	B	Reduces hospitalisations when added to optimal medical therapy in patients in sinus rhythm and heart rate > 70bpm.
ICD (implantable cardioverter defibrillator)	I	A	Improves survival in patients with resuscitated cardiac arrest, VF or sustained VT.
	I	A	Improves survival in patients > 40 days post MI, LVEF ≤ 30%, with non-sustained VT AND inducible sustained VT or VF during an EP study and on optimal medical treatment, and in NYHA II or III.
	I	B	Improves survival in patients with prior MI and > 40 days post MI and 3 months after revascularisation, LVEF ≤ 35% and NYHA class II - III.
	I	B	Improves survival in patients (no prior MI), LVEF ≤ 35%, on optimal medical treatment, and in NYHA II or III.
CRT (cardiac resynchronisation therapy)	I IIa	A B	Improves survival in patients having all of the following): sinus rhythm, LVEF ≤ 35%, LBBB and QRS duration on resting 12-lead ECG: • > 150ms • > 120-149 msec

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] In nearly all regions of the world HF is both common and increasing, affecting between 1 - 2% of the population.[2,3]

The main causes of HF amongst adult Malaysians were ischaemic heart disease (68%), valvular/rheumatic heart disease (29%) and non-ischaemic cardiomyopathy (28%).[4] Vascular risk factors such as hypertension, diabetes mellitus, and dyslipidaemia were common in Asian HF patients, particularly so in Malaysia (75%, 67%, and 52%, respectively).[4] In-patient mortality was 6%, with a 30-day readmission rate of 30%.[4]

HF is an important cause of hospitalisation accounting for about 6% - 10% of all acute medical admissions in Malaysia.[5,6]

It is also an important cause of hospital re-admissions.[7,8] About 25% of patients with HF are readmitted within 30 days for acute decompensation.[7,8] The prognosis for HF remains poor. The 1-year mortality rate varies between 5% to 52% depending on the severity and the presence of co-morbidity.[9,10] With a 5-year mortality at 48%, HF is deadlier than many cancers, for example, colorectal cancer (35.5%), non Hodgkin's lymphoma (29.6%), and breast cancer (10%).[9-11]

The overall global economic cost of HF in 2012 was estimated at $USD108 billion (MYR 439 billion) per annum.[12] The economic impact includes both direct and indirect costs.[12,13] Globally, direct costs accounted for ~ 60% ($USD 65 billion - MYR 264 billion) and indirect costs accounted for ~ 40% ($USD43 billion - MYR 175 billion) of the overall spent.[12] With an aging, rapidly expanding and industrialising population this value will continue to rise.

For Malaysia, the estimated overall HF costs was $USD 194 million (MYR 785 million), of which the direct and indirect costs were $USD 12 million (MYR 48.7 million) and $USD 182 million (MYR 740 million).[12] This is approximately 1.8% of total health expenditure, with 3.6% GDP spent on health. In general, in most low and medium economies like Malaysia, the indirect costs of HF in terms of premature mortality, morbidity, lost earning potential and unpaid care costs outweigh the direct costs. HF poses a major health and economic burden and an important goal in management is to prevent readmissions, thus reducing both direct and indirect costs.[12]

This guideline provides evidence-based recommendations to help health care providers in the management of their patients with HF. Beyond the Clinical Practice Guidelines (CPG), clinical management needs to be individualised to take into account patient's overall health goals, values, perspectives and preferences.

Sound clinical judgment plays an important role in formulating appropriate patient-centred care plans.

Key messages 1:

- HF is an important cause of hospitalisation accounting for about 6% - 10% of all acute medical admissions and an important cause of hospital readmissions in Malaysia.
- HF costs was estimated to account for approximately 1.8% of total health expenditure.

2. DEFINITION

HF is a clinical syndrome due to any structural or physiological abnormality of the heart resulting in its inability to meet the metabolic demands of the body or its ability to do so only at higher than normal filling pressures. This may be accompanied by signs and symptoms of systemic hypoperfusion and/or volume overload. Patients may have typical symptoms (e.g. breathlessness, ankle swelling and fatigue) and signs (e.g. elevated jugular venous pressure, ankle oedema, pulmonary crackles, and displaced apex beat). Occasionally, some patients may present without signs or symptoms of volume overload.

3. CLASSIFICATION

HF may be the result of any disorder of the endocardium, myocardium, pericardium or great vessels although commonly, it is due to myocardial dysfunction. It may involve only the left and/or right ventricle (RV).

HF may be classified in many ways. A commonly used classification is by left ventricular ejection fraction (LVEF). (Table 4, Page 36) This has been shown to have prognostic significance.[14-16] Furthermore, aetiology, demographic characteristics and response to therapies differ in the different classes.[14,15]

For practical purposes, HF can also be classified according to the clinical presentation into:

- Acute heart failure (Acute HF) - defined as the rapid onset of symptoms and signs of HF due to an acute deterioration of cardiac function in the presence or absence of previous cardiac disease.

- Chronic heart failure (Chronic HF) - this is a chronic state when patients have stable symptoms. In these patients, an acute precipitating or aggravating factor(s) may cause acute cardiac decompensation.

4. PATHOPHYSIOLOGY

The main pathophysiology of HF is due to a decrease in cardiac output. This will result in the following compensatory mechanisms:

- A higher ventricular end diastolic pressure - This is a compensatory mechanism to increase stroke volume by the Frank Starling mechanism.
- Neurohormonal activation of the:
  - Sympathetic nervous system
  - Renin-angiotensin-aldosterone system
  - Vasopressin

This neurohormonal activation is aimed at increasing stroke volume and cardiac output by:

- An increase in heart rate and ventricular contraction
- Vasoconstriction of arterial resistance vessels to maintain blood pressure
- Venous constriction to increase venous preload
- Salt and water retention to increase preload

In general, these neurohormonal responses are compensatory mechanisms. However they can also aggravate HF by increasing ventricular afterload and increasing preload to the point where pulmonary and/or systemic congestion and oedema occur.

In the setting of LV myocardial dysfunction, LVEF may be:

- Reduced (LVEF ≤ 40%) - Heart failure with reduced ejection function (HF*r*EF).
- Preserved (LVEF ≥ 50%) - Heart failure with preserved ejection fraction (HF*p*EF).
- Mid-range (LVEF 41%-49%) - Heart Failure with the LVEF being in the mid range (HF*mr*EF).

4.1 HF*r*EF

In HF*r*EF, cardiac output is reduced due to depressed myocardial contractility, irrespective of the aetiology. This leads to a cascade of pathophysiological changes as outlined above. There are effective medical and device therapies that have been shown to have survival benefit in HF*r*EF.

4.2 HF*p*EF

About 50% of patients presenting with HF have normal systolic function with predominantly diastolic dysfunction.[7,17,18] 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 are accompanied by predominantly signs of pulmonary and/or venous congestion and occasionally systemic hypoperfusion as well. There is limited data available on therapies that improve survival in HF*p*EF unlike those with HF*r*EF.

4.3 HF*mr*EF

Patients with HF*mr*EF have a clinical profile that are closer to those of patients with HF*p*EF than those of HF*r*EF. This category of patients is poorly studied and their response to therapies is unknown. Data seems to indicate that they have all cause readmission risk that are higher than HF*p*EF. In addition, the 1-year mortality rate appeared comparable to HF*r*EF and HF*p*EF after risk adjustments.[15]

Table 4: Classification Of Heart Failure According To LVEF

Ejection Fraction Terminology	LVEF
Heart Failure with Reduced Ejection Fraction (HF*r*EF)	≤ 40%
Heart Failure with mid-range LVEF (HF*mr*EF)	41% - 49%
Heart Failure with Preserved Ejection Fraction (HF*p*EF)	≥ 50%

Key messages 2:

- HF is a clinical syndrome due to any structural or physiological abnormality of the heart resulting in its inability to meet the metabolic demands of the body or its ability to do so only at higher than normal filling pressures.

- HF can also be classified according to the clinical presentation into:
  - Acute heart failure (Acute HF)
  - Chronic heart failure (Chronic HF)

- In the setting of LV myocardial dysfunction, LVEF may be:
  - Reduced (LVEF ≤ 40%) - Heart failure with reduced ejection function (HF*r*EF).
  - Preserved (LVEF ≥ 50%) - Heart failure with preserved ejection fraction (HF*p*EF)
  - Mid-range (LVEF 41% - 49%) - Heart Failure with the LVEF being in the mid range (HF*mr*EF)

5. AETIOLOGY

HF is not a complete diagnosis. It is important to identify the underlying disease and the precipitating cause(s), if present, so that disease-specific treatment can be initiated early.

The common underlying causes of HF in adults are:

- Coronary artery disease (CAD)
- Hypertension
- 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, cardiotoxic chemotherapy e.g. doxorubicin, trastuzumab (Herceptin), cyclophosphamide.
- Endocrine and metabolic disorders: thyroid disease, acromegaly, phaechromocytoma.
- Collagen vascular disease: systemic lupus erythematosis, polymyositis, polyarteritis nodosa.
- Tachycardia induced cardiomyopathy eg uncontrolled atrial fibrillation.
- Infiltrative cardiac disease e.g. amyloid, hyper-eosinophilic syndrome.
- Miscellaneous.
  - High output HF e.g. severe anaemia, large A-V shunts/malformations.
  - Peripartum cardiomyopathy.
  - Stress (Takotsubo) cardiomyopathy.

Patients with Chronic HF may occasionally develop acute decompensation. Factors that can contribute to this Acute HF are listed in Table 5, Page 39.

The more important causes that need to be recognised and treated appropriately are:

- Acute myocardial infarction/myocardial ischaemia.
- Arrhythmias (e.g. atrial fibrillation).
- Hypertensive emergencies.
- Infections (e.g. pneumonia).
- Non-compliance to medications.
- Excessive fluid and salt intake.
- Anaemia.
- Development of renal impairment.
- Adverse effects of drug therapy (e.g. non-steroidal anti-inflammatory drugs).

Table 5: 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) ● Hypertensive emergencies ● Arrhythmias ● Pulmonary embolism ● Secondary mitral or tricuspid regurgitation
Systemic Conditions ● Superimposed infections ● Anaemia ● Thyroid disease ● Electrolyte disturbances ● Worsening renal disease
Others ● Urinary retention ● Severe emotional or physical stress

6. DIAGNOSIS

HF is a clinical diagnosis based on a detailed history and physical examination.

6.1. Symptoms and signs

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), and a third heart sound. These signs are associated with adverse outcomes.[19] A fourth heart sound is due to atrial contraction and is more frequent in patients with HF*p*EF. It is absent in patients with atrial fibrillation (AF).

These signs may be accompanied by a laterally displaced apical impulse and a cardiac murmur. Other supportive signs include peripheral oedema, tachycardia, narrow pulse pressure, pulmonary crepitations, hepatomegaly and ascites. These clinical findings may be transient and resolve completely following initial therapy.

However, these signs are difficult to detect and are not always easily reproducible in the elderly, the obese and in patients with chronic lung disease. Occasionally symptoms and signs of volume overload may be absent and the patient may present with fatigue only.

In patients presenting with dysnoea, acute LV failure can sometimes mimic an acute exacerbation of bronchial asthma. Thus, a proper history and clinical examination is essential.

Exercise capacity in a patient with heart disease is assessed by the New York Heart Association (NYHA) functional classification. (Table 6, Page 40)

Table 6: New York Heart Association Functional Classification for Patients with Heart Disease

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

Once the diagnosis of HF has been made, it is important to establish the aetiology of the syndrome. (Section 5, Page 37)

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:
- 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).

Key Recommendation # 1:
- In making a diagnosis of Heart failure, a detailed history and a thorough physical examination are important.
- The clinical suspicion of HF should be supported by objective clinical evidence of cardiac dysfunction. (Flow Chart I, Page 28)
- The exercise capacity in a patient with heart disease should be assessed by the New York Heart Association (NYHA) functional classification. (Table 6, Page 40)

6.2 Investigations

BASIC INVESTIGATIONS	
12 lead ECG	- To assess heart rate, rhythm, QRS morphology, QRS duration, QRS voltage, evidence of ischaemia, LV hypertrophy and arrhythmias.
Chest radiograph	- To look for pulmonary congestion, cardiomegaly and presence of 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	To look for proteinuria, glycosuria.
OTHER IMPORTANT INVESTIGATIONS	
Echocardiography	This will allow assessment of: ● LV chamber size, volume and systolic function ● LV wall thickness, evidence of scarring and wall motion abnormalities ● Diastolic function of the heart ● Valvular structure and function ● Congenital cardiac abnormalities ● LV mechanical dyssynchrony ● Pulmonary hypertension. It is the most useful and widely available test to establish the diagnosis in patients suspected of HF.
Natriuretic Peptides (NP): ● Brain natriuretic peptide (BNP) or ● N-terminal pro BNP (NTproBNP)	BNP and NTproBNP are a family of hormones secreted by the ventricles in response to wall stress. They are useful in the following situations: ● In the emergency setting: ➢ NP are useful as a 'rule out' test for patients presenting with acute dyspnoea. A level of < 100pg/ml for BNP and < 300pg/ml for NTproBNP makes the diagnosis of acute HF unlikely.[20-23] These levels are affected by renal function and gender.[24-26] (See Table 7, Page 44 for the optimal cut off values of NP to exclude or diagnose HF in patients with dyspnoea) ➢ A high level supports the diagnosis of acute HF and very high levels correlate with the severity of HF and adverse outcomes.[20-23]

continue to next page...

	• In the community:
	  ➢ They are a useful "rule out" test in the diagnosis of HF in patients presenting with dyspnoea.[27]
	  ➢ Changes in the levels of BNP and NTproBNP predict risk of hospital admissions for HF.[28]
	• The results of studies on the use of NP to guide therapy in HF are conflicting.[29-32]
	
	NP levels are affected by:
	• Atrial fibrillation (AF)[33,34] - levels are increased even in the absence of HF.
	• Age[20,35] - Levels of NP increase with age
	• Renal function[24-26]
	• Obesity[36,37] - Levels are reduced in obesity
	• Certain medications such as Angiotensin - Receptor Blocker - Neprilysin Inhibitor (ARNI) may interfere with the intepretation of BNP levels.
	
	A raised NP level may be due to other causes besides HF. (Appendix I, Page 116)

ADDITIONAL INVESTIGATIONS WHEN INDICATED:	
Blood tests	• Serum cardiac biomarkers: to look for myocardial necrosis-troponins, creatine kinase-muscle/brain band (CKMB). • Thyroid function tests. Other less common tests that may be considered include: • Gamma-glutamyl transferase (GGT) • Viral studies • Iron studies.
Tests for myocardial ischaemia and/or viability	• Treadmill exercise test • Stress echocardiography (exercise or pharmacological) • Radionuclide studies • Cardiac magnetic resonance imaging (Cardiac MRI)
Invasive tests	• Coronary angiography • Cardiac catheterisation • Endomyocardial biopsy
Others	• Holter electrocardiography, loop recorders • Pulmonary function test

Table 7: Optimal Cut Points for Diagnosis or Exclusion of Heart Failure among Patients with Dyspnoea.[20-23]

	BNP (ng/L)	NTproBNP (ng/L)
Heart failure rule out	< 100	< 300
Heart failure possible	> 400	Age < 50 y: > 450
		Age 50 - 75: > 900
		Age > 75: > 1800

Key Recommendation # 2:

- To confirm the diagnosis and determine the type of HF and the aetiology, the following should be performed:
  - Basic investigations such as ECG, Chest Radiography, blood and urine tests .
  - An echocardiogram to help determine the type of HF (HF*r*EF ,HF*mr*EF or HF*p*EF) and identify structural cardiac defects.

Key Recommendation # 3:

- The underlying disease and the precipitating cause(s), if present, need to be identified so that disease-specific treatment can be initiated early.

7. PREVENTION

Prevention of HF should always be the primary objective of management. It should focus on 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.

7.1 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** - Increased systolic blood pressure (SBP) and pulse pressure (PP) are associated with the risk of HF in a continuous and graded manner.[38-40] Diastolic blood pressure (DBP) demonstrates a U-shaped association with HF risk.[38-40]
- **Diabetes** - This is a risk factor for the development of HF independent of coexisting hypertension or CAD.[41-43] (Section 8.5.1, pg 87)
- **Obesity and metabolic syndrome** - Data from the Framingham Heart Study showed that each unit increase in body mass index was associated with a 5% increase in the risk of HF in men and 7% in women.[44]
- **Smoking** - This leads to HF by direct effects on the myocardium and indirectly by causing or aggravating comorbidities that can cause HF.[45, 46]
- **Familial hyperlipidaemia**
- **Family history of cardiomyopathy**
- **Thyroid disorders** - Both hyper and hypothyroidism.[47] In patients with symptomatic HF and LVEF < 35%, abnormal thyroid function was associated with a significant increase in mortality.[48]
- **Renal disease**
- **Cardiotoxins** - excessive alcohol consumption, chemotherapeutic agents, illicit drug use such as cocaine, amphetamine, antidepressants.
- **Sleep-disordered breathing** (both central and obstructive sleep apnoea).[49, 50]
- **Connective tissue diseases** such as rheumatoid arthritis, SLE.
- **Chronic pulmonary disease** with pulmonary hypertension.

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%.[51] Treating isolated systolic hypertension in the elderly reduced risk of HF events by 49% and even in those over the age of 80 years, treating hypertension reduced new onset HF by 64%.[51-55] Aggressive lowering of the target SBP from ≤ 140 to ≤ 120 resulted in a 37% risk reduction of acute HF events in adults > 75 years.[56, 57]

IIa,B
- **Diabetes** - Optimise glycaemic control. Poor glycaemic control has been shown to increase the risk of HF.[41-43] (See Section 8.5.1, Page 87)

I,B
- **Healthy lifestyles** - A normal body weight, absence of smoking, regular exercise, and consumption of fruits and vegetables were individually and jointly associated with a lower lifetime risk of HF.[58]

I,B
- **Smoking cessation** - Current smokers have a higher risk of HF compared to non-smokers and ex-smokers.[59,60] 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.[60]

I,B
- **Regular exercise** - A minimum physical activity of at least 150 minutes per week of moderate intensity activity has been recommended to prevent ischaemic heart disease.[61]

I,B
- **Maintain ideal body weight**[61]

I,C
- **Curbing alcohol consumption** - Chronic long-term abuse of alcohol can lead to alcoholic cardiomyopathy.

I,A
- **Treating lipids to goal** in all individuals with established cardiovascular (CV) disease to reduce mortality. Statins have been shown to reduce the incidence of HF by approximately 20% among patients with hypercholesterolemia and CAD.[51] Even low risk individuals benefit from statin therapy although the use of pharmacotherapy for primary prevention should be individualised.[62-64]

IIb,B
- **n-3 fatty acids** -
  - Studies on the prevention of HF by n-3 fatty acids have been mixed.[65,66] A study in patients with multiple CV risk factors or atherosclerotic vascular disease who had no previous MI, showed that n-3 fatty acids did not reduce CV mortality and morbidity.[67]

IIb,B
  - On the other hand, consumption of fish more than once per month was associated with a lower HF risk.[67]

IIa,B
- **Identifying and monitoring at risk individuals prior to administration of cardiotoxic chemotherapy.** The use of β-blockers/ACE-I/ARB's have been shown to prevent cardiotoxic cardiomyopathy.[68,69] (See Section 8.5.5 Cardio-oncology, Page 100)

IIb,C
- **Screening of first-degree relatives** of patients with known heritable cardiomyopathy.

IIa,C
- **Detecting and treating thyroid disease** early to prevent thyroid heart disease.

IIb,B
- **Obstructive sleep apnoea** is associated with an increase in the risk of HF.[49,50] However, to date, the use of servo-ventilation and/or Continous Positive Airway Pressure (CPAP) for central and /or obstructive sleep apnoea (OSA) has not been shown to prevent HF.[70-72]

7.2. Individuals with cardiac disease but who still have normal cardiac function. Strategies include:

I,A
- Timely triage and appropriate treatment of patients with acute coronary syndromes.[73-75]

I,A
- Patients with CAD should be treated appropriately with antiplatelet agents,[76-79] β- blockers,[80,81] ACE-I[82] and statins.[83,84] Coronary revascularisation should be offered as indicated. ACE-I reduce the incidence of HF incidence 37% among patients with reduced LV systolic function and by 23% among patients with CAD and normal LV systolic function.[51]

I,B
- Patients with hypertension and left ventricular hypertrophy (LVH) should have their blood pressure control optimised. (< 140/< 90mmHG) Regression of LVH has been shown to be associated with a lower incidence of new onset HF.[85]

IIa,C
- Patients with significant valve disease (moderate and above) should bevfassessed for progression and timely intervention as indicated.[86]

IIa,C
- Patients with arrhythmias, when indicated, should be referred for evaluation and treatment.[87]

I,C
- Patients with congenital heart disease should have their cardiac lesions corrected and appropriate follow-up should be available looking for progression and sequelae.

In addition to the measures stated above, the following medical therapy 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.[88] It has also been shown to reduce new onset HF in patients with atherosclerotic vascular disease,[89] diabetes and hypertension with associated CV risk factors.[90,91]

IIa,A
- **ARB** - are non-inferior to ACE-I and should be considered in ACE-I intolerant patients.[92]

IIa,B
- **β-blockers** - in patients post myocardial infarction (MI).[93,94]

I,A
- **Statins** in patients with CAD.[62-64]

IIa,A
- **Sodium-glucose cotransport-2 inhibitors** (SGLT2i) in patients with diabetes.[95-98]

7.3. 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 symptomatic HF by guideline directed therapy.

Key Recommendation # 4:
- The primary objective of management should be prevention of HF and early intervention, wherever appropriate.

8. MANAGEMENT

8.1. ACUTE HEART FAILURE

Acute heart failure (AHF) is a clinical syndrome of new or worsening signs and symptoms of HF. It can be manifested as a first occurrence (de novo) or more commonly, as a result of deterioration of a previously diagnosed stable patient with HF.

AHF may present as:
- Pulmonary and/or peripheral oedema (“wet” - volume overload).
- Low output state - shock (“dry” - usually due to pump failure).
- Combination of pulmonary oedema and a low output state.

The onset and severity of symptoms can vary depending on the nature of the underlying disease and the rate at which the syndrome develops. The spectrum of clinical findings may range from worsening of peripheral oedema to life threatening pulmonary oedema or cardiogenic shock. It often requires urgent evaluation and treatment, which typically leads to hospitalisation.

Assessment and management must be made promptly and simultaneously.

The principles of management are:
- Rapid recognition of the condition.
- Identification and stabilisation of life threatening haemodynamics.
- Maintaining oxygenation and perfusion of the vital organs.
- Relieving clinical symptoms and signs.
- Identification and treatment of the underlying cause and precipitating/ aggravating factors.

8.1.1 Classification of AHF

There are a number of ways to classify patients with AHF. These classifications allow physicians to systematically assess the risk, prognosis and treatment approach.

- According to aetiology and precipitating causes (Table 5, Page 39). The more important causes are:
  - Myocardial infarction/Ischaemia
  - Arrhythmias – commonly rapid AF
  - Acute valvular dysfunction e.g. acute mitral regurgitation from chordal rupture
  - Severe and uncontrolled hypertension
  - Infection e.g. pneumonia
  - Non-compliance to treatment especially oral diuretics
  - Fluid overload

- According to clinical presentation (Table 8, Page 50)
  - Warm and wet - adequate perfusion but congested** (lungs and/or periphery)
  - Cold and dry - hypoperfusion* and dehydrated/not congested**
  - Cold and wet - hypoperfusion* and congested** (lungs and/or periphery)
  - Warm and dry - adequate perfusion and dehydrated/not congested.** These patients have either mild HF or are in the compensated stage of HF.

*__Hypoperfusion:__ cold peripheries, capillary refill time more than 2 seconds, diaphoresis, oliguria, dizziness, confusion, narrow pulse pressure, hypotension.

**__Congestion__: peripheral oedema, orthopnoea, paroxysmal nocturnal dyspnoea, lung crepitations, jugular venous dilatation, hepatojugular reflux, congested hepatomegaly, gut congestion, ascites

Table 8: Classification of AHF according to Clinical Presentation and a Guide to Management

Warm/Wet **Perfusion:** Adequate **Fluid status:** Congested **Management:** • **Diuretics -** Yes • **Vasodilators -** Yes • **Inotropes -** No	**Warm/Dry** **Perfusion:** Adequate **Fluid status:** Not congested **Management:** • **Diuretics -** No • **Vasodilators -** No • **Inotropes -** No
Cold/Wet **Perfusion:** Poor **Fluid status:** Congested **Management:** • **Diuretics -** Yes • **Vasodilators -** Cautious depending on BP • **Inotropes -** Yes	**Cold/Dry** **Perfusion:** Poor **Fluid status:** Not congested **Management:** • **Diuretics -** No • **Vasodilators -** Cautious depending on BP • **Inotropes -** Yes Consider fluid challenge cautiously

The aim is to obtain optimal perfusion and fluid status (warm/dry).

8.1.2. Investigations

Essential Investigations in AHF include (See Section 6.2, Page 42)

- Electrocardiogram (ECG)
- Chest radiograph
- Blood investigations: haemoglobin, serum electrolytes, urea, creatinine, cardiac biomarkers (troponin, CKMB, Natriuretic Peptides - BNP or NTproBNP)
- Blood gases may be considered
- Echocardiography

8.1.3. Decision for hospitalisation and care-setting

I,C Initial care in the critical care unit (ICU/CCU) should be considered for high-risk patients with features such as:

- Haemodynamic instability
- Arrhythmias
- Hypoperfused state-cold peripheries, capillary refill time more than 2 seconds, diaphoresis, oliguria, dizziness, confusion, narrow pulse pressure, hypotension
- Need for invasive ventilatory support
- Oxygen saturation (SpO_2) < 90% despite supplemental oxygen.

I,C The remaining patients with AHF can be managed in a high-dependency unit or normal ward depending on the clinical circumstances. However clinical deterioration may occur and hence, frequent re-assessments are necessary.

I,C Step-down care from the ICU/CCU is dictated by clinical improvement. Similarly, should the patient not improve, he should be considered to be transferred to a tertiary hospital with a Cardiology Unit.

8.1.4. Management (Flow Chart II, Page 29; Table 2, Page 30 & Table 9, Page 57)

The management of patients with AHF is largely based on clinical judgement and experience rather than on randomised controlled trials. Most clinical trials have been small and of low quality.

8.1.4.1 Oxygen

I,C
- Measurement of oxygenation by pulse oximetry (SpO_2) is recommended.

I,B
- Supplemental oxygen therapy is recommended when the SpO_2 < 95% or PaO_2 < 60mmHg. It should be titrated to achieve SpO_2 > 95%.[99-101]

III,B
- Routine use in non-hypoxic patients is not recommended as it can cause deleterious effects such as vasoconstriction and a reduction in cardiac output.[102-104]

IIa,B
- High flow nasal cannula (HFNC) seems more effective than conventional oxygen therapy and non-inferior to non-invasive positive pressure ventilation in most studies.[105,106] It is also better tolerated.

IIa,B
- Non-invasive positive pressure ventilation (NIV) such as CPAP and BiPAP should be considered early in patients with respiratory distress (respiratory rate > 25 breaths/min, SpO2 < 90%) despite high-flow oxygen administration.[107-111] There are no significant differences in clinical outcomes when comparing CPAP with BiPAP and the choice will depend on the equiment that is available.[111-113]

- NIV reduces respiratory distress and may decrease the need for intubation although data regarding mortality are less conclusive.[110,111]

I,C
- Intubation may be considered in patients with respiratory failure, who cannot be managed non-invasively, show signs of exhaustion and respiratory muscle fatigue.

- Some helpful indicators of respiratory failure include:

  - Hypoxaemia (PaO_2 < 60mmHg),
  - Hypercapnia ($PaCO_2$ > 50mmHg), and
  - Acidosis (pH < 7.35)

8.1.4.2 Diuretics

- Diuretics is the cornerstone therapy in patients who are fluid overloaded (wet).

I,B
- Intravenous (i.v.) frusemide 40 - 100mg is the diuretic of choice.[114] The dose should be individualised depending on the severity of the clinical condition. Patients who have already been on diuretics or have chronic renal disease, may require a higher dose.

- Further doses can be adjusted according to response, blood pressure, and renal function.

- Target 0.5 - 1kg decrease in body weight/day when the patient is volume overloaded. Less than 0.5kg of weight loss/day may indicate inadequate diuretic dose or diuretic resistance.

- To date, there has been no difference between continuous infusion or bolus dosing of frusemide for all-cause mortality, length of hospital stay and electrolyte disturbance, but continuous infusion was superior to bolus administration with regard to diuretic effect, safety profile and reduction in brain natriuretic peptide.[115-118]

8.1.4.3. Vasodilators

- Vasodilators can confer symptomatic relief and an improvement in haemodynamics but there is, however, a lack of data to draw any firm conclusions concerning their effects on CV outcome data.[119,120]

- **Nitrates :**

I,B
  - Nitrates are the most widely studied vasodilator.[119-124]

I,C
  - They are most useful if there is concomitant myocardial ischaemia, severe hypertension or aortic or mitral regurgitation.
  - They should be considered if the BP is adequate (SBP > 100mmHg).
  - It should be administered preferably intravenously for ease of titration.
  - Patients should be closely monitored for hypotension. This commonly occurs with concomitant diuretic therapy.

IIa,B
  - The combination of i.v. nitrate and low dose frusemide was shown in a small study to be more efficacious than high dose diuretic treatment alone.[123]

IIb,C
  - Extreme caution should be exercised in patients with aortic and mitral stenosis.

III,C
  - Nitrates are contraindicated in severe valvular stenosis.

- **Nitroprusside:**

IIa,C
  - This is most useful in AHF due to hypertensive emergencies and acute valvular regurgitation.

IIa,B

- Sodium nitroprusside would be useful in patients not responsive to nitrates.[125]

- Patients should be closely monitored for hypotension preferably using an intra-arterial line.

8.1.4.5 Inotropes (Table 9, Page 57)

IIb,B

- Inotropes are not routinely administered in patients with an adequate BP.[126,127]
- They are indicated in the presence of persistent signs of hypoperfusion (hypotension and low cardiac output cold patients) despite an adequate filling status.

- **Dopamine infusion:**
  - Low dose at < 2 - 3mcg/kg/min to improve renal flow and promote diuresis.[128]

IIb,B

  - The combination of low dose dopamine and low dose frusemide was as effective as high-dose furosemide but associated with less worsening of renal function.[118,128] There was however, no difference in the CV outcomes.[118]

- **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.

IIb,B

  - Dobutamine improved cardiac output but did not reduce pulmonary capillary wedge pressure or hospital stay. It was associated with significant ventricular tachyarrhythmias.[127,129,130]

- **Noradrenaline infusion:**

IIa,B

  - It was as efficacious as dopamine in terms of 28 day mortality but safer especially in the subset of patients with cardiogenic shock.[131,132]

IIa,B

  - The combination of noradrenaline-dobutamine appeared to be associated with more favorable haemodynamics and a safer strategy than adrenaline alone.[133]

8.1.4.6 Morphine

- i.v. 1 - 3mg 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.[134]

IIb,B

- May reduce anxiety and dyspnoea however due to paucity of data, routine use cannot be recommended.[135,136]

- Dose-dependent side effects include nausea, hypotension, bradycardia and respiratory depression.

- Consider co-administrating intravenous antiemetics (metoclopramide 10mg or prochlorperazine 12.5mg).

8.1.5 Response to therapy

Response should be assessed continuously using the following parameters:

- 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 may be considered in patients who despite pharmacological treatment present refractory symptoms (particularly with hypotension and hypoperfusion). This includes:

IIb,B

    - 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. However use of pulmonary artery catheters did not confer additional benefit beyond clinical assessment on CV outcomes.[137-139]

An adequate response would be reflected by all of the following:

- An improvement in the patient's clinical condition and symptoms,
- Warm peripheries,
- Decrease in his heart rate,
- An improvement in his oxygen saturation and
- An improvement in the urine output.

Generally, a SBP ≥ 90mmHg would be considered adequate if the patient has all of the following:

- Feels well,
- Has good tissue perfusion as shown by the absence of giddiness, warm skin ***and***
- Stable renal function with good urine flow.

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

Suggest (see Table 9, Page 57)

IIa,B
- Noradrenaline infusion[131,132] - initial inotrope and if BP is still low, add:

IIb,B
- Dopamine infusion[131]

I,C
- Avoid vasodilators (nitrates, nitroprusside) and morphine until the blood pressure has stabilised.

I,C
- Over diuresis or hypovolaemia - correct accordingly. In Right Ventricular (RV) infarction, the hypotension may respond to volume loading.

Other measures

I,C
- Intubation and mechanical ventilation

IIa,C
- Correction of acidosis

IIb,C
- Invasive haemodynamic monitoring

- Intra-aortic balloon counterpulsation (IABP):

IIa,B
  - 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.[140,141]

III,C
  - 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.[142-144]

IIa,B
  - IABP is contraindicated in patients with aortic regurgitation or aortic dissection.

Table 9: Drugs Commonly Used in Acute HF

	Route of Admin	Dosages
Diuretics		
Frusemide	IV	40-100mg **Initial dose:** New onset AHF and frusemide-naive: 20-40mg Known HF and on oral frusemide: 40-80mg
	Infusion	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
Inotropes		
Noradrenaline	Infusion	0.02-1mcg/kg/min till desired blood pressure is attained
Dopamine	Infusion	< 2-3mcg/kg/min - renal arterial vasodilation 2-5mcg/kg/min - inotropic doses 5-15mcg/kg/min - peripheral vasoconstriction
Dobutamine	Infusion	2-20mcg/kg/min
Adrenaline	Infusion	0.05-0.5µg/kg/min

- **Ventricular Assist Devices (VAD)** - would be useful as a bridge in patients for whom recovery from AHF is expected or for whom heart transplant is an option.[145-147]

There are other agents such as tolvapton, levosimendan and nesiritide which have shown symptomatic improvement in AHF but have been associated with either neutral or an increase in adverse events.[148-151]

8.1.6 Conversion to oral therapy and discharge

Following adequate response to intravenous therapy, the patient should be converted to optimal oral medications. (See Flow Chart III, Page 31)

I,B
- Diuretics[114,152]
  - Oral diuretics may be commenced following resolution of symptoms of congestion and the patient achieving his "dry weight".
  - The initial dose of oral diuretics required is generally higher than the intravenous dose since the oral version of frusemide has approximately 50% bioavailability compared with the i.v. preparation.[153]
  - The dose at discharge needs to be individualised.

I,A
- ACE-I/ARB[9,10,154,155]
  - Oral Renin Angiotensin System (RAS) blockers may be commenced at admission if the inital BP is adequate (systolic BP > 120mmHg).
  - In all other cases, it is best to defer for at least 24 hours till the BP is stable.
  - If the patient is already on a RAS blocker, it is advisable to stop it for at least 24 hours if the BP is low. It can be recommenced at a lower dose once the BP is stable. If the BP is adequate (systolic BP > 120mmHg), it can be continued at the same dose.
  - The dose should be uptitrated depending on the BP and renal function.

I,A
- β-blockers[156-161]
  - It is advisable to commence oral β-blockers if the BP is adequate and the patient is no longer congested i.e. his lungs are clear and there is no more oedema.
  - If already on a β-blocker, this can be continued depending on the patient's symptoms and haemodynamics.

I,A
- MRA[162-164]
  - These can be commenced at admission. Renal function and potassium levels need to be monitored.

- ARNI
  - At present, there is inadequate data to recommend it as first line in AHF.

IIa,B
  - There is data from one study at present, that suggests in-hospital initiation of this drug in patients with AHF in lieu of ACE-I is safe.

The patient should be observed for at least 24 hours for the stability of symptoms, weight and haemodynamics prior to discharge. The follow-up plans must be tailored according to the availability of facilities and expertise to manage the patient on outpatient basis. (See Section 9 Organisation of Care, Page 110)

8.1.7 Deep vein thrombosis (DVT) prophylaxis

IIa,C HF patients especially if they are bed-bound for protracted periods are at risk for DVT. Prophylactic measures include:

- TED stockings
- Direct oral anticoagulants (DOAC)
- Unfractionated or low molecular weight heparin.

8.1.8 Special situations

- **Myocardial Ischaemia / Infarction:**
  - Reversible myocardial ischaemia causing AHF needs early recognition, rapid stabilisation and referral for urgent coronary angiography.
  - In acute MI, reperfusion therapy by fibrinolytic or primary Percutaneous Coronary Intervention (PCI) may significantly improve or prevent AHF.
  - Long term management strategy should include adequate coronary revascularisation, antiplatelet therapy, ACE-I and/or ARB, β-blockers and statins.

- **Hypertensive Emergency:**
  - Typically presenting as "flash pulmonary oedema" with hypertensive crisis.
  - Systolic LV function tends to be normal.
  - The blood pressure needs to be reduced relatively quickly.
  - 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:**
  - AHF can be caused by valvular conditions such as acute mitral or aortic valve incompetence or stenosis, bacterial endocarditis, aortic dissection and prosthetic valve thrombosis.
  - Vasodilator therapy would be beneficial in acute valvular regurgitation, but is contraindicated in severe valvular stenosis.
  - Early access to echocardiography is crucial for the diagnosis and management.
  - Percutaneous intervention such as mitral valve commissurotomy can be life saving in patients with severe mitral stenosis.

- Arrhythmias:
  - Unstable tachy - or bradyarrhythmias need to be identified and treated appropriately e.g. electrical or pharmacological cardioversion or temporary pacemaker.
- Renal Failure:
  - AHF and renal failure can co-exist and either may give rise to the other.
  - Renal failure influences the response to drug therapy.[165] In these patients with refractory fluid retention, continuous ultrafiltration may be considered. (See Section 8.5.6, Page 103)

8.1.8 Cardiogenic Shock

Cardiogenic shock carries a very high mortality rate. The In hospital mortality was > 70% decades ago but recently improved at 27-51% with current therapy and management.[166,167]

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.
- PCWP >=15mmHg
- Serum Lactate > 2.0 mmol/L.

*cardiac index = cardiac output/body surface area

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).

Wherever possible, these patients should be transferred to a tertiary centre with PCI capable facilities.

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. Judicious administration of fluids (usual recommended volume: 100-200 mls) tapered to clinical response and signs of fluid overload.
  - 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 antiarrhythymic drug therapy or radiofrequency ablation.

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: IABP or LVAD.[142-147]

Key messages:

- AHF may present as:
  - Pulmonary and/or peripheral oedema ("wet"- volume overload).
  - Low output state - shock ("dry"- usually due to pump failure).
  - Combination of pulmonary oedema and a low output state.

Key Recommendation # 5:

- In Acute HF, it is important to:
  - Rapidly recognise the condition.
  - Identify and stabilise haemodynamics.
  - Maintain oxygenation and perfusion of the vital organs.
  - Relieve clinical symptoms and signs.
  - Identify and treat the underlying cause and precipitating/ aggravating factors.
- After initial clinical assessment, management should be instituted as in Flow Chart II, Page 29.

8.2 CHRONIC HEART FAILURE DUE TO HF*r*EF

Goals of management of HF include:

- Reducing symptoms, improving functional capacity and quality of life.
- Preventing hospitalisations and unplanned hospital visits.
- Improving patient survival.

8.2.1 NON-PHARMACOLOGICAL MEASURES

8.2.1.1 Education

I,B HF patients and their family members should be educated on the definition, causes, signs, symptoms and the progressive nature of the disease. They should:

- Be educated on self care management.
- Recognise the changes in their signs and symptoms - a sudden weight gain - more than 2kg in 3 days is a sign of worsening HF.
- Know when to contact their healthcare provider.
- Understand the indication, dosing, side effects and drug interaction of each medication they are prescribed.
- Be warned about self-medication and potential drug interactions.
- Adhere to treatment and be informed of the potential complications resulting from non-adherence to prescribed medication.
- 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, more lethal than several common malignancies.

In advanced HF, treatment options must be discussed tactfully and realistically with the patient and family.

8.2.1.2 Exercise training

I,B Several systematic reviews and meta-analyses support exercise training as an integral part of the non-pharmacological treatment of HF.[168-172]

Exercise training:

- Is safe in patients with chronic stable HF.[168-173]
- In patients with HF*r*EF, is associated with a trend towards reduction in all-cause mortality.[168]
- In patients with HF*p*EF, the clinical data is sparse. Small trials show that exercise training leads to an improvement in exercise capacity and quality of life.[174-176]

Exercise-based rehabilitation:

- Reduced the risk of hospital admissions.[168,171,173]
- Improved health related quality of life.(HRQoL)[168,169,171]
- Enhanced exercise capacity.[169,172]

Regular aerobic exercises are encouraged in NYHA I – III patients. These include:

- Walking, treadmill, stationary bicycle as well as swimming with a target goal of 5 days per week, 30 minutes per session.

Moderate intensity aerobic interval may be incorporated for selected patients.

For more details, refer to the 2017 Malaysian Clinical Practice Guidelines on Primary and Secondary Prevention of Cardiovascular Disease,1st Ed.

8.2.1.3 Diet and nutrition

IIa,B

It has been widely accepted that sodium intake has to be restricted in patients with HF especially in those with symptoms. However, clinical evidence to support this has been sparse and conflicting.[177-182] Excessive salt and fluid restriction can lead to intravascular depletion resulting in activation of the renin-angiotensin-aldosterone and sympathetic systems leading to deleterious tachycardia.[183]

The current recommendation is to avoid adding salt and flavouring sauces such as soya sauce, tomato ketchup and chilli sauce while cooking or at the table. Refer to Appendix II, Page 117 on salt content of common Malaysian food.

A good balanced diet plays an an important role to prevent energy depletion which can lead to cardiac cachexia and malnutrition.

8.2.1.4 Fluid restriction

IIa,C

The current evidence on fluid restriction is mixed.[182-185] As with salt, excessive fluid restriction can also lead to worse outcomes.[182-185] This may also be due to reverse causality - sicker patients tend to take less salt and water.

Fluid intake should be individualised. A general recommendation is 1-1.5 litres per day in patients with normal renal function.

8.2.1.5 Lifestyle measures

These include:

- Weight monitoring - Patients should be encouraged to monitor their own weight. In obese patients, weight loss should be emphasised.
- Alcohol - This should be avoided in patients with HF as it can lead to acute decompensation.[186] Patients with alcoholic cardiomyopathy must abstain from alcohol.
- Smoking should be stopped.[60]

8.2.1.6 Sexual activity, pregnancy and contraception

Physiological and psychological changes in patients with HF often result in sexual dysfunction.[187] These patients, in turn, often report a lower Health-related quality of life (HRQoL).[188] This problem is further compounded by their unmet need for information on sexual activities from their health care providers.[187,189]

IIa,B It is imperative that enquiries on sexual activities or dysfunction be addressed to provide a holistic approach to patient care.[190] The physician must take over the initial approach since patients are often embarrassed to initiate the topic. Some helpful tools to initiate the conversation include:

- PLISSIT (permission, limited information, specific suggestion and intensive therapy).[191]
- Needs of Sexual Counselling Scale for Chronic Heart Failure (NSCS-CHF)[187]
- Sexual Adjustment Scale (SAS).[187]

Patients should be taught:

- To pay attention to their symptoms of HF.
- The potential dangers and how to manage them when they occur during sexual activities.
- To defer sexual activities if in NYHA III-IV.
- Not to resume until his/her heart condition stabilises.
- To modify sexual practices to accommodate impaired effort tolerance.

HF patients need to be told that certain cardiac medications have important side effects and drug interactions :

- Nitrates may dangerously interact with drugs for erectile dysfunction - phosphodiesterase-5-inhibitors (Viagra, Cialis, Levitra).
- β-blockers, may contribute towards worsening erectile dysfunction but it is important that HF patients remain compliant to them.

I,C Patients with LVEF < 30% and those with NYHA III and IV should be advised against pregnancy because of high maternal mortality.[192,193] If pregnant, termination of pregnancy should be considered.[193]

When pregnancy is contraindicated, then appropriate contraceptive advice becomes paramount to the safety of the patient by preventing unwanted pregnancy. The World Health Organization Medical Eligibility criteria (WHO-MEC) for contraceptive use offers guidance in women with specific medical conditions.[194]

Contraceptive counselling should begin early. In the absence of randomised controlled studies, the choice of contraceptive method is almost always based on expert opinion of the attending cardiologists, obstretician and the patient's choice. In most cases, the ease of use and efficacy of the progestogen-only long-acting reversible contraceptive methods make them a good method for patients with CVD.[193,195] (Appendix III and IV, Pages 118 and 119)

8.2.1.7 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 sleep apnoea (CSA) or OSA.[196-198] OSA or CSA or combination of both, is commonly known as sleep disordered breathing (SDB).

OSA may occur in normal population or in HF patients, while CSA, which may present as Cheyne-Stokes respiration, is more uniquely associated with HF.[199] Independent predictors of SDB include older age, male gender, obesity, low ejection fraction and the presence of AF.[196,197] Polysomnography (PSG) is the gold standard in diagnosing OSA and CSA. However, a screening using overnight pulse oximetry is useful to preselect a patient for PSG.

Not only does SDB affect HRQoL, it leads to harmful effects on cardiac function, arrthymias and poorer prognosis due to the repetitive hypoxaemia, hypercapnia and swings in blood pressure and intrathoracic pressure.

I,C OSA patients are encouraged to lose weight.

IIa,B CPAP improves daytime sleepiness for OSA patients.[196] In HF patients with OSA, CPAP have been shown to improve HRQoL, LVEF function and HF symptoms.[196] However, none of the evidence so far can suggest improvement in terms of cardiovascular or all-cause mortality.[196]

Treatment of CSA in HF patients remains uncertain.[194] To date, trials using a CPAP or adaptive servo-ventilation in patients with HF have not been shown to be beneficial.[70-72,200]

As CSA tends to worsen when HF worsens, optimising medical therapy remains the main strategy in CSA.

8.2.1.8 Psychosocial support

During the course of HF, psychological problems tend to occur that may be due to change in lifestyle, medication therapy, implanted device and other procedures. Social support reduces stress and helps in maintaining a healthy lifestyle and compliance to treatment. Absence of social support has been associated with higher hospitalisation.[201-203]

I,C Thus, it is important that family members and carers are included during counselling sessions. Depressive symptoms may affect adherence and should prompt referral to specialist for psychological support.

Key Recommendation # 6:

- In Chronic HF, non-pharmacological measures play an important role and it is important to :
  - Educate patient and family about the disease, treatment options and prognosis.
  - Encourage lifestyle measures.
  - Individualise fluid intake - A general recommendation is 1-1.5 litres per day in patients with normal renal function.
  - Provide advice regarding sexual activities and pregnancy.

8.2.2 PHARMACOLOGICAL MANAGEMENT

Drug therapy is the mainstay of management of Chronic HF as outlined in Flow Chart III, Page 31. For grading of recommendations and levels of evidence, see Table 3, Page 33.

The majority of patients with HF*r*EF, regardless of symptom severity, require lifelong optimal medical treatment (OMT) which would include an ACE-I, β-blocker and a Mineralocortocoid Receptor Antagonist (MRA), unless contraindicated. An ARB shall be given to those who are intolerant to ACE-I.

Drugs should be initiated at a low dose and uptitrated to the target doses, or

at least up to maximum tolerated doses. Drugs with less proven survival benefits (e.g. diuretics) should be re-evaluated for reduction in dosage when OMT is not well tolerated due to a low BP. Alternatively, administering drugs at different timing may be considered for those with symptomatic hypotension.

Wherever possible, OMT should be continued during an acute illness. If discontinued, they should be restarted as soon as the condition has stablised.

III,C Non-steroidal anti-inflammatory drugs (NSAIDs) should be avoided in patients with HF.[204]

A) Diuretics (Table 10, Page 68)

I,B Diuretics are indicated in all patients with HF in whom there are signs and symptoms of fluid retention.[152]

The dose of diuretic used is variable and dependent on individual requirements. In the presence of severe congestive HF and in the acute decompensated stage, 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.

Patient should be educated on ‘dry weight’ management and advised to record their daily weight. If there is a consistent increase in weight of more than 2kg in 3 days, patients should be educated to self-adjust their diuretic (frusemide) dose together with restriction of their fluid intake until their “dry weight” is regained. However, if the weight increase is associated with worsening symptoms or fails to respond to these measures, the patient should seek medical help immediately.

The diuretic of choice in patients with fluid overload is a loop diuretic i.e. frusemide. The goal is a reduction of body weight of about 1kg/day.

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. Uptitration of loop diuretics may be a preferred strategy if diuresis is inadequate. Alternatively, bumetanide, a second generation loop diuretic, may be used because of its more predictable absorption.

IIb,B Combination of thiazides and loop diuretics may also be used as these drugs work synergistically to improve diuresis.[205-207] However, this combination has been associated with hypokalaemia, hyponatremia, worsening renal function and increased mortality.[207,208]

Metolazone is a once-daily oral thiazide diuretic. It is given in combination with a loop diuretic in patients with severe HF and refractory oedema.[207,209] At present, there is inadequate data to show that it is superior to the other thiazides in this setting.[207,210] It may also be used in patients with refractory oedema and advanced renal failure.[211-213]

When combination therapy is used, there can be a marked diuresis.[207] Careful monitoring of fluid and electrolyte balance and BP, is essential.

Table 10: Diuretics Used In Heart Failure

	Route of Administration	Usual Daily Dose
LOOP DIURETICS		
Frusemide	IV / Oral	20-80mg
Bumetanide	IV / Oral	0.5-2mg
THIAZIDES		
Hydrochlorothiazide	Oral	12.5-50mg
Metolazone	Oral	2.5-10mg
MINERALOCORTICOID ANTAGONISTS		
Spironolactone	Oral	12.5-50mg
Eplerenone	Oral	25-50mg

B) Inhibitors of the Renin Angiotensin Syste - Angiotensin Converting Enzyme Inhibitors (ACE-I) and Angiotensin Receptor Blockers (ARB) (Table 11, Page 70)

I,A ACE-I improve survival and quality of life in all classes of HF.[9,10,154,155,214] Hence, this first line drug should be given to all HF*r*EF patients. There are no differences among available ACE-Is in their effects on symptoms or survival.[154]

I,A ARBs are also indicated in HF*r*EF in ACE-I intolerant patients.[215-217]

IIa,B ARBs are also indicated in HF*r*EF. There is no difference between ACE-I and ARBs in terms of CV outcomes such as mortality and HF hospitalisation.[218] ARBs are however better tolerated because of their better side effect profile.[219]

IIa,B In patients post MI with impaired LV function, the ARB, Valsartan, was found to be as effective as captopril.[220]

In the initiation of ACE-I/ARB, the following should be considered:

- Patients with underlying low SBP (< 100mgHg) and/or elevated serum creatinine (> 250µmol/L) should be initiated with a low-dose of ACE-I/ARB cautiously.
- Avoid excessive diuresis before treatment. If patients are on large doses of diuretics, the BP 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 11, Page 70) or the maximum tolerated dose.
- Orthostatic hypotension should be avoided.
- Renal profile should be checked periodically. Serum creatinine or estimated Glomerular Filtrate Rate (eGFR) may increase up to 30% from baseline at 7-14 days, after introduction of either an ACE-I or an ARB. Dose adjustments is not required if the increase stabilises at ≤ 30%. The renal function should however be monitored periodically on a regular basis.

There is no significant difference in rates of hypotension, hyperkalaemia, or renal dysfunction between ACE-Is and ARBs.

ACE-I intolerance denotes the presence of a bothersome cough (most common, incidence:10-20%) or the experience of angioedema (uncommon, incidence <1%) with ACE-I therapy. Patients with this condition may be switched to an ARB, although, some may still develop angioedema.[222]

III,A Routine combined use of both ACE-I and an ARB should be avoided, as this combination causes more adverse effects (hypotension, hyperkalaemia, and renal dysfunction).[220,223]

Table 11: Recommended Doses of ACE-I and ARBs used in HF

Drug	Initial Daily Dose(s)	Target Dose(s)
ACE-I		
Captopril	6.25mg BD	50mg TDS
Enalapril	2.5mg OD	10-20mg BD
Lisinopril	2.5-5mg OD	20-40mg OD
Perindopril	2mg OD	8-16mg OD
Ramipril	2.5mg OD	10mg OD
ARBs		
Candesartan	4-8mg OD	32mg OD
Losartan	25-50mg OD	50-150mg OD
Valsartan	40mg OD	160mg BD

C) β-Blockers (Table 12, Page 71)

I,A Large clinical trials have shown that β-blockers reduce morbidity and mortality in patients with NYHA Class II-IV, of both ischaemic and non-ischaemic aetiology, on top of standard therapy.[156-161,240-226]

However, objective improvement in cardiac function might not be apparent for 6-12 months after β-blocker initiation.

Patients with AHF should be clinically stabilised and preferably no longer in overt HF (i.e. lungs are clear), before β-blocker initiation. Those in NYHA III-IV require close monitoring.

Patients who decompensate and are admitted in AHF 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 stabilised, an attempt should be made to uptitrate to the target or maximum tolerated dose of β-blockers.

The dose of the β-blocker may be doubled gradually every 2-4 weeks. The dose of diuretics may need to be adjusted at β-blocker initiation or uptitration as patients may experience transient fluid retention.

Contraindications include:
- Bronchial asthma
- In the presence of atrioventricular (AV) block (e.g. second or third degree heart block without a pacemaker)
- Symptomatic bradycardia or hypotension
- A requirement for β agonist therapy or positive inotropic support.

Initiating therapy with a β-blocker first is non-inferior to the standard approach of starting with an ACE-I.[159] The benefits seen with both these drugs are additive.

Table 12: Recommended Doses of β-Blockers used in HF*

Drug	Initial Daily Dose(s)	Target Dose(s)
Bisoprolol	1.25mg OD	10mg OD
Carvedilol	3.125mg BD	25mg BD (50mg, if > 85kg)
Metoprolol Succinate CR/XL**	12.5-25mg OD	200mg OD
Nebivolol***	1.25mg OD	10mg OD

** 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 hospitalisation with no reduction in mortality.[226]*

D) Mineralocorticoid Receptor Antagonists (MRA) (Table 10, Page 68)

I,A The addition of spironolactone to ACE-I, loop diuretics and digoxin in patients with severe HF reduces mortality and rehospitalisation.[162] Similarly, eplerenone, another MRA, when added to β-blockers and ACE-I in patients with mild HF, has been shown to reduce both morbidity and mortality.[163,164]

Care should be exercised in patients with renal impairment, especially during an acute dehydrating illness. Serum creatinine and potassium should be monitored regularly especially in high-risk groups. This includes those with:
- Diabetes
- Pre-existing renal impairment and/or
- Older age

Potassium supplements may need to be reduced or discontinued. If despite these measures, hyperkalaemia 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.

Table 13: Other Drugs Recommended for HF Management and their Dose Regime

Drug	Initial Daily Dose(s)	Max Dose(s)
ARNI		
Sacubitril/valsartan	50-100mg BID#	100-200mg BID
If Channel Inhibitor		
Ivabradine	(2.5-) 5mg BID	7.5mg BID
Others		
Isosorbide dinitrate*	20mg TDS	40mg TDS
Digoxin	0.0625-0.125mg	0.25mg daily

**(PO) Hydralazine-nitrate combination is not available.*
#Consider lower doses and once daily dose in patients with low BP.

E) Angiotensin Receptor Neprilysin Inhibitor (ARNI) (Table 13, Page 72)

ARNI is a combination of an ARB (valsartan) and an inhibitor of neprilysin (sacubitril), an enzyme that degrades natriuretic peptides-bradykinin, adrenomedullin, and other vasoactive peptides.

In a large study comparing the first approved ARNI (valsartan/sacubitril) versus enalapril in symptomatic patients with HF*r*EF on an adequate dose of either ACE-I or ARB, ARNI reduced the primary composite endpoint of CV death or HF hospitalisation by a significant 20%.[227] Patients with a serum potassium > 5.2mmol/L, an eGFR < 30ml/min, and symptomatic hypotension with a systolic BP of < 100mmHg were excluded from the trial.[227]

The use of an ARNI is associated with hypotension and a low incidence of angioedema. To facilitate initiation and titration, the approved ARNI is available in 3 doses (50mg, 100mg, 200mg).

I,B ARNI should be considered as a replacement to ACE-I/ARB in patients with HF*r*EF who remain symptomatic to decrease CV death, HF hospitalisations, and symptoms. The benefit of this ARNI over an ACE-I, was consistent

regardless of background therapy and irrespective of previous coronary revascularisation or β-blocker dose.[228]

ARNI should not be administered:

- Concomitantly with ACE-I or within 36 hours of the last dose of an ACE-I.[229,230]
- To patients with a history of angioedema.

The tolerability of ARNI and its side effect profile is similar to that of ACE-I or ARB. Laboratory monitoring is also similar. The long term safety of this group of drugs is, however, still not established.[231-233]

When initiating an ARNI:

- Initial dosing and rate of titration is dependent on the pre-existing treatment and associated comorbidities. It should, preferably, be individualised.
- When switching between an ACE-I and an ARNI, a washout period of at least 36 hours is required to decrease the risk of angioedema. No washout period is required for conversion between an ARB and an ARNI.

The drug should be uptitrated to the target dose shown to improve important HF outcomes.

In patients taking ARNI, NTproBNP is a more reliable biomarker than BNP. BNP levels may be spuriously elevated as the drug prevents its breakdown.

F) Ivabradine (Table 13, Page 72)

Ivabradine selectively inhibits the I*f* current in the sinoatrial node, providing heart rate reduction. It has no effect on the ventricular rate in AF.

IIa,B Ivabradine resulted in a reduction in hospitalisation, improvement in LV function and quality of life without an effect on mortality in patients who are:[234,235]

- On optimal medical therapy with diuretics, ACE-I, MRA and β-blockers, *and*
- Still symptomatic (NYHA class II-III), *and*
- Having a LVEF ≤ 35%, *and*
- Having a resting heart rate of ≥ 70 beats /min.

Every effort should be made to achieve target or maximally tolerated doses of β-blockers before initiation of ivabradine. It would be useful in patients who have contraindications to β-blockers or not able to tolerate higher doses of

β-blockers due to its side effect. Ivabradine has no effect on BP or myocardial contractility. It can, however, cause symptomatic bradycardia and visual disturbances.

G) Digoxin

The use of digoxin in HF in the contemporary era remains controversial. It has no proven survival benefits but it relieves symptoms and reduces hospitalisations.[236-238] It has a narrow therapeutic range and thus close monitoring of renal function and serum electrolytes (particularly potassium and magnesium levels) is required, prior to initiation of digoxin and periodically during use.

IIa,B Digoxin may be added to OMT and diuretics for patients with HF*r*EF and in sinus rhythm, who continue to have moderate to severe symptoms.[236-238]

IIa,B In patients with AF, combination of digoxin and β-blockers is superior to either agent alone.[239,240]

Hence, digoxin may be considered in patients with HF and AF in the following situations:

- Rate control is inadequate on β-blockers alone.
- β-blockers are contraindicated.
- Rapid control of the ventricular rate with parenteral drugs is required.

No loading dose is required for the management of chronic HF. Lower doses of digoxin and lower levels of serum digoxin (0.5-0.8ng/ml or 0.65 to 1nmol/L) are efficacious and appear adequate in most patients with compensated HF.[241-243] The maintenance dose of digoxin may range between 0.0625mg to 0.25mg daily, which may be lower in elderly patients, women and those with renal impairment.

Regular monitoring of digoxin levels is not required other than to assess for toxicity. The levels should not be used to guide dose adjustment in chronic therapy. Digoxin levels may be elevated in the presence of worsening renal function, electrolyte imbalance (hypokalaemia, hypomagnesaemia, or hypocalcaemia) or interacting drugs (e.g. amiodarone), which may lead to atrial and ventricular arrhythmias particularly in the presence of hypokalaemia.

H) Nitrates

IIa,C HF symptoms such as orthopnoea, paroxysmal nocturnal dyspnoea, exercise-induced dyspnoea, or angina may be relieved with the use of nitrates alone, in the form of tablets, sprays, or transdermal patches.

Nitrates are mainly used in AHF. In chronic HF, the trials on nitrates have been in combination with hydralazine.[244,245] This combination has been shown to improve survival in the African-American population with HF. [244,245]

Continuous (i.e. around the clock) use should generally be avoided to prevent nitrate tolerance and pseudotolerance.[246]

I) Antiplatelet and Anticoagulation Therapy

III,A There is no role for routine antiplatelet or anticoagulant therapy in patients with HF*r*EF.[247-251]

HF patients with the following risk factors for thromboembolism should be given an appropriate anticoagulant, unless contraindicated:

I,A
- AF - This is a common problem among patients with HF. All patients with AF should be given an anticoagulant, unless contraindicated.[252-257]

I,C
- Intracardiac thrombus (except for organised mural thrombus).

J) Antiarrhythmic Drug Therapy

Arrhythmias are common in HF. The more common ones are:
- Atrial fibrillation
- Ventricular tachyarrhythmias
- Bradyarrhythmias

J.1 Atrial fibrillation (AF)

New-onset AF in a patient with established HF is associated with a poor prognosis irrespective of the LVEF.[258-260] On the other hand, patients who developed AF first, followed by HF usually have a more benign course.[259]

Persistent ventricular rates > 150bpm may cause an arrhythmia induced HF that resolves with rate and/or rhythm control. (See Section 8.5.4, Page 98)

Patients with AF can be managed by either rate control or rhythm control.[261-264]

- **Rate control**
  - The optimal resting ventricular rate in patients with AF and HF is unknown, but probably between 75-90/min.[265-267] Excessive rate control, which may be associated with an increase in pauses, carries a risk.[266]
  - The optimal ventricular rate during exercise is also uncertain, but may be <110/min during light exercise.[264,267,268]

This can be achieved by using either:

I,A
- β-blockers[239,240, 268-270] and/or

IIa,B
- Digoxin[268]

β-blockers are preferred over digoxin as it provides better rate control during exercise and improves morbidity and mortality in patients with HF although the latter effect is attenuated in patients with AF.[266,271]

IIa,B Rate control is better when digoxin and β-blockers are used in combination rather than with each drug individually.[239,240]

In patients with marked congestion who cannot tolerate β-blockers, suggest:
- Oral or intravenous (i.v.) digoxin
- Oral or i.v. amiodarone[272,273]

- **Rhythm control**

IIa,B 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.[268]

Sinus rhythm can be maintained by using:[268]

IIa,B
- Amiodarone or

IIa,A
- Radiofrequency ablation[274]

J.2 Ventricular Arrhythmias

The exact prevalence of sudden cardiac death (SCD) in patients with HF in the contemporary era is not known. It varies depending on the aetiology of the HF and the LVEF.[275] Patients with HF and reduced LVEF (< 30 or 35%) (HF*r*EF) account for < 20% of all SCDs.[276]

SCD 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.[277,278] Occasionally rapid supraventricular tachycardias may deteriorate to malignant ventricular tachyarrhythmias.[278]

The following medications have been shown to reduce the incidence of 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.[279-281]

IIa,B
- **MRA:** have been shown to reduce the incidence of SCD.[162,163,282]

IIa,B
- **ACE-I:** Analysis of trials done following MI showed that ACE-I reduced SCD.[283-286]

IIa,B
- **ARNI:** this reduced both sudden cardiac deaths and deaths from worsening HF.[287]

IIa,B
- **Statins:** have a modest beneficial effect on SCD.[288]

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

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

I,A
- Implantable cardioverter defibrillator (ICD).[289-293] (Section 8.2.3.2, Page 79)

IIa,B
- Antiarrhythymic 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.[294]

IIa,C
- Radiofrequency ablation may be considered in the event of VT storms.

I,C Patients with significant bradyarrhythmias, trifascicular blocks and high-degree Atrio-ventricular (AV) blocks should be considered for pacemaker therapy.[295]

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

K) Calcium Channel Blockers (CCBs)

III,A Routine use of CCBs is not recommended in patients with HFrEF as they do not confer any morbidity or mortality benefit but worsen HF outcomes.[296-301] Diltiazem, verapamil and nifedipine should be avoided.

However, amlodipine and felodipine may be considered for other indications such as persistent hypertension despite use of OMT.[300,302]

Key Recommendation # 7:

- Management of chronic HF due to HF*r*EF is as in Flow Chart III, Page 31.
- Pharmacological Agents that should be administered are those that have been shown to improve survival in HF*r*EF and these include:
  - ACE-I/ARB if ACE-I intolerant
  - ARNI
  - β-blockers
  - MRA
- The doses of these medications should be slowly up-titrated to the maximal tolerated doses. (Tables 10-13,Pages 68,70-72)

8.2.3 DEVICE THERAPY IN HEART FAILURE

8.2.3.1 Cardiac Resynchronisation Therapy (CRT)

Patients who remain symptomatic (NYHA class II-III) despite OMT should be considered for CRT.

CRT has been shown to improve symptoms, hospitalisations and mortality, though up to 30% of patients may be non-responders.[303-307]

Patients with all of the following criteria can be considered for CRT:[304,305,308-312]

- Sinus rhythm
- LVEF ≤ 35%
- Left Bundle Branch Block (LBBB)

- QRS duration on resting 12-lead ECG:

IIa,B
  - ≥ 129-149ms

I,A
  - ≥ 150ms

Mechanical ventricular dyssynchrony is no longer a criteria in selecting patients for CRT.[313,314]

Patients with AF are less likely to respond to CRT. They may be considered for CRT together with atrio-ventricular node ablation to improve biventricular pacing.[315-317]

Regular monitoring of these patients is mandatory after device implantation to adjust medical therapies and reprogram the device as necessary.

8.2.3.2 Implantable Cardioverter Defibrillator (ICD)

SCD in patients with HF is often due to VF or VT. This risk can be reduced with the implantation of an ICD.

An ICD can be implanted as secondary prevention in patients with previous sudden cardiac arrest or documented sustained ventricular arrhythmias.[289-293]

It should be considered in patients who fulfil the eligibility criteria, who otherwise have good clinical function and prognosis (life expectancy of more than 1 year) to improve their survival.

Secondary prevention:

The following should be considered for implantation of ICD:[289-293]

I,A
- Patients resuscitated from SCD due to ventricular fibrillation or haemodynamically unstable sustained ventricular tachycardia. These cardiac arrest survivors have a high risk of recurrent events and implantation of an ICD has been shown to reduce mortality.

IIa,B
- Patients with chronic HF and LVEF ≤ 35% who experience syncope of unclear origin have a high risk of subsequent SCD.

I,A
- Prior MI and LVEF ≤ 40% with non-sustained VT **AND** inducible sustained VT or VF during an electrophysiological (EP) study.[318,319]

Primary prevention (prophylactic ICD implantation)

Prophylactic ICD implantation to reduce the risk of SCD may be considered in patients with:

- Prior MI and at least 40 days after an MI and 3 months after revascularisation by PCI or CABG and:

IIa,B
  - LVEF ≤ 30% with no HF symptoms (NYHA class I).[320]

I,B
  - LVEF ≤ 35% with mild to moderate HF symptoms (NYHA class II-III).[321]

- Non-ischaemic cardiomyopathy LVEF ≤ 35% and:

I,B
  - Mild to moderate HF symptoms (NYHA class II–III).[322-324]

IIa,B
  - No HF symptoms (NYHA class I).[322-324]

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

Key Recommendation # 8:

In patients with HF*r*EF, Device therapy should be considered in patients who fulfil the eligibility criteria, who otherwise have good clinical function and prognosis (life expectancy of more than 1 year) to improve their survival.

- CRT can be considered in patients with ***all*** of the following criteria:
  - Sinus rhythm
  - LVEF ≤ 35%
  - LBBB
  - QRS duration ≥ 150ms

- An ICD is indicated for secondary prevention in:
  - Patients resuscitated from SCD due to ventricular fibrillation or haemodynamically unstable sustained ventricular tachycardia.
  - Patients with chronic HF and LVEF ≤ 35% who experience syncope of unclear origin.
  - Prior MI and LVEF ≤ 40% with non-sustained VT **AND** inducible sustained VT or VF during an EP study.

8.2.4 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) Revascularisation Procedures

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

The STICH extension trial found a lower risk of total mortality in the CABG group compared to medical therapy in patients with severe HF (LVEF < 35%) and significant CAD, after a median follow-up of 9.8 years.[325] There was also a significant reduction in the risk of cardiovascular (CV) death and the combined outcome of all cause death and CV hospitalisations in the CABG group. There was an early risk of mortality following CABG, but benefits of CABG was seen after 2 years, and this benefit in favour of CABG was seen whether viability or angina was present or absent.

IIa,B Coronary revascularisation (by either CABG or PCI) should be considered in patients with HF and suitable coronary anatomy.[325]

B) Valve Surgery

Patients with HF and severe mitral regurgitation, non-ischaemic 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.[326]

Patients with LV systolic dysfunction undergoing surgical coronary revascularisation who also have severe mitral regurgitation secondary to ventricular dilatation may be considered for concomitant mitral valve repair or replacement.[327,328]

IIb,B In patients with moderate to severe MR and who are not surgical candidates, the use of mitralclip has shown mixed results.[329,330]

C) LV Reduction Surgery

LV aneurysmectomy may be considered in patients with a large discrete LV aneurysm who develop HF, angina pectoris, thromboembolism, and tachyarrhythmias due to the aneurysm.[331]

III,B Patients with HF undergoing surgical coronary revascularisation, who have areas of LV dyskinesia or akinesia do not benefit from concomitant LV reduction surgery.[332]

D) LV Assist Devices

Left ventricular assist devices have been used to:

- Bridge patients with HF to heart transplant.
- Support patients with acute severe myocarditis with a view to recovery.
- Provide long term haemodynamic support in eligible patients (destination therapy).[333-335]

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

Key Recommendation # 9:

- In patients with HF*r*EF, coronary revascularisation (by either CABG or PCI) should be considered in patients with HF and suitable coronary anatomy.

8.3 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%.[336,337]

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 hospitalisation was 8%.[9,338] Outcomes are worse if effective therapy is initiated after patients develop overt HF.[339]

Asymptomatic moderate to severe LV diastolic dysfunction is also common (5.6%) and associated with an adverse prognosis.[340] There is a higher risk of progression to HF and death when asymptomatic diastolic dysfunction is present, particularly in patients with diabetes and CAD.[340]

Screening may be done by:[341]

- **Resting ECG** - not very specific or sensitive
- **Echocardiography** - this is the most specific test
- **Natiuretic Peptides (NP) level** - 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.[341-343] These include patients with:

- CAD especially if there is a history of ACS
- Hypertension that has been long standing or poorly controlled
- Diabetes mellitus associated with complications
- Peripheral arterial or cerebrovascular disease
- Excessive alcohol intake
- Metabolic syndrome[344]
- Family history of cardiomyopathy

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

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 hospitalisation.[9,338,345,346]

IIa,C
- **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.[220]

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%.[157,347]

IIa,B
- **MRA:** In post MI patients with diabetes and reduced EF, eplerenone was beneficial.[348,349] Eplerenone also reduced the risk of an increase in natriuretic levels post STEMI.[350]

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

III,B
- **Calcium channel blockers:** The use of calcium channel blockers with negative inotropic effects is not recommended in asymptomatic post MI patients with LVEF < 40%.[351]

Key message 7:
- 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.

8.4 HEART FAILURE WITH PRESERVED LEFT VENTRICULAR SYSTOLIC 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.[18,352] HF*p*EF constitutes more than half of HF in older adults and the prevalence is increasing over time.[18,352] Commonly, these patients are older women who have hypertension.

8.4.1 Diagnosis

The diagnosis of HF*p*EF is challenging as symptoms and signs can be attributable to other co-existing conditions and LVEF is normal. Other co-morbidities that can contribute to dyspnoea in these patients include chronic obstructive pulmonary disease and obesity.
Criteria that is used to diagnose HF*p*EF include:[353,354]
- Clinical signs or symptoms of HF such as exertional dyspnoea, orthopnoea, atrial gallop sounds, and pulmonary rales combined with a suggestive chest X-ray and a favourable response to diuretics.
- Biochemistry - Elevated NP.
- Echocardiographic criteria;
  - Preserved or normal LVEF (> 50% or more within 72 hours of the event) and LV end diastolic volume index (LVEDVI) < 97ml/m^2.
  - Left ventricular hypertrophy (increased LV wall thickness or LV mass index > 115g/m^2 for men and > 95g/m^2 for women) or left atrial enlargement (LA volume index > 34ml/m^2).
  - Diastolic dysfunction if E/e′ ≥ 13 and the mean e' septal and lateral wall < 9cm/s or tricuspid valve regurgitation velocity > 2.8m/s.

- Invasive haemodynamic criteria:
  - Pulmonary capillary wedge pressure > 15mmhg or LV end diastolic pressure of > 16mmHg indicates elevated LV filling pressures.

8.4.2 Aetiology and Associated Comorbidities

Diastolic dysfunction may be due to myocardial or pericardial disease. (See Table 14, Page 87).

Hypertension remains the most prevalent comorbidity of HF*p*EF, with a prevalence of 60% to 89% from large controlled trials, epidemiological studies, and HF registries.[355]

Other comorbidities include overweight or obesity, diabetes mellitus, chronic obstructive pulmonary disease, obstructive sleep apnoea, anaemia, CAD and chronic kidney disease.[18,352,356]

The presence of diabetes, a lower systolic BP, haemoglobin and eGFR were associated with a poorer outcome.[356]

AF is common in HF*p*EF and increases risk of adverse outcomes.[357]

8.4.3 Management

The management of these patients remains empiric, since trial data are limited. Compared with HF*r*EF patients, hospitalisations and deaths in patients with HF*p*EF are more likely to be non-cardiovascular.

The important aim of therapy is to alleviate symptoms, improve well-being and reduce hospitalisations. Screening for comorbidities and appropriate interventions of these comorbidities is important. It includes:

- Identifying and treating the underlying cause(s) appropriately.
  - I,A Hypertension should be treated to target goals.[55,358] Improved BP control has been shown to reduce hospitalisation for HF.[358]
  - 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 AF, β-blockers or calcium channel blockers (verapamil, diltiazem) alone or in combination are the usual first line agents used for rate control.
- I,A Patients with paroxysmal or persistent AF should be anticoagulated to reduce the risk of thromboembolic events.[359,360]

Pharmacological options include:

I,C
- **Diuretics:** These are necessary to control pulmonary congestion and peripheral oedema 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.[226,361]

IIa,B
- **Non-dihydropyridine Calcium Channel Blockers (verapamil and diltiazem):** These may be used to lower the heart rate and has been shown to be beneficial.[362] Verapamil has been shown to improve functional capacity in patients with hypertrophic cardiomyopathy.[363]

IIa,B
- **ARB** trials have shown mixed results. One large trial showed a reduction in hospitalisation while another large trial was neutral.[364,365]

IIa,B
- **ACE-I** may improve relaxation and cardiac distensibility directly and may have long term effects 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 hospitalisations for HF while another trial was neutral.[366,367]

IIa,B
- **MRA:** A large study with spironolactone showed no difference in the combined primary end point of cardiovascular death, aborted cardiac arrest, or HF hospitalisation, though there was a reduction in HF hospitalisation endpoint alone.[368] Hyperkalaemia was more common in those on MRA and close monitoring of potassium and renal function is recommended for those treated with MRA.

I,B
- **Exercise training:** This is safe and improves exercise capacity and quality of life.[169] Combined endurance/resistance training appears safe for patients with HF*p*EF and improves exercise capacity (as reflected by an increase in peak oxygen consumption), physical functioning score and diastolic function.[369] It should consist of dynamic isotonic and not static exercise (e.g. walking or cycling).

- The use of an implantable pulmonary artery pressure monitoring system can guide augmentation of diuretic therapy and reduce HF hospitalisations.[370]

Key Recommendation # 10:

- In managing patients with HF*p*EF:
  - Hypertension is an important cause and should be treated according to guidelines.
  - Treat volume overload with diuretics
  - Manage comorbidities.

Table 14: Causes of Diastolic Dysfunction

MYOCARDIAL DISORDERS	
Myocardial diseases	• Infiltrative • Sarcoidosis • Fatty infiltration
Non-infiltrative	• Ischaemic cardiomyopathy • Idiopathic cardiomyopathy • Diabetic cardiomyopathy • Hypertrophic cardiomyopathy
Endomyocardial diseases	• Endomyocardial fibrosis • Hypereosinophilic syndrome
Storage disease	• Haemochromatosis • 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, et al. Diagnosing diastolic heart failure. Eur J Heart Failure 2002;4:419-30.

8.5 SPECIAL GROUPS

8.5.1 DIABETES AND HEART FAILURE

Heart failure and diabetes often co-exist in as many as 35-45% of cases irrespective of whether it is HF*r*EF or HF*p*EF.[371] The presence of diabetes increases both morbidity and mortality in these HF patients.[371-374] This is particularly so in patients with HF*p*EF who have co-existing microvascular complications.[375]

Patients with HF were shown to be at an increased risk of developing diabetes during a 3 year follow-up.[376,377] The mechanisms for this are not clear and may be the result of drug therapy (diuretics), reduced physical activity or from increased catecholamine and sympathetic activity.

Conversely, men and women with diabetes have 2 x and 4 x respectively,

increased risk of HF as compared to those without diabetes.[378] Associations have also been reported between absolute blood glucose levels, glycaemic control, and HF.[41,43,368,379,380] The risk for hospitalisations for HF was increased by almost 45% over a 5.7 year period despite having five risk factor variables within the target range ie glycated haemoglobin level, low-density lipoprotein cholesterol level, blood pressure, absence of albuminuria and smoking.[381]

HF is one of the earliest, most common and the most serious cardiovascular complication of diabetes.[382] Once HF develops, the clinical course is marked by frequent hospitalisations and eventually death.[383-385] Most sudden deaths are due to LV dysfunction rather than a new ischaemic event. Advanced age, duration of the disease, insulin use, the presence of CAD and an elevated serum creatinine are all independent risk factors for the development of HF.[386]

Diabetes can lead to HF due to:

- Coronary atherosclerosis
- Co-existing hypertension
- Diabetic cardiomyopathy - this can present as either systolic or diastolic LV dysfunction in an otherwise healthy diabetic person in the absence of clinically significant coronary, valvular or hypertensive disease.[387]

The link between diabetes and HF has been postulated to be multifactorial. In these patients advanced glycation end products, formed by a non-enzymatic reaction between protein and sugar residues, are increased and correlate inversely with left ventricular ejection fraction, the severity of the disease and its prognosis.[388,389] In addition, other proposed mechanisms include abnormal cardiac handling of free fatty acids, decreased myocardial levels of adiponectin, presence of cardiotoxic inflammatory cytokines and hyperinsulinaemia by itself.[390]

8.5.1.1 Diagnosis of HF in diabetes

Diabetics with HF present in a similar manner as non-diabetics. In diabetics though, dyspnoea may also be a symptom of ischaemia and CAD.

The investigative work up is also similar to non-diabetics.

8.5.1.2 Treatment of HF in patients with diabetes

Conventional therapies for HF*r*EF are equally effective in both diabetics and non-diabetics. These include:

I,A

- Inhibitors of the renin angiotensin system – ACE-I/ARB.[214]

I,A
- β-blockers - diabetics with HF had a reduction in morbidity and mortality that was as great as, if not greater than non-diabetics.[214,391]

I,A
- MRA - spironolactone and eplerenone. In the EPHESUS trial, eplerenone was shown to reduce mortality in patients with diabetes and mild HF, post MI[163]

I,B
- Sacubitril/valsartan (ARNI)[227]

IIa,B
- Ivabradine[234,235]

In patients with HF*p*EF,

IIa,B
- Spironolactone was shown to reduce morbidity and mortality in obese diabetic patients.[368]
- Sacubitril/valsartan and empagliflozin are being assessed in ongoing trials in HF patients with and without diabetes.

8.5.1.3 Treatment of diabetes in patients with HF

The optimal target HbA1c levels in these patients is still unknown. A large meta-analysis showed that intensive glucose lowering is not associated with any significant reduction in CV risk.[392] Conversely there was a 47% increase in the risk of HF.[392] Tight control of diabetes especially with the occurrence of hypoglycaemia is associated with increased mortality.[392-395]

In considering pharmacotherapy of diabetes in patients with HF:

I,A
- The sodium-glucose cotransport-2 inhibitors (SGLT2i) have been shown to reduce the risk of HF and in addition, in patients with HF at baseline, it also reduces CV mortality and HF hospitalisations.[95-98]

IIa, B
- Glucagon like Peptide -1 (GLP-1) agonists should be used with caution in patients with HF although recent large CV outcome trials have not demonstrated an increase in HF hospitalizations.[396,397]

III,B
- Saxagliptin, a dipeptidyl peptidase 4 inhibitors (DPP-4i), was shown to be associated with an increase in hospitalisation for HF.[398]
- This increased risk of HF was however, not seen with the other agents of the same class.[399]

III,A
- Thiazolidinediones are associated with an increase in the incidence of HF and should be avoided in those in NYHA Functional class III & IV.[400,401]

IIa,C
- Sulphonylureas are generally safe in HF patients although caution must be exercised with the short acting formulations which may cause hypoglycaemia.

IIa,C
- Biguanides like metformin and alpha-glucosidase inhibitors like acarbose are generally safe in patients with HF.

Key message 9:

- Persons with diabetes and, in general, managed in the same manner as persons without diabetes.
- When managing diabetes in patients with HF:
  - The sodium-glucose cotransport-2 inhibitors (SGLT2i) have been shown to reduce CV mortality and HF hospitalisations.
  - Saxagliptin and thiazolidinediones are best avoided because of a trend towards harm.
  - Sulphonylureas, biguanides like metformin and alpha-glucosi dase inhibitors like acarbose are generally safe.

8.5.2 HEART FAILURE IN PREGNANCY

About 0.5-4% of pregnant women have cardiac disease.[402,403] In our National Obstetrics Registry, CVD occurred in about 0.45 and 0.55% of cases in 2013 and 2014 respectively.[193]

HF may develop in pregnancy:[193]

- For the first time in a patient with pre-existing heart disease (congenital and/or valvular) due to decompensation from the stress.
- May occur in a patient who had HF previously and still has a depressed myocardial function. (LVEF < 40%).
- In a patient with a previously unrecognised genetic cardiomyopathy or a latent cardiac viral infection which has been unmasked or activated by the stress of pregnancy.[404-407]
- In a patient with a previously normal heart due to:[408-410]
  - Hypertensive complications of pregnancy i.e. gestational hypertension and the more severe forms preeclampsia, the HELLP syndrome (H: haemolysis, EL: elevated liver enzymes, LP: low platelet count).
  - Peripartum cardiomyopathy.

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 Caesarean 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.

8.5.2.1 Diagnosis

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

8.5.2.2. Management

The management of HF in pregnancy is more difficult than in the non-pregnant state and should be managed by a multidisciplinary team consisting of physicians, obstetricians and paediatricians.[193,402,411]

In the management of HF in pregnancy, the following issues need to be considered:[193,402]

- Gestational age at presentation.
- Clinical presentation, either as Acute HF or Chronic HF.
- Response to medical therapy.
- Potential maternal and foetal risks.
- Review and replace all fetotoxic drugs
- Timing and mode of delivery.

Predictors of maternal cardiac complications are as in Table 15, Page 91.

Table 15: Predictors of Maternal Risk for Cardiac Complication

Predictors of cardiac complication in the mother:[193,402,407,408]

- Cyanosis (oxygen saturation< 90%)
- Repaired or unrepaired cyanotic heart disease
- History of HF before pregnancy
- Prior cardiac event (HF, transient ischaemic attack, stroke, arrhythmia)
- Prior arrhythmia (symptomatic sustained tachyarrhythmia or bradyarrhythmia requiring treatment)
- NYHA class > II
- Valvular stenosis (aortic or mitral valve area < 1.5cm^2) and LV outflow tract obstruction (peak gradient > 30mmHg)
- Reduced systemic ventricular dysfunction (LVEF < 40%)
- Mechanical valve
- High risk aortopathy
- Reduced subpulmonary ventricular function (TAPSE <16 mm)
- Pulmonary arterial hypertension
- Systemic and pulmonary atrio-ventricular valve regurgitation (moderate to severe)
- Natriuretic peptide levels (NT-proBNP >128pg/mL at 20 weeks predictive of event later in pregnancy)
- Cardiac medication before pregnancy
- Maternal history of smoking
- No prior cardiac intervention

A. Preconception counselling

I,C Patients with LVEF < 30% and those in NYHA Class III and IV should be strongly advised not to get pregnant.[193,412] Preconception counselling should be for all women in the childbearing age with known or suspected heart disease. If pregnant, termination should be considered.

Management during pregnancy involves:

- **Non-pharmacological measures**

I,B The management of patients with mild symptoms consists mainly of non-pharmacological measures such as:[193]

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

- **Pharmacological measures**

The following drugs may be used in the pregnant patient with HF:[193]

I,C
- Diuretics are the first line therapy in patients who are fluid overloaded.

IIa,C
- Nitrates and/or hydralazine are used for preload and afterload reduction.

IIa,C
- β-blockers can be used cautiously.

IIa,C
- Digoxin is safe in pregnancy and during breast feeding.

III,C
- ACE-I, ARB and ARNI are contraindicated in pregnancy.

IIa,C
- ACE-I (enalapril and captopril) can be used in the post partum period.

III,C
- Ivabradine should not be used in pregnancy.

III,C
- Spironolactone is best avoided (FDA Category C) in pregnancy and during breast feeding.

- Other treatment considerations in the pregnant patient.

  - Patients with AF who are haemodynamically unstable should be promptly electrically cardioverted. This is safe in pregnancy.
  - Anticoagulation is indicated in the presence of AF, 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.

I,C

- Commonly recommended antihypertensive drugs include methyldopa, labetalol, calcium channel blockers and hydralazine.[413-417]
- In patients with peripartum cardiomyopathy and severe AHF, bromocriptine may be considered.[402]

B. Antenatal care

The principles of management of HF in pregnancy are similar to that in the non-pregnant state. If the patient is in decompensated HF requiring inotropes, she should be transferred to a cardiac centre.[402]

C. Labour and delivery

Timing and mode of delivery should be carefully planned by the multidisciplinary team. In the majority of patients, vaginal delivery with epidural anaesthesia is the preferred mode of delivery.

- Caesarean section is indicated:[193]
  - For obstetric reasons.
  - In patients on warfarin or who have discontinued their warfarin for < 2 weeks and who now are in imminent labour.
  - In patients with severe pulmonary hypertension.
- It is beneficial to shorten the second stage of labour by forceps or vacuum assisted delivery.[193]
  - Left lateral decubitus position is preferred to attenuate the haemodynamic effects in the supine position.
  - A slow i.v infusion of oxytocin immediately after birth, (2 U of oxytocin given over 10 min followed by 12 mU/min for 4 h) reduces the risk of post partum haemorrhage and has a minimal impact on cardiovascular parameters.[418]
- Routine antibiotic prophylaxis is not recommended in patients with valvular heart disease undergoing uncomplicated vaginal delivery or Caesarean section.

D. Post partum care

After delivery, careful monitoring of haemodynamic status should be done for at least 24 hours, or longer in high risk patients. In patients with severe cardiac lesions, haemodynamics may be abnormal up to 10 days after delivery.[193]

These patients should be evaluated post partum to assess the need for corrective surgery.

The risk of recurrence of HF in subsequent pregnancies should also be made known to the patient.

Follow-up visit at 6 weeks post partum should be attended by the multidisciplinary team, a full cardiac assessment should be done, and appropriate contraception should be advised.

Key message 9:

The management of HF in pregnancy is more difficult than in the non-pregnant state and should be managed by a multidisciplinary team consisting of physicians, obstetricians and paediatricians.

- Patients with LVEF < 30% and those in NYHA Class III and IV should be strongly advised not to get pregnant. If pregnant, termination should be considered.
- HF that develops during pregnancy can be managed with the judicious use of diuretics, digoxin, nitrates, β-blockers and/or hydralazine.

8.5.3 HEART FAILURE IN ADULT CONGENITAL HEART DISEASE (ACHD)

Adult congenital heart disease (ACHD) includes patients who are born with congenital heart disease (CHD) and survived to adulthood (age 18 years and above). These include those:

- Diagnosed during childhood and did not require intervention.
- Diagnosed and treated during childhood either surgically or transcatheterly. A significant proportion of this group of patients have residual haemodynamic lesions predisposing them to develop complications later during adult life. Eg: most of the repaired cyanotic heart lesions, palliated single ventricle.
- Diagnosed in adulthood either incidentally or when presenting with complications. eg. atrial septal defects (ASD), congenitally corrected transposition of the great arteries (CCTGA) and Ebstein's anomaly of the tricuspid valve.

8.5.3.1 Prevalence

Advances in diagnosis, medical and surgical management, interventional techniques and perioperative care have resulted in an improvement in the survival of children with CHD into adult life. The population of ACHD is thus increasing rapidly.[419]

The overall mortality rate of these patients is about 8% with the mean age of death occurring at 37 years.[420] The main causes of death were sudden cardiac death, HF due to systemic ventricular failure or tachyarrhythmias or a combination of both.[420-422]

8.5.3.2 Pathophysiology of heart failure

The underlying pathophysiology of HF in ACHD is multifactorial and complex and is highly dependent on the underlying anatomy, haemodynamic severity, timing and type of intervention, myocardial protection during surgery, presence of residual haemodynamic lesions and acquired comorbidities. In general, HF in ACHD may be due to:[423]

- Hemodynamic significant lesions- these need surgical/catheter interventions
- Myocardial failure - the mainstay of management is drug therapy and correction of the underlying causes eg CAD.
- Arrhythmias - management is a combination of drug therapy, CRT and or ICD
- Undetermined or a combination of factors

8.5.3.3 Diagnosis

It is important to determine the cause of the HF. It may be due to:

- An undiagnosed cardiac defect.
- A worsening residual lesion.
- Arrhythmias.
- A compounding extra cardiac pathology such as thyroid dysfunction or severe anaemia.

Knowing the baseline cardiac lesion and the history of previous surgeries and/or catheter interventions is absolutely important in the management of these patients. Due to chronic adaptation to abnormal haemodynamic state since childhood, many ACHD patients with HF may not report any symptoms or reduced exercise tolerance. Traditional echocardiographic parameters to assess ventricular function (volume, ejection fraction) are not applicable in many situations such as systemic RV or single ventricle. Longitudinal monitoring of individual patients is of paramount importance.

Investigations are similar to those mentioned in Section 6, Page 39.

- ECG - baseline abnormalities are common and a change in ECG morphology should trigger further investigation. New tachyarrhythmia is a common triggering factor for HF in ACHD patients
- Chest Xray - cardiomegaly, pulmonary congestion, pleural effusion, size of pulmonary arteries, concomittant lung pathology

Table 16: Common etiology and treatment of heart failure in ACHD

Etiology	Common examples	Treatment
Systemic left ventricular failure	**Structural** **Volume loading lesions** e.g. aortic regurgitation, mitral regurgitation and VSD **Pressure loading lesions** e.g. subvalvular, valvular and supravalvular aortic stenosis and coarctation of aorta	Surgical or catheter intervention whenever
	Myocardial disease, cardiomyopathy from any	Standard heart failure therapy (refer to Table 3, Page 32; Flow Chart III, Page 31)
Systemic right ventricular failure	ccTGA, DTGA post Mustard or Senning atrial switch procedure	Consider tricuspid valve repair CRT Standard heart failure therapy (refer to Table 3, Page 32; Flow Chart III, Page 31)
Systolic dysfunction of the subpulmonic RV	**Structural** **RV volume overload:** (i) chronic pulmonary insufficiency after TOF repair (ii) Ebstein's anomaly of tricuspid valve with TR (iii) Shunt e.g. ASD, TAPVD	Consider surgical correction e.g. Repair or replace the dysfunction valve, relief of RV outflow tract obstruction, ASD (if still operable) Symptomatic treatment for HF
	Chronic RV pressure overload e.g. pulmonary stenosis, conduit stenosis), DORV post TOF with residual RVOTO, Branch PA stenosis	
	Myocardial dysfunction e.g. ischemia, cardiomyopathies due to any etiology	HF therapy: diuretics, MRA and ACE
	PAH/Eisenmengers syndrome	PAH targeted therapy[424] Standard heart failure therapy (refer to Table 3, Page 32; Flow Chart III, Page 31)
Fontan failure	Functioning single ventricular hearts e.g. DILV, Tricuspid atresia, unbalance AVSD	Surgical or catheter intervention of residual structural lesion Fontan failure Standard heart failure therapy (refer to Table 3, Page 32; Flow Chart III, Page 31)
Arrhythmia	Atrial flutter/fibrillation Ventricular arrhythmias Common lesions: ASD, Ebstien's, Fontan, Post TOF correction	Standard antiarrhythmic therapy RFA CRT Pacemaker, ICD implantation
Acquired ischemic heart disease	(i) Cardiovascular risk factors (ii) Congenital coronary artery abnormalities or acquired (extrinsic compression, coronary artery kinking)	Treatment of risk factors CABG or PCI
	iii) Anaemia	Look for underlying cause and treatment
	iv) Thyroid disease	

**Diuretics should be used with caution*

- Echocardiography - establish underlying anatomical diagnosis, identify residual or new lesions and sequelae, assess ventricular function
- Cardiac MRI - the new "gold standard" for comphrehensive assessment of anatomy, haemodynamic, ventricular function and detection of myocardial fibrosis
- Cardiac CT - assessment of stents, conduit, coronary artery and collateral arteries
- Cardiac catheterisation - invasive quantification of shunts, measurements of pressure gradients across stenotic lesions, assessment of severity of pulmonary hypertension and vasoreactivity to help determine surgical operability. Lesions which are amenable to transcatheter interventions can be treated at the same time.
- Natriuretic peptides - the level correlates with the severity of haemodynamic lesions in many ACHD
- Cardiopulmonary exercise test - valuable tool with prognostic implications

8.5.3.4. Management

The aim of management is to:
- Reduce morbidity and mortality.
- Improve quality of life and functional capacity.
- Reduce hospitalisations.

All patients with ACHD and HF are best managed at a tertiary cardiac centre by a multidisciplinary team with ACHD expertise.[425]

Management includes:
- Surgical or catheter-based interventions is indicated where amenable.[426]
- Pharmacological therapy is less well studied in CHD. Selection of choice of pharmacological agents should be based on understanding of the underlying pathophysiology of HF. (Table 16, Page 96).[423,427-429]
  - Systolic failure of systemic LV - diuretics, ACE-Is, ARB, β-blockers and mineralocorticoid receptor antagonists should be used in both symptomatic and asymptomatic patients.
  - Systolic failure systemic RV - evidence is lacking but the above standard HF agents may be used in symptomatic patients.
  - Systolic failure of subpulmonic RV - diuretics are the mainstay treatment for symptomatic patients. If RV failure is secondary to pulmonary arterial hypertension (eg. Eisenmenger syndrome), PAH-targeted therapy such as phosphodiesterase-5 inhibitors (PDE5i), endothelin receptor antagonists or prostacycline analog should be used (see Malaysian CPG on Management of Pulmonary Arterial Hypertension, 2011)

  - Systolic failure of single ventricle - treatment is challenging and options are limited. Diuretics may be used to reduce congestive symptoms but high doses may reduce preload and effective cardiac output. In patients with raised pulmonary vascular resistance, PDE5i may improve Fontan haemodynamics.
- Tachyarrhythymia is a frequent precipitating factor of HF in ACHD and should be treated aggressively with either pharmacological therapy, catheter ablation or with devices such as cardiac implantable electronic devices (CIEDs).[430,431]
- Thromboembolism using anticoagulants (warfarin or Direct Oral Antico agulants - DOAC).
- Iron deficiency is not uncommon in ACHD patients, especially in patients with cyanotic lesions. Iron replacement improves functional capacity and reduces number of HF hospitalisations.
- Routine phlebotomy is no longer recommended for cyanotic patients with secondary erythrocytosis as it increases the risk of stroke and mortality. It is only indicated in symptomatic hyperviscosity syndromes.
- Individualised exercise rehabilitation.[432]
- Antibiotic prophylaxis against infective endocarditis (See Malaysian CPG for Prevention, Diagnosis and Management of Infective Endocarditis,1st Edition 2017).
- Contraception and pregnancy (See Malaysian CPG on Heart Disease in Pregnancy, 2nd Edition 2016 and Sections 8.2.1.6, Page 64 and 8.5.2 , Page 90)

8.5.4 ARRHYTHMIA-INDUCED HEART FAILURE

Arrhythmia-induced HF (also known as Tachycardia-induced cardiomyopathy) is a reversible cause of HF characterised by LV dysfunction resulting from an increased ventricular rate. The degree of dysfunction correlates with the duration as well as rate of the tachyarrhythmia.

Recognition of this entity is important clinically, as treatment of the underlying arrhythmia can result in either partial or complete recovery of LV function which, in turn, would result in an improvement in morbidity and mortality.[433,434]

Arrhythmia suppression should be considered as part of the holistic evaluation in treating patients with HF although the underlying mechanisms are not fully understood.

8.5.4.1 Supraventricular Arrhythmias

Any supraventricular tachycardia (SVT) with a rapid ventricular response may induce HF. Commonly encountered SVTs in clinical practice include:[435]

- Incessant atrial tachycardia (AT),
- Very frequent episodes of atrioventricular nodal re-entrant tachycardia (AVNRT), and
- Atrioventricular re-entrant tachycardia (AVRT).

Successful treatment, usually via electrophysiological study and radiofrequency ablation, could potentially restore LV function.

8.5.4.2 Atrial Fibrillation

AF is the commonest cardiac arrhythmia encountered in clinical practice.[436] AF with a rapid ventricular response may induce HF.[436,437]

Rate control or rhythm control with antiarrhythmic drug is the first line therapy. See Section 8.2.2-J1, Pages 75 and 76.

8.5.4.3 Ventricular Arrhythmias

Ventricular arrhythmias, including frequent premature ventricular complexes (PVC) or VT, may also induce HF. Maintenance of sinus rhythm or control of ventricular rate is critical in treating patients with HF.[434]

Curative or suppressive therapies with either radiofrequency ablation or antiarrhythmic drugs (AAD) may be considered in patients with PVC burden:

IIb,C
- 10% over 24 hours (high)

IIb,B
- 20% over 24 hours[438] (very high)

Radiofrequency ablation is preferred, since most antiarrhythmic drugs are contraindicated in the presence of HF.

8.5.4.4 Ventricular Pacing

Ventricular pacing at high rates may cause HF. Additionally, right ventricular pacing (more evidently at the apical position) may exacerbate HF symptoms, increase hospitalisation for HF and increase mortality.[439,440]

In patients with HF who have bradyarrhythmias and where pacing is indicated, biventricular pacing (CRT) is the pacing mode of choice.[441]

Key message 9:

- Arrhythmia-induced heart failure (also known as tachycardia-induced cardiomyopathy) is a reversible cause of HF.
- Successful treatment of the arrhythmia by drug therapy or catheter ablation can result in normalisation of LV function.

8.5.5 CARDIO-ONCOLOGY AND HEART FAILURE

Heart disease and cancer are often linked due to:

- Common risk factors (e.g. increasing age and cigarette smoking)
- Treatment strategies
  - Chemotherapy drugs has been associated with HF, arrhythmias, vasculitis and thromboembolic disease.
  - Radiotherapy of the mediastinum and left chest can lead to CAD, myopericardial fibrosis and valvular dysfunction.

Dyspnoea in cancer patients could be due to:

- Fluid overload.
- Cardiomyopathy due to chemotherapeutic agents, stress (Takotsubo), or underlying CAD.
- The primary cancer causing anaemia, lung and pericardial involvement.

Chemotherapy-induced cardiomyopathy is not common, clinical HF occurs in 1-5% and an asymptomatic decrease in LV function in the range of 5% to 20%.[442] Prognosis in the patients who develop HF is poor.[443]

The anthracycline class of chemotherapeutic agents remain the major cause of chemotherapy-induced cardiomyopathy.[444,445] In the current era, newer agents have also been implicated in a reversible form of cardiomyopathy.[446]

Chemotherapy-induced cardiomyopathy as defined by the Cardiac Review and Evaluation Committee is the presence of at least one or more of the following:[447]

1. Cardiomyopathy characterised by a decrease in Ejection Fraction (EF) globally or due to regional changes in interventricular septum contraction.
2. Symptoms of HF.
3. Signs associated with HF including but not limited to S3 gallop, tachycardia, or both.
4. Decline in initial EF of at least 5% to < 55% with signs and symptoms of HF or asymptomatic decrease in EF of at least 10% to < 55%.

Chemotherapy drugs that have been associated with HF include (Appendix V, Page120):

- Doxorubicin
  - 5% at a cumulative dose of 400mg/m2 (the higher the cumulative dose, the greater the risk of HF.[445]
  - Even at lower doses of 180 to 240mg/m2, subclinical events can occur in up to 30% of patients about 13 years post treatment.[448]
  - These suggest that there is no 'safe' dose for doxorubicin.
- Cyclophosphamide especially in high doses and ifosfomide.[449,450]
- Newer agents such as monoclonal antibodies (trastuzumab and pertuzumab), small molecule tyrosine kinase inhibitor (imatinib, sunitinib, sorafenib) and the proteasome inhibitor (bortezomib).
  - Trastuzumab especially when administered together with anthracyclines and cyclophosphamide, has been associated with an increased incidence of HF of 27% compared to 1.7% to 4.1% when anthracycline was not part of the therapeutic regimen.[451-453] Symptoms are usually mild to moderate and improve following medical management and termination of drug administration. Improvement is usually seen in about 4-6 weeks after withdrawal of the agent.[454-456] After symptomatic improvement, reinstitution of treatment is usually possible.[454-456]
  - Vascular endothelial growth factor signaling pathway (VSP) inhibitors (bevacizumab) can cause hypertension. Bevacizumab also blocks receptors that are involved in the compensatory response to stress in the cardiomyocytes and when the heart is unable to compensate for the hypertension, it could lead to HF.[457,458] Maintaining good blood pressure control can prevent HF associated with this agent. Heart failure due to VSP inhibitors is usually reversible with cessation of the agent.[459]

One must consider both the efficacy and the toxicity in choosing chemotherapeutic agents. Many of the newer targeted agents cause a reversible form of HF and symptoms usually resolve after the initiation of anti-failure medications.[454-456,459,460]

Risk factors for anthracycline toxicity include: [461-465]

- The total cumulative dose
- Intravenous bolus administration versus infusion
- Higher single doses
- History of prior irradiation
- Use of concomitant agents known to have cardiotoxicity
- Female gender
- Underlying CV disease
- Age (young and elderly)

An increase in cardiac biomarkers such as troponins during and after administration is an indication of toxicity.

8.5.5.1 Management

- Patients undergoing chemotherapy should have a careful clinical evaluation and assessment and treatment of CV risk factors.[464,465]
- Blood pressure control is important in all patients especially in those being considered for VSP inhibitors.
- All patients with potential cardiotoxic chemotherapy should have an echocardiogram prior to treatment. An important parameter is the LVEF determined using the biplane method of discs (Simpson's method) or three-dimensional echocardiography where available. Newer techniques to detect and quantitate regional and global myocardial dysfunction (strain assessment with global longitudinal strain) can be used to detect pre-clinical and subtle changes in function.[466-469]
- Biomarkers such as troponin and natriuretic peptides can help identify patients at higher risk.[462,463,470,471]

Close collaboration between the oncologist and the cardiologist is important.

For the oncologists, the strategy (prior to commencement) includes:[465]

I,C
- Identifying high risk patients (pre-existing heart disease, presence of CV risk factors, age - young and old, female gender, use of high dose anthracycline regimens).

I,C
- High risk patients should:
  - Have a pre-treatment cardiac function evaluation. If the LVEF is < 50%, refer to the cardiologist.
  - Be considered for non-cardiotoxic alternatives.
  - Have their therapy protocols adjusted where necessary (e.g. reduction in doses, continuous infusions rather than bolus injections, liposomal doxorubicin, dexrazoxane etc).

For the cardiologists/general physicians, the strategy includes:

I,C
- Treating CV risk factors.

I,C
- Assessing, repeating (if necessary) imaging studies. (e.g. using high quality LVEF measurement, strain evaluation etc).

I,C
- Assessing cardiac biomarkers (troponin and/or NP).

IIa,B
- Considering cardio-protection prior to/or during treatment using β-blockers, MRA and/or ACE-I/ARB if:[69,465,472-474]
  - EF < 50%,
  - EF drops by > 10%
  - Abnormal global longitudinal strain (GLS) (> 15% drop).

- Monitoring LVEF during therapy is important with repeat echocardiography at 3-monthly intervals and/or according to symptoms. If cardioprotective medications are given, monitoring may be necessary at closer intervals of time depending on the clinical condition of the patient e.g. 1-monthly interval.
- Withholding cardiotoxic therapy only as a last resort. (for anthracycline LVEF < 45%, for anti-HER2 therapy LVEF < 40%).
- Monitoring even after completion of therapy:
  - Obtain post therapy LVEF.
  - Repeat echocardiography in 6 months or 1 year. Most cases of treatment-associated cardiac dysfunction develop within the first year after completion of therapy.[475,476]
  - If EF remains abnormal, follow guidelines for management of HF.[465]

Key message 9:

- Chemotherapy-induced cardiomyopathy is not common; clinical HF occurs in 1-5%.
- Close collaboration between the oncologist and the cardiologist is important.
- Patients undergoing chemotherapy should have a careful clinical evaluation, assessment and treatment of CV risk factors.

8.5.6 HEART FAILURE AND KIDNEY DYSFUNCTION

8.5.6.1 Epidemiology, definitions and classifications

Cardiac and pre-existing kidney disease at admission frequently co-exist, varying from 45.4% in patients with chronic HF to > 60% in those with AHF.[477,478]

In addition, during treatment of AHF, a significant proportion of patients will develop varying degrees of worsening renal function (WRF).

The definition of WRF is:[479]

- An increase in serum creatinine by ≥ 26.5μmol/ L (0.3mg/dl) ***and/or***
- A ≥ 25% increase in serum creatinine or a ≥ 20% drop in eGFR.

The rise in serum creatinine usually occurs in the first three to five days of hospitalisation.

The incidence of WRF is estimated to be between 19 and 45%.[165] This large observed range is due to variations in the definitions of WRF, the observed time-at-risk and the study population.[165]

Risk factors for WRF during admission for HF include:[480]

- A prior history of HF or diabetes,
- An admission serum creatinine of > 133µmol/L, ***or***
- Systolic blood pressure > 160mmHg.

WRF may fulfill criteria for type 1 or type 2 cardiorenal syndrome (CRS). The term "cardiorenal syndrome" refers to disorders of the heart and kidneys whereby acute or chronic dysfunction in one organ may induce acute or chronic dysfunction of the other.[165]

This syndrome has been classified by the Acute Dialysis Quality Initiative working group into 5 subtypes as shown in Table 17, Page 105.[165] Many patients however, may belong to more than one subtype and may move between subtypes during the course of their disease.[165]

8.5.6.2. Pathogenesis of CRS

Multiple mechanisms are involved in the pathogenesis of CRS. These include:

- Increased renal venous pressure - venous congestion is probably the most important factor.[481]
- RV dysfunction.
- Reduced renal perfusion with reduced cardiac output.
- Neurohumoral adaptations (e.g. activation of the sympathetic nervous system and the renin-angiotensin-aldosterone system, increases in vasopressin and endothelin-1).

8.5.6.3 Clinical significance /Impact of kidney dysfunction in HF

The combination of cardiac and kidney disease increases the complexity and costs of care, and may interact to worsen prognosis.

A. Pharmacologic considerations

- Safety:
  - Dosing of renally-excreted cardiac drugs need adjustment in the presence of renal impairment (e.g. digoxin, insulin, low molecular weight heparin).
  - Patients with HF are at increased risk of contrast-induced acute kidney injury.

- Efficacy:
  - Impaired renal function will affect drug choices and dosing. If eGFR < 30mls/min/1.73m^2, most thiazide diuretics are no longer effective and loop diuretics are preferred. Higher doses of loop diuretics may be required with increasing renal impairment.

B. Prognostic implications

- Preexisting CKD is a bad prognostic indicator in patients with HF - the more severe the CKD, the worse the mortality.[482,483]
- In patients with HF, WRF may not always indicate a poor outcome.[484] The prognostic value of WRF is mainly determined by:
  - The presence of persistent congestion
  - Baseline renal function and magnitude of renal changes
  - Duration - persistent WRF is usually associated with hemodynamic derangements and poor prognosis as compared with transient WRF as a result of agressive decongestive therapy.[485-487]

Table 17: Classification of Cardiorenal Syndrome (CRS)

Cardiorenal (CRS) Subtypes	Description
CRS Type 1 (acute CRS)	Rapid worsening of cardiac function leading to acute kidney injury e.g. MI with cardiogenic shock.
CRS Type 2 (chronic CRS)	Chronic abnormalities in cardiac function leading to progressive Chronic Kidney Disease (CKD) e.g. chronic HF*r*EF or HF*p*EF.
CRS Type 3 (acute renocardiac syndrome)	Worsening of renal function leading to acute cardiac dysfunction e.g. in Acute Kidney Injury.
CRS Type 4 (chronic renocardiac syndrome)	Primary chronic kidney disease contributing to decreased cardiac function and an increased risk of CV events e.g. CKD leading to LVH, CAD.
CRS Type 5 (secondary CRS)	Presence of comorbid cardiac and renal dysfunction due to either acute or chronic systemic disease e.g. diabetes, sepsis, amyloidosis.

Adapted from Ronco C, McCullough P, Anker SD, et al. Cardio-renal syndromes: report from the consensus conference of the Acute Dialysis Quality Initiative. Eur Heart J 2010;31:703–11.

8.5.6.4. Management

I,C
- A multi-disciplinary approach is recommended. Early referral to a nephrologist is advisable.

I,C
- Exclude potentially reversible causes for increasing renal dysfunction such as hyper - or hypovolaemia, concomitant medications such as aminoglycosides and NSAIDs, ACE-I or ARB and renal artery stenosis.

I,C
- Closely monitor electrolytes and kidney function, especially during acute illnesses, dehydration and when increasing doses of cardiac drugs including diuretics. The baseline renal function will determine how frequently this should be done.
- The recommended range for serum potassium is 4-5.5mmol/L.[488]

I,C
- Wherever possible, avoid nephrotoxins, e.g. contrast media for angiography
- Intravenous diuretics
  - Loop diuretics are the first choice.

I,B

IIa,B
  - Continuous infusion may not have greater benefits compared with bolus dosing.[115-118,489]
  - Start initially with 2-2.5 times the usual oral dose.

IIa,B
  - Combination therapy (loop diuretic and thiazide/thiazide-like diuretic/ mineralocorticoid) may be required to enhance diuresis.[205-207] However, care is required to avoid electrolyte disturbances, hypovolaemia and worsening renal dysfunction.

- Careful use of Renin Angiotensin System (RAS) blockers

I,A
  - HF patients with stable, chronic mild-moderate renal insufficiency (eGFR > 30mls/min/1.73m^2) should receive standard therapy with an ACE-I/ ARB and an MRA.[490]
  - A serum creatinine rise or GFR decrease by up to 30% from baseline may be acceptable before it becomes necessary to consider stopping or decreasing doses.[221]

I,C
  - In patients with advanced renal failure, the decision to start or stop RAS blockers should be individualised.[490]

I,C
  - Consider withholding RAS blockers during aggressive diuresis in patients at high risk for WRF.
  - RAS blockers (and β-blockers) can be used in patients with HF who are on chronic dialysis therapy.

- Ultrafiltration
  - This involves the removal of plasma water across a semi-permeable membrane in response to a transmembrane pressure gradient.
  - It may be considered for congestive symptoms refractory to diuresis, but should be used in consultation with a nephrologist.[491]

IIa,B
  - Evidence for its efficacy in fluid removal is mixed at present.[491]

- Haemodialysis
  - Criteria for possible need to initiate renal replacement therapy include:
    - Oliguria unresponsive to fluid resuscitation.
    - Severe hyperkalaemia (serum potassium > 6.5mmol/L).
    - Severe acidaemia (pH < 7.2).
    - Serum urea > 25mmol/L.
    - Serum creatinine > 300μmol/L.

Key message 9:

- Cardiac and kidney disease frequently co-exist and this increases the complexity and costs of care, and may interact to worsen prognosis.
- Management includes the use of intravenous diuretics, careful use of Renin Angiotensin System blockers, β-blockers and occasionally ultrafiltration and haemodialysis.

8.6 ADVANCED HEART FAILURE/REFRACTORY HEART FAILURE

These are patients with severe symptoms of HF despite maximal medical therapy. Hospital admission is necessary for stabilisation. Meticulous control of fluid balance is important. Aggravating causes of HF as listed in Table 5, Page 39 should be identified and treated.

These patients may need specialised treatment in CCU or ICU. The following may be required:

- Intravenous infusion of frusemide. These patients may require combination loop diuretics and thiazides.
- Intravenous infusion of inotropes - low dose dobutamine (5mcg/kg/min) or milrinone. These improve symptoms but no survival benefit has been demonstrated.[126,492]
- Ultrafiltration in patients who are fluid overloaded.[493] In most patients, however, the relief is temporary.

The prognosis of these patients is poor. They should be referred to assess whether they may be potential candidates for mechanical circulatory support (e.g. LVAD) and consideration for heart transplant.

8.6.1 HEART TRANSPLANT

Heart transplantation is a well-established treatment of refractory end stage HF. This definitive therapy for HF however is limited by the lack of donor organs.[494,495]

All patients with severe symptomatic HF despite optimal medical therapy and no other alternative therapy option should be considered for heart transplant. They need to be referred to a HF specialist cardiac hospital for further evaluation.

Assessment for heart transplant is done by a multispeciality, multidisciplinary team and appropriate work up will be performed for eligibility.

Eligibility criteria to be considered for heart transplant include:
- Poor LVEF (< 25%).
- Recurrent HF hospitalisations.
- Major limitation of the patient's daily activities.
- Poor effort tolerance i.e. peak VO2 (maximal oxygen consumption or peak oxygen uptake) less than 10ml/kg/min (or < 50% predicted). VO2 max is the maximum rate of oxygen consumption measured during incremental exercise ie exercise of increasing intensity and is widely used as an indicator of cardiorespiratory fitness.
- Intravenous inotropic dependence for symptomatic relief or to maintain end organ function.
- Motivated, psychologically stable and compliant to therapy.

Contraindications to heart transplant
- Active infection.
- Severe peripheral arterial or cerebrovascular disease.
- Malignancy within 5 years.
- Diabetes mellitus with widespread microvascular complications.
- Systemic disease with multi-organ dysfunction.
- Irreversible chronic kidney, liver or lung disease.
- Pharmacologically irreversible pulmonary hypertension.
- Other medical or psychosocial issues that would impact survival.

8.6.2 MECHANICAL CIRCULATORY SUPPORT

The use of mechanical circulatory support (e.g. LVAD), should be considered for patients with potentially reversible or treatable conditions or as a bridge to heart transplant in suitable candidates.

LVAD may also be used as destination therapy in candidates who are not suitable for transplant. Patients have improvement in their symptoms when compared to optimal medical therapy.[496,497] However, the rate of rehospitalisations due to complications of bleeding, thrombosis and infections are high.[496-498] Many patients also go into major depression. Thus, extensive discussion with the patient and family is necessary prior to LVAD implantation.

Key message 10:

- Patients with Advanced Heart Failure should be referred to assess whether they may be potential candidates for mechanical circulatory support (e.g. LVAD) and consideration for heart transplant.

8.7 PALLIATIVE AND END OF LIFE CARE

Despite recent advances in therapy, for some patients, HF remains a progressive disease and carries a poor prognosis. Patients with refractory symptoms despite guideline-directed medical therapy, should be considered for palliative and end of life care if they have the following characteristics:[499]

- Progressive functional decline (mental and physical) and dependence in most activities of daily living.
- Severe HF symptoms with poor quality of life despite optimal pharmacological and non-pharmacological therapies.
- Frequent hospital admissions or serious episodes of decompensation despite optimal therapies.
- Heart transplantation and mechanical circulatory support ruled out.
- Cardiac cachexia.
- Clinically judged to be near end of life.

The aim of palliative care in HF is to prevent and relieve suffering and to promote the best quality of life for patients and their families.[500]

Despite the complexities of end-of-life issues in HF patients, there is minimal evidence-based guidance on the care of this population.[501] The key components of end-of-life care are:

1. Advanced care plan with directives and informed decisions on:
   - Use or withdrawal of treatment including advanced therapies such as V inotropes, ICD and mechanical circulatory support.
   - When it would be appropriate to switch off devices such as ICD or CRT.
   - Resuscitation status.
   - Preferred location of death (i.e. at home or hospital).

2. Symptom management
   Goals of care at this stage should shift from extending life to controlling symptoms and maximising quality of life. Common symptoms include:
   - Dyspnoea
   - Fatigue
   - Pain
   - Urinary retention

- Constipation
- Cachexia
- Depression

Medications that may be useful include analgesics, antiemetics, anxiolytics, opioids, laxatives, and diuretics, etc.

3. Psychosocial support
   The impact of HF on quality of life for the patient and family is complex and extends beyond physical symptoms.[502]

   Emotional, spiritual and social support should be provided to alleviate patient anxiety about dying, and to guide patient towards a peaceful journey at the end of life.

9. ORGANISATION OF CARE

9.1 LEVEL OF CARE AND SHARED MANAGEMENT

The care of patients with HF should ideally take place in a multidisciplinary system, allowing for shared care between the hospital (secondary or tertiary settings) and community (primary setting). A multidisciplinary approach encompasses patient education, cardiac rehabilitation, psychosocial support and palliative care, and has been proven to reduce HF hospitalisations and mortality in discharged patients.[503-505] The multidisciplinary team usually consists of cardiologists and or general physicians, HF nurses, pharmacists, dieticians, physiotherapists, primary care providers, social workers as well as geriatricians, psychologists, occupational therapists and when necessary, palliative care specialists. Care can be done in two different settings:

- In the patient's own home - home-based interventions are associated with significantly lower healthcare costs, reduced hospital readmissions and an improvement in the patient's quality of life.[506] This may however, not be feasible in our local setting.
- Specialist outpatient clinic - the Heart Failure Clinic (HFC).

HFCs can either be:

- Nurse-directed - these are run by nurses with special training in HF.
- Physician-directed - run by general physicians and/or cardiologists.

HFCs can be established in the tertiary hospitals or in the primary care setting. The minimum human resource requirements are a:

- Cardiologist or general physician with an interest in cardiology and HF,
- Dedicated nurse and
- Medical technologist for blood taking, doing echocardiography and 6 minutes walk tests.

In bigger clinic settings, the involvement of physiotherapists to encourage physical activity, pharmacists and counsellors for end of life care would be advisable.

These clinics will be the intermediary between in-patient hospital care and community primary care. Patients who can be seen in these clinics include those:[507]

- Recently discharged after an admission for decompensated HF (a waiting time of 7-12 days post discharge has to be the maximum wait-time).
- Who are in the early decompensation phase and need treatment modification.
- Who are stable but need uptitration of HF medications.
- With ICD or CRTs.
- With comorbidities, such as renal dysfunction, diabetes and COPD.
- With advanced HF who may benefit from:
  - Heart transplant
  - Left Ventricular Assist Device (LVAD)
  - Palliative care.

The objectives of these HF clinics may vary based on local settings. These include:[507,508]

- Optimisation of medical therapy particularly the uptitration of β-blockers, ACE-I and MRA.
- Education of the patient and caregiver on the nature of the disease and its progression.
- Promotion of self-care such as :
  - Compliance to medical therapy and fluid restriction.
  - Regular weighing and adjusting diuretic doses according to symptoms and body weight.

Patient with optimised HF medications/treatment plans can be discharged to the community with appropriate care plans to primary care. Close partnership between these HF clinics and primary care helps to reduce unnecessary admissions to hospital.

In 2018, the Heart Failure Medication Therapy Adherence Clinic (MTAC) was introduced. These clinics are conducted by pharmacists in collaboration with doctors and other healthcare providers to improve HF management. The objectives of the Heart Failure MTAC are:[509]

- Enhance patient's adherence to HF pharmacotherapy and non-pharmacological interventions.
- To reduce unscheduled emergency department visits or hospitalisations of HF patient due to acute decompensation.
- To provide consultative service to doctors on evidence-based HF pharmacotherapy and related issues.
- To collaborate with doctors and other health care professionals in HF management program.

9.2 MONITORING AND FOLLOW-UP

Patients with HF require regular follow-up and monitoring. Serial evaluations serve to assess a patient's status, response to therapy, development of complications and disease progression. Key components of assessment include:

- Functional capacity - NYHA functional class or 6-minute walk test
- Fluid status and body weight
- Blood pressure, heart rate and rhythm
- Examination of the cardiovascular and respiratory systems
- Cognitive status and nutritional status
- Review of pharmacotherapy - uptitration, compliance and side effects
- Serum urea, electrolytes, creatinine and eGFR as necessary
- Diet and sodium intake
- Consumption of alcohol or illicit drugs
- Smoking history.

The frequency of follow-up will depend on the patient's clinical stability and need for pharmacotherapy optimisation. A patient with a recent episode of decompensation or clinical instability, for instance, should ideally be seen again soon, usually within 2 weeks. Ultimately, the intensity and type of follow-up would be determined by the local organisation of care and resources.

Routine serial echocardiogram is not recommended. However, if there has been a recent change in clinical status or if the patient has received treatment that might significantly change certain echocardiographic parameters, a follow-up echocardiogram is reasonable to assess the LVEF and structural remodeling.

Serial brain natriuretic peptide measurements to guide and tailor HF therapy cannot be broadly recommended at the present time due to a lack of consistent evidence.[29-32]

9.3 CARDIOLOGY REFERRAL

HF patients with stable symptoms may be managed at the primary care level. Referral to the cardiologist should be considered in the following situations:

- De novo HF for a comprehensive workup to confirm the diagnosis and determine the aetiology, and to devise a management plan.
- Episodes of acute decompensation.
- Worsening HF symptoms despite appropriate therapy.
- HF complicated with symptomatic hypotension or excessive bradycardia, limiting uptitration of pharmacotherapy.

- Symptomatic stable CAD and/or acute coronary syndrome for consideration of revascularisation (PCI or CABG).
- Resuscitated cardiac arrest.
- Documented or suspected significant arrhythmias e.g. AF, VT.
- Significant valvular disease not previously assessed or worsening valvular dysfunction.
- Pre-conception assessment and counselling of women with significant structural heart disease and a past history of HF or LV dysfunction.
- Complex congenital cardiac lesions and/or Eisenmenger's syndrome.

Key message 11:

- Heart Failure clinics will serve as an intermediary between in-patient hospital care and community primary care.

10. OTHER THERAPIES FOR HEART FAILURE

Despite taking conventional HF therapy, patients may seek alternative therapy and healing approaches that are not considered as allopathic medicine. The National Centre for Complementary and Alternative Medicine (NCCAM) defines complementary and alternative medicine (CAM) as a group of diverse medical and healthcare interventions, practices, products or disciplines that are not generally considered part of conventional medicine.

10.1 Enhanced External Counter Pulsation (EECP)

There is inadequate evidence of clinical effectiveness of EECP in HF.[510-513] There is concern that it could precipitate or exacerbate HF.

10.2 Stem cell therapy

A global position paper on cardiovascular regenerative medicine stated that cell-based therapy in HF patients is neither positive nor consistent.[514]

10.3 Omega 3 fatty acids

In patients with HF*r*EF, it may be considered as an adjunctive therapy based on a single randomised controlled trial (RCT) which showed a small benefit in CV death and/or hospitalisations.[515,516]

10.4 Coenzyme Q10

There is no convincing evidence to support or refute the use of coenzyme Q10 for patients with HF.[517]

10.5 Tai Chi

Tai Chi may improve 6 min walk test distance, quality of life and LVEF in patients with HF.[518,519] Its effect on hard CV outcomes such as rehospitalisation, MI and mortality is not known.

10.6 Yoga

A meta-analysis in 2014 that includes two RCTs concluded that yoga improved peak VO2 (exercise capacity) and quality of life in chronic HF patients.[520] There is an ongoing RCT to look at the effect of yoga in HF*p*EF patients.[521]

11. FUTURE DEVELOPMENT

The focus of future development for HF in Malaysia should be towards service enhancement working to meet the World Heart Federation mandate of a 25% reduction in premature non-communicable disease mortality by 2025.

Finding the balance between costs and quality remains a global challenge, and the understanding of the disease in our healthcare context is imperative to making sure we move forward regarding service delivery, human resource allocation, medical expense costs and patient outcomes. To achieve this, the following need to be undertaken:

- Epidemiological studies to understand the disease profile in the country.
- Establishment and expansion of HFCs leading to more patient-centred HF care.
- Expanding service delivery, human resource allocation, medical expense cost and patient outcomes.
- Education of healthcare personnel.

Efforts should be directed to the knowledge and understanding of the epidemiology of HF in our country, its phenotype, presentation, current adherence to guideline-directed therapy and outcomes. Regular cluster sampling cohorts or a nationwide registry should be considered. Understanding the limitations of service delivery albeit geography or human resources and making plans for better service delivery systems are important.

Development of HFCs, can lead to a more patient-centric HF care. (See Section 9, Pages 110-113)

Modules for HF care need to be initiated in order to train and educate general internal medicine physicians. A core-curriculum for education needs to be formed to ensure adequate training has been disseminated to HFC personnel.

Incentives regarding HF guidelines compliance should be implemented and HF innovative practice should be encouraged with awards for best clinical practice and innovation be made available.

This streamline approach to HF care with engagement of connected groups hopefully will help in better overall patient care and experience.

12. PERFORMANCE MEASURES

Performance measures should be used with the goal of improving quality of care for HF.[518,519]

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 for in-patients with HF includes:[522-524]

- % of patients who had documentation of NYHA Functional Class.
- % of patients who had LVEF measurement.
- % of patients with current or prior LVEF < 40% and without contraindications discharged with ACE-I/ARB.
- % of patients with current or prior LVEF < 40% and without contraindications discharged on β-blockers.
- % of patients with current or prior LVEF < 40% and without contraindications discharged on MRA.
- % of patients with chronic or paroxysmal AF/atrial flutter without contraindications on anticoagulant therapy at discharge.
- % of patients given a post discharge appointment.

The accepted performance measure should be more than 60%.

Outcome measures indicators include:

- In-hospital mortality
- 30-day readmission for HF

Refer to Appendix VI, Page 121 for calculation of these measures.

Appendix I: Causes of Elevated Natriuretic Peptide Levels*

Cardiac

- HF, including RV syndromes
- Acute coronary syndromes
- Heart muscle disease, including LVH
- Valvular heart disease
- Pericardial disease
- Atrial fibrillation
- Myocarditis
- Cardiac surgery
- Cardioversion
- Toxic-metabolic myocardial insults, including cancer chemotherapy

Non-cardiac

- Advancing age (Table 7, Page 44) for optimal cut off values according to age)
- Anaemia
- Renal failure:
  - NTproBNP lost its prognostic value in patients with GFR < 30ml/min/1.73 m^2.
  - BNP levels are relatively independent of GFR.
- Right ventricular overload from:
  - Pulmonary causes: obstructive sleep apnoea, severe pneumonia
  - Pulmonary hypertension whatever the cause
- Critical illness
- Bacterial sepsis
- Severe burns
- Liver cirrhosis

**Adapted from*

- *Yancy WC, Jessup M, Bozkut B, et al. 2017 ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure. A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. Circulation 2017;136:e137-61.*
- *Goei D, Schouten O, Boersma E, et al. Influence of renal function on the usefulness of N-terminal pro-B-type natriuretic peptide as a prognostic cardiac risk marker in patients undergoing noncardiac vascular surgery. Am J Cardiol 2008;101:122-6.*
- *Tagore R, Ling LH, Yang H, Daw HY, Chan YH, Sethi SK. Natriuretic peptides in chronic kidney disease. Clin J Am Soc Nephrol 2008;3:1644-51.*

Appendix II: Salt Content of Common Malaysian Foods

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

Appendix III: Risk of Combined Contraceptive Pills for the Different Cardiac Conditions WHOMEC Risk Classification for the Use of Combined Hormonal Contraceptives*

MEC CLASS	WHOMEC 1	WHOMEC 2	WHOMEC 3	WHOMEC 4
Category of Use Cardiac Conditions	Condition with no restriction for the use of contraceptive method	Condition where the advantages of the method generally outweigh the risks	Condition where the risks of the method usually outweigh the advantages and to consider all alternatives first	Conditions where the method represents an unacceptable health risk
	Always usable	Broadly usable	Caution in use	Do not use
Cardiac Conditions	Physiological murmurs in absence of heart disease	Most arrhythmias otherthan atrial fibrillation and flutter	Atrial fibrillation or flutter on warfarin	Atrial fibrillation or flutter if not anticoagulated
	Mitral valve prolapse with or trivial mitral regurgitation	Uncomplicated mild native mitral and aortic valve disease	Bi-leaflet mechanical valve in mitral or aortic position taking warfarin	Pulmonary hypertension or pulmonary vascular disease (e.g. Eisenmenger syndrome)
	Bicuspid aortic valve with normal function	Tissue prosthetic valve lacking any of the features noted in WHOMEC 3 and WHOMEC 4	ASD with left to right shunt that may reverse with physiological stress (e.g. Valsalva manoeuvre)	Dilated left atrium > 4 cm
	Mild pulmonary stenosis	Surgically corrected congenital heart disease lacking any features noted in WHOMEC 3 and WHOMEC 4	Marfan syndrome with aortic dilatation unoperated	Fontan heart on warfarin
	Repaired coarctation with no hypertension or aneurysm	Small left to right shunt not reversible with physiological manoeuvres (e.g. small VSD, small PDA)	Past thrombotic event on Warfarin	Cyanotic heart disease
	Simple congenital lesions successfully repaired in childhood and with no sequelae e.g. • Ostium secundum atrial septal defect • VSD • PDA • Total anomalous pulmonary venous drainage	Uncomplicated Marfan syndrome		Pulmonary arteriovenous malformation
				Past thromboembolic event (venous and arterial) not on warfarin
				Poor left ventricle function of any cause (e.g. dilated cardiomyopathy) Ejection fraction < 30%
		Hypertrophic cardiomyopathy lacking any of the features noted in WHOMEC 3 and WHOMEC 4		Coronary artery disease
		Past cardiomyopathy fully recovered including peripartum cardiomyopathy		Coronary arteritis (e.g Kawasaki's disease with coronary involvement

*World Health Organization. Medical Eligibility Criteria (MEC) for Contraceptive use. (5thed) 2015. Available at: www.who.int/reproductivehealth/publication/family_planning/Ex-SummMec-5/en/

Adapted From: Thorne S et al. Pregnancy and contraception in heart disease and pulmonary arterial hypertension. J Fam Plann Reprod Health Care. 2006; 32:75-81

Appendix IV: Safety of Progesterone Only Contraceptive Methods in Women with Cardiac Disease

Progesterone Only Contraceptive Method	Cardiac Condition	WHOMEC# Class
Progesterone only pill[a] ● Noriday® ● Cerazette®[b]	All cardiac conditions *(should not normally be advised where pregnancy poses a high or unacceptable risk - WHOMEC Class 3 and 4 conditions)*	1
Depo Provera	All cardiac patients who are not on warfarin	1
	All cardiac patients on warfarinc	3
Implants e.g. (Nexplanon® previously known as Implanon®)	All cardiac patients	1
Intra-Uterine System e.g. Mirena®	Cardiac patients generally even if taking warfarin[d]	1
	Structural heart disease[e]	2
	Prosthetic heart valves[d,e]	3
	Previous endocarditis[e]	3
	Pulmonary hypertension, Fontan circulation or other condition in which vagal reaction at insertion would be poorly tolerated	4(3)
Emergency contraception	All cardiac disease	1

#WHOMEC: *World Heart Organization Medical Eligibility Criteria (see Appendix III, Page 118)*
[a]Although safe, the standard progestogen-only pill is less effective than all the other progestogen-only methods.
[b]Efficacy reduced by Bosentan
[c]Risk of haematoma at injection site
[d]The INR may be altered after initiation of any progesterone hormone therapy. It needs to be monitored.
[e] Risk of Infective Endocarditis

From: Thorne S, MacGregor A, Nelson-Piercy C. Pregnancy and contraception in heart disease and pulmonary arterial hypertension. J Fam Plann Reprod Health Care 2006;32:75-81.

Appendix V: Anticancer Agents Associated with Heart Failure / LV Dysfunction)

Chemotherapy Agents	Management
Anthracyclines Doxorubicin Epirubicin Idarubicin	• Monitor LVEF, strain assessment with global longitudinal strain, • Measure troponins • Consider use of dexrazoxane, continuous infusion, liposomal preparations, β-blockers, ACE-I
Alkylating agents Cyclophosphamide Ifosfamide	
Antimetabolites Decitabine Clofarabine	
Antimicrotubule agents Docetaxel	
Monoclonal antibody-based tyrosine kinase inhibitors Trastuzumab Bevacizumab Adostratuzumab emtacine Pertuzumab	Avoid concomitant use with anthracyclines
Small molecule tyrosine kinase inhibitors Pazopanib Sorafenib Sunitinib Lapatinib	Treat hypertension aggressively
Proteasome inhibitor Carfilzomib Bortezomib	

APPENDIX VI: 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 thattime 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 discharged during this time period who had no contraindications to ACE-I/ARB	X 100
% of patients discharged on β-blockers	=	Number of patients who were on β-blockers at discharge Number of HF patients who were discharged during that time period who had no contraindications to β-blockers	X 100
% of patients discharged on MRA	=	Number of patients who were on MRA at discharge Number of HF patients who were discharged during that time period who had no contraindications to MRA	X 100
% of patients with chronic or paroxysmal AF/Atrial Flutter on anticoagulant therapy(OAC) at discharge.	=	Number of patients who had AF/Atrial Flutter who were on OAC at discharge Number of HF patients who had AF/Atrial Flutter during that time period who had no contraindications to OAC at discharge	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

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PART 2

Management of Heart Failure in Paediatrics

13. HEART FAILURE IN THE PAEDIATRIC POPULATION

TABLE OF CONTENTS

GLOSSARY

Abbreviation	Description
DACE-I	Angiotensin-converting enzyme inhibitors
ALCAPA	Anomalous left coronary artery to pulmonary artery
AP window	Aortopulmonary window
AS	Aortic stenosis
AVSD	Atrioventricular septal defect
CHD	Congenital heart disease
CXR	Chest X-ray
CoA	Coarctation of aorta
ECG	Electrocardiogram
HF	Heart Failure
HLHS	Hypoplastic left heart syndrome
MRI	Magnetic resonance imaging
PBF	Pulmonary blood flow
PDA	Patent ductus arteriosus
PHF	Paediatric heart failure
PS	Pulmonary stenosis
TGA	Transposition great arteries
VSD	Ventricular septal defect

13.1 Introduction

Paediatric heart failure (PHF) is a complex syndrome with heterogeneous aetiology and presentation.[1] It is an uncommon condition with a reported incidence of 0.87 to 7.4 per 100,000 population.[2] It, however, causes significant morbidity and mortality.

Unlike adults with HF, PHF is commonly due to congenital heart disease (CHD) or cardiomyopathies. However, the general principles of management are similar to those in adults, except that there is a lack of randomised clinical trials and international guidelines for PHF.[3]

13.2 Definition

There are various definitions of PHF.[1,4,5] PHF can be defined as

- "The failure of the heart to supply blood to either systemic or pulmonary circulation at an appropriate rate of flow, or to receive venous return at an appropriate filling pressure, resulting in adverse effects on the heart, the circulation, and the patient"[4] or
- "A clinical and pathophysiologic syndrome that results from ventricular dysfunction, volume or pressure overload, alone or in combination that leads to characteristic signs and symptoms, and is associated with circulatory, neurohormonal and molecular abnormalities".[5]

13.3 Aetiology

In children, cardiac failure is most often due to CHDs and cardiomyopathies.[6] (Table 18, Page 152).
Common etiologies are:

- At birth - foetal cardiomyopathies, foetal arrhythmias or non-cardiac conditions (i.e., perinatal asphyxia, sepsis, hypoglycaemia, and hypocalcaemia).
- Within the first week of life - duct dependent systemic circulation, i.e. closure or restriction of ductus arteriosus leading to a severe reduction of end-organ perfusion in patients with critical aortic stenosis (AS), aortic coarctation (CoA), and hypoplastic left heart syndrome (HLHS).
- Within the first year of life - left to right shunts (i.e. large ventricular septal defect (VSD), patent ductus arteriosus (PDA), atrioventricular septal defect (AVSD), aortopulmonary window (AP window), or cyanotic CHD with non-protective pulmonary blood flow (i.e. transposition great arteries with VSD, truncus arteriosus). In both these conditions, pulmonary blood flow (PBF) progressively increases with the fall of pulmonary vascular resistance.
- Children and adolescence (1-18 years of age) - more often due to rheumatic carditis, myocarditis or cardiomyopathies other than congenital heart disease.

13.4 Clinical Presentation

The clinical presentation of HF varies with age. It may present at birth (because of foetal disease) or can develop at any stage of childhood. Table 19, Page 153 summarises the clinical presentation of paediatric HF according to the different age groups.

The clinical presentation of HF in neonates and infants are non-specific, and cardiac murmurs may be absent or very soft. Absence of femoral pulse or presence of radio-femoral delay may suggest coarctation of aorta.

Hence, it is very important to exclude underlying cardiac disease in younger infants with feeding difficulties, respiratory distress, and growth failure. Furthermore, features of HF in adults such as ankle oedema are rarely seen in infants and children.

The severity of HF is staged based on modified Ross classification as shown in Table 20, Page 153. Briefly, class 1 is absence of symptoms and class 4 is severe symptoms of HF.

Acute heart failure in children may present with hypotension or tachycardia with narrow pulse pressure, cool extremities, and irritable or decreased consciousness. It is usually seen in cardiomyopathies, myocarditis, and left ventricular outflow tract obstructions such as critical/severe aortic stenosis or coarctation of aorta.

13.5 Diagnosis

PHF is a clinical diagnosis, and any child presenting with symptoms and signs of HF needs assessment to establish the diagnosis and haemodynamic status.[7] The initial steps of management are non-invasive investigations to look for the aetiology and assess the severity of HF.

These include blood investigations, electrocardiogram (ECG), chest radiograph, echocardiogram. Occasionally, other investigations such as cardiac catheterisation, cardiac magnetic resonance imaging (MRI) or CT scan may be necessary.

13.5.1 Essential investigations (Tables 21 and 22, Pages 154 and 155)

Initial therapy to reduce pulmonary congestion or to improve perfusion should not be delayed while waiting for the results of the investigations.

Chest X-ray (CXR)

I,C CXR is indicated as the first-line investigation in all children with suspected HF.

Features to look for are:

- Size of the heart (small, normal or, large) -
  - In the neonate and small infant, the thymic shadow may be confused as cardiomegaly. In these cases, a lateral CXR may be helpful.
  - The incidental finding of cardiomegaly in asymptomatic infants would warrant further investigations with an echocardiogram.
- Contours of the heart
- Pulmonary vascularity (increase, normal, and decrease)
- Signs of fluid overload such as cardiomegaly, septal lines (or Kerley B lines), and pleural effusions.

ECG

I,C

- The ECG is always abnormal in children with HF. However, the findings are generally non-specific - e.g. sinus tachycardia and left ventricular hypertrophy.
- ECG may be diagnostic in HF secondary to tachy - or bradyarrhythmias (e.g. supraventricular tachycardia, atrial ectopic tachycardia, heart block).
- A continuous ECG monitoring (Holter) is indicated in any patient presenting with unexplained dilated cardiomyopathy for possible tachycardia-induced cardiomyopathy.

2D-echocardiogram

This will provide information on:

- Structural cardiac defects (volume or pressure overload),
- Chamber sizes (dilated left atrium and ventricle in left to right shunt), and
- Cardiac function (a poor cardiac function with dilated left ventricle in myocarditis or dilated cardiomyopathies.

13.6 Management

The therapeutic approach should be tailored to the clinical status at presentation and the underlying cause of HF. (Table 23, Page 156).

Treatment goals are:

- Treat the underlying problem, i.e., corrective surgery/intervention in a child with significant left-right lesions,

- Minimise morbidity and mortality, and
- Improve functional status and quality of life.

Children with decompensated HF are preferably managed in an intensive care unit for stabilisation.

General principles of management include:

- Oxygen therapy in acute HF.
- Correcting acidosis, hypoglycaemia, and anaemia.
- Correcting electrolyte disturbances.
- Treating respiratory infections.
- Nasogastric tube feeding in children with poor weight gain.
- Treating gastroesophageal reflux.
- Adequate nutritional intake.
- Fluids should be carefully administered - symptoms may be related to fluid overload, under perfusion or both. Therefore, the goal of therapy is to return the patient to a euvolemic state with good perfusion.
- Anaemia should be treated cautiously. If indicated, blood transfusion should be given in small volumes (5-10ml/kg) to avoid worsening symptoms.

Following stabilisation, efforts should be made to identify and treat the underlying cause. All treatable structural heart defects should have corrective surgery and/or interventional therapy as early as possible.

In cases of HF due to cardiomyopathy or myocarditis, long-term medical therapy is necessary.

Common medications include: (Table 24, Page 157)

- Loop diuretics - frusemide
  - Indicated in the treatment of HF due to volume overload.

I,C

  - In decompensated HF, a slow intravenous infusion of frusemide would avoid worsening the hypotension as compared to intermittent bolus injections.[8]
  - The addition of spironolactone (potassium sparing) avoids the need for potassium supplements. It has the additional beneficial effect of attenuating the development of aldosterone-induced myocardial fibrosis and catecholamine release.[9]
  - In euvolemic patients, diuretics should be used judiciously.

IIa,B
- Angiotensin-converting enzyme inhibitors (ACE-I)
  - Captopril is commonly used in infants.[4,6]
  - In those more than 2 years of age, enalapril can also be used.[4,6]
  - Close monitoring of renal function is required to avoid renal impairment particularly in the neonate and small infant.

- β-blockers
  - Indicated in the treatment of HF with moderate to severe systolic left ventricular dysfunction.

IIa,B
  - In dilated cardiomyopathy, carvedilol shall be started together with diuretics and ACE-I.[10,11] Start a low dose and gradually titrate up to the targeted dose.

- Phosphodiesterase type III inhibitor (Milrinone)[12,13]

IIa,B
  - Milrinone is indicated for the prevention of low cardiac output syndrome (poor perfusion, decreased urine output, cool extremities) after cardiac surgery.[12,13]

IIa,B
  - It is also indicated in decompensated HF with a low cardiac output syndrome.[4,13]
  - It is to be used cautiously in the presence of hypotension.

- Digoxin
  - Indicated in symptomatic patients with left and/or right ventricular systolic dysfunction but is rarely used at present.
  - It has a narrow therapeutic index, hence needs close monitoring for toxicity.

- Inotropes
  - Dopamine and dobutamine have been shown to be effective inotropes and vasopressors in neonates, infants, and children with circulatory failure.
  - However, these inotropes may also cause tachycardia and other tachyarrhythmias and should be used cautiously.

IIb,C
- Corticosteroid and intravenous immunoglobulin in myocarditis
  - In children with acute HF due to suspected myocarditis, routine use of corticosteroid and intravenous immunoglobulin is not indicated due to lack of benefit.[4]

13.7 Prognosis

The outcome of infants and children with HF depends largely on the aetiology. When due to structural congenital defects, surgery and/or interventional treatment can be curative. In some patients, however, it may only be palliative with some improvement in clinical symptoms.

Table 18: Causes of Paediatric Heart Failure

Type	Mechanisms	Example
Congenital heart disease	Left to right shunt (volume overload)	Large VSD, PDA, AVSD, AP window, and coronary fistula
	Outflow tract obstruction (pressure overload)	Severe or critical PS, AS or CoA
	Inflow obstruction	Cor triatriatum Pulmonary vein stenosis Mitral stenosis
	Complex CHD with non-protected pulmonary flow	TGA with large VSD Univentricular heart with no PS Truncus Arteriosus
	Anomalous pulmonary venous drainage	TAPVD
	Severe valvular regurgitation	Severe Ebstein anomaly, common AV valve regurgitation
	Coronary insufficiency (decreased O2 supply to cardiomyocyte)	ALCAPA
Acquired heart disease	Severe valvular regurgitation	Rheumatic carditis Infective endocarditis
Cardiomyopathies	Systolic dysfunction (low cardiac output)	Dilated cardiomyopathies: • Familial • Metabolic disease • Post myocarditis • Neuromuscular Disease • Drug induce (Anthracycline)
	Pressure overload Decrease preload	Hypertrophic cardiomyopathy: • Infant of diabetic mother • Noonan syndrome • Pompe disease
	Diastolic dysfunction (elevatedpulmonary capillary pressure)	Restrictive cardiomyopathies • Familial RCM
Arrhythmias	Low cardiac output	Supraventricular tachycardia
		Complete heart block
Infection	Myocardial dysfunction	Severe sepsis
Miscellaneous	High output	Severe anaemia
		Systemic arteriovenous malformation
		Thyrotoxicosis
	Myocardial ischaemia	Kawasaki disease
	Fluid Overload	Acute glomerulonephritis

ALCAPA, anomalous left coronary artery to pulmonary artery; AP, aortopulmonary; AVSD, atrioventricular septal defect; AS, aortic stenosis; CHD, congenital heart disease; CoA, coarctation of aorta; PDA, patent ductus arteriosus; PS, pulmonary stenosis; RCM, restrictive cardiomyopathy; TAPVD, total anomalous pulmonary venous drainage; TGA, transposition great arteries; VSD, ventricular septal defect.

Table 19: Clinical Presentation of Paediatric Heart Failure

Age group	Clinical presentation
Infants and young children	Difficulty in feeding (interrupted feeding, prolonged feeding time)
	Tachypnoea
	Diaphoresis
	Pallor
	Rarely with ascites, facial oedema, ankle swelling
Children and adolescence	Shortness of breath
	Dyspnoea
	Decrease effort tolerance
	Abdominal pain, nausea, and vomiting
	Rarely ankle oedema, ascites, chest pain, and palpitation

Table 20: Modified Ross Classification for Paediatric Heart Failure[1]

Class	Age groups	Symptoms
I	All	Asymptomatic
II	Infant†	Mild tachypnoea or diaphoresis during feeding No growth failure or failure to thrive
	Older children‡	Dyspnoea on moderate exertion
III	Infants	Marked tachypnoea or diaphoresis during feeding Growth failure or failure to thrive
	Older children	Dyspnoea on mild or minimal exertion
IV	All	Tachypnoea, diaphoresis or respiratory distress at rest

†Infants refer to age 0-1 year.
‡Older children refer to age 1-10 years
[1]Ross RD, Daniels SR, Schwartz DC, Hannon DW, Shukla R, Kaplan S. Plasma norepinephrine levels in infants and children with congestive heart failure. Am J Cardiol 1987;59:911-4.

Table 21: The ECG, CXR, and 2d-Echocardiography and Possible Cardiac Diagnosis in Paediatric Heart Failure

4.1 ECG findings	Interpretation
LVH	Left to right shunt
RAD, RVH	Right sided lesion
T inversion and Q waves in inferolateral leads	ALCAPA
Bilateral atrial enlargement (bifid p and peak p)	RCM
Supraventricular tachycardia	Tachycardia-induced dilated cardiomyopathy
4.2 CXR findings	**Interpretation**
Left ventricular and atrial enlargement and pulmonary artery dilation	Left to right shunt
Right atrial and ventricular enlargement, pulmonary artery dilation	Right-sided lesion
Left ventricular enlargement, Rib notching	Bigger children with CoA
“Snowman” sign	Supracardiac TAPVD
Small heart with increase pulmonary vascular marking	Obstructed TAPVD
4.3 2d-echocardiography findings	**Interpretation**
Dilated LA and LV with a normal function	Left to right shunt
LVH +/- LV dysfunction	Left sided obstructive lesion
RVH +/- LV dysfunction	Right-sided obstructive lesion
Dilated LV with LV dysfunction	DCM, ALCAPA
Global IVS thickening	HOCM
Biatrial enlargement	RCM
Dilated RA and RV	Neonatal CoA
	TAPVD
	Pulmonary hypertension
	ASD (rarely cause symptomatic heart failure in infancy)

LCAPA, anomalous left coronary artery to pulmonary artery; AS, aortic stenosis; ASD, atrial septal defect; CoA, coarctation of aorta; CXR, Chest X-ray; DCM, dilated cardiomyopathy; ECG, electrocardiogram; HOCM, hypertrophy obstructive cardiomyopathy; IVS, interventricular septum; LA, left atrium; LV, left ventricle; LVH, left ventricular hypertrophy; PS, pulmonary stenosis; RA, right atrium; RAD, right axis deviation; RCM, restrictive cardiomyopathy; RV, right ventricular; RVH, right ventricular hypertrophy; TAPVD, total anomalous pulmonary venous drainage.

Table 22: Other Tests for Heart Failure in Children

Test	Indication and findings
FBC	Low haemoglobin (anaemia) may cause or aggravate HF.
Electrolyte	Prolong use of diuretic may cause low potassium or chloride.
Renal profile	Renal impairment may result from medication used for treatment of HF (diuretic or ACE inhibitor) particularly in neonate and small infant.
Liver function test	In acute HF, raised liver enzyme is commonly noted due to liver congestion particularly in infant and children with right-sided
	volume and pressure overload.
Natriuretic peptides	BNP or NT-proBNP levels are useful in distinguishing HF from respiratory or other non-cardiac disease.
Lactate	Useful in patients with acute decompensated HF, helps guide management.
Arterial blood gases	In acute stage for oxygen (hypoxia) and metabolic acidosis.
Thyroid function test	If clinically indicated to exclude thyrotoxicosis.
Cardiac troponins	Useful in HF i.e. increase troponin T in acute myocarditis and increase troponin I in dilated cardiomyopathy.
Metabolic and genetic testing	Indicated in children with unexplained cardiomyopathy. Should be based on clinical presentation and a discussion with genetic and/or metabolic specialist.
Viral studies	Indicated in infant and children with suspected acute myocarditis. Viral studies includes enterovirus, adenovirus, parvovirus, hepatitis C, and the herpes group viruses (EBV, CMV, HSV, HHV6/7, VZV) from blood, stool, and/or nasopharyngeal samples as appropriate.
Endomyocardial biopsy	Useful in suspected acute myocarditis, but the yield is low. Not advisable in non-stable patients and infant less than 10kg.
Cardia MRI/CT scan	Shall be guided by echocardiogram. Useful in diagnosis of primary CMs and myocarditis, complex CHD or rare extracardiac malformation i.e. vascular ring and sling, pulmonary sequestration, abdominal CoA.
Cardiac catheterisation	Shall be guided by echocardiogram. Indicated for complex CHD. Assessment of pulmonary pressure and haemodynamic.

ACE, angiotensin-converting enzyme; BNP, B-type natriuretic peptide; CHD, congenital heart disease; CMV, cytomegalovirus; CoA, coarctation of aorta; CT, computerised tomography; EBV, Ebsteins Barr virus; FBC, full blood count; HSV, herpes simplex virus; HF, heart failure; MRI, magnetic resonance imaging; NT-proBNP, N-terminal pro b-type natriuretic peptide; VZV, varicella zoster virus

Table 23: Summary of Principles of Management of Paediatric Heart Failure by Aetiology/Pathophysiology

Type of heart failure	Suggested treatment and medication†	Comments
Volume overload	Frusemide, spironolactone, and/or ACE-I. Corrective surgery or intervention.	Corrective surgery or intervention should be considered early in an infant with poor weight gain and recurrent chest infection.
Pressure overload††	Supportive care in the acute stage. Urgent corrective surgery or intervention to release the obstruction.	Inotropes shall be used cautiously, may worsen HF. Avoid ACE-I in CoA.
Single ventricle/ complex CHD with no pulmonary stenosis	Surgical repair Frusemide, spironolactone, and/or ACE-I	Unnecessary use of O2 supplement, may worsen HF.
ALCAPA††	Supportive care in the acute stage. Frusemide, spironolactone, and ACE-I Corrective surgery	May mimic left-sided obstructive lesion In the acute stage: • May need a slow infusion of frusemide and inotrope. • Add each medication in a stepwise manner.
Dilated cardiomyopathy††	Frusemide, spironolactone, and ACE-I, β-blocker	In the acute stage: • May need a slow infusion of frusemide and inotrope. • Add each medication in a stepwise manner. • β-blocker after stabilisation.
Hypertrophic cardiomyopathy	β-blocker Surgical resection	In the acute stage: • Inotropes shall be used cautiously, may worsen HF.
Restrictive cardiomyopathies	Diuretic, β-blocker and ACE-I	• To administer medications cautiously. Associated with poor prognosis.
Tachyarrhythmias	Antiarrhythmias to control SVT. β-blocker	In the acute stage: • Inotropes shall be used cautiously, may worsen arrhythmias.
Complete heart block	Temporary pacing or intravenous isoprenaline in the acute stage.	Permanent pacing
Acute myocarditis††	Supportive care in the acute stage. Frusemide, spironolactone, and ACE-I	In the acute stage: May need a slow infusion of frusemide and inotrope Add each medication in a stepwise manner
Rheumatic carditis	Steroids in severe carditis. Frusemide, spironolactone, and ACE-I	As steroids are being weaned off, aspirin is added. Early valve repair in severe valvular regurgitation.
Infective endocarditis	Supportive care in the acute stage Appropriate antibiotic Frusemide, spironolactone, and ACE-I	Early valve repair in severe . valvular regurgitation

† No. of medication used is depending on clinical response
†† Commonly associated with ventricular dysfunction

ACE-I, angiotensin-converting enzyme inhibitor; ALCAPA, anomalous left coronary artery to pulmonary artery; CHD, congenital heart disease; CoA, coarctation of aorta; SVT, supraventricular tachycardia.

Table 24: Common Drugs Used in Paediatric Heart Failure

Medication	Standard dose†	Indication and comments
Diuretics		
Frusemide	Oral 0.5-1mg/kg 6-24H Infusion 0.1-1mg/kg/hr.	A slow intravenous infusion may be required in children with impaired or depressed cardiac function.
Spironolactone*	Oral 0-10kg: 6.25mg 12H 11-20kg: 12.5mg 12H 21-40kg: 25mg 12H > 40kg: 25mg 8H	Potassium sparring, used in combination with frusemide.
ACE-I		
Captopril	Oral 0.1mg/kg 8H up to max 2mg/kg 8H	Introduce slowly and monitor renal function. Monitor for hypotension.
Enalapril	Oral 0.1 mg/kg daily up to max 0.5mg/kg 12H	Only for children more than 2 years of age.
β-blocker		
Propranolol	Oral 0.2-0.5mg/kg 68H up to max 1.5mg/kg 6-8H	SVT, HOCM
Metoprolol	Oral 1-2mg/kg 6-12H	SVT, HOCM, DCM
Carvedilol	Oral 0.1mg/kg 12H, up to max 0.5-0.8mg/kg 12H	Stable DCM in addition of diuretics and ACE-I Increase gradually, 0.1mg/kg every 1-2 week to max dose.
Milrinone	Infusion 75mcg/kg over 1 hour, then 0.5-0.75mcg/kg/min	For low cardiac output syndrome.
Digoxin	3-5mcg/kg 12H	Rarely used except in tachyarrhythmia and ventricular dysfunction. Monitor the digoxin level.

ACE-I, angiotensin converting enzyme inhibitors; HOCM, hypertrophy cardiomyopathy; SVT, supraventricular tachycardia.
†*Adapted from Drug Doses Frank Shann 17th edition*

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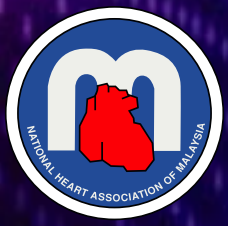

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