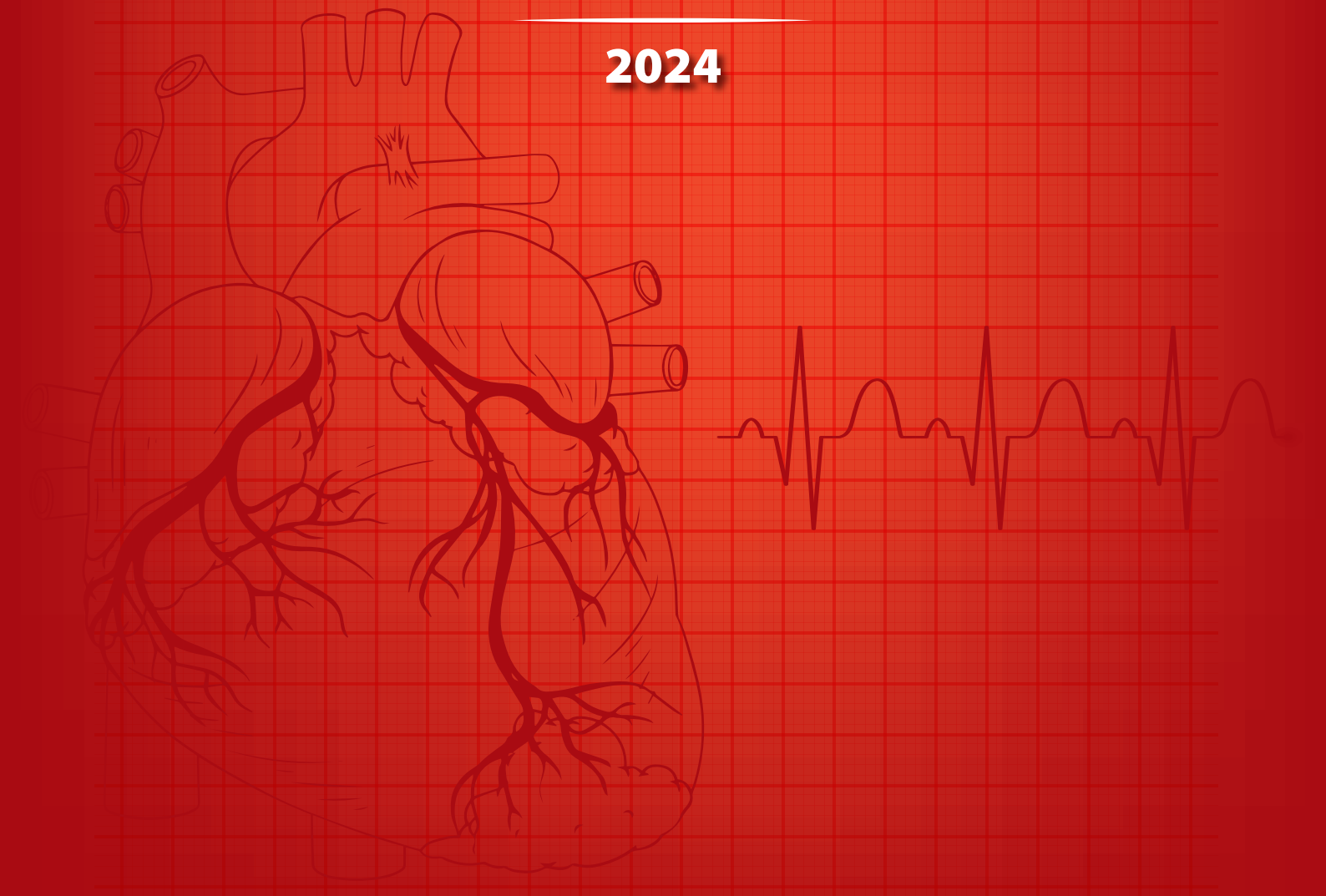
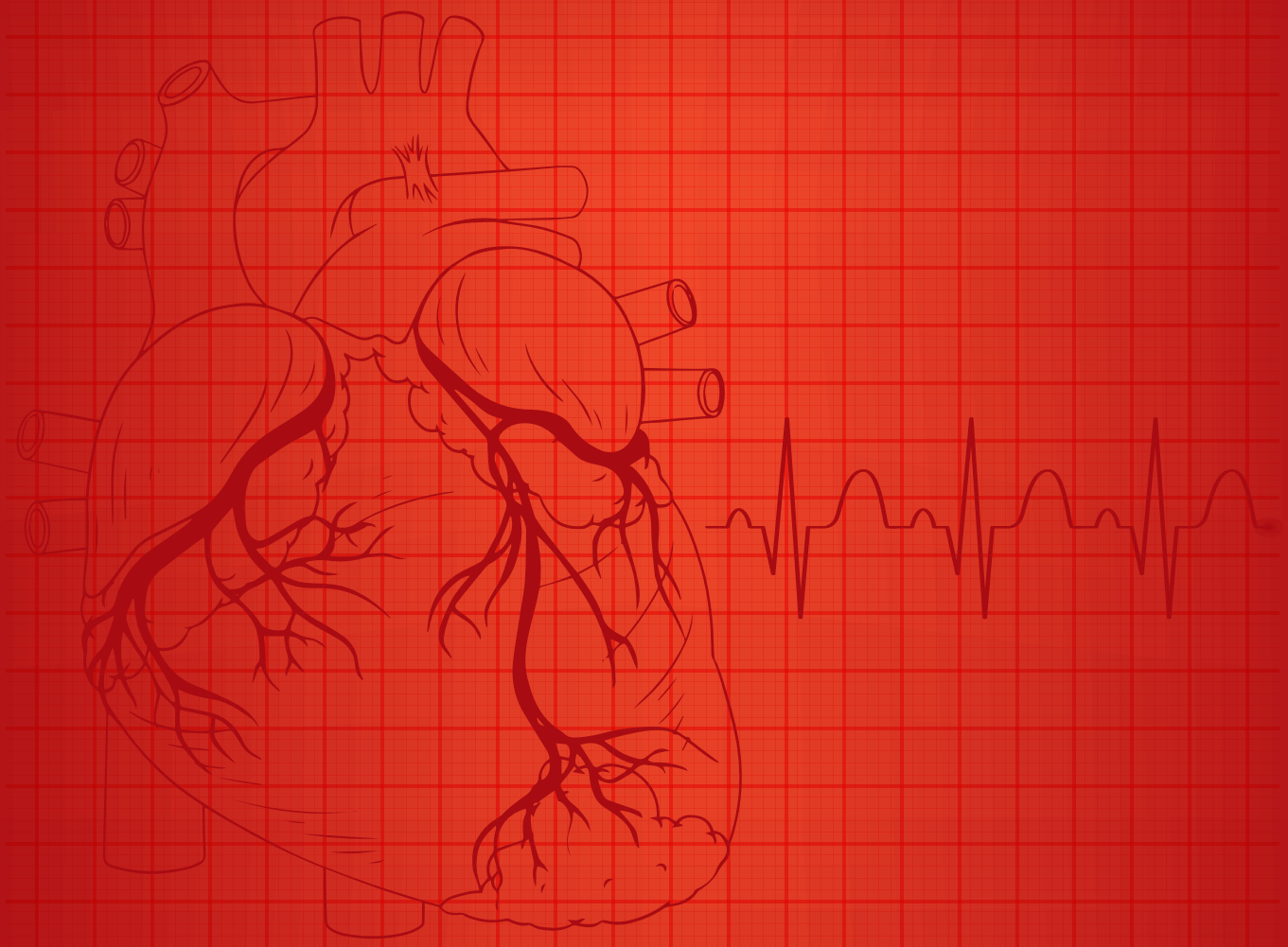
REPUBLIC OF KENYA

MINISTRY OF HEALTH

KENYA NATIONAL GUIDELINES FOR THE MANAGEMENT OF CARDIOVASCULAR DISEASES

2024





KENYA NATIONAL GUIDELINES FOR THE MANAGEMENT OF CARDIOVASCULAR DISEASES

Developed by the Division of Non-Communicable Diseases - Ministry of Health

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FOREWORD

The Kenyan government is dedicated to attaining Universal Health Coverage (UHC) as guided by the Sustainable Development Goal Agenda 3.8 and the constitutional right to achieve the highest standards of care for all Kenyan citizens. This commitment is anchored on strengthening four key pillars, including human resources for health, health financing, health products and technology, and the strategic utilization of digital technologies. Additionally, the government has committed to strengthening primary healthcare, prioritizing a strategic shift from a focus on curative to preventive and promotive health services, thereby enhancing the nation's ability to proactively address the health needs of all citizens. Non-communicable diseases (NCDs), particularly cardiovascular diseases such as hypertension, have been prioritized in these initiatives.

The Kenya Health Policy 2014-2030, the Ministry of Health's roadmap for achieving the constitutional goal, places a high priority on tackling the escalating burden of non-communicable diseases (NCDs). These diseases, which currently account for 41% of all deaths in Kenya, are not just health issues but also significant barriers to social and economic development. To combat this growing NCD burden, the Ministry of Health has formulated the National Strategic Plan for the Prevention and Control of Non-communicable Diseases 2021/22-2025/26, with a target of reducing premature NCD-related deaths, including cardiovascular diseases (CVDs), by one-third.

Given that cardiovascular diseases (CVDs) are a leading cause of mortality, it is imperative to implement comprehensive strategies to mitigate their impact on individuals, families, and communities. The second edition of the Kenya Cardiovascular Disease Guidelines serves as a comprehensive framework for proactive prevention, diagnosis, treatment, and management of cardiovascular conditions at all levels of care. These guidelines advocate for integrating multidisciplinary approaches, with a strong emphasis on primary prevention, risk assessment, lifestyle modifications, early detection, timely intervention, and holistic patient-centred care. This approach aligns with the government's focus on strengthening preventive and promotive health services and ensuring that populations can access quality cardiovascular care without financial hardships.

We are committed to ensuring the effective dissemination and use of these guidelines. However, we recognize that our efforts alone are not enough. We need the active participation of county governments and other stakeholders, as their involvement is not just beneficial, but crucial for the impactful strengthening of cardiovascular care in Kenya. We value your role in this process and look forward to the positive impact that will arise from our collective efforts in implementing these guidelines.

Dr. Patrick Amoth, EBS
AG. Director General For Health
Ministry of Health Kenya

PREFACE

Cardiovascular diseases (CVDs) are the leading cause of death globally. In Kenya they are the second contributing to 13% of total mortalities and 25% of hospital admissions. CVDs pose a formidable challenge to public health, carrying substantial economic implications in terms of healthcare needs, lost productivity, and premature deaths. Their impact on individuals during their most productive years greatly strains our economy and hampers economic growth. With the rising prevalence of risk factors such as hypertension, diabetes, obesity, and sedentary lifestyle, the burden of CVDs continues to escalate, underscoring the critical need for targeted interventions and evidence-based guidance.

Most cardiovascular diseases can be prevented by addressing behavioural risk factors such as tobacco use, unhealthy diet, obesity, physical inactivity, and harmful use of alcohol, using population-wide strategies. People living with cardiovascular conditions or those at high risk (due to the presence of one or more risk factors such as hypertension, diabetes, hyperlipidemia or already established disease) need early detection and management, as appropriate.

In response to this crisis, the Ministry of Health in collaboration with the Kenya Cardiac Society (KCS) spearheaded the development of the second edition of the National Guidelines for the Management of Cardiovascular Diseases to provide a standardised way of managing cardiovascular diseases in the country. These guidelines were developed through a collaborative effort of esteemed healthcare professionals, researchers, policymakers, and stakeholders and encapsulates the latest advancements in cardiovascular care, tailored to the unique context and healthcare landscape of Kenya. They embody the collective wisdom, expertise, and dedication of numerous experts who have committed themselves to the advancement of cardiovascular health across our nation. They offer practical recommendations, informed by the latest scientific evidence, and guided by international best practices, to empower healthcare providers in delivering optimal care to individuals at risk of, or living with, CVDs.

The cardiovascular disease guidelines are suitable for all health workers and health institutions from both public and private sectors. They give clear directions on what needs to be done for people living with cardiovascular diseases and provide a guide on the continuum of care required throughout their life course. We encourage their thorough adoption and implementation across all levels of healthcare provision to enhance the quality of care and ultimately reduce the burden of cardiovascular diseases on our society.

Dr. Issak Bashir
Director – Directorate of Family Health
Ministry of Health

ACKNOWLEDGEMENT

The publication of the 2nd edition of the Kenya Cardiovascular Disease Guidelines stands as a testament to numerous individuals' and organizations' collaborative efforts and invaluable contributions. The development process was marked by active participation and consultation, with significant efforts from our esteemed partners and stakeholders. The Ministry of Health extends heartfelt gratitude to all stakeholders for their unwavering contributions, commitment, and both technical and financial support.

Our sincere thanks go to the leadership of the Ministry of Health for their indispensable support, with special mention to the offices of the Cabinet Secretary, Principal Secretary, Director General, and Director- Directorate of family Health, whose guidance played a pivotal role in the successful development of this document.

We express deep appreciation to the editorial team, whose tireless efforts were instrumental in ensuring the successful completion of this process. Special recognition for the Division of Non-communicable Diseases for providing strategic leadership during the development process, led by Dr. Gladwell Gathecha, Dr. Elizabeth Onyango, and the focal person for cardiovascular diseases, Dr. Yvette Kisaka, who effectively coordinated the entire effort. Special recognition is also extended to Dr. Bernard Samia, the President of Kenya Cardiac Society, who tirelessly marshalled all the authors and other stakeholders to compile and release the document. Well-deserved recognition goes to Prof. Elijah Ogola, Dr. Anders Barasa, Dr. Felix Barasa, Dr. Loise Mutai, Dr. Jeilan Mohamed, Dr. Mzee Ngunga, Dr. Lilian Mbau, Dr. Tabitha Wambaire, and many others not mentioned here whose dedicated contributions were integral to this undertaking.

We extend our sincere gratitude to our partners for providing both technical expertise and financial support. In particular, we recognize the Kenya Red Cross, PATH, and others who played a crucial role in this endeavour. Special recognition to Getz Pharma for their technical input and liaison to support external editorial review. We are greatly indebted to the Clinton Health Access Initiative (CHAI) for their financial support in designing and initial printing of the booklet.

The success of this collaborative effort underscores the collective commitment to advancing cardiovascular health in Kenya. We acknowledge and appreciate the dedication and support of each individual and organization involved in this significant undertaking.

Dr. Gladwell Gathecha,
Head; Division of Non-communicable Diseases
Ministry of Health

ABBREVIATIONS

ACS	Acute Coronary Syndrome
aPTT	Activated Partial Thromboplastin Clotting Time
ASCVD	Atherosclerotic Cardiovascular Disease
CAD	Coronary Artery Disease
CHP	Community Health Promoter
CKD	Chronic Kidney Disease
CVD	Cardiovascular Disease
DBP	Diastolic Blood Pressure
DIC	Disseminated Intravascular Coagulation
DM	Diabetes Mellitus
DVT	Deep Venous Thrombosis
EF	Ejection Fraction
ESC	European Society of Cardiology
GFR	Glomerular Filtration Rate
HF	Heart Failure
HIV	Human Immunodeficiency Virus
HMOD	Hypertension-mediated Organ Dysfunction
HTN	Hypertension
LMWH	Low Molecular Weight Heparin
MI	Myocardial Infarction
NSTEMI	Non-ST elevated MI
NYHA	New York Heart Association
PE	Pulmonary Embolism
PERT	Pulmonary Embolism Response Team
PT	Prothrombin Time
SBP	Systolic Blood Pressure
STEMI	ST- elevated MI
UFH	Unfractionated Heparin
VTE	Venous Thromboembolism

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INTRODUCTION

The World Health Organization (WHO) estimates that cardiovascular diseases (CVDs) are the leading cause of mortalities worldwide. In 2019 alone, an estimated 17.9 million individuals succumbed to CVDs, constituting 32% of all global deaths. Predominantly, 85% of these fatalities were attributed to heart attacks and strokes. Alarmingly, more than three-quarters of CVD-related deaths occur in low- and middle-income nations. Moreover, out of the 17 million premature deaths (those under 70 years old) caused by noncommunicable diseases in 2019, CVDs accounted for 38%.

In Kenya, approximately a quarter of hospital admissions are attributed to cardiovascular diseases (CVDs), with 13% of autopsies identifying CVDs as the primary cause of death. This places CVDs as the second leading cause of mortality, following infectious, maternal, and perinatal causes. The diagnosis and management of CVDs entail significant costs, and when these are not met often results in premature death among productive members of households and society at large. Moreover, these diseases play a pivotal role in perpetuating poverty due to the financial burden of healthcare expenses, leading to high levels of out-of-pocket spending and catastrophic health expenditures.

The National Cardiovascular Disease Management guidelines has outlined essential messages to support health workers in delivering top-quality care for CVDs. These guidelines are intended for adoption by policymakers, program developers, implementers of noncommunicable disease (NCD) interventions, healthcare professionals, community educators, and academic institutions alike.

Organization of the Guideline

The guidelines begin with an introduction, underscoring the necessity of the document and explaining the responsibilities of both levels of government in its dissemination. A pivotal emphasis is placed on the role of community health interventions in supporting CVD care, aligning with the government's transformative agenda to promote preventive and promotive healthcare while bolstering primary healthcare services. This underscores the significance of community health promoters as integral components of Kenya's healthcare workforce.

Following the introduction, the guidelines elaborate on the prevention of cardiovascular diseases, offering specific recommendations for managing risk factors. Subsequently, they delve into a comprehensive discussion of various conditions and their management across the healthcare system. Moreover, they provides guidance on managing CVD in special populations, including athletes, older individuals, and people living with HIV, diabetes, and kidney disease. Palliative care guidance follows this section, with the document concluding with annexes.

Dissemination and Use of the National Guidelines for Prevention and Control of Cardiovascular Disease

Roles of the Different Levels of Care

a. Level one (Tier 1) – Community

Community Health promoters (CHPs) are the core resource persons at this level; they should be well-trained and equipped with a kit designed to assess CVD risk in the community. The kit should include:

- A blood pressure machine
- A Glucometer and strips
- A weighing scale
- A tape measures

- Waist/hip charts
- BMI charts T

The CHPs are the link between households, communities, and health facilities. Community health assistants (CHAs) should be trained in CVDs and coordinate CHP activities. The main intervention entails carrying out public awareness campaigns on CVD risk management through mass media, e.g. posters, mass media outlets, e.g. vernacular radio stations, barazas, community health education forums, community dialogue and action days.

b. Level two and three (Tier 2) – Dispensaries and Health Centres

The CVD package at this level includes:

- Provision of lifestyle intervention/advice
- CVD risk assessment and this entails blood pressure (BP) monitoring, blood sugar assessment, electrocardiography, measuring of lipid profiles, renal functions and urinalysis
- Provision of the initial treatment for type II diabetes mellitus and hypertension
- Referral and follow-up for patients on management for CVD in higher levels of care

c. Level four and five (Tier 3) – Subcounty and County referral health facilities

- The CVD package at this level entails a comprehensive CVD risk assessment using the appropriate risk assessment tools.
- Complete cardiovascular imaging and laboratory assessment (echocardiogram etc.)
- Comprehensive management of both primary and secondary prevention interventions
- Referral up (to level 6) for further management and down to lower levels for follow-up after management is initiated.

d. Level six (Tier 4) – National referral health facilities.

These facilities should offer advanced cardiovascular assessment and treatment, including cardiac catheterization, angioplasty, bypass surgery, endarterectomy, prostheses and pacemakers, ventricular devices, heart transplants, and rehabilitation services.

Service Delivery Model for CVD Management: Adapted from the WHO Hearts Technical

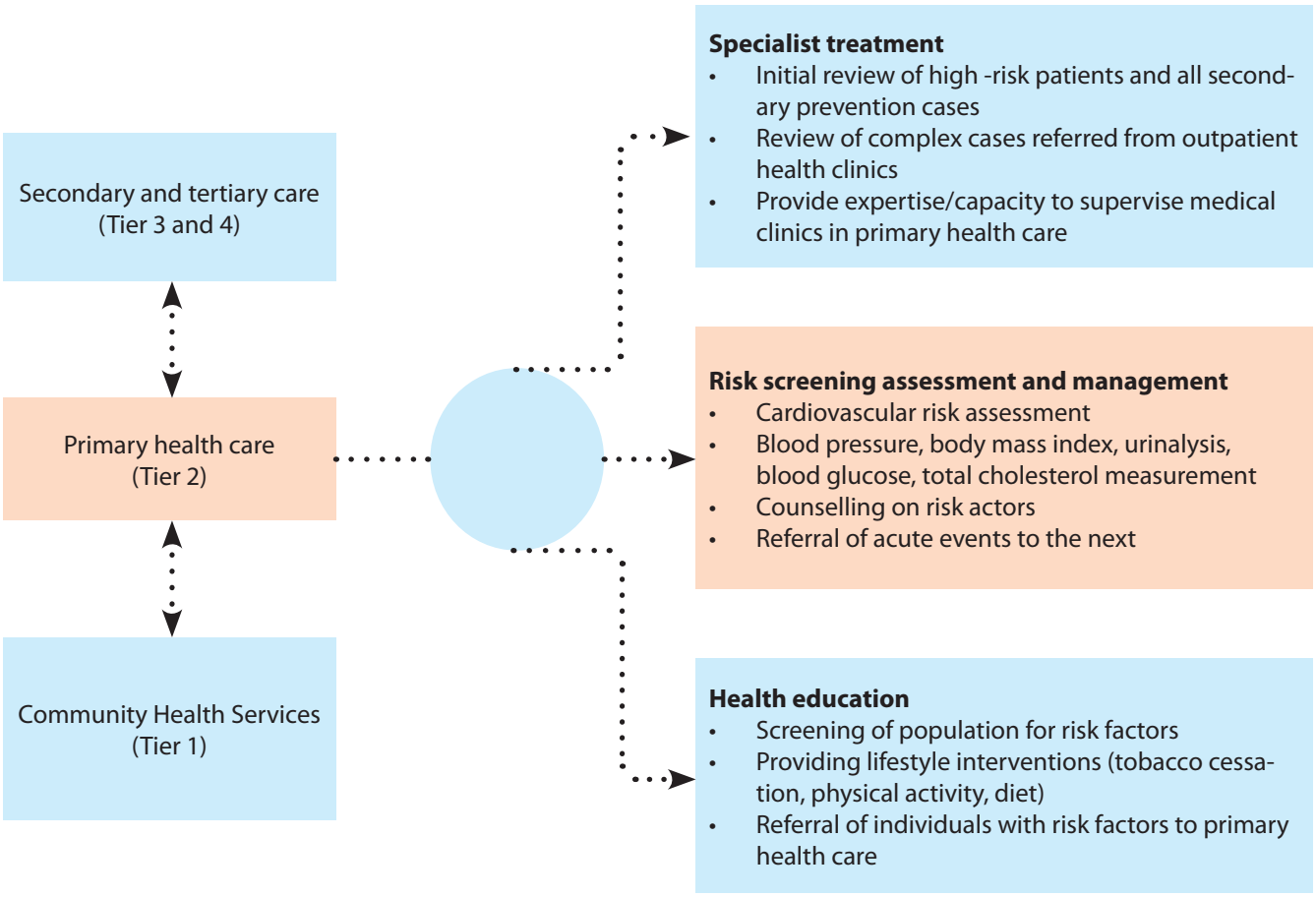

Figure 0.1: Service Delivery Model for CVD Management: Adapted from the WHO Hearts Technical

Resources needed for cardiovascular healthcare delivery

The table below lists the recommended resources for the management of CVD in health facilities:

Table 0:1 Resources Needed for CVD Care Delivery

Resources needed	Level 1	Level 2 and 3	Level 4	Levels 5 and 6
Human resources	• Community health promoters • Community health assistants • Community health extension workers	• Nurses • Clinical officers • Nutritionist • Medical Officer • Lab personnel • Radiographers • Pharmacists • Pharmaceutical Technologists	• Cadres in level 2 and 3 • Physician • Pediatrician • Echocardiographer • Radiologist	• Cadres in Level 2,3,4 • Cardiologist • Pediatric Cardiologist • Perfusionists • Cardiac anesthetists • Specialized nurses • Cardiothoracic surgeons • Clinical pharmacist • Pathologist

Screening/Diagnostic equipment	BP machine Weighing scale Thermometer Height meter BMI charts	BP Machine • Stethoscope • Weighing scale • Height meter • Thermometer • CVD risk assessment tools • Strips for urinalysis • Glucometer • Hematology equipment and reagents • Biochemistry equipment and reagents • X-Ray • ECG machine	Equipment in level 2 and 3 • Echo machine • Biochemistry and Haematological machines • Ophthalmoscope	Equipment in level 2, 3 and 4 • Echo machine (high specification) • Blood analysis: fasting blood sugar, electrolytes, creatinine, cholesterol and lipoproteins • Cardiac catheterization lab • Ambulatory BP • 24 hr Holter machine • Treadmill • Facilities for telemedicine • A critical care unit
Medications	None	• Thiazide-like* diuretic • Calcium-channel blocker* • ACEI/ARB* • Furosemide** • Statins** • Aspirin**	Diuretics (including spironolactone and furosemide) • Beta-blockers*** • Digoxin**** • Warfarin • Clopidogrel	• Diuretics (including spironolactone and furosemide) • Beta blockers • Angiotensin converting enzyme inhibitors/ARBs/ARNi • Calcium channel blockers • Aspirin SGLT2i • Digoxin**** • Dopamine • Dobutamine Sildenafil/tadalafil
Main Services	• Awareness creation • Detection • Referral and linkage to care • Follow up	• Detection Diagnosis • Initiate treatment • of uncomplicated • hypertension • Follow-up clinic • for hypertension • Referral	Services offered in level 2&3of general medical conditions • Comprehensive diagnosis • Management of complications e.g heart failure as you prepare for referral • Referral rehabilitation and follow up Training	Services offered in level 4 • Cardiac catheterization and open heart surgery • Treatment of non-cardiac and cardiac surgical complications • Management of pregnancy in a cardiac patient including safe delivery
KEY: *Medications can be initiated at level 2 or 3 **Medications are not to be initiated, but prescription can be refilled at level 2/3 ***Beta-blockers recommended for children are propranolol and carvedilol *****Digoxin use limited to physicians and other specialist				

Priority Research Areas

- Regional mapping of the burden of priority CVDs at the population level and health facilities in Kenya
- Determinants of occurrence, severity and outcome of priority CVDs in Kenya
- Qualitative studies on the quality of CVD care across counties in Kenya
- Integration of CVD care in communicable diseases service e.g. HIV – outcomes, feasibility, cost, ROI, models of integration

1

1. PREVENTION OF ATHEROSCLEROTIC CARDIOVASCULAR DISEASES

Key Messages

- Early detection and appropriate control of hypertension is the hallmark of preventing atherosclerosis.
- CVD risk assessment refers to the use of a systematic approach to enable identification and classification of individuals who are at an increased risk of cardiovascular disease. To keep cost of risk stratification low, it is advisable that CVD risk factors already available in the individuals' medical records be utilized.
- An informed discussion about CVD risk and treatment benefits tailored to the needs of a patient is recommended.
- Treatment of ASCVD risk factors is recommended in apparently healthy people without DM, CKD, genetic/rarer lipid, or BP disorders who have high CVD risk assessment scores.

1.0 Introduction

Majority of cardiovascular diseases are preventable with control of risk factors, early detection, and prompt management. Cardiovascular disease (CVD) can be categorized into atherosclerotic and non-atherosclerotic disease based on the underlying pathophysiologic mechanisms. Non-atherosclerotic cardiovascular diseases include rheumatic heart disease, endocarditis, congenital heart disease, venous thromboembolism, pericardial heart disease, and cardiomyopathies among others. Prevention of the non-atherosclerotic cardiovascular disease has been discussed in the various relevant chapters.

Atherosclerotic cardiovascular disease (ASCVD) results from the build-up of cholesterol plaques in arteries due to deposition of fatty material, cholesterol, and other substances in the walls of the vessels which may in turn reduce blood flow to end organs such as the heart, brain, kidneys, and limbs.1 They include coronary heart disease, stroke, peripheral artery disease, and aortic disease. The most important way to prevent atherosclerotic cardiovascular disease (ASCVD) is to promote a healthy lifestyle throughout life. A team-based care approach is an effective strategy for the prevention of CVD. Additionally, a comprehensive patient-centred approach that addresses all aspects of a patient's lifestyle habits and estimated risk of a future ASCVD event forms the key aspect in prevention.

1.1 Aetiology and Risk Factors

A small proportion of the population have genetic conditions that predispose them to CVDs, while the majority who develop them do so because of a combination of modifiable and non-modifiable risk factors as listed below:

Table 1.1: Risk factors for CVD

Modifiable Risk Factors	Non-Modifiable Risk Factors
• Tobacco use and exposure to tobacco smoke • Unhealthy diet- • Overweight/obesity • Physical inactivity • Harmful use of alcohol • Hypertension • Diabetes • Dyslipidaemia • Infections e.g., HIV	• Sex (male) • Age (Male >50; female >60) • Race- Blacks, Asians • Family history

Source: Kenya National Stepwise Survey for NCD risk factors[2]

There are many risk factors that contribute to CVDs. Hypertension is the single most important risk factor. The figure below demonstrates a proposed causal pathway for Atherosclerotic CVD.

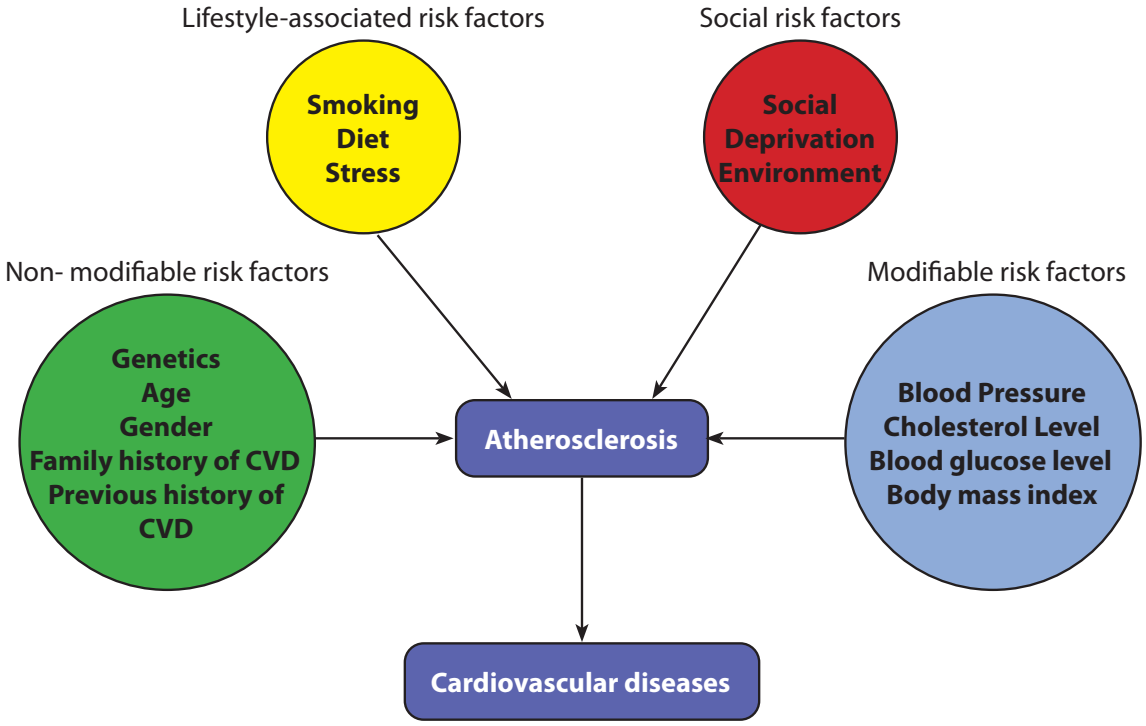

Figure 1.1: Causal Pathway for ASCVD

(Adapted from: Front. Cardiovasc. Med., 22 August 2022 Sec. Atherosclerosis and Vascular Medicine)

1.2 Classification of Prevention Strategies in Cardiovascular Disease

Prevention strategies involve a wide array of interventions that aim to reduce the risk of developing cardiovascular disease. Strategies to prevent cardiovascular disease in people at higher risk are crucial to reduce the global burden of CVD. Prevention strategies are mainly classified into four: primordial prevention, primary prevention, secondary prevention, and tertiary prevention.

- Primordial prevention is a strategy to prevent the development of cardiovascular risk factor at the population level.
- Primary prevention represents the earliest possible interventions and aims to prevent the onset of disease in people who are at high risk of CVD but have not developed a cardiovascular condition.
- Secondary prevention is any strategy aimed at reducing the probability of a recurrent cardiovascular event in patients with known cardiovascular disease.
- Tertiary prevention targets people who are already affected by cardiovascular disease and who are experiencing its long-term effects by slowing, arresting, or reversing disease to prevent recurrent symptoms, further deterioration, and subsequent events. It is generally more costly and more invasive than primary and secondary prevention.

Table 1.2: CVD Prevention Strategies

Prevention Strategy	Health Promotion/ Primordial Prevention	Primary Prevention	Secondary Prevention	Tertiary Prevention
Target	Entire population	People with one or more risk factors	People at early stage of disease	People with symptomatic or advanced diseases
Effects	Prevent risk factors, lower population risk	Prevent development of disease at early age	Prevent disease progression or recurrence	Reduce complications or disability
Examples	Public awareness campaigns Increased taxes on cigarettes and alcohol and banning of smoking in public places Encourage safe pregnancy by avoidance of exposure to risk factors and unnecessary and non-prescribed use of medicines. Use folate and iron supplements in women of childbearing age.	Early detection, appropriate screening, and surveillance Vaccination Lifestyle modification: cessation of tobacco and alcohol use, consumption of healthy diet low in saturated fat, salt, and refined sugars, and high in fruits and vegetables	Providing appropriate treatment and care, support groups Promoting medication adherence together with lifestyle modification (cardiac rehabilitation)	Cardiac Rehabilitation and palliative care at the various stages of the disease pathway. Revascularization i.e., percutaneous coronary intervention, coronary artery bypass grafting (CABG), carotid artery endarterectomy, pacemakers, defibrillators, and left ventricular assist devices

1.3 Cardiovascular Risk Assessment

Cardiovascular risk refers to the likelihood of an individual developing ASCVD over a defined period of time; usually 10 years.

Cardiovascular risk assessment/stratification refers to the use of a systematic approach to enable identification and classification of individuals who are at an increased risk of CVD. The total CVD risk is thus an estimate of the combined risk posed by each of the risk factors. The assessment helps health care workers and patient to make appropriate decisions on effective prevention and management of CVD.

CVD risk estimation helps in prioritization of individuals for further formal and more elaborate risk assessment. This is based on key risk factors using the World Health Organization/International Society of Hypertension (WHO/ISH) assessment tools. The recommended tool for the Kenyan context is the WHO Eastern Sub-Saharan region charts.3 Recommendations for prevention and care of CVD based on individual risk level are then made, focusing on tobacco and alcohol control, dietary modification, physical activity, and pharmacological management as shown below.

Assessment of total CVD risk can be used for routine management of hypertension (HTN) and diabetes mellitus (DM), and for targeting the following categories of people who are/have:

- ✓ aged >40 years
- ✓ smokers
- ✓ obesity
- ✓ known to have HTN
- ✓ known to have DM
- ✓ history of premature CVD in first-degree relative
- ✓ history of DM or kidney disease in first-degree relative.

(Adapted from the HEARTS technical package,2020)

WHO/ISH Risk Prediction Charts for Eastern Sub-Saharan Africa Region

These are 10-year risk prediction tools for a fatal or non-fatal cardiovascular event by gender, age, systolic blood pressure, total blood cholesterol, smoking status, and presence or absence of diabetes mellitus. The charts are shown below.

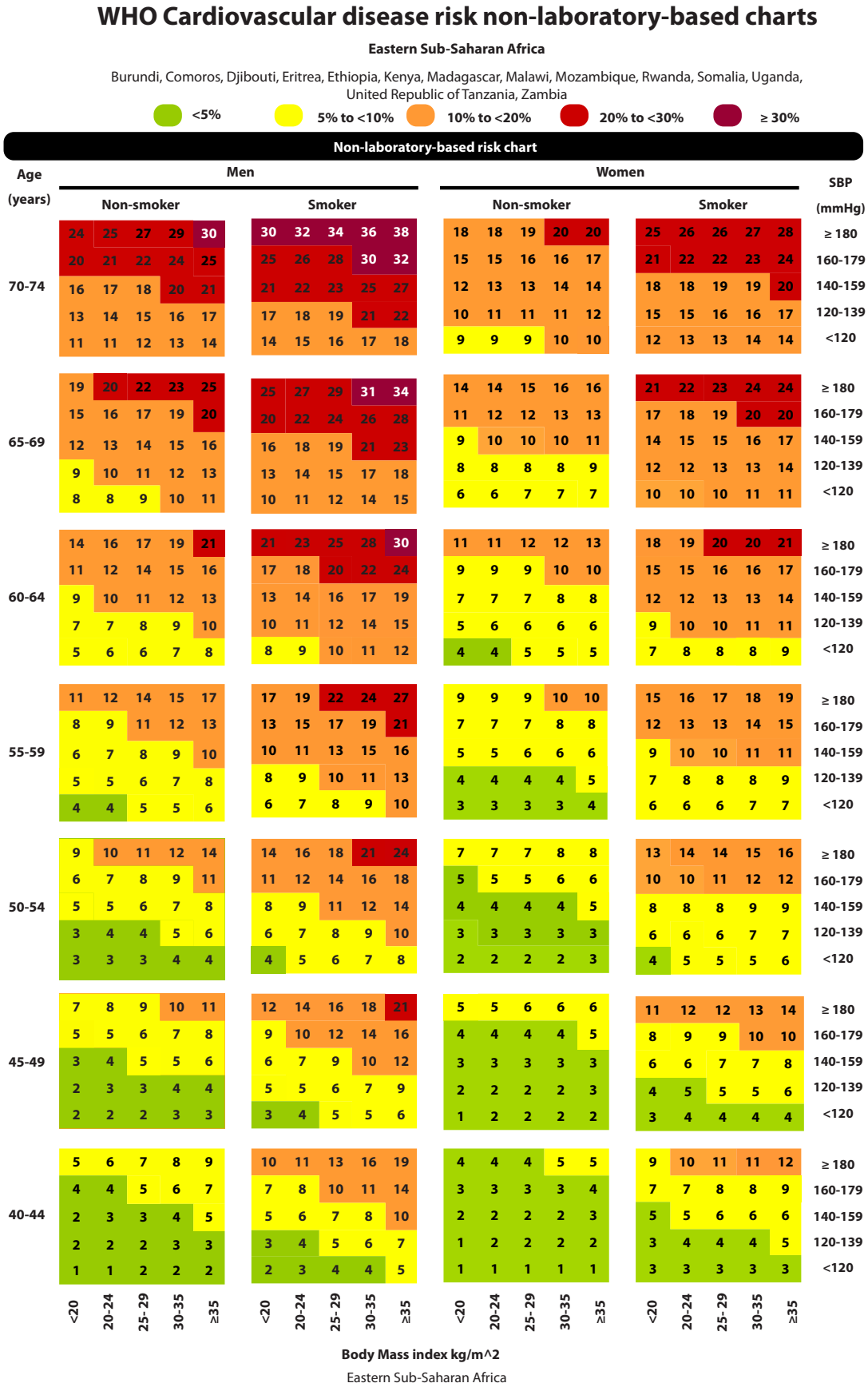

Figure 1.2: WHO Cardiovascular Disease Risk Non-laboratory Based Charts

WHO Cardiovascular Disease Risk Laboratory-based Charts

Eastern Sub-Saharan Africa

Burundi, Comoros, Djibouti, Eritrea, Ethiopia, Kenya, Madagascar, Malawi, Mozambique, Rwanda, Somalia, Uganda, United Republic of Tanzania, Zambia

People without Diabetes

Age (years)	Men										Women										SBP (mmHg)
	Non-smoker					Smoker					Non-smoker					Smoker					
	<4	4-4.9	5-5.9	6-6.9	≥7	<4	4-4.9	5-5.9	6-6.9	≥7	<4	4-4.9	5-5.9	6-6.9	≥7	<4	4-4.9	5-5.9	6-6.9	≥7	
70-74	22	24	27	29	32	28	30	33	36	39	16	17	17	18	19	22	23	24	25	26	≥ 180
	18	20	22	24	26	23	25	28	30	33	14	14	15	15	16	19	20	20	21	22	160-179
	15	17	18	20	22	19	21	23	25	28	12	12	13	13	14	16	17	17	18	19	140-159
	12	14	15	16	18	16	17	19	21	23	10	10	11	11	12	14	14	15	15	16	120-139
	10	11	12	14	15	13	14	16	17	19	8	9	9	9	10	12	12	12	13	14	<120
65-69	16	19	21	23	26	23	26	28	31	34	12	13	14	14	15	19	19	20	21	23	≥ 180
	14	16	17	19	21	19	21	23	25	28	10	11	11	12	13	15	16	17	18	19	160-179
	11	12	14	15	17	15	17	19	21	23	9	9	9	10	10	13	13	14	15	16	140-159
	9	10	11	12	14	12	14	15	17	19	7	7	8	8	9	11	11	12	12	13	120-139
	7	8	9	10	11	10	11	12	14	15	6	6	6	7	7	9	9	10	10	11	<120
60-64	14	15	17	19	21	19	21	24	27	30	10	10	11	11	12	15	16	17	18	20	≥ 180
	11	12	13	15	17	15	17	19	21	24	8	8	9	9	10	13	13	14	15	16	160-179
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50-54	8	9	10	12	13	13	15	17	19	22	6	6	7	7	8	11	12	12	14	15	≥ 180
	6	7	8	9	10	10	11	13	15	17	4	5	5	6	6	8	9	10	11	12	160-179
	5	5	6	7	8	8	9	10	11	13	3	4	4	4	5	6	7	8	8	9	140-159
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	2	2	2	3	3	3	4	5	5	7	1	1	2	2	2	3	3	4	4	5	120-139
	1	1	2	2	2	2	3	3	4	5	1	1	1	1	2	2	3	3	3	4	<120

Eastern Sub-Saharan Africa

Burundi, Comoros, Djibouti, Eritrea, Ethiopia, Kenya, Madagascar, Malawi, Mozambique, Rwanda, Somalia, Uganda, United Republic of Tanzania, Zambia

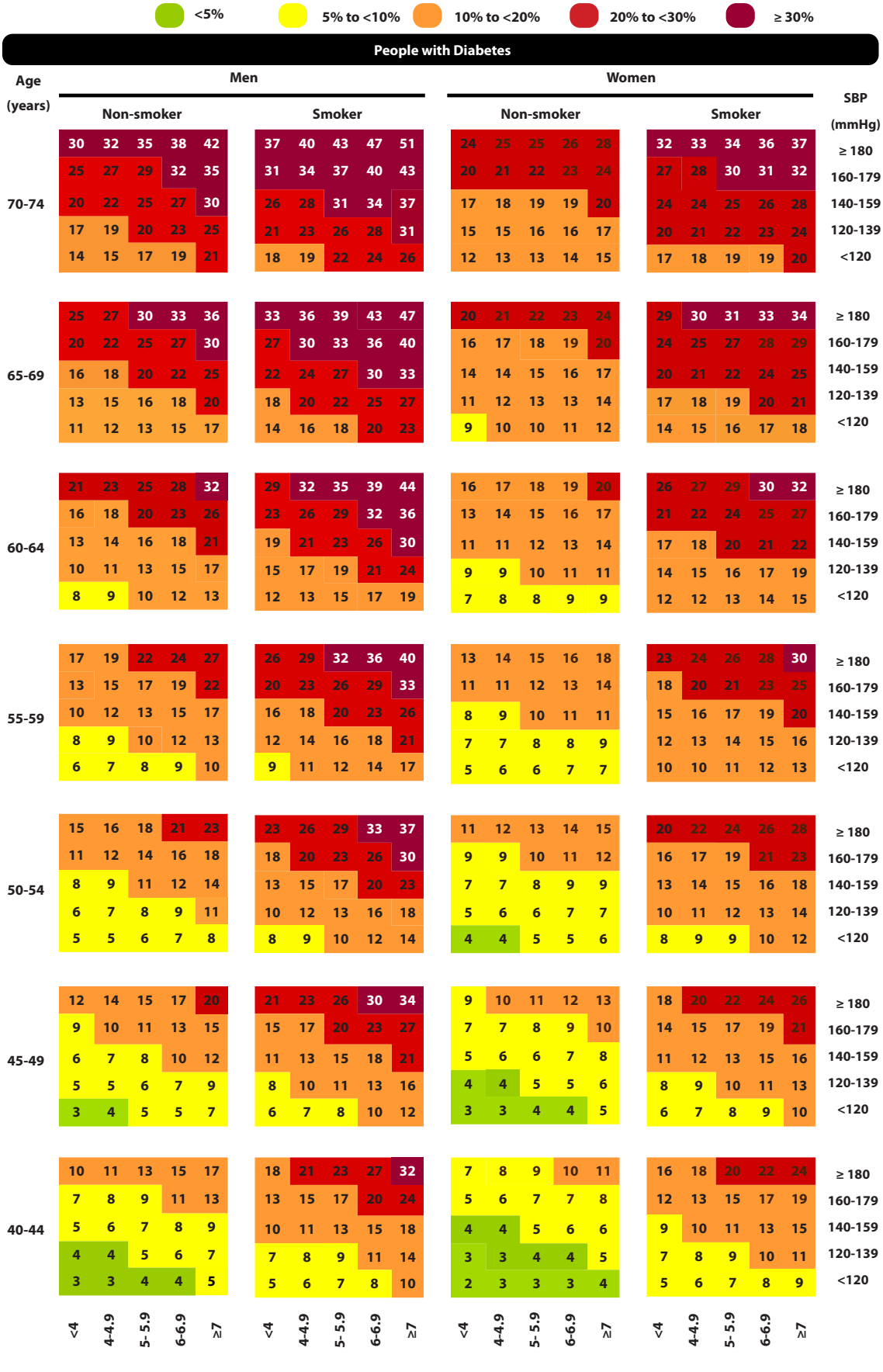

Figure 1.3: WHO Cardiovascular Disease Risk Laboratory-based Charts

1.4 Recommendations for Prevention and Care of CVD Based on Individual Risk Level

Table 1.3: Management of total 10-year risk of fatal or non-fatal CVD event

<10 % (Low risk)	10% to <20% (Moderate risk)	>20% (High and very high risk)
Counsel on diet, physical activity, smoking cessation and avoiding harmful use of alcohol		
• If risk is <5%, follow up in 12 months • If risk is 5% to <10% follow up every 3 months until targets are met, then 6-9 months	• Persistent BP >140/90 mmHg: consider drugs • Follow up every 3-6 months	• Persistent BP ≥ 130/80 mmHg: consider drugs • Give a statin • Follow up every 3 months • If there is no reduction in CVD risk after 6 months of follow-up, refer
Important practical points • For the management of hypertension, refer Chapter 2: Hypertension. • For the management of diabetes, refer to Chapter 16: Cardiovascular Disease in Diabetes. • Consider drug treatment for the following: ○ All patients with established DM, CVD, and renal disease. If stable, continue with the medication already prescribed. They should be considered as having risk >20% (high and very high risk) ○ Patients with albuminuria, retinopathy, left ventricular hypertrophy ○ All individuals with persistently raised BP >160/100 mmHg ○ All individuals with total cholesterol at ≥8 mmol/L (refer to the chapter on dyslipidaemia) • Follow-up visits: ○ Ask about: new symptoms, adherence to advice on tobacco and alcohol use, physical activity, healthy diets, medication ○ Assess (physical exam) ○ Estimate cardiovascular risk ○ Counsel and treat as shown in the protocol		

(Adapted from the HEARTS technical package, 2020)

1.5 Prevention Interventions

Cardiovascular disease prevention includes both non-pharmacological and pharmacological therapies.

1.5.1 Non-Pharmacological Therapy

Non-pharmacological interventions are largely lifestyle interventions. Graded lifestyle advice is appropriate for everyone and needs to consider the individual's circumstances. Specific lifestyle interventions are based on a behaviour counselling approach.

Nutrition and Healthy Diets

Healthy diet

An unhealthy diet characterized by high salt intake, low fruits and vegetables intake, high fat intake, and high sugar intake increases the risk of CVDs. The composition of a healthy diet should take into consideration individual needs such as age, sex, lifestyle, degree of physical activity, cultural context, and locally available foods.

The table below summarizes the basic elements of a healthy diet:

Table 1.4: Basic Elements of a Healthy Diet

1.	Include a variety of foods:
	• Range of fruits and vegetables (at least 5 portions per day). A portion is equivalent to:
	  ○ ½ cup/ ½ fist/ 3 tablespoons of fresh vegetables/fruits
	  ○ 1 cup/1 fist of leafy vegetables
	  ○ ¼ cup/cupped hand of dried fruits
	  ○ A single whole fruit of orange, apple, small mango, banana or 3 tablespoons of cooked vegetables
	• Legumes (beans, lentils)
	• Nuts
	• Whole grains (unprocessed maize, millet, oats, wheat, and brown rice)
	• Starchy tubers or roots (potato, yam, cassava)
	• Food from animal sources (meat, fish, eggs, milk)

2.	Less than 5g of salt per day (1 teaspoon) • This includes salt added to food while cooking or eating. • Avoid processed foods as they tend to have higher salt content. • Eat food prepared at home as much as possible. • Use herbs, spices, vinegar, and citrus to flavour food instead of salt. • Avoid adding salt to ready meals.
3.	Fats • Fats should constitute less than 30% of daily energy intake. • Unsaturated fats are preferred (mainly from plants such as seeds, grain, nuts, vegetables, and fruits. Examples include sunflower oil, corn oil, olive oil and avocado oil). They are also found in fish. • Less than 10% of daily energy intake should be from saturated fats (fats found in animal products such as meat, milk, butter cream, cheese, ghee, lard as well as palm and coconut oil) • Avoid trans-fats (these are hydrogenated or partially hydrogenated oils found in processed foods, fast foods, snacks, fried foods, pizza, cookies, margarines and other spreads). Check food labels to identify foods with trans fats.
4.	Sugars • Take less than 5-10% of daily energy from free sugars (sugars added to foods such as processed drinks, cakes, cookies, and sweets. They are also found naturally in honey, syrups, and fruit juices) • Avoid sugar sweetened beverages such as soft drinks and fruit juices. • Make water the drink of choice.

Adapted from: HEARTS: healthy-lifestyle counselling 2018, ESC Guidelines on cardiovascular disease prevention in clinical practice 2021

Physical activity and weight management

WHO defines physical activity as any movement produced by skeletal muscle that uses energy.

Physical activity prescription

Physical activity should be individually assessed and prescribed in terms of frequency, intensity, time (duration), type, and progression.

How much physical activity is recommended?

WHO guidelines and recommendations provide details on how much physical activity is needed for good health for different age groups and specific population groups.

- **Adults aged 18–64 years**
  - Should do at least 150–300 minutes of moderate-intensity aerobic physical activity;
    - or at least 75–150 minutes of vigorous-intensity aerobic physical activity;
    - or an equivalent combination of moderate- and vigorous-intensity activity throughout the week.

- Should also do muscle-strengthening activities at moderate or greater intensity that involve all major muscle groups on 2 or more days a week, as these provide additional health benefits.
- Should limit the amount of time spent being sedentary. Replacing sedentary time with physical activity of any intensity (including light intensity) provides health benefits.

- **Adults aged 65 years and above**
  - Same as for adults aged 18-65 years;
  - And as part of their weekly physical activity, older adults should do varied multicomponent physical activity that emphasizes functional balance and strength training at moderate or greater intensity, on 3 or more days a week, to enhance functional capacity and to prevent falls.

Table 1.5: Classification of Physical Activity Intensity and Examples

Intensity	Example	Criteria for evaluating intensity
Light	• Walking • Light household work	Can have a normal conversation while doing it
Moderate	• Walking at a moderate or brisk pace • Slow cycling	Breathing and heart rate is noticeably faster; one can still carry on a conversation.
Vigorous	• Race-walking • Jogging or running • Cycling	Heart rate is increased substantially and breathing is too hard and fast to have a conversation.

Recommendations for weight management

- Limit energy intake from total fats and sugars.
- Increase consumption of fruit and vegetables, as well as legumes, whole grains, and nuts. (Refer to section on Nutrition and Healthy Diet above.)
- Engage in regular physical activity. (Refer to section on Physical Activity above.)

Tobacco Dependence Treatment, Cessation and Prevention

Health care professionals should provide regular and tailored counselling interventions for those who meet the criteria for tobacco dependence. Tobacco dependence treatment and cessation programs should combine behavioural support (such as psychological interventions, telephone support, and self-help) with pharmacotherapy treatment where necessary. Before deciding on which intervention to use, it is essential to document tobacco use status and conduct screening. Healthcare providers of tobacco dependence treatment and cessation should receive suitable training.

There are three main categories of interventions:

a. Brief advice by a healthcare professional
b. Behavioural support
c. Pharmacotherapy

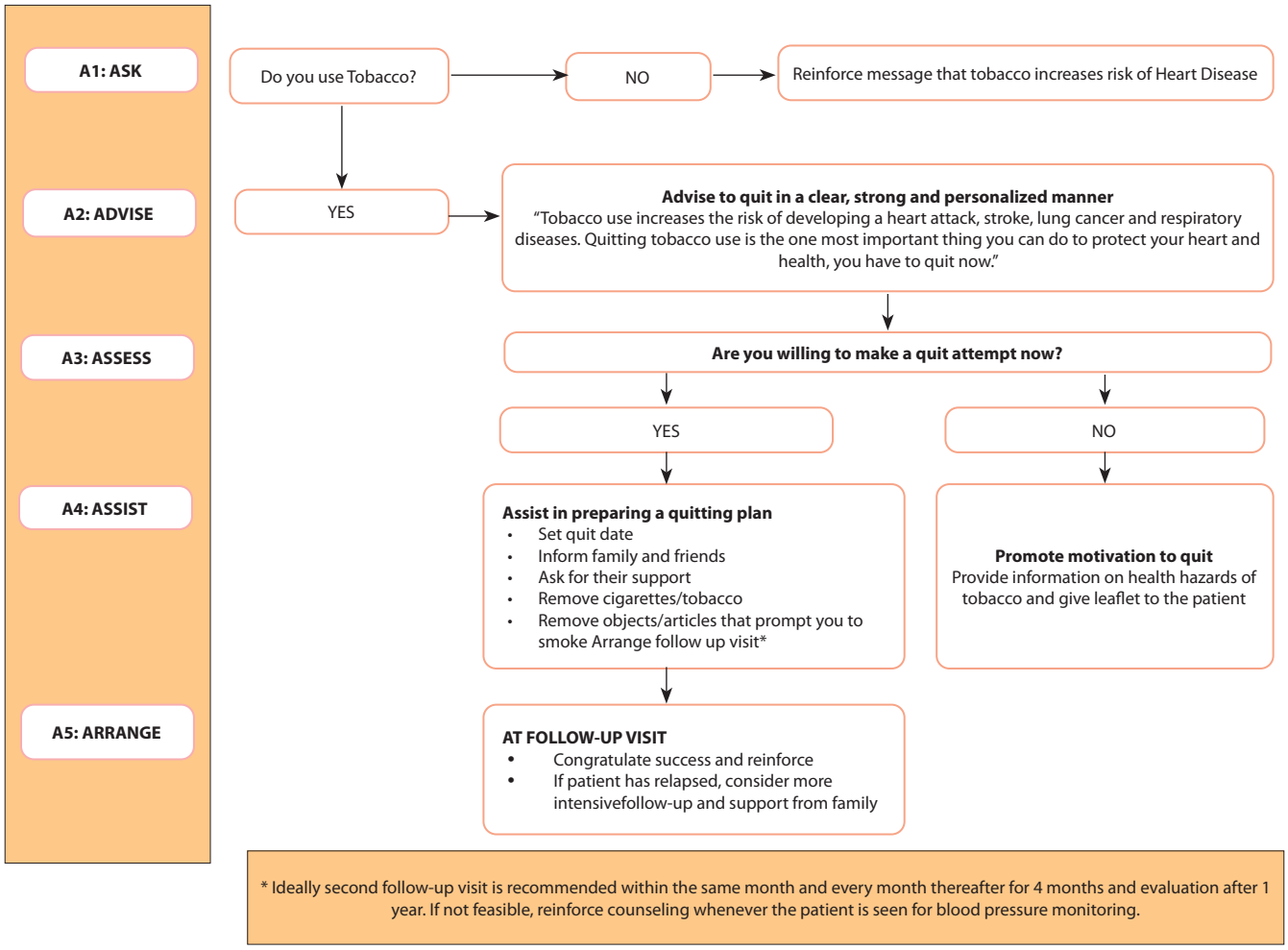

Figure 1.4: Counselling on Cessation of Tobacco Use.
(Adapted from WHO)

Behavioural support

Behavioural strategies that can support a client to cope with the triggers and high-risk situations for tobacco use include:

- Face to face support
- Individual behavioural counselling
- Group behaviour therapy
- Telephone counselling or quit lines.
- Self-help materials

Pharmacological interventions

These include:

A. Nicotine replacement therapies
   - Nicotine gums
   - Nicotine patches
   - Nicotine lozenges/sublingual tablets
   - Nicotine inhalers
   - Nicotine nasal spray

B. Non-Nicotine replacement therapies
   - Bupropion
   - Varenicline

For further details on behavioural and pharmacological interventions, refer to the Kenya National Guidelines for Tobacco Dependence Treatment and Cessation.

1.5.2 Pharmacological Therapy

Pharmacological management is largely disease-specific and is handled in greater detail in the relevant chapters. Discussed below are general principles of lipid lowering and antiplatelet therapy.

Lipid Lowering Therapy

This therapy is given to patients depending on the individual's risk of developing CVD as per the assessment described previously. However, in patients with diabetes, total cholesterol (TC) ≥8 mmol/L or a total cholesterol-to-high-density lipoprotein cholesterol (TC:HDL-C) ratio ≥8, lipid-lowering treatment is usually recommended irrespective of the combined CVD risk.

- For patients with combined CVD risk between 10 % and 20 %, discuss the benefits and risks of therapy and initiate statin therapy
- Following lifestyle management, repeat lipid profile (non-fasting) to recalculate risk and use the results to inform shared treatment decision-making in 6–12 months.
- The aim is to achieve a moderate reduction in low-density lipoprotein cholesterol (LDL-C); no target is required for those with a combined risk ratio under 20 %.
- Re-measurement the lipids at the next formal combined risk assessment.

Antiplatelet Therapy

The table below gives the general principles for antiplatelet therapy.

Table 1.6: Recommendations for antiplatelet therapy

• Antiplatelet therapy is not recommended in individuals with low/moderate CV risk due to the increased risk of major bleeding. Consult with a physician before initiating aspirin in high-risk patients. • Aspirin 75 - 100 mg daily is recommended for secondary prevention of CVD. • Clopidogrel 75 mg daily is recommended as an alternative to aspirin in secondary prevention in case of aspirin intolerance or if aspirin is not available. • Concomitant use of a proton pump inhibitor is recommended in patients receiving antiplatelet therapy who are at high risk of gastrointestinal bleeding.

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2

2. HYPERTENSION

Key messages

- Hypertension is highly prevalent in Kenya, affecting a quarter of the adult population.
- Awareness levels are low, and treatment plus control rates are poor in those on follow-up even after diagnosis.
- Evaluation of affected patients should assess both global risk for cardiovascular events as well as the presence of hypertension-mediated organ damage (HMOD).
- Calcium channel blocker-based combination therapy is the preferred initial treatment with the use of single pill combinations advocated to enhance adherence.

2.1 Introduction

Hypertension is defined as persistently elevated, systolic and/or diastolic blood pressure (BP) of 140/90 mmHg or more in adults. This is defined by the level of BP at which pharmacologic treatment has been demonstrated to provide benefit. The goal of treatment is to achieve blood pressure below 140/90 mmHg at minimum for most patients, but preferably below 130/80 mmHg. Modification of lifestyle factors can delay onset of hypertension, contribute to lowering of blood pressure in treated patients, and in some cases, abolish need for antihypertensive therapy, as well as controlling concurrent cardiovascular risk factors.[1]

2.2 Epidemiology

According to the World Health Organization, approximately 1.3 billion people worldwide between the ages of 30 and 79 have hypertension with 78% of these cases reported in low- and middle-income countries.[1] Among adults aged 30–79 years with hypertension, an estimated 54% have been diagnosed with hypertension, 42% are being treated for their hypertension, and 21% have had their hypertension control.[1]

The number of people with hypertension in Africa has steadily increased over the years. From 54.6 million in 1990, it rose by 70% to 92.3 million in 2000, and then by 41% to 130.2 million in 2010. Experts predict that this number will continue to rise and reach 216.8 million by 2030. It is common for sub-Saharan African countries, particularly in rural areas, to have limited knowledge, management, and control of hypertension. Tanzania and Kenya are among the countries in the region with the highest rates of hypertension.[2] The 2015 Kenya STEPS survey reported the estimated prevalence of hypertension at 25%, with a large majority (92%) not on treatment.[3]

2.3 Classification and Grading of Hypertension

Classification

Classification is based on etiology as either primary or secondary. The table below describes the characteristics of the two classes of hypertension.

Hypertension is graded based on the blood pressure measurement.

Table 2.1: Definition and Grading of Hypertension[4,5]

Category	Systolic (mmHg)		Diastolic (mmHg)
Optimal	<120	and	<80
Normal	<120 - 129	and/or	<80 - 84
High normal	130–139	and/or	85 - 89
Grade 1 hypertension	140 -159	and/or	90–99
Grade 2 hypertension	160 - 179	and/or	100 - 109
Grade 3 hypertension	≥180	and/or	≥110
Isolated systolic hypertension*	≥140	and	<90

*Isolated systolic hypertension is graded 1,2, or 3 according to SBP values in the ranges indicated.
The same classification is used for all ages from 16years.

Table 2.2: The Differences Between Primary and Secondary Hypertension

Primary	Secondary
Over 95% of cases	Less than 5%
No known causes	Hypertension with a specific cause
Develops gradually over time	Sudden onset: Often severe and refractory
Multiple associated risk factors	May occur in younger persons

2.4 Causes and Risk factors of Hypertension

The aetiology of hypertension is unknown in up to 95% of cases. This is referred to as essential/primary hypertension. In 5% of cases the cause can be identified and sometimes treated, and this is referred to as secondary hypertension.

Risk factors that are known to be associated with primary hypertension and causes of secondary hypertension are listed in the table below.

Table 2.3: Types and Risk Factors for Hypertension

Risk factors for primary hypertension	Causes of secondary hypertension	
	Endocrine, renal and vascular causes	**Drugs and other causes**

• Age
• Race (more in blacks)
• Family history
• Overweight/central obesity
• Metabolic syndrome
• Physical inactivity
• Tobacco use
• High dietary salt
• Low dietary potassium
• Stress
• Chronic/heavy alcohol use
• Low calcium intake
• Environmental pollution
	Endocrine
	• Primary hyperaldosteronism (Conn's syndrome)
	• Cushing's disease
	• Pheochromocytoma
	• Acromegaly
	• Polycystic ovarian syndrome
	• Hyperthyroidism
	
	Renal
	• Renal parenchymal disease: chronic glomerulonephritis, polycystic disease, or any cause of CKD
	• Renal vascular disease – renal artery stenosis.
	
	Vascular
	• Coarctation of the aorta
		Drugs
		• Anabolic steroids
		• Combined oral contraceptive pills
		• NSAIDS
		• Sympathomimetic drugs
		• Psychoactive/recreational drugs:
		  • Amphetamines
		  • Cocaine
		
		Others
		• Sleep apnoea
		• Pregnancy
		• Intracranial tumours

2.5 Clinical Presentation and Diagnosis

2.5.1 History

Patients with hypertension are often asymptomatic; however specific symptoms can suggest secondary hypertension or hypertensive complications. A complete medical and family history should include the following:

Table 2.4: Components of Past Medical and Family History

Component	Description
Blood Pressure	• Onset and duration of hypertension • Current and previous antihypertensive medication • Other medications including over-the counter medicines that can influence BP levels • History of intolerance (side-effects) of antihypertensive medications • Adherence to antihypertensive treatment • Previous hypertension with oral contraceptive use or during pregnancy • Family history of hypertension

Assessment of CV risk factors	• Personal history of:
	  • Cardiovascular disease: myocardial infarction, heart failure (HF), stroke, transient ischemic attacks (TIA), peripheral arterial disease
	  • Diabetes
	  • Dyslipidaemia
	  • Chronic kidney disease (CKD)
	• Diet
	• Smoking status
	• Alcohol intake
	• Physical activity (See Chapter 1: Prevention of Atherosclerotic Cardiovascular Disease for more information)
	• Psychosocial aspects (e.g., history of depression)*
	• Family history of:
	  • Premature cardiovascular disease
	  • Familial hypercholesterolemia
	  • Diabetes

Symptoms and signs of hypertension and coexistent illnesses	• Chest pain • Shortness of breath • Palpitations • Intermittent Claudication • Peripheral oedema • Headaches • Blurred vision • Urinary symptoms e.g. nocturia, oliguria, haematuria • Dizziness
Symptoms suggestive of secondary hypertension	• Muscle weakness/tetany/cramps, arrhythmias (hypokalaemia/ primary aldosteronism) • Flash pulmonary oedema (renal artery stenosis) • Sweating, palpitations, frequent headaches (pheochromocytoma) • Snoring, daytime sleepiness (obstructive sleep apnoea) • Symptoms suggestive of thyroid disease • Symptoms suggestive of renal disease as above.

*As diagnosed by a qualified mental health professional using established criteria.

Adapted from the ISH Guidelines, 2020

2.5.2 Physical Examination

A thorough physical examination can confirm the diagnosis of hypertension, identify hypertension mediated organ dysfunction (HMOD), and/or secondary hypertension. It should include:

- **Cardiovascular examination:**
  - Examination of the pulses including rate, rhythm, volume character and examination of the peripheral pulses including radio-femoral and radio-radial delay.
  - Jugular venous pulse/pressure
  - Apex beat, extra heart sounds
  - Basal crackles
  - Peripheral oedema
  - Bruits (carotid, abdominal, femoral)

- **Other organs/systems:**
  - Enlarged kidneys
  - Neck circumference >40 cm (obstructive sleep apnoea)

- Enlarged thyroid
- Increased body mass index (BMI)/waist circumference
- Fatty deposits and coloured striae (Cushing's disease/syndrome)
- Other signs of heart failure: tender hepatomegaly, ascites

2.5.3 Blood Pressure Measurement

The accurate diagnosis of hypertension depends on the accurate measurement of BP. Figure 2.1 gives details of the procedure of BP measurement at the clinic.

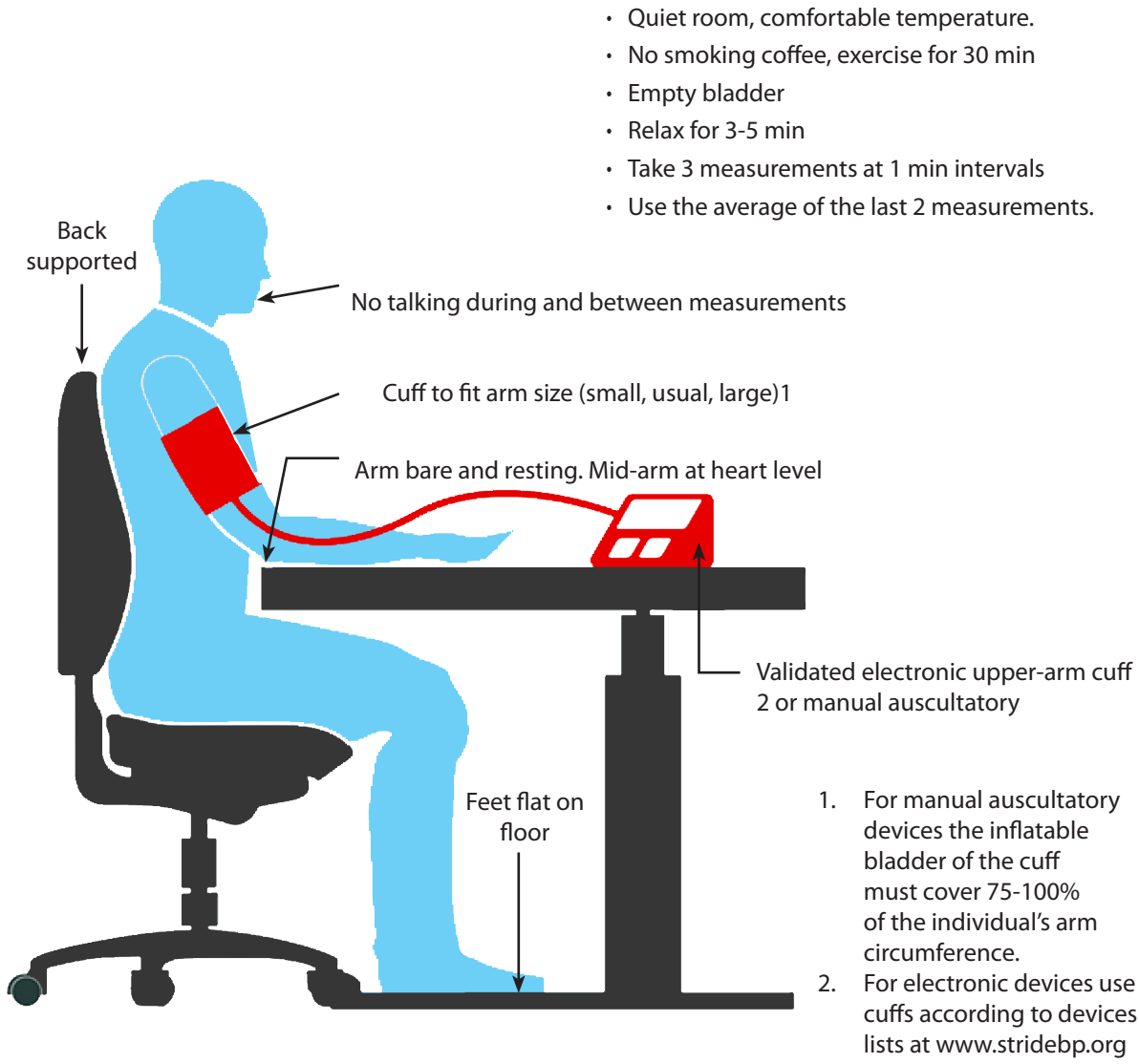

Figure 2.1: BP Measurement

Source: Unger T, Borghi C, Charchar F, Khan NA, Poulter NR, Prabhakaran D, et al. 2020 International Society of Hypertension Global Hypertension Practice Guidelines. Hypertension (Dallas, Tex : 1979). 2020;75(6):1334-57. Copyright © American Heart Association, Inc.

2.5.4 Out of Office Blood Pressure Monitoring

Measuring blood pressure outside of a health facility has proven to be important for diagnosing and treating hypertension. There are two main methods: home blood pressure monitoring, where patients use automated devices to measure their own blood pressure, and ambulatory blood pressure monitoring, where patients wear a device that measures their blood pressure every 15 minutes to 1 hour. These methods can help identify various BP phenotypes as described below:

A Normal blood pressure (BP normal both at health facility and outside health facility)

B Masked hypertension (individuals who BP is normal at the health facility and elevated outside)

C White-coat hypertension (individual whose BP is elevated in the health facility and normal outside)

D Sustained hypertension (those who are truly hypertensive-BP is elevated both at the health facility and outside)

Detection of white coat and masked hypertension in patients not on drug therapy is described in the figure below:

Table 2.5: Detection of White Coat or Masked Hypertension in Patients Not on Drug Therapy

Method	SBP (mmHg)		DBP (mmHg)
Office BP	≥140	and/or	≥90
Ambulatory BP			
Awake mean	≥135	and/or	≥85
Asleep mean	≥120	and/or	≥70
24-hr mean	≥130	and/or	≥80
Home BP mean	≥135	and/or	≥85

2.5.5 Actions After Health Facility BP Measurement

After initial BP measurement, the next course of action is dictated by the BP readings, as shown in the table below.

Table 2.6: Actions After Initial BP Measurement

<140/90 mmHg	140–159/90–99 mmHg (Grade 1)	≥160/100 mmHg (Grade 2)
Re-measure within 1 year	Confirm with out-of-office BP measurements (to r/o white coat or masked hypertension); alternatively confirm with repeated 2-3 clinic visits at 1 to 4-week intervals, depending on the BP level.	Confirm diagnosis within a few days; otherwise start treatment immediately in patients at high risk.

2.5.6 Basic Investigations

The basic package of investigations after hypertension diagnosis or during follow-up includes:

Blood tests: Total blood count, Urea Electrolyte Creatinine, lipid profile, blood glucose

- **Urine test:** Dipstick urine test.
- **12-lead ECG:** Detection of atrial fibrillation, left ventricular hypertrophy (LVH), ischemic heart disease
- **Pregnancy test** in women of childbearing potential

Additional tests may be ordered depending on the specific needs of the patient and the healthcare setting. These include microalbuminuria, HbA1C levels, echocardiogram, ankle-brachial index, carotid Doppler ultrasound, and serum uric acid.

2.5.7 Assessment for Complications

The table below shows the main complications of hypertension, and the suggested evaluation approaches.

Table 2.7: Hypertension Complications and Diagnostic Approaches

Complication	Assessment
TIA or strokes	CT or MRI brain should be considered in patients with neurologic disturbances, cognitive decline and memory loss
Heart (CAD, LVH)	A 12-lead ECG, two-dimensional transthoracic echocardiogram (ECHO)
Kidney damage	UEC and eGFR, albuminuria (dipstick or urinary albumin creatinine ratio), ultrasound/renal artery Doppler, CT/MR angiography
Peripheral artery disease	Carotid ultrasound, carotid-femoral pulse wave velocity, ankle-brachial index
Hypertensive retinopathy	Fundoscopy, preferably done by a trained professional after pupil dilation

CT, computed tomography; MRI, magnetic resonance imaging; ECG, electrocardiogram; UEC, urea, electrolytes, creatinine; eGFR, estimated glomerular filtration rate.

(Adapted from the ISH guidelines, 2020)

Risk stratification according to additional risk factors, presence of hypertension-mediated organ damage and previous disease should then be done. A simplified classification of hypertension risk in a 60-year male patient is shown in the table below:[4]

Table 2.8: Simplified Classification of Hypertension Risk in a 60-Year Male Patient

Other risk factors, HMOD, or disease	High-normal SBP 130-139 DBP 85-89	Grade 1 SBP 140-159 DBP 90-99	Grade 2 SBP ≥160 DBP ≥100
No other risk factors	Low	Low	Moderate / High
1 or 2 risk factors	Low	Moderate	High
≥3 risk factors	Low / Moderate	High	High
HMOD, CKD Grade 3, diabetes mellitus, CVD	High	High	High

HMOD, hypertension-mediated organ damage; SBP, systolic blood pressure; DBP, diastolic blood pressure; CKD, chronic kidney disease; CVD, cardiovascular disease.

2.6 Management of Hypertension

The overall aim of the treatment of hypertension is the adequate control of blood pressure and the control of other risk factors to reduce morbidity and mortality.

2.6.1 Non-pharmacologic Therapy/Lifestyle Modification

At every clinic visit, all patients should receive advice about lifestyle modification. Healthy lifestyle choices can reduce blood pressure and cardiovascular risk and reduce the dose and number of antihypertensive medications required. The appropriate lifestyle advice includes avoidance of alcohol and tobacco use, daily adequate physical activity, consumption of a healthy diet (like DASH diet), stress reduction, and reduced exposure to air pollution. Refer to Chapter 1 for more details on lifestyle interventions (physical activity, healthy diet, tobacco cessation, and avoidance of alcohol). The components of the DASH diet are described in Chapter 1.

2.6.2 Pharmacologic Therapy

The decision to initiate pharmacologic treatment on the level of BP and the overall CV risk as shown in figure 2.2 below.

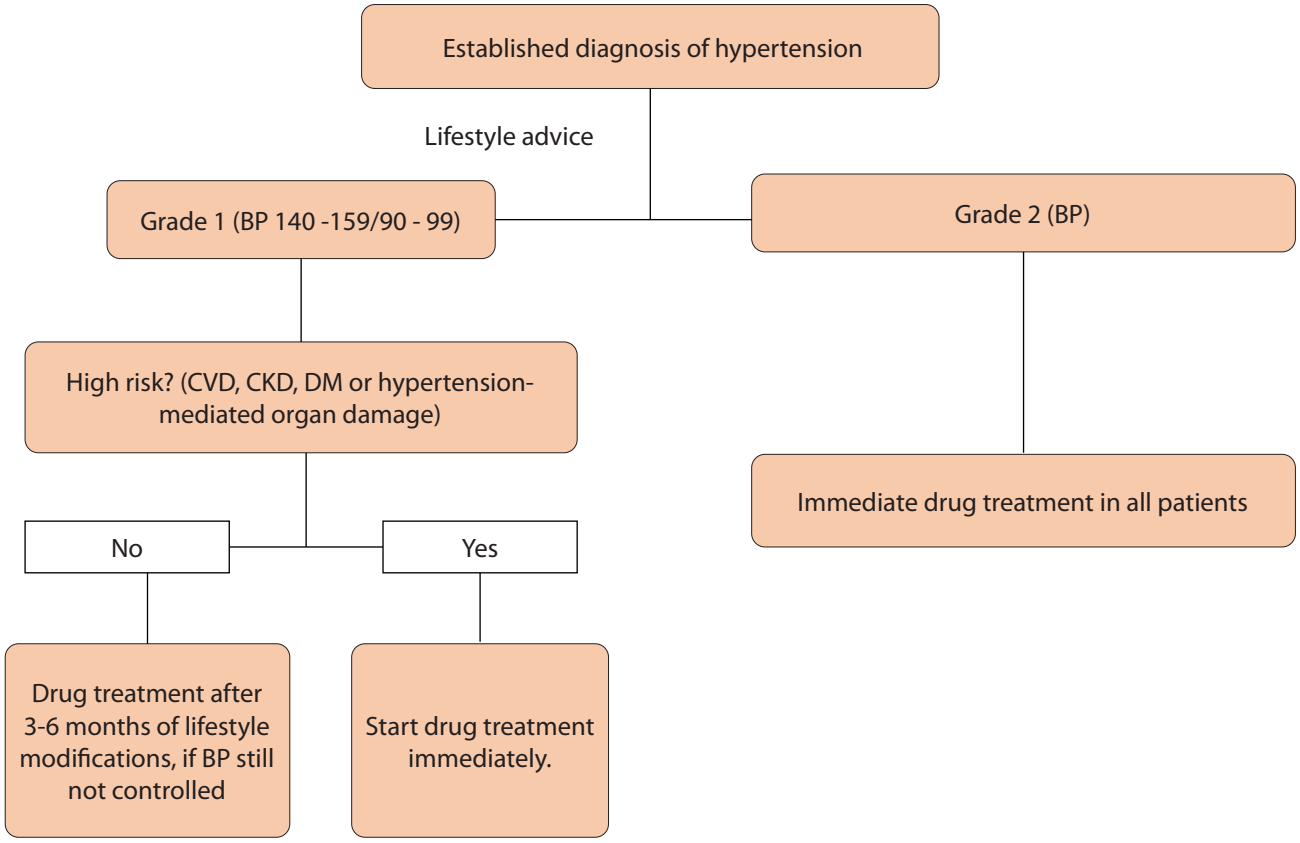

Figure 2.2: Threshold for Treatment Initiation

(Adapted from the ISH guidelines, 2020)

Pharmacologic treatment should be titrated stepwise, to attain desired treatment targets, as shown in the chart below:

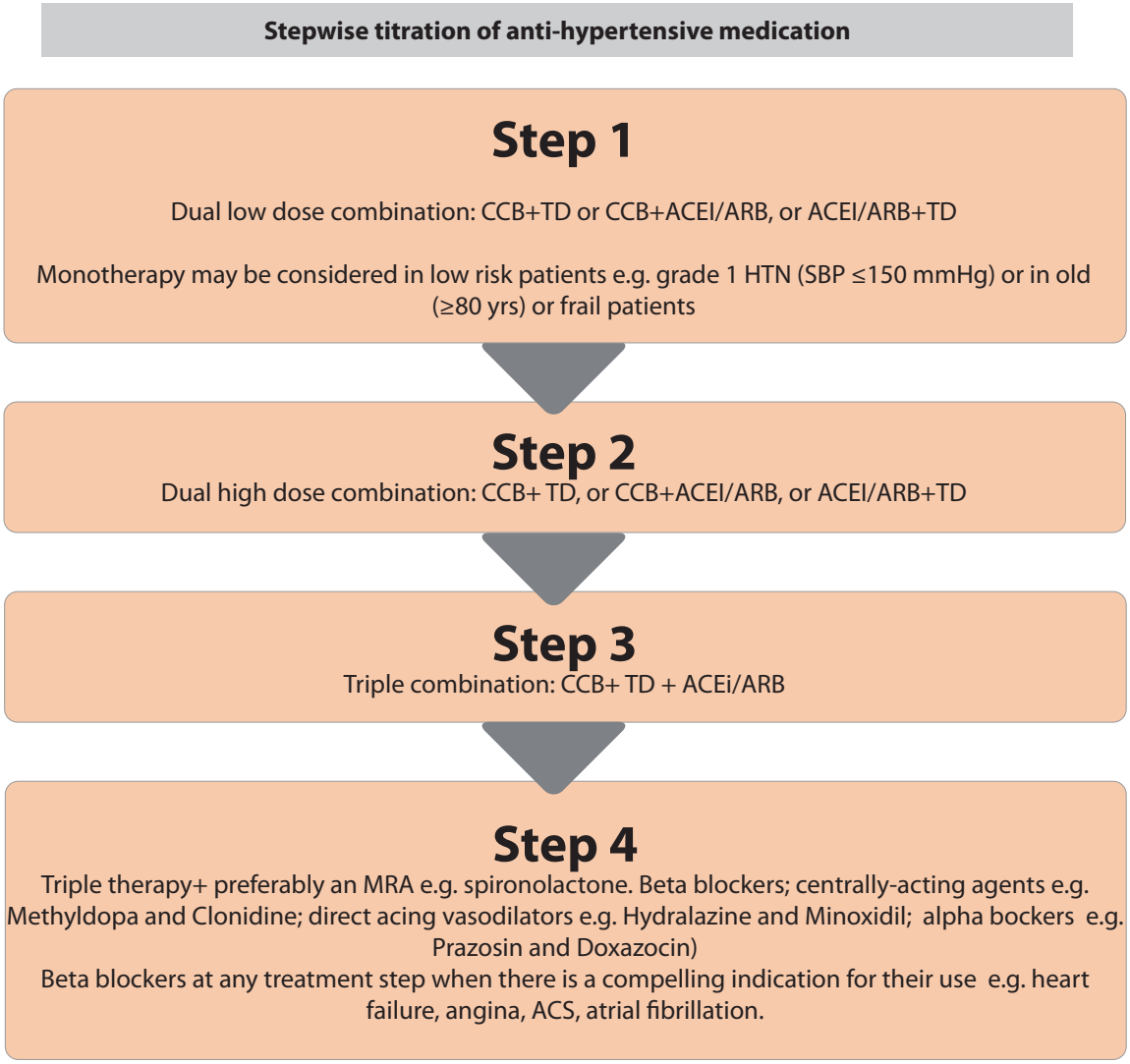

Figure2.3: Stepwise Titration of Anti-Hypertensive Medication

CCB, calcium channel blocker; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; HTN, hypertension; ACS, acute coronary syndrome; TD – thiazide or thiazide like diuretic.

Long acting agents that can be given once a day are preferred. They should preferably be given as single pill combinations. The recommended dosages and common side effects of various antihypertensive medications is outlined below.

Table 2.9: Antihypertensive Agents and Their Common Side Effects

Drug class	Examples	Recommended Initiating doses	Maximum daily dose	Possible side effects
CCB	Amlodipine	5 mg OD	10 mg OD	Oedema Fatigue Headache Palpitations
	Felodipine	5 mg OD	10 mg OD	
	Nifedipine	LA tabs: 30 mg OD (Preferred) Retard tabs: 10 mg BD	LA tabs: 90 mg OD Retard tabs: 30 mg BD	

Thiazide diuretic	Chlorthalidone	25 mg OD	50 mg OD	Hypokalaemia Hyponatraemia Hyperuricaemia Hypocalciuria Hyperglycaemia Rash Dyslipidaemia
	Hydrochlorothiazide (HCTZ)	12.5 mg OD	25 mg OD	
Thiazide-like diuretic	Indapamide	2.5 mg OD	5 mg OD	
ACE inhibitor	Captopril	25 mg BD or TDS	50 mg TDS	Cough (ACEI) Hyperkalaemia Increased serum creatinine Angioedema
	Enalapril	2.5 mg BD or 5mg OD	10 mg BD or 20 mg OD	
	Lisinopril	10 mg OD	40 mg OD	
	Perindopril	4 mg OD or 5 mg OD	8 mg OD or 10 mg OD	
	Ramipril	2.5 mg OD	10 mg OD	
ARB	Candesartan	8 mg OD	32 mg OD	
	Irbesartan	150 mg OD	300 mg OD	
	Losartan	50 mg OD	100 mg OD	
	Telmisartan	40 mg OD	80 mg OD	
	Valsartan	80 mg OD	160 mg OD	
Beta blockers	Atenolol	25-50mg OD	100mg OD	Hypotension, bradycardia
	Carvedilol	6.25mg BD	25mg BD	Hypotension, dizziness
	Nebivolol	5mg OD	40mg OD	Headache, dizziness
	Metoprolol	25-100mg OD/BD	400mg	Headache, dizziness
MRA	Spironolactone		100mg OD	dizziness, slow or irregular heartbeat
	Eplerenone	50mg OD	50mg BD	Hyperkalemia, dizziness
To add blocker (Atenolol, carvedilol, nebivolol, metoprolol, MRA (eplerenone, spironolactone)				
CCB: Calcium channel blocker; ACE: angiotensin converting enzyme; ARB: angiotensin receptor blocker; MRA: mineralocorticoid receptor antagonist; OD: administer once daily (every 24 hours); BD: administer twice daily (every 12 hours); TDS: administer 3 times daily (every 8 hours)				

(Adapted from the ISH guidelines, 2020)

Blood pressure treatment targets

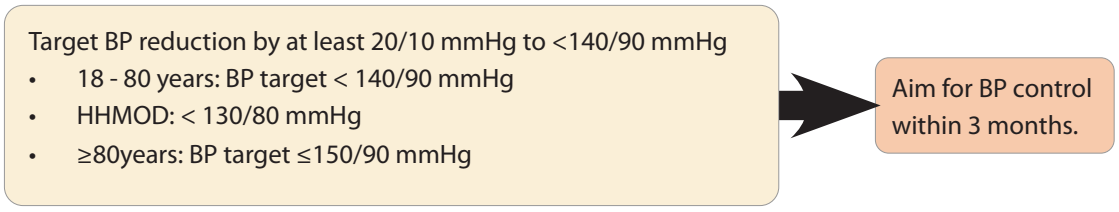

Figure2.4: Blood Pressure Treatment Targets

Other treatment considerations

- Treatments should be evidence-based in relation to morbidity/mortality prevention.
- Use whatever drugs are available with as many of the ideal characteristics as possible.
- Use a once-daily regimen which provides 24-hour blood pressure control.
- Treatment should be affordable and/or cost-effective relative to other agents.
- Treatments should be well-tolerated.
- Consider ACE inhibitors and thiazide diuretics in persons who have had previous strokes, the very elderly, those with incipient heart failure, or who cannot tolerate calcium channel blockers.
- Exercise caution with potassium-sparing diuretics in reduced renal function.

2.7. Follow-up Considerations

- Evaluate adherence to antihypertensive treatment as appropriate at each visit and prior to escalation of antihypertensive treatment.
- Consider the following strategies to improve medication adherence:
  - reducing polypharmacy – use of single pill combinations
  - once-daily dosing over multiple times per day dosing
  - linking adherence behaviour with daily habits
  - providing adherence feedback to patients
  - home BP monitoring
  - reminder packaging of medications
  - empowerment-based counselling for self-management
  - electronic adherence aids such as mobile phones or short messages services
  - multidisciplinary healthcare team approach (i.e., pharmacists) to improve monitoring for adherence.
- Once the goal BP has been achieved, the patient should be followed up every 3 - 6 months, or monthly if there is change in antihypertensive medications.

2.8 Indications for Referral

The following patients require specialized care and should be referred if the requisite expertise is not available at the facility of initial contact:

- All pregnant women (refer to the chapter on CVD in pregnancy)
- Patients who are not reaching their goal BP after a reasonable trial of antihypertensive therapy (3 months)
- Hypertensive patients aged ≤18 years.
- Patients with an associated clinical condition: coronary heart disease, heart failure, chronic kidney disease, stroke or transient ischaemic attack, peripheral arterial disease, diabetes
- Patients in whom a secondary cause of hypertension is suspected – characteristics of secondary hypertension are outlined in the table below:

Table 2.10: Characteristics of Secondary Hypertension

Characteristics
Younger patients (<40 years) with grade 2 hypertension or onset of any grade of hypertension in childhood
Acute worsening of hypertension in patients with previously documented chronically stable normotension
Resistant hypertension (BP uncontrolled despite treatment with optimal or best-tolerated doses of three or more drugs including a diuretic, and confirmed by ABPM or HBPM)
Severe (grade 3) hypertension or a hypertension emergency
Presence of extensive HMOD
Clinical or biochemical feature suggestive of endocrine causes of hypertension or CKD
Clinical features suggestive of OSA
Symptoms suggestive of pheochromocytoms or family history of pheochromocytoma
ABPM = ambulatory blood pressure monitoring; BP= Blood pressure; CKD = chronic kidney diseases, HBPM = home blood pressure monitoring; HMOD = hypertension-mediated organ damage; OSA = obstructiv sleep apnoea.

2.9 Treatment of Hypertensive Emergencies

Hypertensive emergencies are situations where there is marked elevations in SBP or DBP e.g., > 180/120 mmHg associated with impending or progressive organ damage/dysfunction. Suspected hypertensive emergencies include:

- acute ischemic stroke
- acute intracerebral haemorrhage
- subarachnoid haemorrhage
- aortic dissection
- acute coronary syndrome
- acute heart failure
- pre-eclampsia/eclampsia

Management of such a patient should be done in an inpatient setting; preferably in a specialized unit such a critical/ intensive care unit (CCU/ICU) or a high-dependency unit (HDU). The treatment should be with intravenous drugs and sublingual short acting preparations e.g. nifedipine should be avoided because of the risk of catastrophic drop in BP. The table below summarizes the choice of drugs and dosages for use in hypertensive emergencies.

When there is marked elevation of BP but no acute HMOD, these are hypertensive urgencies. They don't require rapid reduction in BP.

Table 2.11: Drugs of Choice in Hypertensive Emergencies

AGENT	MOA	DOSE	ONSET/ DURATION OF ACTION (AFTER DISCONTINUATION	PRECAUTIONS
Parental Vasodilators				
Nitroglycerine	Decreases coronary vasospasm, which increases coronary blood flow. Also, induces vessel dilatation, decreasing cardiac workload.	5-20 µg/min as infusion	2-5 min /5-10min	Headache, tachycardia, vomiting, flushing, metheglobinemia; requires special delivery system due to drug binding to plastic tubing
Hydralazine	Decreases systemic resistance through direct vasodilation of arterioles	10min/>1hr	10min/>1hr	Tachycardia, headache, vomiting, aggravation of angina pectoris
Parental Adrenergic Inhibitors				
Labetalol	α, β1, β2 Blocker	20mg IV bolus over 10 mins then 1-2mg/min IV infusion	5-10min/>15-30min	Bronchoconstriction, heart block, ortµhostatic hypotension
Esmolol	Ultra-short acting β-andrenergic blocker	500 µg/kg bolus injection IV or 25 -100 µg/kg/min by infusion. May repeat bolus after 5min or increase infusion rate to 300µg/kg/min	1-5 min/15-30min	First-degree heart block, congestive heart failure, asthma

Hypertension care per level of health service delivery		
Level of care	**Services offered**	**Requirements**
Level 1 (Community)	• Health education and awareness creation • Risk modification and behaviour change • BP screening • Referral and linkage to care • Patient follow up	• Trained community health promoters • CHP Kit - BP machine, weighing scale, tape measure, height meter, BMI charts • IEC materials • Data collection tools / system
Level 2 and 3	**level 1 services plus:-** • Confirmation and diagnosis of hypertension • Initiation of treatment • Hypertension management (grade 1 and 2) • Patient follow up • Referral and linkage to care • Patient follow up	**level 1 plus:-** • Essential antihypertensives • Basic laboratory tests - FHG, Urinalysis, Uecs
Level 4 and 5	**level 2 and 3 plus:-** • Management of hypertension complications and secondary hypertension • Management of hypertensive urgencies and emergencies • Specialist care • Referral and linkage to care • Patient follow up • Training	**level 2 and 3 plus:-** • Advanced laboratory support • Imaging -ECG, Echo, Doppler, CT scans, MRI • Antihypertensives (as per KEML) • Data collection tools • ICU care
Level 6	**Level 4 and 5 plus** • Cardiac catheterization • Advanced specialist care • Specialist training	**Level 4 and 5 plus** • Advanced laboratory and Imaging support • Specialised skills lab for training

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3

3. DYSLIPIDAEMIA

Key messages

- A heart-healthy lifestyle should be recommended for all patients at all stages of life.
- A full lipid profile is recommended to identify individuals at high risk of ASCVD, diagnose dyslipidaemia, and estimate CVD risk. For individuals without CVD risk factors, screening should begin at age 40 with a full lipid profile, or at least total cholesterol (TC) or LDL cholesterol (LDL-C) if the full profile is not available.
- Patients should be stratified according to their cardiovascular risk using available and validated tool and managed appropriately according to their risk category.
- Define treatment targets for (LDL-C and/or TG levels) for each patient.
- If treatment targets are not met despite the use of maximum-tolerated statin therapy, non-statin cholesterol-lowering medication should be added to the treatment.

3.0 Introduction

Lipids play vital roles in energy utilization, lipid storage, hormone production, and bile acid formation. Lipoproteins, including chylomicrons, very low-density lipoproteins (VLDL), intermediate-density lipoproteins (IDL), low-density lipoproteins (LDL), lipoprotein (a) (Lp(a)), and high-density lipoproteins (HDL), transport lipids in the bloodstream. The accumulation of lipoproteins in arterial walls contributes to atherosclerosis, resulting in the formation of plaques. The risk of acute cardiovascular events is influenced by the exposure to Apolipoprotein B (ApoB)-containing lipoproteins and plaque burden, with LDL particles directly impacting event likelihood [1-5].

Dyslipidaemia refers to an abnormal lipid profile characterized by deviations from the recommended levels of lipids, such as elevated levels of total cholesterol, low-density lipoprotein cholesterol (LDL-C), triglycerides, or reduced levels of high-density lipoprotein cholesterol (HDL-C). It is a common risk factor for cardiovascular diseases [1].

The prevalence of dyslipidaemia in the general adult population in Africa is 25.5%, similar rates in men and women, higher rates in urban areas, and higher rates in individuals with major cardiovascular risk factors, such as diabetes, hypertension, or HIV, primarily characterized by low HDL-C concentrations and less commonly by elevated TG concentrations [4,6]. A study in Nairobi reported overall prevalence of metabolic syndrome at 34.6%, with incidence of individual factors suggesting low HDL-C, raised blood pressure, and higher waist circumference as major contributors [13]; while another study in Western Kenya reported 47% prevalence exacerbated by old age, overweight, abdominal obesity, and low fruit and vegetable intake [14].

This guideline informs prevention, risk assessment, treatment, and surveillance options for at-risk populations.

3.1 Screening

A full lipid profile is recommended for identifying individuals at high risk of ASCVD, diagnosing dyslipidaemia, and estimating CVD risk. For individuals without CVD risk factors, screening should begin at age 40 with a full lipid profile, or at least total cholesterol (TC) or LDL cholesterol (LDL-C) if the full profile is not available. However, certain individuals with genetic predispositions, family history, and other risk factors should be screened earlier. Cascade screening for Familial Hypercholesterolemia (FH) is recommended for all potentially affected relatives of patients with severe dyslipidaemia, and priority in screening children, adolescents, and young adults should be given to identifying those with FH and estimating lifetime ASCVD risk.

Table 3.1 Who to Screen for Dyslipidaemia

Who to screen
Children from 8 years of age with • Family history of severe dyslipidaemia • Relative of subject with FH (if both parents have FH, testing should be undertaken within the first 6 months of life to identify infants with homozygous FH) Men ≥40 years of age; women ≥40 years of age (or postmenopausal) All patients with any of the following conditions, regardless of age: • Clinical evidence of atherosclerosis • Abdominal aortic aneurysm • Diabetes mellitus • Arterial hypertension and/or on antihypertensive medication • Smoking: any smoking • Stigmata of dyslipidaemia (corneal arcus, xanthelasma, xanthoma) • Family history of premature CVD* • Family history of dyslipidaemia • CKD (eGFR ≤ 60 mL/min/1.73 m2 or ACR ≥ 3 mg/mmol) • Obesity [BMI ≥ 30 kg/m2 or waist circumference >94 cm (men), >80 cm (women)] • Inflammatory diseases (RA, SLE, PsA, AS, IBD) • HIV infection • Erectile dysfunction • COPD • History of hypertensive disorder of pregnancy

*ACR,albumin-to-creatinine ratio; AS, ankylosing spondylitis; BMI, body mass index; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; IBD, inflammatory bowel disease; PsA, psoriatic arthritis; RA, rheumatoid arthritis; SLE, systemic lupus erythematous. * Men younger than 55 years of age and women younger than 65 years of age in first-degree relatives*

Screening frequency

Table 3.2: Frequency of Screening in Different Populations

Risk group	Frequency
Adults (40-75yrs) with no risk factors for ASCVD	Every 5 years

• People (Men >45, Women 50-55) with one or more risk factors including:
  • High cholesterol on a prior test
  • Previous CVD
  • Smoking – any smoking
  • Being overweight or obese
  • Eating an unhealthy diet
  • Not getting enough physical activity
  • Hypertension
  • Family history of premature ASCVD (men, age <55 years; women, age <55 years).
  • Having diabetes or prediabetes
• People >65 years
	Annually

Children with familial hypercholesterolaemia	Age 3yrs, between 9 and 11 years, and at age 18.

Measurement of Lp(a) should be considered at least once in each person's lifetime, if available, to identify people who have inherited an extremely elevated level of Lp(a) ≥430 nmol/L and therefore have a very high lifetime risk of ASCVD; and in patients with a family history of premature CVD and those who have an estimated 10-year risk of ASCVD that is close to the threshold between high and moderate risk (2).

3.2 Measurement of Lipids and Lipoproteins

Laboratory measurement of lipids and lipoproteins is crucial for assessing the risk of ASCVD and guiding treatment decisions. Specific measurements, such as total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglycerides (TG), are used to estimate the risk and guide therapeutic interventions.

TC is necessary for risk calculation, HDL-C improves risk estimation, and LDL-C helps estimate the modifiable risk of ASCVD and identify individuals with significantly elevated levels. Measurement of TG is essential for identifying individuals with a higher modifiable ASCVD risk due to increased levels of atherogenic lipoproteins and their remnants, especially in patients with diabetes or metabolic syndrome. Apolipoprotein B (ApoB) provides a more accurate assessment of atherogenic particle concentration and is preferred for refining ASCVD risk estimation and guiding lipid-lowering therapy.

The table below provides guidance on how to evaluate the patient with dyslipidaemia in adults at risk. Non-fasting lipid testing is generally advised for most adults to enhance patient adherence and facilitate measurement of plasma lipids during clinic visits, while fasting lipid levels should be measured for individuals with a history of TG levels exceeding 4.5 mmol/L (3,6). When interpreting lipid results, prioritizing non-HDL-C or ApoB levels over LDL-C is recommended, especially when TG levels are ≥1.5 mmol/L, where available.

Table 3.3: How To Screen for Dyslipidaemia

For all:

- History and physical examination
- Standard lipid profile (TC, LDL-C, HDL-C, NON-HDL-C, TG)
- FPG or A1c
- eGFR
- Lipoprotein(a) – once in a patient's lifetime, with initial screening

Optional:

- ApoB
- Urine ACR (if eGFR<60mL/min/1.73m2, hypertension or diabetes)

A1c, glycated haemoglobin; ACR, albumin-to-creatinine ratio; ApoB, Apolipoprotein B; eGFR, estimated glomerular filtration rate; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; TG, triglycerides.

3.3 Management of Dyslipidaemia

3.3.1 Primary Prevention

Primary prevention aims to prevent or delay the onset of ASCVD through efforts targeted at populations or individuals. Starting early in life, primary prevention involves managing ASCVD risk factors and promoting healthy behaviours like maintaining a healthy weight, following a nutritious diet, engaging in regular exercise, quitting smoking, limiting alcohol consumption, and getting enough sleep. For individuals with a Lp(a) level of ≥100 nmol/L, more intensive health behaviour modification, counselling, and management of other ASCVD risk factors are recommended. Individual CV risk should be estimated (See Section 1.3: Cardiovascular risk assessment) and appropriate treatment instituted according to the risk category.

3.3.2 Secondary Prevention

Secondary prevention involves treating known ASCVD and preventing progression and recurrence of disease manifestations. Patients with ASCVD are considered at high risk and require aggressive treatment with risk factor modification and lipid lowering therapy, including statins. Lifestyle therapy is recommended for all patients with a history of ASCVD to optimize cardiovascular health. The effectiveness of lifestyle and statin therapy is measured by the percentage reduction in LDL-C levels compared to baseline [19].

Lifestyle therapy

With regards to diet, two dietary patterns that have been shown to be effective in reducing CVD risk factors: Dietary Approaches to Stop Hypertension (DASH) diet and Mediterranean diet, detailed further in the table below. Alcohol consumption should generally be avoided, but moderate intake (up to 10g/day or 1 unit) is acceptable for individuals without elevated triglyceride levels, according to the ESC dyslipidaemia guidelines. Smoking and exposure to second-hand smoke have negative effects on cardiovascular health, and all smokers are strongly encouraged to quit due to the clear benefits, especially on HDL-C levels.

Adults should aim for at least 150 minutes of moderate-intensity physical activity or 75 minutes of vigorous exercise per week. Reducing sedentary behaviour along with regular exercise can further decrease the risk of cardiovascular events. High-risk individuals with or without existing cardiovascular disease should receive appropriate advice and support to achieve and maintain a healthy weight.

Table 3.4: Cardio-protective Diets

Dietary Approaches to Stop Hypertension (DASH)
(https://www.hsph.harvard.edu/nutritionsource/healthy-weight/diet-reviews/dash-diet)
This diet emphasizes foods that are lower in sodium as well as foods that are rich in potassium, magnesium and calcium — nutrients that help lower blood pressure.
This diet is based on the following foods:

- Fruits
- Vegetables
- Low-fat milk
- Whole grains
- Fish
- Poultry
- Bean
- Nuts
- Reduction of sodium, foods and beverages with added sugar and red meat
- Limits saturated and trans fats

Mediterranean diet
(https://www.escardio.org/Education/ESC-Prevention-of-CVD-Programme/Treatment-goals/Risk-factor-control/nutrition)
A cardio-protective diet that can be used in primary or secondary prevention and in conjunction with specific dietary advice related to individually relevant risk factors (diabetes, high cholesterol, high blood pressure, overweight).
Characteristics of the Mediterranean diet are:

- High in unsaturated fats (e.g., olive oil, nuts, seeds)
- Low in saturated fats (e.g., red meat, full fat dairy)
- Contains more fresh than processed food items (e.g., fruit, vegetables, whole grains)

Pharmacological Management of Dyslipidaemia

CV risk in the context of these guidelines means the likelihood of a person developing an atherosclerotic CV event over a defined period of time. Dyslipidaemia management is guided by cardiovascular risk classification of patients.

Table 3.5: Cardiovascular risk stratification

Primary Prevention (NICE guidelines)

Risk Category	Definition/Subjects with the following:
Very High risk	Documented CVD Patients with type 2 diabetes, patients with type 1 diabetes with target organ damage (such as microalbuminuria) Patients with moderate to severe CKD (eGFR<60 mL/min/1.73 m^2). A calculated 10-year risk SCORE ≥10%.
High risk	Markedly elevated single risk factors such as familial dyslipidaemias and severe hypertension. A calculated SCORE ≥5% and <10% for 10-year risk of fatal CVD.
Moderate risk	SCORE of ≥1% and ,5% at 10 years. (Many middle-aged subjects belong to this risk category. This risk is further modulated by a family history of premature CAD, abdominal obesity, physical activity pattern, HDL-C, TG, hs-CRP, Lp(a), fibrinogen, homocysteine, apo B, and social class.)
Low risk	SCORE ,1%.

Before starting lipid modification therapy for primary prevention, the following should be carried out:

1. A sample to measure lipid profile comprising the following should be taken (fasting is not required):
    - Total cholesterol (TC)
    - HDL cholesterol (HDL)
    - Non-HDL cholesterol
    - Triglycerides (TG)
2. Exclude familial lipid disorder (clinical findings, family history, lipid profile) – TC 7.5mmol/L and family history of premature coronary heart disease
3. Exclude secondary caused of dyslipidaemia (excess alcohol, uncontrolled diabetes, hypothyroidism, liver disease, nephrotic syndrome)
4. If TC is >9mmol/l, non-HDL >7.5mmol/L or triglyceride > 20mmol/L (not related to poor glycaemic control or alcohol intake) refer for specialist assessment
5. If TG is between 10 – 20mmol/L
    a. Repeat measurements with fasting blood sample (between 5 – 14 days later)
    b. Review for secondary causes
    c. If levels remain >20mmol/L seek specialist advise
6. If TG is 4.5 – 9.9mmol/L
    a. CVD risk may be underestimated by CVD risk assessment tools
    b. Address other CVD risk factors
    c. Seek specialist advise if non-HDL is >7.5mmol/L
7. Discuss the decision to initiate lipid lowering drugs with the patients taking into consideration the following:
    a. Benefits from lifestyle modification
    b. Informed patient preference
    c. Comorbidities

d. Polypharmacy
e. General frailty
f. Life expectancy

8. Perform blood tests and clinical assessment, treat comorbidities and secondary causes of dyslipidaemia. The assessment should include:
    a. smoking status
    b. alcohol consumption
    c. blood pressure (see NICE's guideline on hypertension)
    d. BMI or other measure of obesity (see the NICE guideline on Obesity: identification, assessment, and management)
    e. total cholesterol, non-HDL cholesterol, HDL cholesterol and triglycerides
    f. HbA1c
    g. renal function and eGFR
    h. transaminase level (alanine aminotransferase or aspartate aminotransferase)
    i. thyroid-stimulating hormone. [new 2014]

Lipid modification therapy for primary prevention:

- Offer lifestyle modification and manage other modifiable risk factors. Reassess the CVD risk again after lifestyle modification.
- After risk assessment, offer statin treatment if lifestyle modification is not effective or appropriate.
- For individuals with 10% or greater risk of developing CVDs, start with Atorvastatin 20mg
- For people 85 years or older consider atorvastatin 20 mg as statins may be of benefit in reducing the risk of non-fatal myocardial infarction. Be aware of factors that may make treatment inappropriate.
- Patients at very-high risk, but without FH, if LDL goal is not achieved with maximum tolerated statin and ezetimibe, a PCSK9 inhibitor may be considered.

Secondary Prevention

Secondary prevention strategies apply to individuals at a very high risk i.e., individuals with atherosclerotic cardiovascular disease including acute coronary syndromes, myocardial infarction, history of coronary revascularization, stroke, TIA, or peripheral arterial disease of atherosclerotic aetiology.

Table 3.6: Definition of Very High Risk (Clinical ASCVD) & High-risk Conditions [19]

Very High-risk Conditions
Recent ACS occurred within the past 12 months
History of myocardial Infarction (other than recent ACS)
History of ischemic stroke
Symptomatic peripheral arterial disease (history of intermittent claudication with ABI <0.85, previous amputation, or revascularization)
High-risk Conditions
Age ≥65 y
Heterozygous familial hypercholesterolemia
History of prior coronary artery bypass surgery or percutaneous coronary intervention outside of the major ASCVD event(s)
Diabetes mellitus
Systemic hypertension
CKD (eGFR 15-59 mL/min/1.73 m^2)
Current smoking
Persistently elevated LDL-C (LDL-C ≥2.6mmol/L (100 mg/dL) despite maximally tolerated statin therapy and ezetimibe
History of congestive HF

ACS, acute coronary syndrome; ABI, ankle-brachial index; ASCVD, atherosclerotic cardiovascular disease; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; LDL-C, low-density lipoprotein cholesterol; HF, heart failure.

The recommendations regarding secondary prevention include [23):

- Below age 75 years, high-intensity statins should be initiated to achieve a drop in LDL-c of ≥50% from baseline, with a target of <1.4mmol/L.
- For individuals who are intolerant to high dose statins, moderate-intensity should be initiated to achieve a 30 to 49% reduction in LDL-C levels
- For individuals in whom a target LDL-C of <=1.8mmol/L is not achieved despite maximally tolerated statins, consider the addition of ezetimibe.

Table 3.7: Recommended Treatment for Patients with Established ASCVD [2]

Available drugs	Dosage	Expected LDL reduction	Note
Atorvastatin	40 – 80 mg once daily	≥50%	
Rosuvastatin	20 – 40 mg once daily	≥50%	
Ezetimibe	10 mg once daily	18% as monotherapy 20 – 25% when added to statin therapy	Consider as add on statin therapy in patients with baseline LDL ≥2.6 mmol/L

Consideration to make:

1. Start statin treatment in people with CVD with atorvastatin 80 mg.
2. Use a lower dose of atorvastatin if any of the following apply: potential drug interactions, high risk of adverse effects, patient preference
3. Initiate statin treatment promptly in secondary prevention, including acute coronary syndrome, without delay, take lipid sample at admission and monitor lipid levels within 3 months of treatment initiation.
4. For patients who fail to achieve their goals with the maximum tolerated dose of statin, combination therapy with ezetimibe is recommended.
5. If patients at very-high risk still do not reach their goal with the maximum tolerated dose of ezetimibe, a combination with a PCSK9 inhibitor is recommended.

3.4 Treatment Targets and Goals

After initiating lipid lowering therapies, individuals should undergo a repeat lipid profile after three months to assess treatment progress. Monitoring can be done using either LDL-C or non-HDL-C, with optimal lipid parameters and targets for different risk categories outlined in the table below:

Table 3.8: Lipid Parameter Targets for Different Risk Categories

Lipid parameter	Risk category	Target
LDL-C	Very high risk	≥50% LDL-C reduction from the baseline and LDL-C level < 1.4mmol/L(55mg/dl)
	High risk	≥ 50% LDL-C reduction from the baseline and LDL-C level < 1.8mmol/L(70mg/dl)
	Low-moderate risk	LDL-C < 2.6mmol/L (100mg/dl)
Non-HDL	Very high risk	<2.2 mmol/L (85mg/dl)
	High risk	<2.6 mmol/L (100mg/dl)
	Low -moderate risk	<3.4 mmol/L (130mg/dl)
Triglycerides	All categories	< 1.7 mmol/L (150mg/dl)

Adapted from ESC/EAS guidelines for the management of dyslipidaemia (Mach et al., 2020)

3.5 Common Side Effects of Lipid-lowering Therapies

Statin therapy is generally considered safe and well-tolerated. The cardiovascular benefits far outweigh the risks of statins (24).

Adverse events include:

- "statin-associated muscle symptoms" (myopathy, rarely rhabdomyolysis)
- diabetes and
- haemorrhagic stroke
- drug-drug interactions (elderly, patient on polypharmacy)

It is recommended that a statin is started at a low dose if there is significant renal impairment and/or the potential for drug interactions, and then titrated upwards to achieve LDL-C treatment goals (2).

The figure below summarized the algorithm for managing statin intolerance. If statin-based regimen is not tolerated at any does (even after rechallenge), ezetimibe should be considered. PCSK0 can also be added to ezetimibe in this situation.

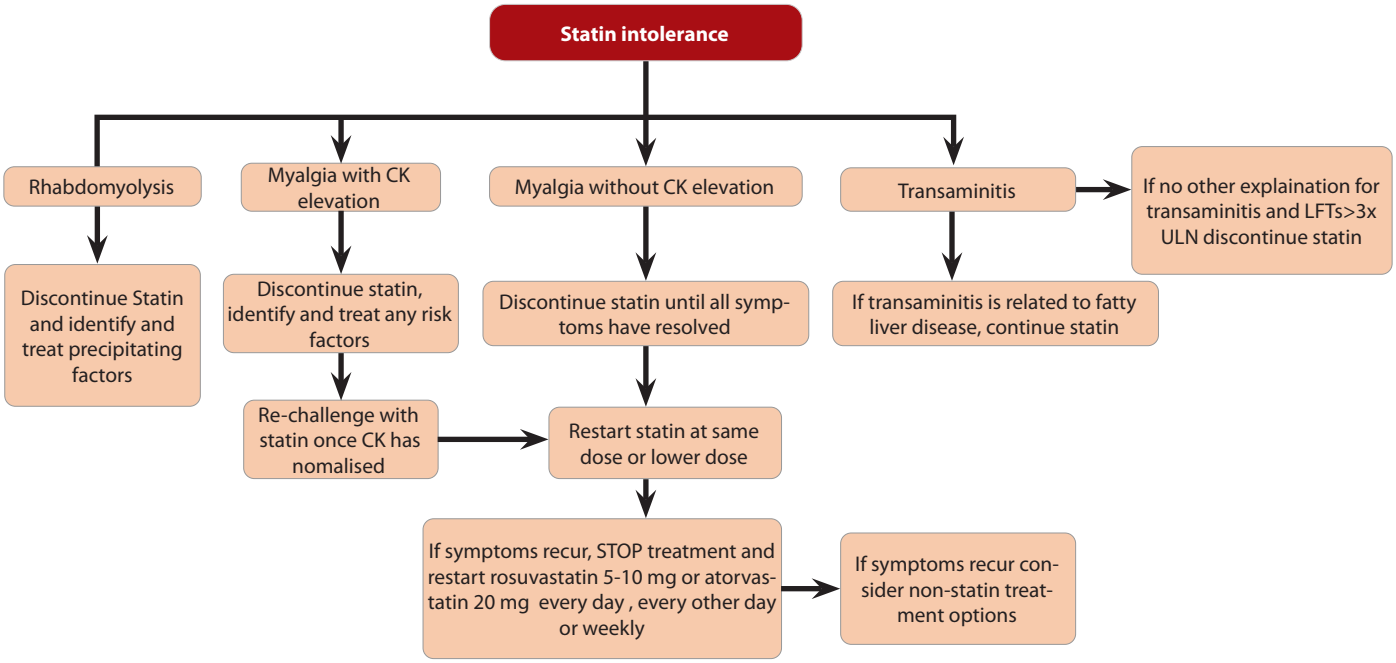

Figure 3.1: Algorithm for management of statin intolerance

3.6 Dyslipidaemia In Special Populations

Cardiovascular risk assessment should be offered to all patients. Certain groups of patients however deserve special mention when undergoing evaluation and management for lipid disorders. These groups of patients either have inherently elevated cardiovascular risk or have certain unique considerations when planning their treatment.

3.6.1 Familial Dyslipidaemias

Data on the prevalence of familial dyslipidaemias in Kenya and Africa are lacking, but these conditions are frequently observed in clinical practice. Identifying affected patients is crucial due to their high risk of cardiovascular events if not properly managed. Genetic factors play a significant role in plasma lipid composition. While most dyslipidaemia cases result from the combined effect of multiple genes (polygenic), some are caused by specific mutations (monogenic), such as familial hypercholesterolemia (FH). Table X provides an overview of common familial dyslipidaemias.

Table 3.9: Genetic Disorders of Lipoprotein Metabolism

Disorder	Prevalence	Gene(s)	Effect on lipoproteins
HeFH	1 in 200-250	LDLR APO B PCSK9	↑ LDL-C
HoFH	1 in 160 000-320 000	LDLR APO B PCSK9	↑↑ LDL-C
FCH	1 in 100/200	USF1+ modifiying genes	↑ LDL-C 1VLDL-C 1ApoB
Familial dysbetalipoproteinaemia	1 in 5000	APO E	↑↑ DL and chylomicrons remnants (BVLDL)
Familial lipoprotein lipase deficiency	2 in 106	LPL APO C2 ApoAV, GPIHBP1 LMF1	↑↑ chylomicrons and VLDL-C
Tangier disease (analphalipoprotein-aemia)	1 in 106	ABCA1	↓↓ HDL-C
Familial LCAT deficiency	1 in 106	LCAT	↓ HDL-C

Apo = apolipoprotein; FCH = familial combined hyperlipidaemia; HDL-C = high-density lipoprotein cholesterol; HeFH = heterozygous familial hypercholesterolaemia; HoFH = homozygous familial hypercholesterolaemia; IDL = intermediate-density lipoprotein; LCAT = lecithin cholesterol acyltransferase; LDL-C = low-density lipoprotein cholesterol; VLDL = very low-density lipoprotein cholesterol

Adapted from 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk.

Familial Hypercholesterolaemia (FH)

FH is an inherited disorder causing high LDL cholesterol, increasing cardiovascular disease risk. Heterozygous FH raises coronary artery disease (CAD) risk before 55 years (men) or 60 years (women). Homozygous FH is rare but life-threatening, with CAD by age 20 and death before 30. FH diagnosis is based on clinical features and genetic testing. Treatment involves lipid-lowering therapy (statins, ezetimibe) to reduce LDL-C. Cascade screening is recommended (i.e., relatives must also be checked for elevated LDL-C). Manage FH with close monitoring and specialized therapy by knowledgeable physicians or cardiologists.

Recommendations

1. A diagnosis of FH should be considered in patients with personal or familial history of premature CAD (<55 years and <60 years for men and women respectively), tendon xanthomas, and severely elevated LDL-C (>5mmol/L)
2. FH should be diagnosed using clinical criteria, and if possible, confirmed using genetic testing.
3. Familial cascade screening of relatives is recommended once a case of FH is diagnosed.
4. Lipid lowering therapy should be started as soon as possible in patients with FH to target an LDL-C reduction of >50% and a goal LDL-C of <1.8. In patients at very high risk (patients with ASCVD or the presence of another major risk factor) a goal LDL-C of <1.4mmol/L should be targeted
5. High intensity statins, or statin-ezetimibe combination should be used as first line therapy. In patients who cannot achieve treatment targets with this, then consideration should be given to the use of PCSK-9 inhibitors.
6. Familial lipid disorders are best referred for management by a physician or cardiologist experienced in management of lipid disorders due to the need for aggressive risk modification, close monitoring, and frequent need for additional therapies.

3.6.2 Diabetes

Patients with diabetes are at substantially higher risk of cardiovascular events compared to patients without diabetes. Other cardiovascular risk factors such as hypertension, abdominal obesity, fatty liver, and dyslipidaemia commonly coexist in diabetic patients and further exacerbate the risk. The presence of target organ damage such as retinopathy, nephropathy (including microalbuminuria) and neuropathy also determine the risk of ASCVD.

Recommendations

1. In patients with type 2 diabetes who are high risk, treatment with lipid lowering therapy should be initiated to target an LDL-C reduction of >50% from baseline and an LDL-C goal of <1.8mmol/L.
2. In patients with type 2 diabetes at very high risk (presence of target organ damage, or at least three major risk factors, or long duration of diabetes >20 years) an LDL-C goal of <1.4mmol/L is recommended.
3. If the above goals cannot be achieved by intensification of statin therapy, then combination of statin-ezetimibe should be considered.
4. Statins are recommended in patients with type 1 diabetes mellitus who are at high risk.

3.6.3 Patients with Established ASCVD

Atherosclerotic cardiovascular disease (ASCVD) is the leading global cause of mortality, characterized by the presence of atherosclerosis, leading to ischemia or acute malperfusion in target organs such as the heart (coronary artery disease), brain (cerebrovascular disease), and peripheral arteries.

Patients who present with ASCVD are at high risk of recurrent events and lipid lowering therapy should be initiated as early as possible.

Recommendations

1. In all patients with ASCVD without contraindications, high-intensity statin therapy should be initiated as soon as possible regardless of the initial LDL-C.
2. Patients undergoing percutaneous coronary intervention (PCI) should receive a periprocedural loading dose of high-intensity statin.
3. Lipid levels should be reassessed in 4-6 weeks. Aim for a target reduction in LDL-C >50% from baseline and an LDL-C goal of <1.4mmol/L.
4. If the above LDL-C goal cannot be achieved with high-intensity statins alone then consideration should be given to addition of ezetimibe.
5. If LDL-C goal of <1.4mmol/L cannot be achieved with statin-ezetimibe combination in 4-6 weeks then the use of PCSK9 inhibitors should be considered.
6. In patients with statin intolerance or contraindication to statin use, ezetimibe should be considered.

3.6.4 Chronic Kidney Disease

Chronic kidney disease (CKD) independently increases CVD risk. Current risk models may not accurately assess CVD risk in CKD patients. CKD stage 3 is considered high risk, while stages 4-5 or dialysis are very high risk. Statins or statin/ezetimibe combinations are effective in reducing CVD risk in CKD stages 3-5, but not for primary prevention in patients undergoing haemodialysis. Dose adjustments are necessary when prescribing statins in CKD (see the table below).

Table 3.10: Dose Adjustment of Statins in Patients with CKD

Statin	GFR 60-90 ml/min/1.73m^3	GFR 15-59 ml/ min/1.73m^3	GFR <15ml/ min/1.73m^3	Notes
Atorvastatin	No	No	No	
Fluvastatin	No	Not defined	Not defined	↓ dose to one-half at GFR < 30 ml/ min/1.73m^3 not to exceed 40mg/day
Lovastatin	No	↓ to 50%	↓ to 50%	↓ dose to one-half at GFR < 30 ml/ min/1.73m^3 not to exceed 20mg/day unless careful monitoring
Pravastatin	No	No	No	Start at 10 mg/day for GFR < 60 ml/ min/1.73m^3
Rosuvastatin	No	5-10mg	5-10mg	Start at 5 mg/day for GFR < 30 ml/ min/1.73m^3 max dose 10mg/day
Simvastatin	No	No	5mg	Start at 5mg if GFR < 30 ml/min/1.73m^3
Pitavastatin	No	1-2 mg	1-2 mg	Dose should not exceed 2mg a day if GFR < 30 ml/min/1.73m^3

Harper CR,Jacobson TA. J AM Coll Cardiol. 2008;51:2375-2384

Recommendations

1. Patients with CKD stages 3-5 are at high risk of ASCVD and should be initiated on statins or statin/ezetimibe combination to modify the risk.
2. In patients on haemodialysis, initiation of statin therapy for primary prevention is not recommended.
3. In patients already on statin or statin/ezetimibe combination at the time of dialysis initiation, these drugs may be continued
4. In patients with CKD and other indication for lipid lowering therapy (such as familial dyslipidaemias and ASCVD) dose adjustment should be made based on creatinine clearance.

3.6.5 Women

Women have been underrepresented in statin trials, but pooled data show similar reduction of cardiovascular events with LDL-C reduction as in men. Pre-menopausal women have lower cardiovascular risk than men, but after menopause this risk increases. High-risk women should receive lipid-lowering therapy to reduce cardiovascular events.

Recommendations

1. Women at high cardiovascular risk, and those with established cardiovascular disease should be offered lipid lowering therapy with similar LDL-C goals as in men.
2. Women who are planning pregnancy, and who are pregnant or breastfeeding should not be given lipid lowering therapy due to the lack of safety data. However, where there is a strong indication for lipid lowering such as in severe FH, then bile acid sequestrants and/or LDL apheresis may be considered.

3.6.6 Older Patients (>75 years)

Statins are underused in elderly patients despite a higher absolute risk of CAD and a larger risk increase with age. Uncertainty about clinical benefits may contribute to this underuse.

Pooled data from multiple randomized controlled trials demonstrate a clear benefit of statins in reducing major vascular events in patients over 75 years old, regardless of age. However, older patients are more prone to adverse effects due to altered pharmacokinetics, comorbidities, and potential drug interactions.

Recommendations

1. Statins should be used in the treatment of ASCVD in older patients.
2. Initiation of statins for primary prevention may be considered in patients >75 years of age if they are deemed to be at high risk of CVD.
3. If there is renal impairment or the potential for drug interactions, it is recommended to start statins at a lower dose and then titrate upwards if necessary.

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4

4. HEART FAILURE

Key messages

- Heart failure is highly prevalent and carries a high risk of morbidity and mortality.
- A cardiologist should be involved as early as possible in the care of patients with HF.
- Causes of HF are varied and are generally attributed to structural or functional abnormalities of the heart. Determination of the cause helps direct therapy.
- Classification of HF according to the left ventricular ejection fraction (LVEF) has been endorsed by both the AHA and ESC and is recommended for all clinicians to follow. This classification helps direct clinical and other management.
- Guideline-directed medical therapy (GDMT) is key in management and improves outcomes.
- The foundational therapies for HF are ACEi/ARB/ARNi + Beta blockers + SGLT2 inhibitors + MRAs.
- Loop diuretics are still a cornerstone in management of HF.
- New modalities of treatment are available including mechanical devices, and these should be considered for patients who might benefit from them.

4.1 Definition

Heart failure (HF) is a clinical syndrome with symptoms and/or signs caused by a structural and/or functional cardiac abnormality and corroborated by elevated natriuretic peptide levels and/or objective evidence of pulmonary or systemic congestion. As such HF encompasses a recognizable cluster of signs and symptoms; notably dyspnoea with or without fluid retention/oedema, fatigue, activity intolerance, and exercise limitation; and some form of structural or functional heart disease together with markers of congestion.

The universal definition of heart failure proposed in 2021 puts into perspective the evidence of structural heart disease, a history of symptoms that are commonly reported in HF, and objective signs commonly seen in HF.

4.2. Epidemiology of Heart Failure

HF affects more than 64 million people worldwide and the prevalence is projected to increase due to the ageing of the population (Savarese G,2023). It has been shown to disproportionately affect individuals living in low- and middle-income countries (LMICs) who face growing health disparities, extreme poverty, difficult access to healthcare, and potential differences in genetics and risk factor distribution. The outcomes of HF in high-income countries have improved over the past three decades while that in low and middle income countries continues to worsen (Bragazzi NL2017).

HF has a morbidity and mortality at par with most cancers. Guideline-directed medical treatment (GDMT) is associated with improved life quality, reduced morbidity, hospitalization, and mortality.

The goals of care include the following:

1. To provide early and prompt diagnosis
2. To identify the cause of heart failure (aetiology)
3. To provide appropriate guideline-directed medical therapy to reduce morbidity and mortality
4. To manage comorbidities including interdisciplinary collaboration
5. To optimize and aid the patient obtain a measure of self-reliance, self-monitoring, and autonomy to manage their disease

4.3 Aetiology

The aetiology of HF varies between different regions of the world. The causes can be attributed to structural abnormalities or functional abnormalities of the heart. Sub-Saharan Africa is unique in the world being the only region where ischemic HF is not the leading cause of heart failure. This requires calibration in terms of diagnostic focus and protocols in the regions health care systems.

Causes of heart failure

- Hypertensive HF – this is the most common aetiology in most parts of Africa including Kenya. This was clearly demonstrated in the THESUS study conducted in the early 2000s (3).
- Valvular heart disease -it is a common cause of HF in Kenya, primarily due to rheumatic heart disease and infectious endocarditis.
- Ischemic heart disease- it is potentially the main emerging cause of HF in Kenya.
- Cardiomyopathies - common in Kenya and they have varied aetiologies. Lack of access to diagnostic tools including cardiac MRI and CT limits the diagnostic work up for these patients.
- Congenital heart disease- this remains a common cause of undiagnosed HF due to lack of country-wide systematic screening.

- Other rare causes include arrhythmias, infiltrative diseases (most prominently amyloid disease), and cardiotoxicity due to alcohol, chemotherapy, and radiation.

4.4 Pathophysiology of Heart Failure

The common pathophysiologic state that perpetuates the progression of heart failure is extremely complex, regardless of the aetiology. Compensatory mechanisms exist at all levels from subcellular to organ-to-organ interactions. These mechanisms (e.g., increases in heart rate and heart size, vasoconstriction) are able to "compensate" for the heart's inability to pump efficiently. Only when this network of adaptations becomes overwhelmed does heart failure ensue.
These adaptations are:

1. The Frank-Starling mechanism, in which an increased preload helps to sustain cardiac performance
2. Alterations in myocyte regeneration and death
3. Myocardial hypertrophy with or without cardiac chamber dilatation, in which the mass of contractile tissue is augmented
4. Activation of neurohumoral systems

The release of norepinephrine by adrenergic cardiac nerves augments myocardial contractility and includes activation of the renin-angiotensin-aldosterone system (RAAS), the sympathetic nervous system (SNS), and other neurohumoral adjustments that act to maintain arterial pressure and perfusion of vital organs. The release of epinephrine and norepinephrine, along with the vasoactive substances endothelin-1 (ET-1) and vasopressin, causes vasoconstriction, which increases calcium afterload. The calcium overload may induce arrhythmias and lead to sudden death.
In addition, the activation of the RAAS leads to salt and water retention, resulting in increased preload and further increases in myocardial energy expenditure.

4.5 Classification of Heart Failure

The classification of heart failure is important to help clinicians deal with complex patient scenarios, communicate effectively and guide therapy. The following classification is recommended for all clinicians to follow and has been endorsed by the American Heart Association-AHA and the European Society of Cardiology-ESC.

1. *HFrEF*-Heart Failure with reduced Ejection Fraction:
    a. LVEF: ≤40%, AND
    b. symptoms of HF which may be accompanied by clinical signs.
2. *HFmrEF*-Heart Failure with mildly reduced Ejection Fraction:
    a. LVEF: 41-49% AND
    b. symptoms of HF which may be accompanied by clinical signs. This includes patients with HF whose EF has either worsened or improved.
3. *HFimpEF*- Heart Failure with improved Ejection Fraction:
    a. This refers to those patients with previous LVEF≤ 40% but is now >41%.
4. *HFpEF*-Heart Failure with preserved Ejection Fraction
    a. LVEF: ≥50% AND,
    b. symptoms of HF which may be accompanied by clinical signs, AND
    c. evidence of raised filling pressures as indicated by elevated brain/B-type natriuretic peptide (BNP) or N-terminal prohormone of brain-type natriuretic peptide (NT-proBNP), and structural heart disease such as left ventricular hypertrophy or left atrial enlargement.
    d. Like with HFrEF, the causes of HFpEF are heterogeneous and often require further diagnostic work up with emphasis on other causes of dyspnoea including non-cardiac causes.

4.5.1 The New York Heart Association (NYHA) Classification

The NHYA classification is a simple and useful way to assess symptoms in any HF patient. It has been used to guide therapy and has prognostic implications.

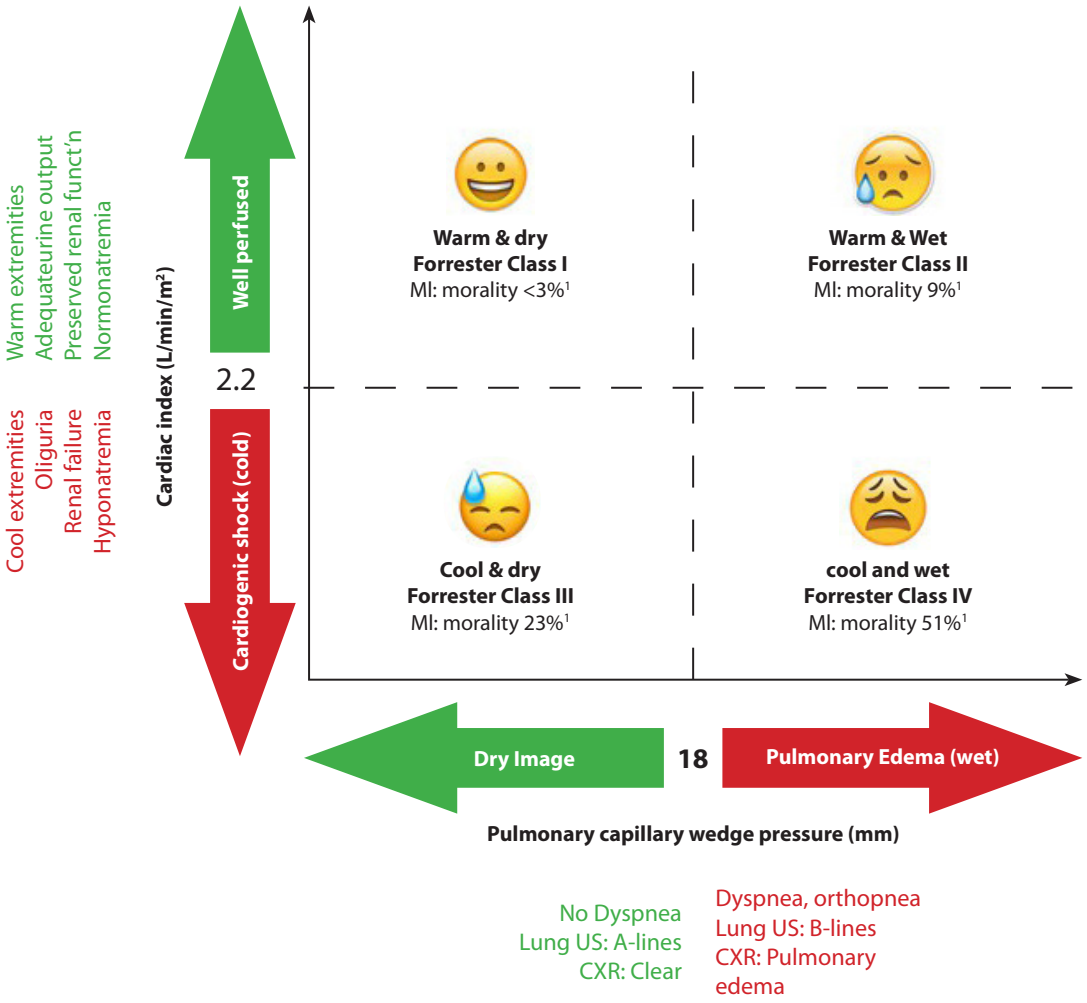
Table 4.1: The NHYA Classification-The Stages of Heart Failure

Class I	No limitation of physical activity. Ordinary physical activity does not cause undue breathlessness, fatigue, or palpitations.
Class II	Slight limitations of physical activity. Comfortable at rest, but ordinary physical activity results in undue breathlessness, fatigue, or palpitations.
Class III	Marked limitation of physical activity without discomfort. Comfortable at rest, but ordinary physical activity results in undue breathlessness, fatigue, or palpitations.
Class IV	Symptoms at rest can be present. If any physical activity is undertaken, discomfort is increased.

4.5.2 Acute Vs Chronic Heart Failure

Another important classification is acute versus chronic heart failure.

Acute heart failure poses a bigger challenge in diagnosis and therapy and carries a poorer prognosis. Patients with acute heart failure require hospitalization and most therapies for chronic heart failure may not apply to them. In acute heart failure physicians are advised to stratify their patients using the Forrester classification as it guides the approach to therapy with a view to improving patient survival.



(1) Morality numbers from Forrester 1976 PMID 790191. Morality is probably lower today.

Figure 4.1: Forrester Classification of Heart Failure

4.6 Diagnostic Work-up for HF

The aim of the diagnostic work-up is to ascertain the cause, severity, and prognosis of HF. In addition, it helps to chart out a management plan that includes pharmacological and non-pharmacological interventions such as devices, advanced care, and rehabilitation.

4.6.1 When to Suspect Heart Failure

The cardinal symptom of heart failure is dyspnoea with or without fluid retention, sometimes combined with a new-onset cardiac murmur. Previously known CVD, ECG changes (such as LVH, atrial fibrillation, T-wave changes, Q-waves, bundle branch blocks) are important in making the differential diagnosis. Elevated BNP or NT-proBNP makes the diagnosis more likely but not definitively. Increased baseline cardiovascular risk including hypertension, renal disease, excessive alcohol use, previous myocardial infarction, or diabetes, cancer, or smoking increase the probability of a heart failure diagnosis.

Common heart failure mimics include:

- lung disease: pneumonia, COPD, asthma, interstitial lung disease, pleural effusions, malignancies
- pericardial disease
- kidney failure
- rarely systemic disease causing anaemia, inflammation
- thyroid disease.

4.6.2 Initial Tests

When HF is suspected, patients should be referred for an echocardiogram. The referral letter should include a good symptom history, NYHA class, physical signs, information about weight changes, and previous history of disease, particularly cardiovascular disease. Finally, a list of current prescription medicine should be included in the referral note.

An ECG and chest radiograph are usually warranted. If the pretest probability is low, pulmonary function tests should be performed prior to referral.

Laboratory tests include a full hemogram, urea, electrolytes, liver function tests, thyroid function tests (TFTs), HbA1c, and a lipid status. BNP or NT-proBNP, when available, are appropriate rule-out tests, although false negative results may occur in a minority of people.

4.6.3 Biomarkers in the Definition of HF

Natriuretic peptides such as brain natriuretic peptide (BNP) and N-terminal prohormone of brain natriuretic peptide (NT-proBNP) are an integral component in making a diagnosis of HF in many clinical settings, especially when the diagnosis is uncertain. The use of these biomarkers has the highest class of recommendation to support a diagnosis or exclusion of HF in contemporary practice guidelines, but are notably absent from most definitions of HF. This is because most care systems lack the capacity to perform these tests in a timely manner and cost may prohibit their routine use. NT pro BNP is a good prognostic maker and a marker for follow-up and also a good renal marker (ref).

4.6.4 Cardiovascular Tests

1. **ECG**
    - All patients with suspected heart failure must have an ECG as soon as possible. The ECG is invariably abnormal in the heart failure patient.
    - Common abnormalities to look out for include LVH, atrial fibrillation, bundle branch blocks and hemiblocks, Q-waves.

2. **Echocardiogram**
   - 2D-echocardiogram is the key examination in HF.
   - It enables classification of the disease at rest and provides a wide array of differential diagnosis including valvular disease, aortic disease, and pericardial disease.
   - An echocardiogram will often not only detect the underlying pathogenesis, but also help grade the severity.
   - An echocardiogram is performed when the GDMT has been fully implemented before device therapy assessment. The timing of this echo remains subjective, but 3 months post diagnosis is appropriate.
   - Consider early repeat echocardiography if reversible causes of HF are suspected e.g., tachycardia induced cardiomyopathies, hypertension with quick resolution of symptoms, alcohol-induced cardiomyopathy, or peripartum cardiomyopathy.
   - An earlier echocardiogram may also be performed if patients continue to worsen despite medical therapy. This can assess, for example, worsening heart valve lesions, and rising pulmonary pressures.
3. **Chest radiograph**
   - All patients with suspected heart failure should have a CXR as part of the initial work-up: look out for differential diagnosis of heart failure and attendant complications.
4. **Ambulatory blood pressure measurement (ABPM)**
   - This reasonable in patients where residual hypertension is suspected.
   - However, the combination of the four pillars of management usually results in good BP control. (Refer to Chapter 3 on Hypertension.)
   - Quick titration of medication is usually possible in hypertension.
5. **Holter monitor**
   - Can be used to diagnose arrhythmia, to optimize heart rate, or pre-empt arrhythmia during up-titration of therapy.
6. **Pulmonary function tests**
   - Used to investigate for differential diagnosis when residual symptoms exist despite appropriate therapy.
7. **Natriuretic peptides**
   - BNP and NT-proBNP are an integral part of the diagnosis of heart failure. NT-proBNP is preferred to BNP as it is not affected by renal insufficiency.

Table 4.2: Recommended Diagnostic Tests in All Patients with Suspected Chronic Heart Failure

Recommendations	Class	Level
BNP/NT - proBNP	I	B
12-lead ECG	I	C
Transthoracic echocardiography	I	C
Chest radiography (X-ray)	I	C
Routine blood tests for commodities , including full blood count, urea and electrolytes, thyroid function, fasting glucose and HbA1c, lipids, iron status (TSAT and ferritin)	I	C

Adapted from the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

The flow chart below derived from the ESC guidelines (www.escardio.org/guidelines/) can be used as a wall chart in the clinical areas to guide clinicians who review patients with HF.

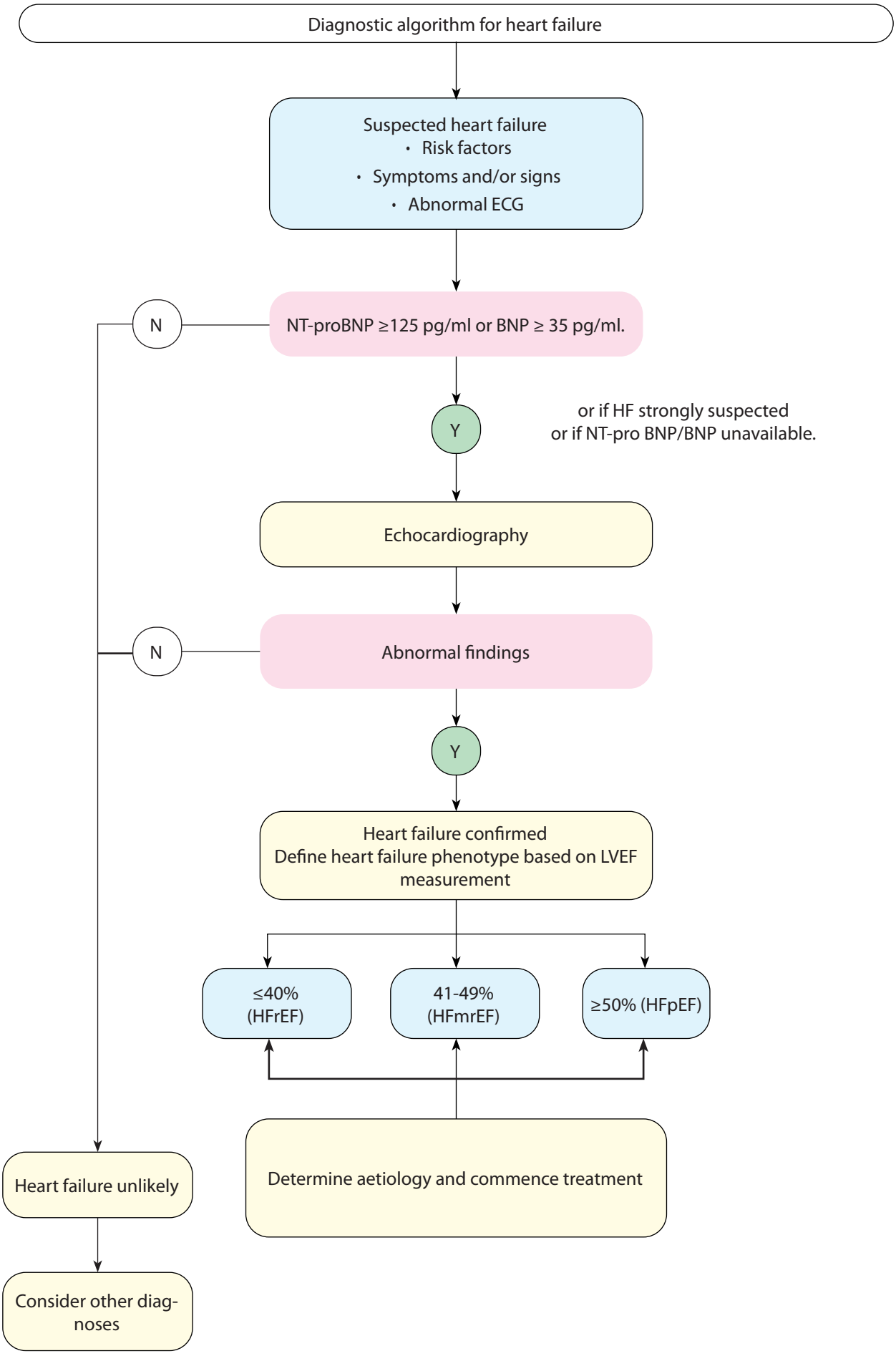


Figure 4.2: The Diagnostic Algorithm for Heart Failure

4.6.5 Additional Tests that may be done in Higher/Specialised Centres

Computed tomography coronary angiography (CTCA) for patients with a low to intermediate pre-test probability of CAD, or those with equivocal non-invasive stress tests to exclude the diagnosis of CAD. Due to excessive calcification CTCA should be avoided in elderly patients and patients with renal failure on dialysis (4,5).

Single-photon emission CT (SPECT) can be used to assess myocardial ischaemia and viability, myocardial inflammation or infiltration.

Coronary angiography is recommended in patients with HF who have angina despite pharmacological therapy to establish the diagnosis of CAD and its severity, and to assess for possible coronary revascularization.

If triple vessel disease is suspected, especially in the diabetic patient, the threshold for coronary angiogram should be lower. An ECG with Q-waves and wall motion abnormalities on echo have been found to increase the likelihood of significant coronary artery disease in this patient population.

Cardiac MR with late gadolinium enhancement (LGE) is recommended if cardiac function is not fully elucidated (e.g., due to poor imaging quality) or the aetiology is not clear, e.g., if infiltrative/sarcoid disease is suspected. Cardiac MR can be used an adjunct to echo when grading moderate to severe aortic regurgitation. Perfusion MR has a relatively high sensitivity for ruling out irreversible ischemia and LV thrombus.

DPD (Technetium-99m)-bone scintigraphy is used to detect and grade amyloid transthyretin cardiomyopathy.

Right heart catheterization (RHC): although invasive and inaccessible to many patients, RHC has utility in patients who need myocardial biopsies (infiltrative disease, myocarditis). RHC may also be indicated in selected patients with HFpEF or out-of-proportion pulmonary hypertension and HF when non-invasive tests are inconclusive.

Work up for genetic disease is still in its infancy but should be considered in patients with familial accumulation of premature sudden cardiac death in the absence of a clear aetiology. This is usually undertaken by subspecialized cardiologists.

4.7 Management 0f Heart Failure

The aim of therapy in heart failure is to reduce morbidity and mortality and to improve quality of life. The underlying aetiology should always be targeted.

The foundational treatment for HFrEF patients comprises:

1. ACE-inhibitors/ARB/ARNI
2. Beta blockers
3. SGLT-2 inhibitors
4. MRAs

All these agents have class IA recommendation in both the ESC and ACC guidelines for management of HF. All four pillars should be initiated in relatively rapid sequence (within 4-6 weeks). Aim to achieve maximum recommended or maximally tolerated doses. This may not be attained in patients who are elderly, frail, or with significant comorbidities.

When fully titrated, the medical treatment should be maintained if possible unless severe side effects occur. Although hypotension is common, it should not routinely lead to stopping or reducing the dosage of any of the drugs.

4.7.1 Pharmacological management of HFrEF

Angiotensin converting enzyme inhibitors (ACEi) & Angiotensin receptor blockers/antagonists (ARB)

- This class of drugs remains the major foundational therapy in HFrEF management. They prolong life and reduce hospitalization. Most patients should receive a drug from this drug class.
- After initiating the treatment, the dose should be carefully titrated upwards in 1 to 2 week intervals in the outpatient setting, but more rapidly in the in-patient setting. If the patient is hypotensive (systolic BP <100 mmHg) at the outset, or if eGFR<30 ml/min, lower doses may be considered. A creatinine level increase of up to 30% from baseline is to be expected. If creatinine increases >50% from patient's baseline, alternative causes should be explored. Cessation or withholding the drug for some days is appropriate.
- The best evidence for available ACEi is for enalapril and ramipril. (Frigerio M 2005)
- ARBs is given to ACEi-intolerant patients who are more common in Kenya than in the RCTs; however, a cough is more likely to be due to decompensation than to ACEi intolerance. The best data for ARBs are for candesartan, valsartan, and losartan. (Frigerio M)

Angiotensin Receptor Blocker and Neprilysin Inhibitor (ARNi)

- ARNi comprises valsartan and a neprilysin inhibitor (sacubitril) in a two-moiety molecule. The target dose for sacubitril/valsartan is 97/103 mg (200mg) every 12 hours. The usual starting dose is 50mg every 12 hours.
- ARNi has been shown to be superior to ACEi in the PARADIGM-HF study (McMurray JJV, 2014).
- When starting ARNi the following should be kept in mind:
  - The systolic BP should preferably be ≥95 mmHg.
  - It is not recommended if eGFR <30 ml/min. Monitor renal function as with ACEi/ARBs.
  - When changing from ACEi to ARNi a 36-hour drug-free interval is required before starting the second drug i.e., stop the ACEi and wait for 36 hours before initiating the ANRi
    - If the patient was on an ARB, there is no need the break beefoe starting thee ARNi.
  - Patients on maximum dose ACEi can usually start on ½-dose ARNi. Titration is to be done biweekly. Other patients start on the lowest dose of ARNi depending on the BP.
  - Changing to ARNi should be considered in the setting of worsening HF.

Beta-blockers (BB)

- Beta blockers typically reduces mortality from HF by approximately 30%.
- They should be given to all patients with HFrEF who do not have contraindications to the use of beta blockers.
- There is evidence for mortality reduction for carvedilol, long-acting metoprolol, and bisoprolol.
- Patients may experience worsening symptoms the first week of treatment.
- BB should not be given in decompensated HFrEF and should be given with caution to patients with compensatory sinus tachycardia.
- Chronic obstructive pulmonary disease (COPD) or peripheral artery disease (PAD) are not contraindications for BB use.
- If the patient has severe asthma, liaise with a chest physician. Ivabradine can be of use in such patients.
- Titration is done at a slower rate than with ACEI/ARNis, however data suggest that reaching the maximal dose used in the trials is more important for beta blockers than in any other class of HF drugs.
  - Slower titration may be warranted depending on patient characteristics.
  - In patients with atrial fibrillation, BB should be prioritized earlier in the algorithm. Sub-analyses from RCTs suggest that up-titration to max doses in HFrEF patients with atrial fibrillation is not associated with better outcomes. Titration therefore should be optimized according to patient symptoms.

Diuretics

- Though there are no placebo-controlled randomized studies available, loop-diuretics are the cornerstones in the management of HF.
- In the furosemide-naive patient with normal eGFR, low doses are initiated and titrated according to response.
- Furosemide, torsemide, or bumetanide can be used. Torsemide and bumetanide have better bioavailability than furosemide. In the recent TRANSFORM-HF trial there was no difference between furosemide and torsemide (Mentz RJ, 2023).
- Loop-diuretics can be dosed once a day in near-volemic patients, but when decongesting a thrice daily dosing (every 8 hours) is preferred due to between-dose salt retention.
- Oral furosemide should be administered ½ hour before or 2 hours after meals to optimize absorption.
- Metolazone is a potent thiazide-like diuretic which can be used as an adjunct in patients where euvolemia cannot be attained on loop-diuretics alone.
    - The risk of electrolyte derangement is significant and close monitoring of sodium and potassium is mandatory.

Mineralocorticoid-receptor-antagonists (MRA)

- MRAs reduce mortality and hospitalization and have a modest natriuretic and diuretic effects. They comprise one of the four pillars of GDMT and should be used routinely if there is no contraindication to their use.
- Both spironolactone and eplerenone are approved for use in HF.
- A minority of patients develop gynaecomastia or tenderness around the nipples when on spironolactone. Switching to eplerenone in these patients usually alleviates the pain.
- MRAs should not be initiated in patients with renal failure (serum creatinine >220 µmol/L, eGFR <30 ml/min) or potassium >5.0 mmol/L
- The starting dose of spironolactone is 12.5 mg to 25 mg once per day, increased to 25-50 mg once per day.
- Monitoring is similar to that of ACEi/ARNi, with particular focus on potassium levels.
- Repeat kidney function tests within a few weeks after introducing MRAs, especially if eGFR <45ml/min.
- If the patient experiences vomiting or diarrhoea MRAs should be held.
- It is reasonable to hold MRA temporarily if potassium >5.5 mmol/L and permanently discontinue the drugs if > 6.0 mmol/L.

SGLT-2-inhibitors

- Evidence-based sodium glucose transporter-2 inhibitors (SGLT2i) (dapagliflozin and empagliflozin) are indicated in all HF patients with or without type-2 diabetes.
- SGLT2i are contraindicated in patients with eGFR <20 ml/min.
- SGLT2i can often be initiated early, even during in-hospital admission as they aid decongestion. A reversible rise in creatinine of approximately 30% from baseline is expected, especially if the patient is dehydrated. This should not cause the drug to be withheld. Reducing loop diuretics may be indicated.
- UEC monitoring is mandatory, and should be done sooner if eGFR <30 ml/min.
- There is a small known risk of diabetic ketoacidosis (DKA) with SGLT-2i use. Diabetic patients who are dependent on insulin have a higher risk of developing DKA.
- Special care should be taken in cachectic or patients who are nil-by-mouth including patients awaiting elective surgery.
- SGLT2i is currently not indicated in T1D. If in doubt liaise with an internist/endocrinologist.

Ivabradine

- Consider it in patients on maximum recommended/tolerated doses of ACEi, BB, and MRA in sinus rhythm with a resting HR >70 bpm and still symptomatic.
- It has proven efficacy on the combined end-point of cardiovascular death and heart failure hospitalization.

- Ivabradine should be reserved for patients optimally treated with beta-blockers.
- It also has some utility in patients who do not tolerate BB.
- Consider other causes of tachycardia, especially compensatory sinus tachycardia in the decompensated patient.
    - Other common causes of tachycardia are hyperthyroidism, dehydration, infection, or anaemia.
- Starting dose of ivabradine is 5 mg twice per day (every 12 hours). Starting dose in the frail is 2.5 mg every 12 hours.
    - Target dose: 7.5 mg every 12 hours.

Digoxin

- It is not used routinely in patients with sinus rhythm, but its utility in atrial fibrillation and flutter is established especially in decompensated HF when blood pressure is low and beta blockers may not be tolerated.
- Even if not associated with mortality reduction evidence supports symptomatic relief and reduced hospitalization.
- Care should be taken to avoid high doses, particularly in patients with chronic kidney disease. Measure potassium prior to initiation.

HYDRALAZINE/isosorbide dinitrate (H/ISDN)

- The combination of H/ISDN has been shown to decrease mortality predominantly in African-Americans on top of baseline therapy with ACEi/BB & MRA.
- H/ISDN is also safe in patients with very low eGFR (CKD 5).
- Starting dose of hydralazine is 25 mg every 12 hours, then every 8 hours.
- Commonly available nitrates in Kenya are isosorbide dinitrate dosed at 20mg twice a day and isosorbide monotrate at 30-60mg daily

Vericiguat

- A novel agent with class IIb recommendation and may be considered to reduce the risk of cardiovascular death and hospitalization for heart failure following a prior hospitalization for heart failure or need for outpatient intravenous diuretics, in adults with symptomatic chronic heart failure on optimal medical therapy.
- Liaise with a cardiologist for its use.

4.7.2 Treatment of Comorbidities

Ischaemic heart failure

- Patients with HF due to ischaemic cause should routinely be put on statins. There remains no evidence for statins in patients with heart failure without dyslipidaemia or coronary artery disease.
- CABG is indicated in patients with LVEF ≤35% and angina and significant CAD (left main or left main equivalent including proximal LAD with 2- or 3-vessel disease).
- Revascularization in patients without angina is not routinely indicated, but it is an evolving area of research (REVIVED-BCIS) (6).

Iron deficiency

- Intravenous iron therapy is associated with reduced readmission and improved quality of life in patients with LVEF<50% and proven iron insufficiency with or without anaemia.
- Iron deficiency in this context is defined as:
    - ferritin <100 mcg/L,or
    - ferritin 100 – 300 mcg/L + transferrin saturation (TSAT) <20%. (AFFIRM-HF)

Malnutrition

- Dietary intervention is an intrinsic part of the treatment of obese patients with heart failure.
- In cachectic patients dietary intervention should also be instituted.

Obstructive sleep apnoea

- Obstructive sleep apnoea (OSA) is common in heart failure.
- Patients in NYHA III or IV more often have central sleep apnoea (CSA). In these patients treatment with adaptive servo-ventilation is associated with increased mortality (SERVE-HF).

4.7.3 Other treatment modalities

Inotropic agents

- No single agent is associated with improved 30-day survival, but in acutely decompensated patients with refractory heart failure inotropic agents may be considered to maintain cardiac output and mean arterial pressure to sustain kidney function.
- The inotropic agents should be reserved for patients with reversible decompensated HF.
- The most studied inotropic agent is levosimendan.
- Dobutamine is however more commonly available and may be used in addition to pressor agents.

Vasopressor agents

- Vasopressor agents are recommended for the decompensated heart failure patient with hypotension and shock.
- The first line agent is noradrenaline.
- Adrenaline may be added to refractory cases.

Antiarrhythmic drugs

- These should be used with caution.
- Amiodarone is the preferred agent if needed although it is associated with significant risk of side effects in the setting of long-term use.
- Dronedarone (not available locally) and class IC agents like flecainide are contraindicated in HFrEF.

Mechanical support devices

- These are reserved for patients with:
    - intractable heart failure
    - valvular lesions such as severe mitral regurgitation
    - mechanical complications of myocardial infarction
- These include intra-aortic balloon pump, Impella pump, extracorporeal membrane oxygenation (ECMO), left ventricular assist device (LVAD).

Heart Transplant

This is done in the developed countries and remains the only definitive treatment for intractable, stage IV heart failure.

Devices in heart failure:

Biventricular pacing – Cardiac Resynchronization Therapy (CRT)

- Cardiac resynchronization is an established treatment which aims to restore interventricular synchronization through pacing the right ventricle (conventionally), and left ventricle (through the coronary sinus).
- It should be offered to patients with LVEF<35% and true left bundle branch block (LBBB) (QRS >150 ms). In this population CRT-implantation is associated with reduced symptoms, hospital readmission, and all-cause death.
- The therapy may be combined with an implantable cardioconverter defibrillator (ICD).

- The suitability and type of device is determined between the treating physician/cardiologist and the implanting centre where factors like ECG-characteristics, age, frailty, aetiology, and overall prognosis are all considered.
- Less robust data suggest benefit in selected patients with symptomatic HFrEF patients (LBBB with QRS 130 – 150 ms) or patients with atrial fibrillation (good rate control is a prerequisite – AV nodal ablation may be indicated in a minority of cases) or high RV pacing burden.
- In non-LBBB the data is ambiguous and individualized assessment is important.
- Post-implant review is key to identifying: loss of capture of the CS-lead, tachyarrhythmias or frequent PVCs or more commonly suboptimal program settings, which will all ensure maximal long-term benefit of the intervention.

Implantable cardioverter defibrillator (ICD)

- ICD for primary prophylactic purposes is indicated in ischaemic HFrEF patients who, despite optimized medical therapy, have NYHA II – III, LVEF ≤35%.
- It is good practice to wait at least 3 months after an acute MI or CABG, though one can be more lenient in patients with malignant arrhythmias or syncope.
- In patients with non-ischaemic HFrEF primary prophylactic ICD may still be indicated in younger patients (no set age-cut off can be determined). According to the DANISH trial patients older than 70 years did not derive any benefit.
- Suspicion of familial cardiomyopathy including death or VT/VF in a close relative should prompt genetic work-up if available.
- CRT-P (CRT with a pacemaker) or CRT–D (CRT+ICD) is generally inappropriate in very elderly, comorbid patients with low life expectancy (< one year). Psychological factors also play a role as ICD may cause significant anxiety in some patients.
- The indication for secondary prophylactic ICDs do not differ significantly for heart failure patients.

Physical Exercises

- Physical exercise is recommended in all patients unless they are very symptomatic or have ongoing unstable angina.
- Exercise may be started the moment the patient is euvolemic.
- Exercise is associated with reduced symptoms and better quality of life.
- Body weight should be monitored and fluid and salt intake reduced moderately (< 2 L per day).
- Referral to a cardiac rehabilitation centre can facilitate this care.

Medications which should be avoided.

- NSAIDs and COX-2 inhibitors reduce the kidney function and cause fluid and sodium retention. They should be avoided as they are associated with increased mortality. Paracetamol should preferably be considered for treatment in the setting of pain.
- Calcium antagonists: non-dihydropyridines (verapamil, diltiazem) are contraindicated in HFrEF.
    - Dihydropyridines (amlodipine, felodipine) may be used in the setting of refractory hypertension or angina, but their isolated use has no indication in HFrEF.

4.8 Right heart failure

Chronic right ventricular (RV) failure is most often secondary to LV failure and accompanied by pulmonary hypertension (WHO class II). Isolated RV failure is seen in the setting of RV myocardial infarction, pulmonary embolism, pulmonary arterial hypertension, valvular disease, congenital disease, or pericardial disease.

Aetiological work-up is essential. Echocardiography is indicated: great care should be taken to assess the right-sided chambers and TR-gradient. Assessment may also include:

- Coronary angiogram
- Cardiac MRI,
- Right heart catheterisation
- Pulmonary function tests
- V/Q-scans and/or CT scan chest.

Patients who need pacing or right-heart catheterization should be referred to a highly specialized cardiac unit.
There are no RCTs to support the use of GDMT in patients with isolated RV failure and it may be detrimental.

4.9 Common challenges in patients with heart failure

Non-sustained ventricular tachycardia (nsVT). A common finding and should not elicit routine referral. BB and optimization of potassium levels and GDMT is the primary treatment.

LV recovery. A number of patients will experience normalization of LVEF. This is often dependent on GDMT and aetiology: e.g., alcoholic cardiomyopathy, Takutsubo cardiomyopathy are well known reversible causes of HF.Currently we do not have data to support cessation of GDMT in these patients.

Atrial fibrillation is a common finding albeit less common in SSA.

AF patients are well represented in the pivotal heart failure trials and should be given GDMT, with known caveats in the case of BB. A resting HR of <110bpm should be achieved – probably lower. A rhythm control strategy can be pursued in younger patients with HF and symptomatic AF if optimally treated. Trial cardioversion (amiodarone may be needed) is a good strategy to determine the effect of sinus rhythm in these patients. Weight optimization is important to maintain sinus rhythm. Anticoagulation should follow guidelines noting that eGFR may fluctuate.

Hypotension occurs commonly in HF and is primarily addressed if symptomatic. Postural hypotension is commonly seen in most patient during titration and should only lead to reduction of drug dosages if it is pronounced or if it leads to creatinine rise >50% above baseline.

Hypo-/hyperkalaemia commonly occurs during titration with ACEi, ARB, SGLT2i, and especially MRA. These agents should not be started if potassium is >5.0 mmol/L. However, if the patient is already on the agents, only consider reduction if K^+ >5.5 mmol/L. Hypokalaemia is best avoided by early treatment with MRA which also has anti-fibrotic properties and prevents sudden cardiac death.

Hyponatremia: institute fluid restriction. Avoid hypersaline fluids. Tolvaptan, a vasopressin receptor 2 antagonist, could be used intermittently in these patients. Avoid use of salt replacement tablets.

Worsening renal function is often caused by dehydration and hypotension. GDMT should be maintained as long as is feasible.

Cough is most often caused by decompensation but is more common in SSA (approximately 25%). If it occurs increase the dose of loop diuretics before changing from ACEi to ARB as decompensation is the more likely cause of cough (7).

Gout is common in HF and can be due to HF itself, CKD, or dehydration. Avoid NSAIDs. Treat with paracetamol, colchicine, and steroid injections. Allopurinol can be used prophylactically according to eGFR (8).

Erectile dysfunction may significantly impact the quality of life and should be addressed. Consider changing the MRA to eplerenone or BB to nebivolol. Sildenafil or tadalafil can be given if no known contraindication exists. Avoid concomitant use of these drugs with nitrates.

4.10 HFpEF and HFmrEF

HFpEF is a difficult condition to diagnose and is essentially a diagnosis of exclusion The ESC risk scoring tool remains the most feasible method for assessing these patients prior to starting therapy.

There is no consensus on which exercise protocol should be used. If criteria for diastolic dysfunction during an exercise echocardiogram through E/e' ratio and tricuspid regurgitant velocity are not met, invasive hemodynamic assessment through a right heart catheterization at rest or at exercise is the next step.

A rest pulmonary capillary wedge pressure (PCWP) ≥15 mm Hg or exercise PCWP ≥25 mm Hg is diagnostic of HFpEF.
Probability of HFpEF

H2FPEF Scoring

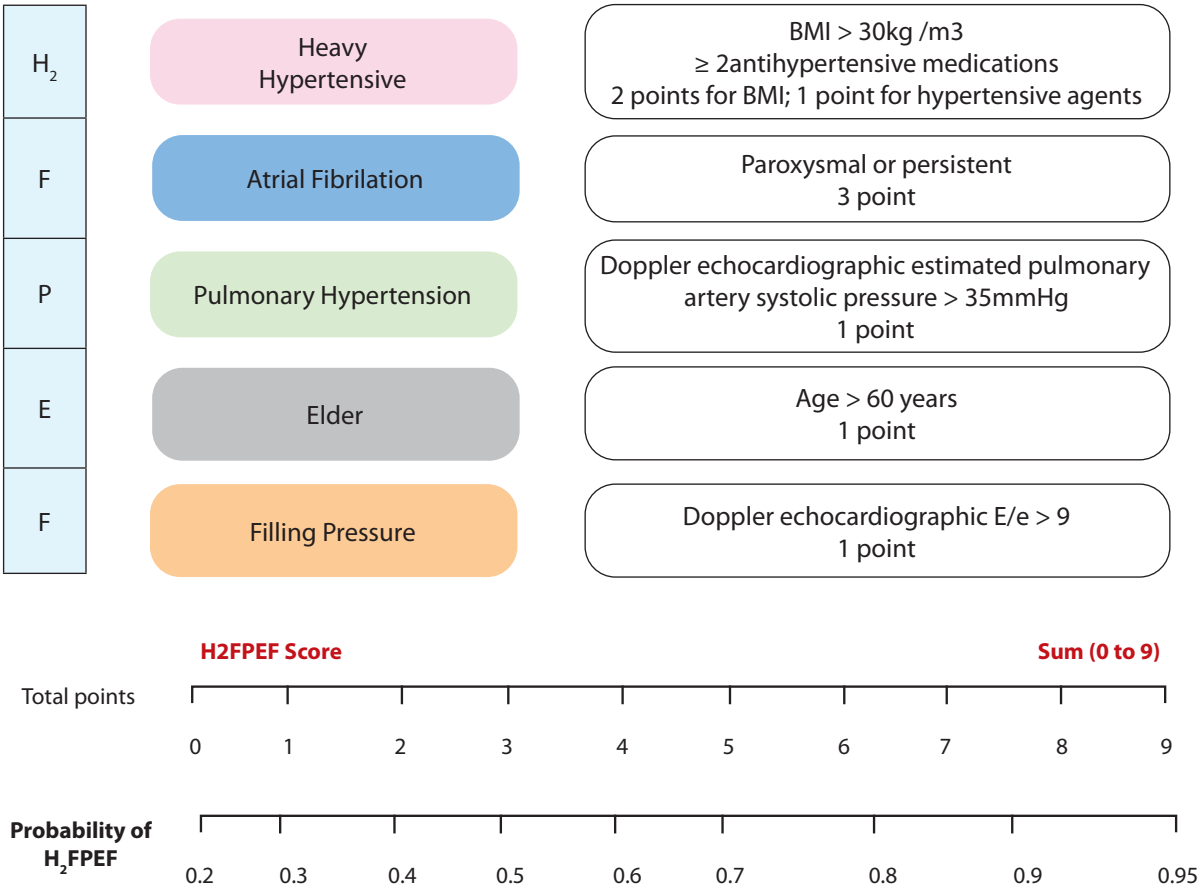


Figure 4.3: ESC HFpEF scoring

For each major criterion met, 2 points are awarded, and 1 point is awarded for a minor criterion. Interpretation:

- Score of ≥5 points based on echocardiographic and natriuretic peptide levels is diagnostic of HFpEF.
- Score of ≤1 points: diagnosis of HFpEF very unlikely.
- Score of 2-4 points: additional workup in the form of diastolic stress echocardiography is recommended.

The treatment of HFpEF (and HFmrEF) centres around managing comorbidities including hypertension, obesity, diabetes, AF, and sleep apnoea. Agents of choice include diuretics, angiotensin receptor–neprilysin inhibitors (ARNIs), angiotensin receptor blockers (ARBs), and mineralocorticoid antagonists (MRAs).

An SGLT2 inhibitor (dapagliflozin or empagliflozin) is recommended in patients with HF with preserved EF (HFpEF) to reduce the risk of HF hospitalization or CV death.

4.11 Palliative Care

A significant number of patients with advanced HF will not be candidates for advanced therapies. Patients with a life expectancy of < 1 year should be offered palliative care. The patient should be informed of his/her prognosis and what to expect. This includes reducing the pill-burden, addressing end of life issues including when to turn off the ICD, transition to home care and/or eventually hospice or liaison with a religious or spiritual adviser.

As the scientific evidence is scanty, the aim of palliative care is primarily to reduce symptoms, improve quality of life, and avoid unnecessary admissions through adjusted the level of care. Palliative care in HF patients is often different from cancer patients as their symptoms may differ.

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5

5. RHEUMATIC FEVER AND RHEUMATIC HEART DISEASE

Key messages

- Rheumatic fever (RF) is an autoimmune inflammatory response to Group A streptococcal infection that tends to occur a few weeks after the infection.
- Repeated episodes of RF can cause recurrent scarring of the heart valves resulting in the chronic form of the disease termed Rheumatic Heart Disease (RHD).
- Diagnosis remains a clinical decision, as there is no specific laboratory test.
- Where available, Echocardiography with Doppler should be performed in all cases of confirmed and suspected ARF.
- Prompt and effective treatment of ARF and prevention of recurrent attacks are critical in preventing RHD.

5.1 Introduction

Rheumatic Heart Disease (RHD) is the most common acquired heart disease in children in developing countries (1). It is a chronic heart condition caused by acute rheumatic fever (ARF) which can be prevented and controlled.

The risk of rheumatic fever (RF) following untreated group A streptococci (GAS) pharyngitis is between 0.3 – 3% (6). For individuals with a history of previous RF, the risk rises to 50%. Up to 30% of sore throats in children and young people are caused by GAS (2). Without antibiotic treatment, some of these children will develop RF a few weeks after their sore throat (3).

Repeated episodes of GAS infection and RF causes progressive heart valve damage and scarring [5]. This persistent valve scarring results in chronic valvular heart disease termed as rheumatic heart disease (RHD).

The most important determinant of disease progression appears to be the number of times RF recurs in an individual. Only some people are susceptible to RF and RHD. A triad of environmental, genetic, and bacterial factors appears to be important in the development of clinically significant disease [7].

5.2 Epidemiology and Burden of Disease

Globally, over 15 million people suffer from RHD [14]. Acute rheumatic fever and rheumatic heart disease are rare in the high-income countries [8]. This is attributed in part to improvement in socioeconomic conditions and the widespread use of penicillin G benzathine to treat streptococcal pharyngitis [9]. The remaining burden of rheumatic heart disease is found mostly in low- and middle-income countries and among immigrants and older adults in high-income countries [10].

The prevalence of RHD in Kenya ranges from 1.7% to 2.7% in hospitalized surgical patients aged 5 to 35 years.

It has been estimated that most children develop at least one episode of pharyngitis per year, 15–20% of which are caused by group A streptococci and nearly 80% by viral pathogens [11]. Group A streptococcal pharyngitis has a peak incidence in children 5–15 years of age [12, 13]. It is less frequent among children in the first three years of life and among adults.

Death and disability from RHD continue to exert an enormous social, economic, and cultural toll on young adults and their communities. The burden is greatest in the most productive years of life for those who can least afford it.

5.3 Etiology and Pathogenesis

Rheumatic fever (RF) is an autoimmune inflammatory response to Group A streptococcal infection that tends to occur a few weeks after the infection. Persons who have experienced an episode of RF are predisposed to recurrence following subsequent group A streptococcal infections.

Streptococcal proteins are similar to some host proteins. The body's immune defences formed against streptococcal proteins will also attack tissues having related proteins (heart, subcutaneous tissues, joints, and the central nervous system) resulting in an inflammatory reaction, which can be mild or intense. This inflammatory reaction is self-limiting in all the tissues except the heart.

Determinants of the disease burden of rheumatic fever and rheumatic heart disease

The table below outlines the key socioeconomic and health-care related risk factors that are associated with development and course of RF and RHD.

Table 5.1: Direct and Indirect Results of Environmental and Health-System Determinants on Rheumatic Fever and Rheumatic Heart Disease

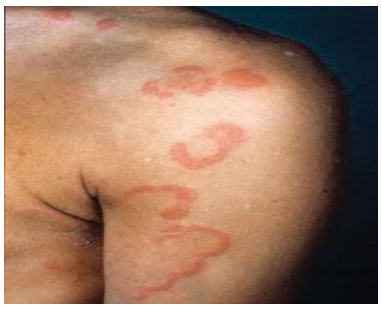
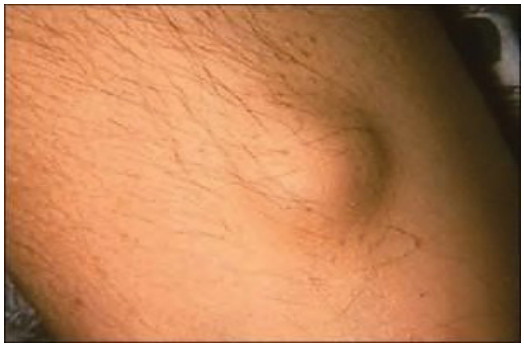
Determinants	Effects	Impact on RF and RHD burden
Socioeconomic and environmental factors		
- Poverty - Undernutrition - Overcrowding - Poor housing	Rapid spread of group A streptococcal strains	- Higher incidence of acute streptococcal pharyngitis and suppurative complications.
	Difficulties in accessing healthcare	- Higher incidence of acute RF - Higher rates of recurrent attacks
Health system-related factors		
Shortage of resources for health care	Inadequate diagnosis and treatment of streptococcal pharyngitis	- Higher incidence of acute RF and its recurrence.
Inadequate expertise of health care providers	Misdiagnosis or late diagnosis of acute RF	- Patients unaware of first RF episode - More severe evolution of disease - Untimely initiation or lack of secondary prophylaxis
Low level awareness of the disease in the community	Inadequate secondary prophylaxis and/or non-compliance with secondary prophylaxis	- Higher rates recurrent attacks with more frequent and severe heart valve involvement - Higher rates of repeated hospital admissions and expensive surgical interventions.

5.4 Clinical Manifestations

RF causes joint pains, fever, skin changes and sometimes abnormal movements (Sydenham's chorea). In most cases the heart also becomes inflamed during RF. However, when other symptoms of RF resolve, changes to the heart valves may persist [4]. Further features are shown in the table below:

Table 5.2: Manifestations of Acute Rheumatic Fever (also referred to as criteria)

Major Manifestations	
Manifestation	**Description**
Carditis	This the only manifestation that has the potential for long-term complications. It usually manifests as a pancarditis involving the endocardium, myocardium, and pericardium. The patient usually presents with general malaise, palpitations, swelling of the feet, shortness of breath, and cough. Clinically, the patient may have tachycardia, a heart murmur, cardiac enlargement, congestive heart failure, a pericardial friction rub, and/or pericardial effusion.
Arthritis	Inflammation of the synovial membranes of several joints characterized by swelling, redness, warmth, and pain. Usually presents as polyarthritis which is migratory in nature. Mostly affects the larger joints, including the knee, ankles and elbows, and wrists. It rapidly improves on NSAIDS. Usually runs a self-limited course lasting ≈4 weeks. Monoarthritis may be a presenting feature in high-risk populations

Sydenham's chorea	Chorea in ARF is characterized by purposeless, involuntary,non-stereotypical movements of the trunk or extremities. It often is associated with muscle weakness and emotional lability.
Erythema marginatum	Distinctive rash marked by the presence of pink rings in the torso or upper (proximal) parts of the body; can appear and disappear within minutes. 
Subcutaneous nodules	Small painless lumps under the skin. Usually present over the elbows, wrists, knees, ankles, Achilles tendon, occiput, and posterior spinal processes of the vertebrae. These are uncommon and are associated with severe carditis. 
Minor manifestations	
Clinical	Fever, polyarthralgia
Laboratory	Elevated acute phase reactants (erythrocyte sedimentation rate or leukocyte count)
Electrocardiogram	Prolonged P-R interval
Supporting evidence of a preceding streptococcal infection within the last 45 days	
• Elevated or rising anti-streptolysin-O or another streptococcal antibody, or • A positive throat culture, or • Rapid antigen test for group A streptococci, or • Recent scarlet fever	

5.5 Diagnosis

An accurate diagnosis of ARF is important. Over diagnosis results in unnecessary treatment over a long time, while under diagnoses leads to further attacks of ARF, cardiac damage, and premature death. Diagnosis remains a clinical decision, as there is no specific laboratory test.

The diagnosis of ARF is guided by the Jones criteria and the more recent World Health Organization (WHO) criteria.

The clinical diagnosis of carditis usually depends on detecting:

i) myocarditis
ii) pericarditis, and
iii) valve regurgitation.

Carditis as a major manifestation of ARF has been a clinical diagnosis based on the auscultation of typical murmurs that indicate mitral or aortic valve regurgitation at either valve or both valves. To increase sensitivity of ARF diagnosis current evidence now supports the use of echocardiography/Doppler as part of the diagnostic criteria for confirmation of the presence of carditis in patients with suspected ARF. Where available, Echocardiography with Doppler should be performed in all cases of confirmed and suspected ARF.

Accordingly, in the Revised Jones Criteria for the diagnosis of ARF in the era of Doppler Echocardiography recommends: -

a) It is reasonable to consider performing follow up echocardiography/Doppler studies in any patient with diagnosed or suspected ARF even if documented carditis is not present on diagnosis.
b) Echocardiography/Doppler testing should be performed to assess whether carditis is present in the absence of auscultatory findings when ARF is considered likely.
c) Echocardiography/Doppler findings not consistent with carditis should exclude that diagnosis in patients with a heart murmur.

5.5.1 Diagnostic Criteria for Rheumatic Fever and RHD

The Revised Jones Criteria was adopted to facilitate standardization of diagnosis. In principle, the Criteria prescribes various combinations of major and minor manifestations.

Any 1 of the following can serve as evidence of a preceding GAS infection, per a recent American Heart Association (AHA) statement:

a) Increased or rising anti-streptolysin O titre or other streptococcal antibodies (anti-DNASE B). A rise in titre is better evidence than a single titre result.
b) A positive throat culture for group A β-haemolytic streptococci.
c) A positive rapid GAS carbohydrate antigen test in a child whose clinical presentation suggests a high pre-test probability of streptococcal pharyngitis.

Table 5.3: Revised Jones Criteria for Diagnosis of Acute Rheumatic Fever

A: For all patient populations with evidence of preceding GAS infection		
Diagnosis	Initial ARF	2 major manifestations or 1 major + 2 minor manifestations
	Recurrent ARF	2 major manifestations or 1 major and 2 minor manifestations or 3 minor manifestations
B: Major Criteria		
	Low-risk populations*	**Moderate- and high-risk populations**
Carditis	Clinical and/or subclinical	Clinical and/or subclinical
Arthritis	Polyarthritis only	Monoarthritis or polyarthritis Polyarthralgia
Chorea	Chorea	Chorea
Erythema marginatum	Erythema marginatum	Erythema marginatum
Subcutaneous nodules	Subcutaneous nodules	Subcutaneous nodules
C: Minor Criteria		
	Low-risk populations*	**Moderate- and high-risk populations**
Arthralgia	Polyarthralgia	Monoarthralgia
Fever	≥38.5^{0}C	≥38^{0}C
ESR and/or CRP[§]	≥60 mm in the first hour and/or CRP ≥3.0 mg/dL	≥3.0 mm/h and/or CRP ≥3.0 mg/dL
ECG	Prolonged PR interval, after accounting for age variability (unless carditis is a major criterion)	Prolonged PR interval, after accounting for age variability (unless carditis is a major criterion)

ARF indicates acute rheumatic fever; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; GAS, group A streptococcal infection.
*Low-risk populations are those with ARF incidence ≤2 per 100,000 school-aged children or all-age rheumatic heart disease prevalence of ≤1 per 1000 population per year.
§CRP value must be greater than upper limit of normal for laboratory. Because ESR may evolve during the course of ARF, peak ESR values should be used.

5.5.2 Differential Diagnosis

Table 5.4: Differential Diagnosis of Arthritis, Carditis and Chorea

Arthritis	Carditis	Chorea
• Septic arthritis (including gonococcal) • Connective tissue and other • autoimmune diseases such as • juvenile idiopathic arthritis • Viral arthropathy • Reactive arthropathy • Lyme disease • Sickle cell anaemia • Infective endocarditis • Leukaemia or lymphoma • Gout and pseudogout • Poststreptococcal reactive arthritis • Henoch-Schoenlein purpura	• Physiological mitral • regurgitation • Mitral valve prolapse • Myxomatous mitral • valve • Fibroelastoma • Congenital mitral • valve disease • Congenital aortic • valve disease • Infective endocarditis • Cardiomyopathy • Myocarditis, viral or • idiopathic • Kawasaki disease	• Drug intoxication • Wilson disease • Tic disorder • Choreoathetoid cerebral palsy • Encephalitis • Familial chorea (including • Huntington disease) • Intracranial tumour • Lyme disease • Hormonal • Metabolic (e.g. Lesch-Nyhan, • hyperalaninemia, ataxia • telangiectasia) • Antiphospholipid syndrome • Autoimmune: Systemic lupus • erythematosus, systemic • Vasculitis • Sarcoidosis • Hyperthyroidism

5.6 Management of Acute Rheumatic Fever

Management of RF/RHD involves four main steps:

1. Primary prevention- eradication of streptococci and prevention of new infections
2. Anti-inflammatory treatment
3. Supportive treatment and management of complications - This is the mainstay treatment of ARF. It includes bed rest, decreased physical activity, and good nutrition.
4. Secondary prevention- prevention of recurrent attacks

Exposure to bacteria (Group A streptococcus) **Bacterial GAS infection** (Sore throat)*	**Primordial Prevention** • Reduction in overcrowding, poverty and malnutrition • Improved access to healthcare	
Rheumatic fevers (RF)	**Primary prevention** • Treating **ALL** sore throats with antibiotics • Development of GAS vaccine	**Penicillin or Amoxycillin** If penicillin allergy give Cephalexin

Rheumatic heart disease (RHD)	**Secondary Prevention** • RF/RHD registers • Regular antibiotics for people at risk of RF recurrence	
Heart failure Complications of RHD	**Tertiary Prevention** • Medical management of symptomatic RHD • Heart surgery	

Figure 5.1: Opportunities for Intervention for RF and RHD

5.6.1 Principles of management

- Adequate penicillin for eradication for GAS.
- Anti-inflammatory treatment with steroids in severe cases of carditis and arthritis.
- The ubiquitous use of anti-inflammatory agents is thought to have masked many cases of ARF. There is still no convincing evidence that this changes the course nor natural history of the disease.
- Symptomatic treatment of cardiac failure using anti-failure medication is required in severe cases.
- In severe carditis with severe valvular regurgitation with intractable heart failure, surgery may be required.

Table 5.5: Priorities in Managing ARF

Admission to hospital
Admit all patients suspected to have severe forms of ARF
Confirmation of the diagnosis
Patients meeting the revised jones criteria for diagnosis
Treatment
Purulent Pharyngitis Single-dose IM BPG (preferable) or 10 days' oral penicillin V (IV not needed; oral erythromycin if allergic to penicillin)
Arthritis and fever Observation prior to anti-inflammatory treatment; Paracetamol and codeine can be used before confirmation of diagnosis. NSAIDs (Aspirin, naproxen or ibuprofen) for fever, arthritis or severe arthralgia or once diagnosis confirmed. Mild arthralgia and fever may respond to paracetamol alone
Chorea No treatment for cases with mild symptoms Severe chorea: Anticonvulsants (carbamazepine, valproic acid) or neuroleptics (haloperidol, risperidone). Use only one of these drugs at any one time.
Severe carditis (Heart failure) Bed rest, with mobilization as symptoms permit Urgent echocardiogram Anti-failure medication Fluid restriction Diuretics (Furosemide and spironolactone) ACE inhibitors in severe heart failure Digoxin in AF or severe heart failure Steroids for severe carditis (patients on steroids should have empirical broad-spectrum antibiotic in the 1st week) Valve surgery for life-threatening valve regurgitation in acute carditis (rare)

Long-term preventive measures
Begin secondary prophylaxis Notify case to ARF/RHD register, if available Contact local primary care staff to ensure follow-up Referral to a medical specialist Provide culturally-appropriate education to patient and family Arrange dental review and ongoing dental care to reduce risk of endocarditis
ACE-angiotensin converting enzyme; AF-atrial fibrillation; BPG-benzathine penicillin G; IM-intramuscular; IV-intravenous

5.6.2 Consideration for Admission

Most patients with ARF can be treated as outpatients. Inpatient treatment should be considered where there is:

- Severe constitutional symptoms
- Severe joint involvement
- Severe carditis
- Severe chorea
- Heart failure

5.6.3 Health Education Activities

Health education activities should address both primary and secondary prevention. These activities may be organized by trained doctors, nurses, or teachers and should be directed at the public, teachers, and parents of school-age children. Health education activities should focus on:

a. Importance of recognizing and reporting sore throats early;
b. Methods that minimize and avoid the spread of infection;
c. The benefits of treating sore throats properly; and
d. The importance of complying with prescribed treatment regimes.

5.6.4 Treatment of Streptococcal Pharyngitis: Antimicrobial therapy

- The goal of therapy is eradication of the pharyngeal streptococcal infection which is mandatory to avoid chronic repetitive exposure to streptococcal antigens.
- Ideally, two throat cultures should be performed before starting antibiotics.
- However, antibiotic therapy is warranted even if the throat cultures are negative.
- Antibiotic therapy does not alter the course, frequency, or severity of cardiac involvement [3].

Table 5.6: Antibiotic Medications for Streptococcal Pharyngitis

Agent	Paediatric dosage	Adult Dosage	Administration	Duration
Benzathine penicillin	<27kg: 0.6 MU	1.2 MU	IM	STAT
Amoxycillin	Mild to moderate pharyngitis 12.5mg/kg BD Or 10mgkg TDS Severe pharyngitis 22mg/kg BD Or 13.3mg/kg TDS	500MG TDS	PO	10 days
Erythromycin*** (if penicillin allergies)	30-50mg/kg per day in 2-4 divided doses	500mg QID	PO	10 days
Azithromycin		500mg OD	PO	5 days

*** *Oral cephalosporins preferred to oral pen ilicin (consider affordability)*

5.6.5 Anti-inflammatory Therapy

- The cornerstone of management of ARF is the suppression of the inflammatory process.
- Anti-inflammatory agents are used to control the carditis, arthritis, fever, and other acute symptoms.
- Salicylates are the preferred agents, although other nonsteroidal agents are probably equally efficacious.
- Steroids are also effective but should probably be reserved for patients in whom salicylates fail.

Table 5.7: Medication for ARF

BPG, IM	Treat streptococcal infection	900 mg (1,200,000 U) ≥20kg 450 mg (600,000 U) <20kg	Single dose
Or phenoxymethylpenicillin PO (penicillin V)	Initial treatment of streptococcal infection	Child: 250 mg, bd Adolescents and adults: 500 mg/bd	10 days
Or Erythromycin ethyl succinate, PO (only if allergic to penicillin)	Initial treatment of streptococcal infection	Child: 20 mg/kg up to 800 mg, bd Adult: 800 mg, bd	10 days
Or Erythromycin stearate, PO (only if allergic to penicillin)	Initial treatment of streptococcal infection	Child: 12.5 mg/kg up to 500 mg, bd Adult: 500 mg, bd	10 days
Azithromycin	Initial treatment of streptococcal infection	Child: 10 mg/kg, od Adult: 500 mg od day 1, then 250 mg od days 2-5	3 days 5 days
Paracetamol, PO	Arthritis or until diagnosis confirmed Arthralgia	60 mg/kg/day (max 4 g) given 4-6 doses/day; may increase to 90 mg/kg/day, if needed, under medical supervision	Until symptoms relieved or NSAID started
Aspirin*, PO	Arthritis or severe arthralgia (or when ARF diagnosis confirmed)	Begin with 50-60 mg/kg/day, increasing, if needed, up to 80-100 mg/kg/day (4-8 g/day in adults) given in 4-5 doses/day If higher doses required, reduce to 50-60 mg/kg/day when symptoms improve, and cease when symptom free for 1-2 weeks Consider ceasing in the presence of acute viral illness.	Until joint symptoms relieved
Ibuprofen, PO	Arthritis or severe arthralgia (or when ARF diagnosis confirmed)	30 mg/kg/day (max 1600 mg) given tds	As for aspirin
Prednisone or prednisolone, PO	Severe carditis, heart failure, pericarditis with effusion	1-2mg/kg/day (max. 80 mg); if used > 1 week, taper by 20-25% per week	Usually 1-3 weeks
Frusemide, PO/IV (can also be given IM)**	Heart failure	Child: 1-2mg/kg stat, then 0.5-1mg/kg/dose 6-24 hourly (max 6mg/kg/day Adult: 20-40mg/dose, 6-24 hourly, up to 250-500 mg/day.	Until failure controlled and carditis improved
Spironolactone, PO	Heart failure	1-3mg/kg/day (max 100-200 mg/day) in 1-3 doses; round dose to multiple of 6.25mg (1/4 of a tablet)	As for frusemide
Enalapril, PO	Heart failure	Child: 0.1 mg/kg/day in 1-2 doses, increased gradually over 2 weeks to max of 1 mg/kg/day in 1-2 doses Adult: initial dose 2.5 mg daily, maintenance dose 10-20mg daily (max 40mg)	As for frusemide

Captopril, PO	Heart failure	Child: initial dose 0.1 mg/kg/dose. Beware of hypotension. Increase gradually over 2 weeks to 0.5-1mg/kg/dose 8 hourly (max 2mg/kg/dose 8 hourly	As for frusemide
Lisinopril, PO	Heart failure	Child: 0.1-0.2mg/kg once daily, up to 1mg/kg/dose Adult:2.5-20mg once daily (max 40mg/day	As for frusemide
Digoxin	Heart failure/atrial fibrillation	Child: 15 mcg/kg stat, and then 5 mcg/kg after 6 hours, then 3-5mcg/kg/dose) max 125 mcg0 12 hourly Adult: 125-250mcg daily Check serum levels	Seek advice from a specialist
Haloperidol* **	Severe chorea	<12 years: 12.5- 25mcg/kg 12 hourly 12 - 18yrs: 0.5- 3mg 2-3 times daily (very severe chorea 3-5mg 2-3 times daily)	Gradual withdrawal once patient is symptom free for at least 1 month
Risperidone	Severe chorea	Only for children above 12 years Day 1: 2mg (stat) Day 2: 4mg in 1-2 divided doses daily	Gradual withdrawal once patient is symptom free for at least 1 month
Carbamazepine	Severe chorea	7-20 mg/kg/day (7-10mg/kg/day usually sufficient) given tds	Gradual withdrawal once patient is symptom free for at least 1 month
Valproic acid, po	Severe chorea (may affect salicylate metabolism)	Usually 15-20mg/kg/day (can increase to 30mg/kg/day) given tds	Gradual withdrawal once patient is symptom free for at least 1 month

KEY: bd - twice daily; BPG - benzathine penicillin G; im - intramuscular; iv - intravenous; NSAID - non-steroidal anti-inflammatory drug; po - per oral; tds - three times daily

***The optimal aspirin dose should ensure an adequate response but avoid toxicity. If symptoms of toxicity are present, they may subside after a few days despite continuation of the medication, but salicylate blood levels could be monitored if facilities are available. However, in patients who are intolerant or allergic to aspirin, ibuprofen (30mg/kg/ day) can be used.**

****More frequent dosing for severe heart failure.**

*****May cause extrapyramidal effects.**

5.6.6 The Role of Surgery in Active Rheumatic Carditis

- Surgical option in acute RF is usually limited to instances of intractable heart failure due to severe valve regurgitation.
- Usually, deferral of surgery till active inflammation has subsided is the preferred option.

5.7 Secondary Prevention and Rheumatic Heart Disease Control

Use of benzathine penicillin G (BPG) is the only RHD control strategy shown to be clinically effective and cost-effective at both community and population levels. Randomized, controlled trials (RCT) have shown that monthly administration on the same date is required to prevent recurrent ARF.

5.7.1 Secondary Prophylaxis

World Health Organisation guidelines for secondary prophylaxis duration:

Disease Classification	Duration of secondary prophylaxis
ARF (no Carditis)	Minimum of 5 years after last ARF, or until age 18 years (whichever is longer)
Mild - moderate RHD (or healed carditis)	Minimum of 10 years after last ARF, or until age 25 years (whichever is longer)
Severe RHD and after surgery	Continue for life

Secondary Prophylaxis guidelines may vary

Figure 5.2: Recommended Duration of Secondary Prophylaxis

Guidelines for Secondary Prophylaxis

Length of time for secondary prophylaxis depends on a number of factors including

- Age at first diagnosis of ARF (or RHD)
- Severity of disease
- If carditis was present with first ARF
- Time (years) since last ARF illness
- Onging risk factors (e.g. level of poverty)
- If medication is received regularly

In pregnant patients, penicillin prophylaxis should continue for the duration of pregnancy to prevent recurrent ARF. There is no evidence of teratogenicity. Erythromycin is also considered safe in pregnancy.

Table 5.8: Selection of Therapy for Secondary Prevention of Rheumatic Fever

Agent	Dosage	Route of administration
BenzathinePenicillin	Patients weighing 27 kg or less: 600,000 units every 4 weeks. Patients weighing more than 27 kg: 1,200,000 units every 4 weeks	Intramuscular
Penicillin V	250 mg BD	Orally
Azithromycin (if penicillin allergies)	250mg OD	Orally
Erythromycin	250mg BD	Orally

5.8 Management of Rheumatic Fever at Different Levels of Care

Table 5.9: Valvular Lesions in Chronic RHD

Level of Service	Services offered	Requirements
Level 1	1. Health education 2. Behaviour change communication Surveil- 3. lance and referral of children with fever and sore throat	IEC materials Sensitization and support of CHW activities
Level two and three	1. Detect streptococcal sore throat Treat sore 2. throat /streptococcal URTI as per the guide-lines 3. Provide secondary prophylaxis for patients with RF to prevent recurrence 4. Detect ARF using the revised Jones criteria and refer 5. Detect heart conditions and refer Carry out epidemiological surveillance	Training of health care providers on the guide-lines Job aids Reliable light source (e.g. solar torches) and spatulas Essential drugs such as penicillin and alterna-tives such as erythromycin Lab support- Throat swabs Data collection tools
Level four and five	1. All activities under level two and three Detec-tion, treatment and follow up RF and RHD 2. Development of a comprehensive manage-ment plan including referral instructions upwards and downwards Epidemiological surveillance 3. Definitive cardiac surgery (at level five)	Training of personnel on the guidelines A functional laboratory Imaging services; 2D echo with appropriate probes, TEE probe CT scans and MRI, Catheterization laboratory. Job Aids Essential drugs Consumables both surgical and medical
	All activities in level four and five Interventional cardiology	Case specific surgical management and refer-ral management protocols Training of accredited courses in cardiovascu-lar disease Research in cardiovascular diseases

5.9 Rheumatic Heart Disease

RHD is sequelae of poorly managed or undiagnosed RF. It evolves over 2-10 years following repeated episodes of RF. The hallmark of this condition is the development of valvular heart lesions.

5.9.1 Clinical Presentation and Recommendations

Table 5.10: Valvular Lesions in Chronic RHD

Valve lesion	Symptoms	Signs
Mitral stenosis	• Fatigue • Dyspnoea • Palpitation • Cough • Haemoptysis • Oedema • Ascites • Chest pain	• Atrial fibrillation • Mitral facies (flushed cheeks) • Crepitations • Diastolic murmur • Loud P2

Mitral regurgitation	• Fatigue • Cough • Palpitation • Oedema • Ascites • Dyspnoea	• Atrial fibrillation • Cardiomegaly • Apical pansystolic murmur • Crepitations • Signs of RHF (oedema, ascites, hepatomegaly)
Aortic regurgitation	• If mild to moderate it is asymptomatic • Palpitation • Breathlessness • Angina	• Large volume or collapsing pulse • Femoral bruit (Duroziez's sign-gradual pressure over femoral artery with stethoscope leads to audible bruit) • Capillary pulsationon light compression of nail bed (Quincke's) sign • Bounding periphery pulse • Head nodding (De Musset's sign-head bobbing with each heartbeat) • Murmurs: systolic murmurs (soft mid diastolic murmur (Austin Flint murmur)
Aortic Stenosis	Mild to moderate –asymptomatic • Dyspnoea • Angina • Exertion syncope • Angina • Episodes of acute pulmonary oedema	• Injection systemic murmur • Slow carotid pulse • Narrow pulse pressure • Thrusting apex beat • Crepitations
Tricuspid regurgitation/ Tricuspid Stenosis	• Oedema • Ascites • Exercise intolerance • Angina (rare; due to RV overload and strain) • Symptoms of heart failure if is underlying cause	• S3 gallop • Jugular venous distention with a prominent V wave • In some patients, a pansystolic murmur • Diminished peripheral pulse volume secondary to impaired forward blood flow; • Right ventricular heave and S 4 gallop that increases with inspiration • Ascites • Peripheral oedema • Cachexia and jaundice • Atrial fibrillation • Pulmonary rales if TR is associated with LV dysfunction or MS

Recommendation

Stabilize the patient and consult or refer to a physician/ paediatrician for definitive diagnosis and management plan.

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6

6. INFECTIVE ENDOCARDITIS

Key Messages

- A high index of suspicion is required for diagnosis based on clinical presentation, as delays in initiating treatment can have serious outcomes.
- Antibiotics should be initiated early after drawing blood for cultures. Results of the culture should then dictate the optimal antibiotics to be used in the remaining phase of treatment, typically 4-6 weeks.
- Surgery should be done early for those with appropriate indications.
- Antibiotic prophylaxis should be individualized based on patient characteristics and based on these guidelines.

6.1 Introduction

Infective endocarditis (IE) is an infection of the endocardial surfaces of the heart, usually of one or more cardiac valves; to a lesser degree the mural endocardium; or a septal defect. IE may lead to severe valvular insufficiency, intractable congestive heart failure, and myocardial abscesses.[1]

6.2 Epidemiology

In a recent meta-analysis of studies from Africa, rheumatic heart disease (RHD) was the most common risk factor for infective endocarditis in adults, whereas congenital heart disease was the most common risk factor for infective endocarditis in children.[1] Microbiological testing (mostly blood cultures) was positive in half of patients with infective endocarditis, with Staphylococcus species and Streptococcus species as the most commonly identified microorganisms.

6.3 Risk Factors for Developing IE

- Heart valve disease, commonly RHD
- Previous heart valve surgery
- Congenital heart disease
- Intravenous drug use
- Previous history of IE
- Indwelling vascular catheters

The table below summarises cardiac and non-cardiac risk factors for development of infective endocarditis.

Table 6.1: Cardiac and Non-Cardiac Risk Factors[2]

Cardiac risk factors
Previous infective endocarditis
Valvular heart disease
Prosthetic heart valve
Central venous or arterial catheter
Transvenous cardiac implantable electronic device
Congenital heart disease
Non-cardiac risk factors
Central venous catheter
People who inject drugs
Immunosuppression
Recent dental or surgical procedures
Recent hospitalization
Haemodialysis

Adapted from the 2023 ESC Guidelines for Management of Endocarditis[2]

6.4 Diagnosis

6.4.1 History and Physical Examination

- Clinical features of infective endocarditis are highly variable and require a high index of suspicion.
- May present with associated complications such as stroke.

Table 6.2: Clinical Presentation of Infective Endocarditis

Symptoms	Signs

• Fever and chills (most common).
• Anorexia
• Weight loss
• Malaise
• Headache
• Myalgias
• Night sweats
• Shortness of breath
• Cough
• Asymmetrical/monoarticular joint pains
• Primary cardiac disease may present with symptoms of congestive heart failure due to valvular insufficiency.
• Secondary embolic phenomena causing vascular obstruction (in up to 20% cases). Could include:
  • Acute meningitis
  • Focal neurologic complaints (e.g., hemiplegia) due to an embolic stroke or
  • Back pain associated with vertebral osteomyelitis
  • Unilateral blindness
  • Painless haematuria
  • Angina/MI
• Dyspnoea, cough, and chest pain are common complaints of intravenous drug users (This is likely related to the predominance of tricuspid valve endocarditis in this group and secondary emboli to the pulmonary vasculature.)
	• Fevers
	• Cardiac murmurs
	• Change in a pre-existing murmur
	• Classical signs:
	  • Petechiae
	  • Subungual (splinter) haemorrhages - dark red linear lesions in the nail beds
	  • Osler nodes - tender subcutaneous nodules usually found on the distal pads of the digits
	  • Janeway lesions – non-tender maculae on the palms and soles
	  • Roth spots - retinal haemorrhages with small, clear centres; rare and observed in only 5% of patients.
	• Signs of congestive heart failure, such as distended neck veins, frequently are due to acute left-sided valvular insufficiency.
	• Splenomegaly may be present in patients with longstanding disease.
	• Other signs include the following:
	  • Stiff neck
	  • Delirium
	  • Paralysis, hemiparesis, aphasia
	  • Conjunctival haemorrhage
	  • Pallor
	  • Gallops
	  • Rales
	  • Cardiac arrhythmia
	  • Pericardial or pleural friction rub

6.4.2 Investigations

1) Blood cultures: collect at least three sets of blood samples, each containing 10 mL, from three different sites at least 30 minutes apart and before starting antibiotic treatment. These samples should be incubated in both aerobic and anaerobic conditions and obtained from a peripheral vein rather than a central venous catheter to minimize the risk of contamination and misinterpretation, using strict sterile techniques.
2) Full blood count- look out for (normocytic normochromic) anaemia, leucocytosis - neutrophilia.
3) C- reactive Protein or Procalcitonin (PCT) may be elevated.
4) Erythrocyte sedimentation rate (ESR)- elevated.
5) Urinalysis- proteinuria, microscopic haematuria.
6) Transthoracic Echocardiography (TTE) - visible vegetations, abscesses. In suspect cases where TTE is normal, do Transoesophageal echocardiography (TEE).
7) Chest radiography - pulmonary pyogenic lesions due to emboli may be visualized.

8) Renal function tests –patient may develop kidney failure.
9) Other studies based on individual symptomatology e.g., CT scan of the head for patients with CNS manifestations.

6.4.3 Diagnostic Criteria for IE

Table 6.3: Diagnosis of infective endocarditis (Adapted from the 2023 ESC Guidelines)[2]

Major Criteria
1. Major blood culture criteria a) Two separate blood cultures positive for organisms found in patients with IE: oral streptococci, Streptococcus gallolyticus (formerly S. bovis), a HACEK group organism, community acquired S. aureus, E. faecalis b) Blood cultures persistently positive for one of the above organisms: • ≥2 positive blood cultures of blood samples drawn >12 hours apart. • All of 3 or a majority of ≥4 separate cultures of blood (with first and last samples drawn ≥1 hour apart). c) Single positive blood culture for C. burnetii or phase IgG antibody titre >1:800 2. Major imaging criteria Valvular, perivalvular/periprosthetic and foreign material anatomic and metabolic lesions characteristic of IE detected by any of: • Echocardiography (TTE and TOE) • Cardiac CT • [18F]-FDG-PPET/CT(A)
Minor Criteria
1. Predisposing conditions, i.e., predisposing heart condition at high or intermediate risk of IE or people who inject drugs. 2. Fever defined as temperature >38°C 3. Embolic vascular dissemination, including asymptomatic events detected by imaging only: • Major systemic and pulmonary emboli/infarcts and abscesses • Haematogenous osteoarticular septic complications (i.e., spondylodiscitis) • Mycotic aneurysms • Intracranial ischaemic/haemorrhagic lesions • Conjunctival haemorrhages • Janeway's lesions 4. Immunological phenomena: • Glomerulonephritis • Osler's nodes and Roth spots • Rheumatoid factor 5. Microbiological evidence: • Positive blood culture but does not meet a major criterion as noted above • Serological evidence of active infection with organism consistent with IE

Adapted from 2023 ESC Guidelines for management of endocarditis

Table 6.4: Diagnostic Criteria for Infective Endocarditis[2]

IE CLASSIFICATIOIN (at admission and during follow-up)
Definite: • 2 major criteria • 1 major criterion and at least 3 minor criteria • 5 minor criteria Possible: • 1 major criterion and at least 1 criteria • 3 – 4 minor criteria Rejected: • Does not meet criteria for definite or possible at admission with or without a firm alternative diagnosis.

Adapted from 2023 ESC Guidelines for the management of endocarditis

Algorithm for Diagnosis of Native Valve IE

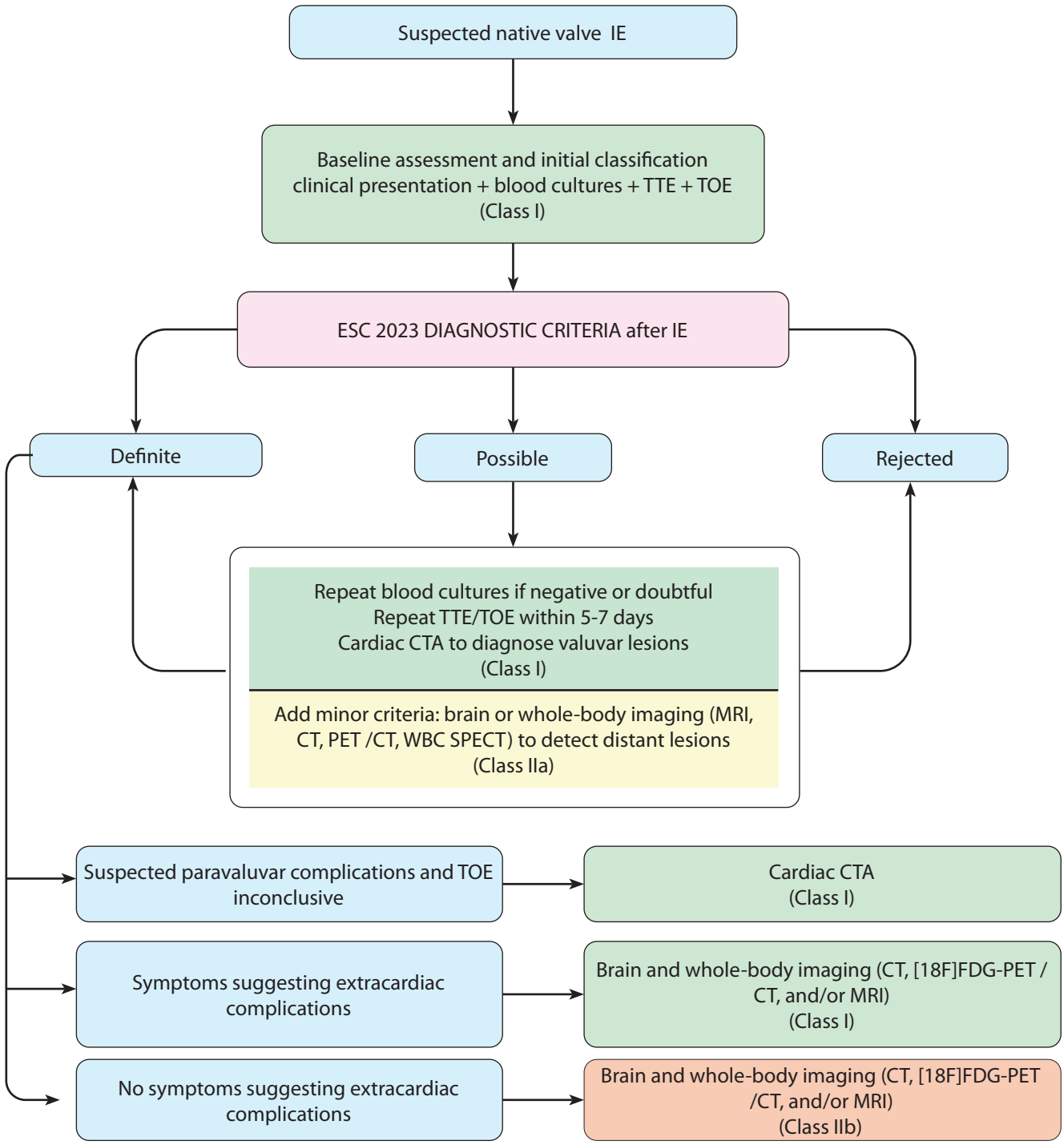

Figure 6.1: Diagnostic Algorithm for Diagnosis of Infective Endocarditis

Adapted from 2023 ESC Guidelines for the management of endocarditis

6.5 Management of Infective Endocarditis

The primary goals of therapy for infective endocarditis (IE) include to:

1. Eradicate infection, including sterilizing vegetations.
2. Address the complications of valvular infection.
3. Address Intracardiac complications
4. Manage Extra-cardiac consequences of IE.

Emergency care should focus on making the correct diagnosis and stabilizing the patient with acute disease and cardiovascular instability. General measures include the following:

- Treatment of congestive heart failure
- Oxygen
- Start empirical therapy
- Bed rest. Limitations to physical activity may also be compounded by the severity of the illness, complications (e.g., stroke), and the presence of significant congestive heart failure.

6.5.1 Antibiotic Therapy

Table 6.5: Antibiotic Treatment of Infective Endocarditis Due to Streptococcus Group

Antibiotic	Dosage and route	Comments
Strains penicillin-susceptible (MIC ≤ 0.125 mg/L) oral and digestive streptococci		
Standard treatment: 4-week duration		
Penicillin G Or Ceftriaxone	12-18 million U/day i.v either in 4-6 doses or continuously 2g/day i.v. or i.m. in 1 dose Pediatric doses Penicillin G 200,000 U/kg/day i.v. in 4-6 doses Cefriaxone 100 mg/kg/day i.v. or i.m. in 1 dose	Preferred in patients 65 years or with impaired renal or VIII (Vestibulocochlear) cranial nerve functions. 6-week therapy recommended for patients with prosthetic valve endocarditis (PVE)
Standard treatment: 2-week duration		
Penicillin G or Ceftriaxone combined with Gentamicin	12–18 million U/day i.v. either in 4–6 doses or continuously Ceftriazone ;2g/day i.v. or i.m. in 1 dose Gentamycin; 3 - 5 mg/kg/ dose i.v. or i.m. in 3 dose Paediatric doses: Penicillin G and ceftriaxone as above Gentamicin 1 month to 12 yr ; 2 .5mg/kg/ dose i.v. or i.m. in 3 Doses 12-18 yrs; 2mg/kg every 8 hrs	Only recommended in patients with non-complicated native valve endocarditis (NVE) with normal renal function.
In beta-lactam allergic patients		
Vancomycin	30 mg/kg/day i.v. in 2 doses Paediatric doses: Vancomycin 40 mg/kg/day i.v. in 2 or 3 equally divided doses	6-week therapy recommended for patients with PVE
Strains relatively resistant to penicillin (MIC 0.250–2 mg/l)k		
Standard treatment		

Penicillin G	24 million U/day i.v. either in 4–6 doses or continuously	6-week therapy recommended for patients with PVE

Antibiotic	Dosage and route	Comments
Strains penicillin-susceptible (MIC ≤ 0.125 mg/L) oral and digestive streptococci		
Standard treatment: 4–6-week duration		
Penicillin G Or Ceftriaxone	12-18 million U/day i.v either in 4-6 doses or continuously 2g/day i.v. or i.m. in 1 dose Pediatric doses Penicillin G 200,000 U/kg/day i.v. in 4-6 doses Cefriaxone 100 mg/kg/day i.v. or i.m. in 1 dose	
In beta-lactam allergic patients		
Vancomycin	30 mg/kg/day i.v. in 2 doses Paediatric dosage Vancomycin 40 mg/kg/day i.v. in 2 or 3 equally divided doses	6-week therapy recommended for patients with PVE
Strains relatively resistant to penicillin (MIC 0.250–2 mg/l)k		
Standard treatment		
Penicillin G or	24 million U/day i.v. either in 4–6 doses or continuously	6-week therapy recommended for patients with PVE

IM, intramuscular; IV, intravenous; MIC, minimum inhibitory concentration

6.5.2 Indications for Surgery in IE

Table 6.6: Indications and Timing of Surgery for IE

Indications for surgery	Timing
1. Acute heart failure	
Persistent heart failure, particularly if Aortic valve is involved	
Aortic or mitral NVE or PVE with severe acute regurgitation, obstruction or fistula causing refractory pulmonary oedema or cardiogenic shock	**Emergency**
Aortic or mitral NVE or PVE with severe regurgitation or obstruction causing symptoms of HF or echocardiographic signs of poor haemodynamic tolerance	**Urgent**
2. Uncontrolled infection	
Locally uncontrolled infection (abscess, false aneurysm, fistula, enlarging vegetation)	**Urgent**
Infection caused by fungi or multi-resistant organisms	**Urgent/elective**
Persisting positive blood cultures despite appropriate antibiotic therapy and adequate control of septic metastatic foci	**Urgent**

PVE caused by staphylococci or non-HACEK gram-negative bacteria	**Urgent/elective**
3. Prevention of embolism	
Aortic or mitral NVE or PVE with persistent vegetations >10 mm after one or more embolic episodes despite appropriate antibiotic therapy	**Urgent**
Aortic or mitral NVE with vegetations >10 mm, associated with severe valve stenosis or regurgitation, and low operative risk	Urgent
Aortic or mitral NVE or PVE with isolated very large vegetations (>30 mm)	Urgent
Aortic or mitral NVE or PVE with isolated large vegetations (>15 mm) and other indication for surgery-	Urgent
Emergency surgery: surgery performed within 24 h; urgent surgery: within a few days; elective surgery: after at least 1–2 weeks of antibiotic therapy. HACEK = Haemophilus parainfluenzae, Haemophilus aphrophilus, Haemophilus paraphrophilus, Haemophilus influenzae, Actinobacillus actinomycetemcomitans, Cardiobacterium hominis, Eikenella corrodens, Kingella kingae and Kingella denitrificans; NVE = Native Valve Endocarditis, PVE = Prosthetic Valve Endocarditis	

6.5.3 Indications for Antibiotic Prophylaxis

Prior to certain dental procedures that involve manipulation of gingival tissue or the periapical region of teeth, or perforation of the oral mucosa for patients with heart valve disease who have any of the following:

- Prosthetic cardiac valves, including transcatheter-implanted prostheses and homografts.
- Prosthetic material used for heart valve repair, such as annuloplasty rings, chords, or clips.
- Previous IE.
- Unrepaired cyanotic congenital heart defect (birth defects with oxygen levels lower than normal) or repaired congenital heart defect, with residual shunts or valvular regurgitation at the site adjacent to the site of a prosthetic patch or prosthetic device.
- Cardiac transplant with valve regurgitation due to a structurally abnormal valve.

Antibiotic prophylaxis may also be considered in high risk patients with rheumatic valvular regurgitant lesions based on clinical acumen or local experience.

In addition, antibiotic prophylaxis is not recommended for patients with valvular heart disease who are at high risk of IE for non-dental procedures (e.g., TEE, esophagogastroduodenoscopy (OGD), colonoscopy, or cystoscopy) in the absence of active infection.

Table 6.7: Recommendations for Prophylaxis of IE in High-Risk Patients according to the Type of Procedure[2]

A. Dental procedures
Antibiotic prophylaxis should only be considered for dental procedures requiring manipulation of the gingival or periapical region of the teeth or perforation of the oral mucosa.
Antibiotic prophylaxis is not recommended for local anaesthetic injections in non-infected tissues, treatment of superficial caries, removal of sutures, dental X-rays, placement, or adjustment of removable prosthodontic or orthodontic appliances or braces or following the shedding of deciduous teeth or trauma to the lips and oral mucosa.
B. Respiratory tract procedures
Antibiotic prophylaxis is not recommended for respiratory tract procedures, including bronchoscopy or laryngoscopy, or trans nasal or endotracheal intubation
C. Gastrointestinal or urogenital procedures or TOE
Antibiotic prophylaxis is not recommended for gastroscopy, colonoscopy, cystoscopy, vaginal or caesarean delivery or TOE
D. Skin and soft tissue procedures
Antibiotic prophylaxis is not recommended for any procedure
E. Cardiac or vascular procedures
Perioperative prophylaxis is recommended before placement of a pacemaker or implantable cardioverter defibrillator
Perioperative antibiotic prophylaxis should be considered in patients undergoing surgical or transcatheter implantation of a prosthetic valve, intravascular prosthetic, or other foreign material
For patients undergoing surgical procedures involving infected skin (including oral abscesses), skin structure or musculoskeletal tissue, it is reasonable that the therapeutic regimen contains an agent active against staphylococci and beta-haemolytic streptococci.

Prophylactic Drugs

Table 6.8: Drugs of Choice for Prophylaxis of IE

Situation	Antibiotic	Adults	Children
No allergy to penicillin	Amoxicillin	2g orally 6 hours preoperatively or intravenously at the start of procedure	50mg/kg orally
	Ceftriaxone	1 g	50 mg/kg intravenously
Allergy to penicillin	**Clindamycin**	**600 mg orally or**	**20 mg/kg orally or intravenously**

6.6 Complications

- The complications of IE affect the cardiac, or extra-cardiac structures if the cause is embolic (due to treatment or because of sepsis.)
- The common complications are:
    - Congestive heart failure, which has the biggest impact on prognosis.
    - Peri annular abscesses.
    - Systemic emboli.
    - Neurological complications.
    - Splenic abscesses and mycotic aneurysms are rare.

6.7 Patient Follow-up

- This is important because of the heightened risk for future endocarditis, typically within 6 months.
- Advise on warning signs of septic embolization should be given across the board, and patients who have chronic heart failure, pacemakers, or have had peripheral embolization should take extra precautions.

Patient Referral

If the current facility is unable to institute the appropriate investigations/management, then upward referral to a more capable facility is warranted urgently.

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7

7. CONGENITAL HEART DISEASE

Key Messages

- Patients suspected to have CHD should be referred as soon as possible to a paediatrician/ cardiologist for a definitive diagnosis and management plan.
- Patients need follow up for life.

7.1 Definition of Congenital Heart Disease

Congenital heart disease (CHD) is a range of birth defects that affect the normal working of the heart. It may be a structural anomaly of the heart or great vessels, or it could be of functional significance. It is the most common congenital disorder in newborns.

7.2 Aetiology

The defects occur mostly at about the fifth week of pregnancy during the development of the heart. The causes are mostly unknown but may be associated with an increased incidence in the following perinatal conditions:

Table 7.1: Perinatal conditions associated with increased incidence of congenital heart disease

Infectious causes	Non-infectious causes
• Toxoplasmosis • Rubella • Syphilis • Herpes • Cytomegalovirus Varicella Parvovirus B19	• Chromosomal abnormalities* (e.g., Downs syndromes) • Phenylketonuria (PKU) • Alcohol abuse • Anti-convulsion medications such as phenytoin sodium, benzodiazepines • Acne medications such as topical retinoids and isotretinoin • Organic solvents such as nail polish and glue • Poorly controlled maternal diabetes

*Babies with chromosomal abnormalities e.g., Down's Syndrome have a higher incidence of CHD as compared to normal babies

7.3 Epidemiology

It is estimated that 8-12 in 1000 live births worldwide have a congenital heart disease. About 50% of these children die within one month of age from critical congenital heart disease (1). In Africa, the prevalence of CHD in different countries showed; Cameroon (13.1%), Mozambique (2.3 per 1000), and Nigeria (9.3%). The defects were predominantly ventricular septal defects (VSD) and Tetralogy of Fallot (TOF) [(1)].

Kenya has hardly any data on the prevalence of CHD. However, there was a study published in 1996 where echocardiography done on 1115 school going children found CHD in 2 of them. The lesions found were secundum atrial septal defect (ASD) and VSD with pulmonary stenosis [(3)].

7.4 Classification of CHD

CHD is generally classified based on how the patients present. This is true for both adults and children. They are broadly classified into 2 groups:

1. Cyanotic: CHD with visible central cyanosis (bluish discolouration of the skin/mucous membranes) often associated with finger clubbing
2. Acyanotic: Congenital heart disease with no cyanosis

The most common acyanotic congenital heart defects are:

1. patent ductus arteriosus (PDA),
2. ventricular septal defect (VSD),
3. secundum atrial septal defect (ASD).

Tetralogy of Fallot (TOF) is the most common of the cyanotic heart defects identified [2].

The adult congenital heart disease population includes those who have:

1. Never undergone cardiac surgery,
2. Have undergone cardiac surgery/intervention and require no further operation/interventions,
3. Have had palliative surgery with or without anticipation of reparative surgery,
4. Inoperable defects needing organ transplant.

Majority of congenital heart diseases are simple and correctable hence the need for a national screening and care program. Early diagnosis improves chances of better outcomes with intervention.

7.5 Clinical Presentation

Patients often present with recurrent respiratory tract infections, excessive sweating, easy fatiguability, recurrent fainting, poor growth, or cyanosis depending on the heart defect present.

The illustration below outlines the common symptoms and signs at presentation.

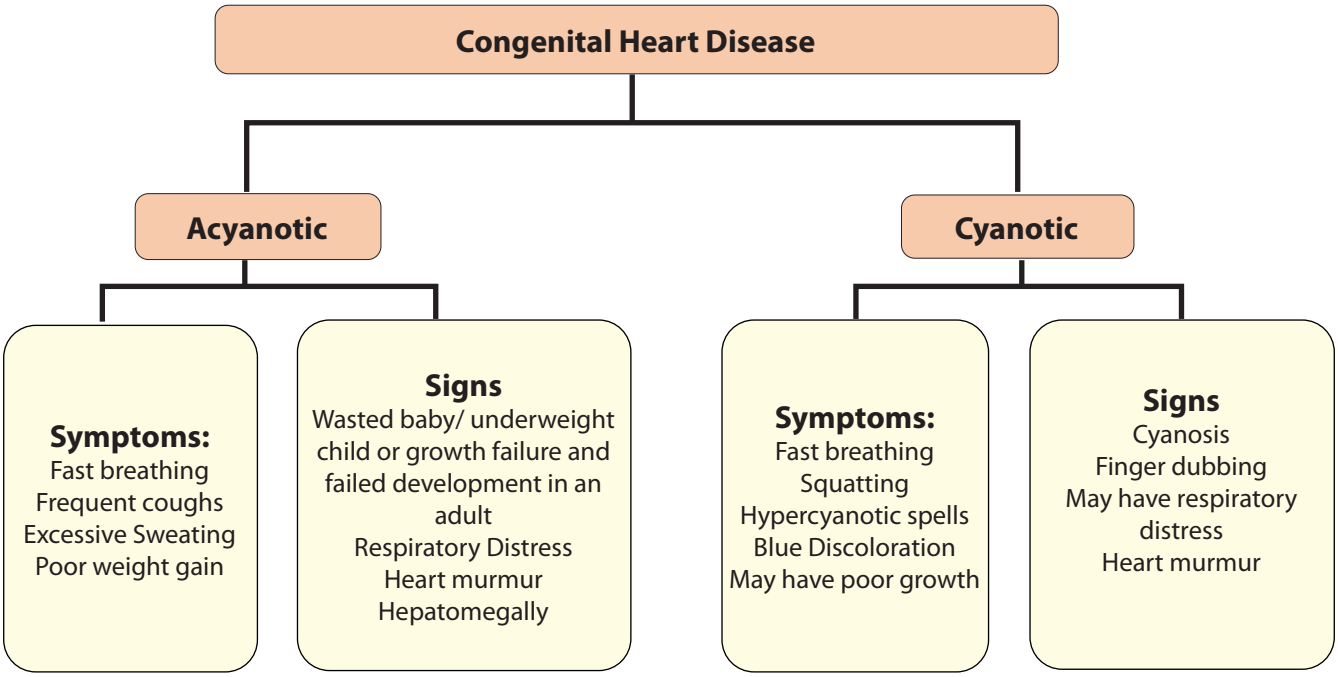

Figure 7.1: Classification and presentation of CHD

7.6 Diagnosis: History, Physical Examination, Laboratory, and Imaging Investigations

Children suspected to have CHD should be referred to a Paediatric specialist/Cardiologist for confirmation of the diagnosis. The following investigations are recommended for accurate diagnosis:

i. Haemogram
ii. Chest radiograph
iii. Echocardiogram
iv. Electrocardiogram if indicated
v. For some selected cases: Cardiac catheterization, Cardiac CT/MRI

7.7 Patient Referral

Patients suspected to have CHD should be referred to a paediatrician/cardiologist for definitive diagnosis and management plan.

7.8 Management

- Management may be non-pharmacological, pharmacological, or surgical.
- This will be based on the diagnosis and the clinical state of the child.
- For infants with critical cardiac lesions, the risk of morbidity and mortality increases when there is a delay in diagnosis and timely referral to a tertiary centre with expertise in treating these patients.
- Supportive care will include nutritional care, management/prevention of other complications, and psychosocial support.
- Pharmacological management will involve treating heart failure and/or preventing complications. If the child is in heart failure manage the heart failure as per the heart failure management guidelines and based on the diagnosis. For appropriate drug dosing refer to the drug index.
- Definitive care may involve catheterization interventions or surgery based on the diagnosis by the paediatric cardiologists.

7.9 Complications

The complications are varied and may include:

- Heart failure
- Failure to thrive
- Infective endocarditis
- Cardiovascular accidents (stroke)
- Death

7.10 Patient Follow-up

Patients with CHD need follow up for life. Once the diagnosis is made, the Paediatric Cardiologist will make a management and follow-up plan. While some patients will require continued follow-up by the Paediatric Cardiologist, some may be referred back to lower facilities after intervention with their follow up plan.

7.11 Prevention

- While causes of congenital heart diseases remain largely unknown, it is important to avoid and manage the known risk factors such as teratogens and infections in pregnancy. This will entail appropriate antenatal care.
- Regular medical check-ups for women of childbearing age to identify and manage any risk factors. Ideally a medical check-up should be done before pregnancy for screening of any infections and appropriate treatment where applicable.
- Health education to avoid teratogens
- Adequate management of diabetes before and during pregnancy will reduce the incidence of severe congenital heart defects such as Tetralogy of Fallot, truncus arteriosus and transposition of the great arteries amongst women with diabetes.
- Genetic counselling. There is an increased incidence of congenital heart disease in children of patients with congenital heart disease and their first-degree relatives.
- Talk about consanguinity if culture permits marriage in the clan/family.

7.12 Recommendations for Delivery of Care

These patients require prompt diagnosis and referral to specialists in tertiary levels for development of a management plan (both short term and long term). There is room for follow up in lower levels of care depending on the individual case management plan.

Table 7.2: Management by level of care

Resource Needed	Level 2 and 3	Level 4	Level 5 and 6
Personnel	• Nurses • Clinical officers • Nutritionist • Medical Officer	Cadres in levels 2 & 3, plus: • Physician • Paediatrician • Clinical Pharmacist • Echo-cardiographers	Cadres in levels 2, 3, & 4, plus: • Paediatric Cardiologist • Perfusionists • Cardiac anaesthetists • Specialised nurses • Cardiothoracic surgeons
Equipment	• BP Machine • Stethoscope • Weighing scale • Height meter Thermometer • CVD risk assessment tools • Strips for urinalysis • Glucometer • X ray machine	Equipment in levels 2 & 3, plus: • ECG machine • Echo screening machine*** • Blood analysis: • -Biochemistry: • FBS, UEC, lipid profile • -Haematological	Equipment in levels 2, 3, & 4, plus: • High specification Echo machine • Ophthalmoscope • Cardiac catheterisation lab • Ambulatory BP • 24 hr Holter machine • Treadmill • Facilities for telemedicine • A critical care unit
Drugs	• Furosemide • Oxygen	All in levels 2 & 3, plus: • Oxygen • Beta blockers* • ACEi* • CCBs (sustained release formulations) • Aspirin • Warfarin • Spironolactone • Digoxin*	All in levels 2, 3 & 4, plus:** • Dopamine • Dobutamine • Sildenafil • Labetalol • Adenosine • Adrenaline • Nitroglycerine
Services	• Detection • Referral • Prophylaxis services	Services in levels 2 & 3, plus: • Treatment of co- morbid general medical conditions (anaemia, heart failure, infections, oxygen for cyanosis) • Comprehensive Care • Referral	• Diagnostic / Intervention Cardiac catheterisation and open-heart surgery • Treatment of non-cardiac and cardiac surgical complications • Management of pregnancy in a cardiac patient including safe delivery • Rehabilitation and follow-up • Training
BP, blood pressure; ECG, electrocardiogram; CVD, cardiovascular disease; FBS, fasting blood sugar; UEC, urea, electrolytes, creatinine; ACEi, angiotensin converting enzyme inhibitors; CCB, calcium channel blockers. *prescribed by paediatrician. **any other medications as deemed fit by cardiac teams in various facilities ***a machine that is not elaborate but functions adequately for screening of heart lesions. There is need to build capacity across all levels of care. This entails training of more cardiologists, specialized nurses, and echo-cardiographers. In addition, there needs to be adequate infrastructure, specifically open-heart surgery.			

Table 7.3: Heart Failure Medications for Children

Drugs for Management of Heart Failure in children and their common side effects				
Class	**Examples**	**Usual starting dose**	**Maximum daily dose**	**Possible side effects**
Diuretic	Furosemide	1mg/kg/dose	QID	Hypokalaemia Hyponatraemia Hypotension Ototoxicity
	HCTZ	2mg/kg/d divided BD	QID	
MRA	Spironolac-tone	1mg/kg OD	3.3mg/kg	Hypotension Hyperkalaemia Hyponatraemia Gynaecomastia
ACE inhibitor Captopril 0.1mg/kg/d PO divided q8h 0.5 mg/kg/d				Cough (ACEI) Hyperkalaemia Hypotension Increased serum creatinine Angioedema Cardiac Arrythmia.Bradycardia
	Enalapril	0.1 mg/kg/d PO divided OD/BD	0.5 mg/kg/d	
Digitalis	*Digoxin	From preterm infants: 0.005 mg/kg/d PO divided BD or 75% of this dose IV From age 10yr: 0.005 mg/kg/d PO QID or 75% of this dose IV		
Beta blockers	Carvedilol	0.2mg/kg/dose PO BD; initiate with lower dose and gradually increase dose every 2-3 weeks to therapeutic range	0.4 mg/kg/dose	Aggravated CHF Malaise Hypo-tension Bradycardia
	Propanolol	0.5mg/kg/dose given BD	1mg/kg/dose	Bradycardia Hair loss Malaise Diarrhoea
CCB: Calcium channel blocker; ACE: angiotensin converting enzyme; HCTZ: Hydrochlorothiazide; MRA: Mineralocor-ticoid receptor antagonists; OD: administer once daily; BD: administer twice daily(12-hourly); TDS: administer 3 times daily (8-hourly); QID: administer 4 times daily (6-hourly)				

7.13 Further Recommendations

Infant Screening for CHD.

All infants should be subjected to a simple screening process as follows:

- Midwife to auscultate the baby's heart with a stethoscope
- Nurse should palpate for pulses in both upper and lower limbs
- Pulse oximetry – see the protocol below:

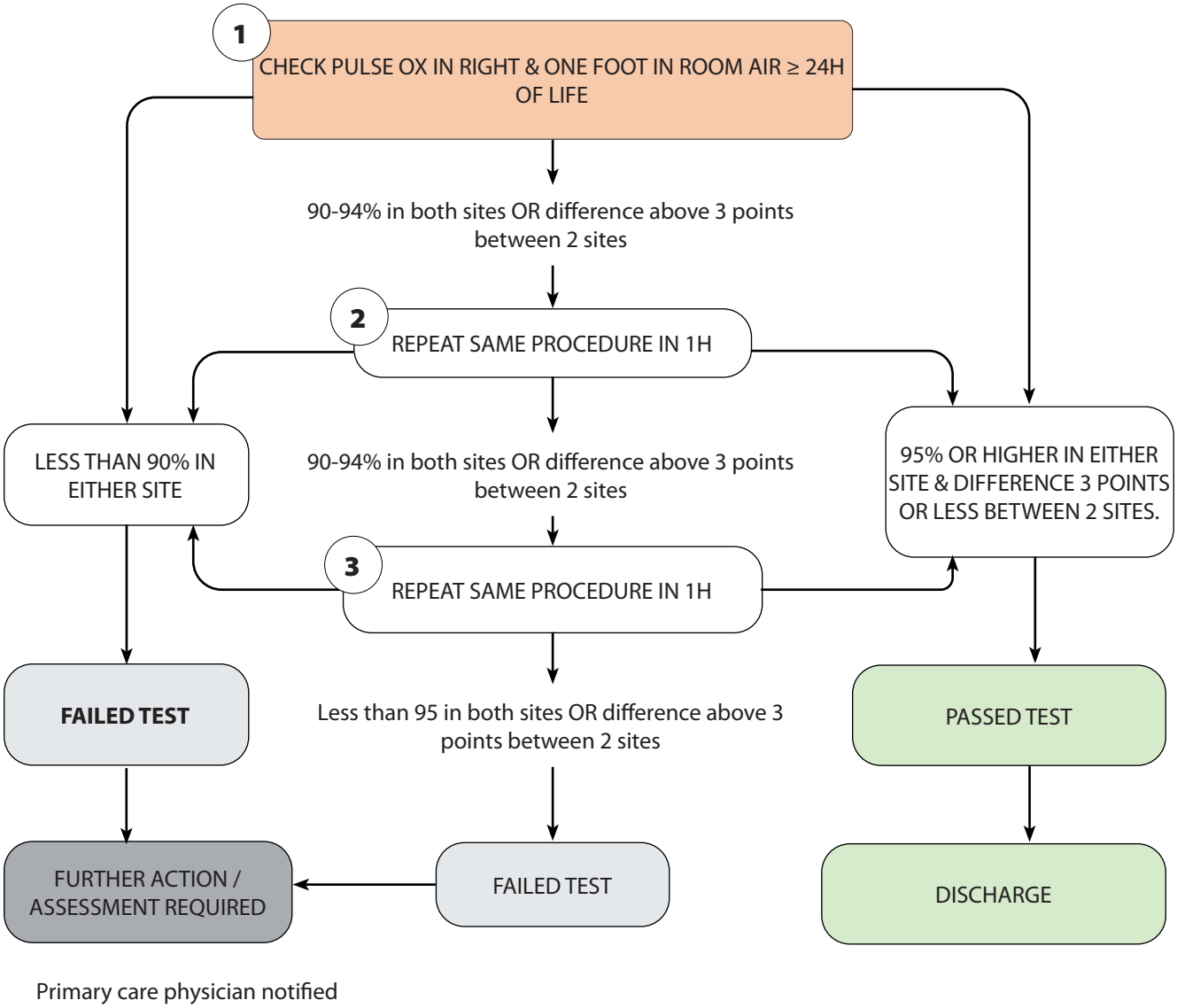

Figure 7.2: Pulse Oximetry Protocol for Screening for CHD in Neonates

Babies suspected to have CHD should be reviewed by the clinical officer, medical officer, or paediatrician/cardiologist (depending on level of facility) before discharge.

Infective endocarditis prophylaxis

Counselling of family/care givers of patients with CHD by health care provider should include education on endocarditis prophylaxis measures where necessary as follows:

- Antibiotic prophylaxis is recommended before urethral instrumentation and/or dental procedures that involve manipulation of gingival tissue, the peri-apical region of teeth or perforation of the oral mucosa. This is in patients with CHD with the highest risk for adverse outcome from Infective Endocarditis (IE), such as:
  - I. Prosthetic cardiac valve or prosthetic material used for cardiac valve repair.
  - II. Previous IE.
  - III. Unrepaired and palliated cyanotic CHD, including surgically constructed palliative shunts and conduits.
  - IV. Completely repaired CHD with prosthetic materials, whether placed by surgery or by catheter intervention, during the first 6 months after the procedure.

Guidelines for physical exertion

- Participation in regular exercise has a well-documented benefit for fitness, psychological well-being, and social interaction, as well as having a positive effect on the future risk of acquired heart disease.
- Recommendations for exercise and sports need to be based on the patient's ability, the impact on underlying haemodynamics, and the risk of acute decompensation and arrhythmias.
- Counselling should be based on the type of sport and the anticipated effort levels. As a general recommendation, dynamic exercise such as walking is more suitable than static exercise such as weightlifting.
- In patients with known cardiac conditions, with advised levels of exercise; sudden death during exercise is very rare.

Information for contraception and pregnancy

- All women with CHD whether treated or untreated should seek medical advice before getting pregnant.
- Counselling before pregnancy is important and should include genetic evaluation for the couple.
- Specifically for women of childbearing age, assessment of the following should be done before pregnancy:
  I. potential foetal risk,
  II. risk of prematurity or low birth weight in the offspring,
  III. review of medications that may be harmful to the foetus,
  IV. appropriate counselling and management of anticoagulation especially for women receiving chronic anticoagulation with warfarin to enable them to make an informed decision about maternal and foetal risks
  V. discussion of potential maternal complications.

If pregnancy occurs,

- Foetal echocardiography is recommended, and its consequences should be discussed.
- Breast feeding is safe in women with CHD.
- Women requiring cardiovascular medications should be aware that many of the medications will cross into breast milk and the potential effect of medications on the infant should be clarified with a paediatrician.

Healthcare providers managing pregnant patients with CHD should have a plan for management of labour and the postpartum period that includes consideration of the appropriate response to potential complications. This care plan should be made available to the patient and to all the healthcare providers.

- Patients in NYHA class III/IV should be referred to a tertiary centre where appropriate heart care can be instituted.
- Patients with oxygen saturation below 85% should be discouraged from attempting pregnancy as the rate of foetal demise is 60% and maternal mortality up to 30%

Other:

Advice on a healthier lifestyle i.e., smoking cessation, weight loss/maintenance, hypertension/lipid screening. Refer to Chapter 1: Prevention of atherosclerotic cardiovascular disease.

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8

8. CARDIAC RHYTHM DISORDERS

Key Messages

- The diagnosis of cardiac rhythm disorders requires an ECG.
- All patients with cardiac rhythm disorders should have an echocardiogram.
- Healthcare workers taking care of patients with cardiac rhythm disorders should be Advanced Cardiac Life Support (ACLS) certified.

8.1 Arrhythmia

- An arrhythmia is an irregularity in the heartbeat – this manifest as either an abnormality with the heart rate or the heart rhythm.
- The heart may beat too slowly (bradycardia <50 beats/ minute), or too quickly (tachycardia >100 beats/minute) or irregularly.
- Initial care of most arrhythmias can be managed by a competent medical officer with consultation from a physician.
- Some require physician input or referral to a cardiologist.
- Specific arrhythmias require specialist assessment by a cardiac electrophysiologist.

8.2 Bradycardia

- Bradycardia is defined as a heart rate of less than 50 bpm.
- Significant bradycardia occurs when the heart rate is <40 bpm; requires more urgent attention.
- Bradycardia can be detected by examination of the patient's arterial pulse but is best confirmed with an electrocardiogram (ECG).
- ECG allows classification according to the pacemaker which is at fault. In most instances, this is the sinus node or the atrioventricular node.

8.2.1 Sinus Node Disease

- The sinus node exhibits automaticity and generates the initiating impulse of the cardiac cycle as a rate of between 50 - 100 bpm, affected by physiological changes.
- In very fit adults, the sinus node will beat at a slower rate.
- Sinus node dysfunction will include abnormal sinus bradycardia, intermittent sinus arrest or sick sinus syndrome.
- Sinus bradycardia may be due to medication; other causes include excessive parasympathetic tone, hypothyroidism, hypothermia, and sleep apnoea.
- Sinus bradycardia can also be the result of rheumatic fever.
- Sinus bradycardia is common and benign in most instances but if the heart rate is less than 40, or there are associated symptoms, treatment may be required.

8.2.2 AV Node Disease

AV node block usually requires an assessment by ECG for confirmation.

i) First-degree AV block

- Means a PR interval of >200 milliseconds (ms) on the ECG. In elderly (> 65yrs), the PR interval of >220ms is diagnostic.
- PR interval prolongs with age.
- Certain drugs should be used in caution including beta-blockers, verapamil, digoxin.
- If first-degree atrioventricular (AV) block is not associated with symptoms no specific therapy is indicated.
- If there are symptoms such as dyspnoea or dizziness, cardiac monitoring may be considered to identify intermittent second or third-degree AV block.

ii) Second-degree AV block type

- Also known as Wenckebach phenomenon, it is characterized by progressive lengthening of the PR interval followed by a dropped non-conducted atrial impulse.
- It is often seen in young adults with high vagal tone especially in the evenings, and usually does not require specific therapy.

- If there are attributable symptoms, or in older patients (>55 years), this degree of AV block can signify a significant risk.

iii) Second-degree AV block type II

- Also known as Mobitz type II, is diagnosed on an ECG.
- The PR interval is constant-either normal or prolonged-for several heartbeats before a sudden failure of a P wave to be conducted to the ventricles.
- This usually indicates more serious conduction system disease and requires an urgent assessment and intervention.
- A careful assessment of drugs and underlying causes should be performed and if the patient has symptoms, permanent pacing should be offered in the absence of a reversible cause.

iv) Third-degree AV block

- This is also an ECG diagnosis.
- There is no association between the P waves and the QRS complexes meaning that the atrial impulses are not conducted through to the ventricles.
- For this to occur an escape rhythm is initiated either at the region of the bundle of His or in the lower conduction tissues.
- Usually, the QRS complexes will be narrow if the escape rhythm arises at or above the the bundle of His and will be broad if the escape rhythm comes from cells below the AV node.
- When the escape rhythm comes from cells below the AV node, the heart rate is usually slower (<45 bpm) and the situation is more acute.
- Patients with a third-degree AV block require urgent pacemaker.

8.2.3 Treatment of Bradycardias

Treatment is offered to patients who are symptomatic.

Atropine

- Should be considered in people with symptomatic bradycardia involving the sinoatrial (SA) or AV node.
- Dosage: 0.6 mg intravenously stat should be given up to a maximum of 2.7 mg

Adrenaline

- Adrenaline infusion should be given in the acutely ill patients with bradycardia and hypotension.
- Dosage: begin at 0.1 mcg/kg/min to obtain a target mean BP of 60mmHg
- Dobutamine
- This can also be given to patients with severe symptomatic bradycardia if adrenaline is not available.
- Dosage: start at 5mcg/kg/min to achieve a mean arterial BP (MAP) of 60mmHg

Device therapies

- Indicated for patients who do not respond to IV medication.
- Immediate therapies:
  a) Transcutaneous pacing
  - Involves use of defibrillator pads to pace the patients who remain hypotensive despite medical interventions and pending transfer for advanced pacing.
  - Choose the pacing option on your defibrillator and aim to pace between 60-100 beats per minute with a pacing output of 10 volts. A VOO pacing mode should be selected. Confirm pacing by palpating the femoral or carotid pulses. If not present it means the pacemaker is not achieving physiologic capture.

- Sedation and analgesia should be considered to all patients undergoing transcutaneous pacing.

b) Transvenous pacing

- This should be attempted with expert advice in patients who are acutely ill pending transfer for a permanent pacing option. This involves putting a temporary pacing wire through the right internal jugular vein to the right ventricle to ensure mechanical and physiologic capture. Pace between 60-100 beats per minute to achieve a mean arterial pressure of 60mmHg.

- Long-term therapies:
  - This is through permanent pacing devices implanted in specialist cardiology units.

8.3 Tachycardias

Tachycardia is defined as a heart rate persistently above 100 bpm.

Tachycardia can be classified into the following:

A) Supraventricular tachycardia

These describes tachycardia arising above the AV node. They are commonly narrow complex but sometimes can be broad complex if there is aberrant conduction through an accessory pathway.

They include:

1. Sinus tachycardia
2. Atrial tachycardia
3. Multifocal atrial tachycardia
4. Atrial fibrillation
5. Atrial flutter
6. AV nodal re-entrant tachycardia (AVNRT)
7. AV re-entrant tachycardia (AVRT)
8. Accelerated junctional tachycardia

B) Ventricular arrythmias

The two types in this group include:

1. Ventricular tachycardia
2. Ventricular fibrillation

These two arrythmias are lethal and require immediate recognition and treatment.

8.3.1 Supraventricular Tachycardias

i) Sinus tachycardia

This is the commonest heart rhythm abnormality. It is usually seen normally in patients with anxiety, stress, exercise, pain, and febrile states, in response to rise in circulating catecholamines. It can also be due to hypovolemia, stimulants, hypoxia, hypothyroidism, sepsis, and cardiac failure.

Occasionally patients have a sinus tachycardia which is not appropriate for the condition and this may be due to a primary problem with the sinus node. These patients may require referral for specialist assessment by a cardiologist. In patients who have symptomatic sinus tachycardia, heart rate slowing drugs like beta-blockers, calcium blockers such as verapamil and diltiazem, and ivabradine can be considered.

ii) Atrial tachycardia

The heart rhythm is from an ectopic sinus focus that is usually faster than the sinus node. It can easily be confused with sinus tachycardia. Note the negative P-wave in lead II, positive P-wave in lead III and unusually positive P-wave in lead V1 on ECG. These are important clues to the diagnosis of atrial tachycardia. Seek expert opinion before making this diagnosis.

iii) Multifocal atrial tachycardia

This occurs when you have three or more atrial foci that act as the pacemaker. In this case the p-wave has at least 3 different morphologies. One of the foci may be the sinus node. It is common in patients with lung disease such as COPD, interstitial lung disease, asthma or underlying heart disease. The ECG shows 3 or more morphologies of P waves, three or more PR intervals and three of more RR intervals. This is the rule of 3.

iv) Re-entry tachycardia

The two common re-entry tachycardias are the AVNRT and the AVRT. These are commonly referred as supraventricular tachycardias (SVT) but inappropriately so as there are many other types of supraventricular tachycardias as detailed above. Therefore, it may be important to describe them as AV node dependent re-entry tachycardia rather than SVTs.

AV nodal re-entry tachycardia (AVNRT) is probably the commonest form of supraventricular tachycardia (SVT) followed by atrioventricular re-entry tachycardia (AVRT) through an accessory pathway. In both instances, there is a re-entrant circuit that involves the AV node. In these scenarios, the QRS complexes will normally be narrow, and regular, and the heart rate will be between 140 and 180 beats per minute in most instances.

In some instances, AVRT may be broad complex tachycardia, which may mean that the AVRT is carried on with either a rate related bundle branch block or with a preexisting bundle branch block. In rares cases the impulse goes down the accessory pathway and comes up the AV node. This is called antidromic AVRT and causes the QRS to be wide as the impulse goes into the muscle. The impulse is conducted in the muscle at a velocity of 0.5 m/s, whereas the impulse travels down the His Purkinje system at a rate of 1-3m/s. If the imulse goes down the AV node in AVRT it produces a narrow complex tachycardia, this is then called orthodromic AVRT. (ref)

v) Treatment of supraventricular re-entrant tachycardias

Immediate therapies in the ER

In patients who are stable with SVT, vagal manoeuvres such as holding the breath, or the Valsalva manoeuvre can slow conduction in the AV node and interrupt the re-entrant circuit and convert to sinus rhythm. If this does not work, carotid sinus massage can be considered especially in younger patients. Massage the carotid sinus for few seconds on the nondominant cerebral hemisphere side, but only consider this after auscultating for bruits because of the risk of stroke from emboli. You should never perform carotid massage on both sides simultaneously and there should usually be a 10-second pause before trying the other side.

When SVT cannot be terminated by vagal manoeuvres adenosine may terminate 90% of tachycardias due to AVNRT or AVRT. Adenosine is given by rapid intravenous injection starting at 6 mg and increased to 12mg and possibly 18 mg if unsuccessful at lower doses. Like vagal techniques, adenosine interrupts the re-entrant circuit involving the AV node. Adenosine has a short half-life and should be administered in a large vein followed by flush with at least 10 mL of sodium chloride 0.9%. Adenosine is contraindicated in patients with severe asthma or obstructive airways disease and should be avoided. In the case of contraindication to medications or rarely hemodynamic compromise direct current cardioversion nis recommended.

Cardioversion under sedation starting at 100 to 150 J can be used in patients who have not responded and are becoming hemodynamically unstable or develop pulmonary oedema, chest pain with ischemia or any other features.

Verapamil 5 to 10 mg by slow IV infusion is an alternative but should not be considered in patients already on beta-

blockers or who have significant left ventricular dysfunction. Intravenous beta-blockers, metoprolol and atenolol, and also amiodarone may also convert rapid SVT into sinus rhythm.

Long term therapies

Long-term therapy includes use of drugs such as flecainide 50 -50 mg twice daily close and sotalol 80 to 160 mg twice daily as well as amiodarone. Amiodarone is also effective but is not recommended as first-line without consideration of its toxicity and long half-life which may make electrophysiological study challenging. Some patients do respond to beta-blockers or rate limiting calcium blockers.

All patients with frequent attacks or side effects to drugs should be reviewed by cardiologist for consideration of electrophysiology study with a view to radiofrequency ablation which provides a cure in more than 95%.

vi) Atrial fibrillation/Atrial flutter

On the ECG atrial fibrillation is recognized as a ventricular rhythm without discernible P-waves on the surface ECG, onlt fibrillatory waves are noted. This is important as misdiagnosis may potent a big risk to the patient because it is a significant risk factor for stroke and other cardioembolic phenomena and may lead to inappropriate long-term therapies. Atrial fibrillation is characterized as either being permanent, persistent, or paroxysmal.

Atrial flutter is recognizable as P-waves with intermittent ventricular contractions, the ratio of p-waves to ventricular beats is constant.

Atrial fibrillation and atrial flutter present with dyspnoea, palpitation, presyncope.

The most common causes of atrial fibrillation include valvular heart disease usually rheumatic mitral valve, hypertension, cardiomyopathy, ischemic heart disease, congenital heart disease especially atrial septal defect, acute infection especially respiratory illness, thyrotoxicosis, alcohol excess, sleep apnoea, pericarditis, and cancer.

Patients with atrial fibrillation should be evaluated for an underlying cause using a full biochemical profile, glucose, thyroid function, lipid profile, and complete blood count.

In addition, the risk of stroke should be carefully assessed using one of the stroke risk calculators including the CHA2DS2-VASc score which is only useful in nonvalvular atrial fibrillation. This usually requires confirmation by echocardiography to assess for structural or functional heart disease and specifically to look for evidence of atrial thrombus and significant mitral stenosis. The introduction of an anticoagulant is usually matched by an assessment and discussion around the risk of bleeding.

8.3.2 Treatment of Atrial Fibrillation/Flutter

Acute treatment

If the patient is hemodynamically unstable, cardioversion is recommended. Start with 50 J for atrial flutter and 150 J for atrial fibrillation. In this acute setting give enoxaparin 1mg/kg subcutaneously stat at the time of cardioversion.

If cardioversion is unavailable give amiodarone 150mg IV stat, can be increased to 300mg IV if the rhythm remains uncontrolled with hemodynamic compromise. Amiodarone infusion over 24hrs should be considered to sustain the heart rate.

In the patient who is hemodynamically stable, treatment depends on the main driver of the atrial fibrillation or flutter. Amiodarone and beta blockers are preferred in patients with significant LV dysfunction whereas long-acting calcium channel blockers e.g., verapamil and diltiazem can be used in those with normal LV function.

Long-term therapies

There are two strategies in treatment of the heart rate in atrial fibrillation and atrial flutter.

- Rhythm control is an attempt to establish normal sinus rhythm.
- Rate control is geared towards achieving a rate of 80-100 beats per minute even atrial fibrillation is persistent.

Rhythm control is achieved by medication that can help convert atrial fibrillation back into sinus rhythm and by cardioversion. These drugs include amiodarone, flecainide, among others.

Rate control is achieved by medications such as beta blockers and long-acting calcium channel blockers such as verapamil and diltiazem.

Cardioversion may revert the patient into sinus rhythm but maintaining sinus rhythm in the longer run may require concomitant use of antiarrhythmic therapy for instance sotalol or flecainide. When cardioversion is planned, the patient should be given anticoagulants for minimum of 21 days. In patients who require more urgent cardioversion transoesophageal echocardiography to look specifically for atrial thrombus should be performed.

Anticoagulation in non-valvular AF

The use of long-term anticoagulation should be considered for all patients after performance the CHA_2DS_2-VASc score. Management of these patients will usually require ongoing follow-up with a cardiologist.

Therapy should be tailored to the individual patient in terms of their bleeding risk with warfarin. A simple method for quantifying risk is by using the HAS-BLED score (hypertension (include only if systolic BP >160 mmHG), abnormal renal/liver function, stroke, bleeding history or predisposition, labile INR, elderly (> 65), drugs/alcohol concomitantly). This score is available through online applications.

CHA_2DS_2 - VASc score

C= congestive cardiac failure; H= Hypertension; A= Age; D= diabetes; S= stroke/TIA; V= vascular disease; S= Sex (female).

The use of online scoring applications should be used to guide clinicians. Patients with a CHA_2DS_2 - VASc score of ≥2 should be anticoagulated.

Patients do not need to be admitted to initiate anticoagulation. The two options for anticoagulation are warfarin (target INR 2-3) or new oral anticoagulants (dabigatran, rivaroxaban, apixaban, endoxaban). NOACs are preferred. All the recommendations for anticoagulation in atrial fibrillation apply to atrial flutter.

Anticoagulation in valvular AF

Patients with rheumatic mitral stenosis of moderate or severe grade have a high chance of cardio-embolic stroke and are an important group. These patients require anticoagulation with warfarin as opposed to the new oral anticoagulants. hm control see further flow chart.

Ablation therapy in atrial fibrillation and atrial flutter

This should be recommended for all patient with atrial flutter as it is therapeutic. Ablation therapy is recommended for atrial fibrillation for those with incessant symptoms, younger patients and those with heart failure.

8.3.3 Ventricular Arrythmias

As stated previously, the two most common ventricular arrythmia are ventricular tachycardia and ventricular fibrillation.

These arrythmias are associated with high mortality and immediate recognition and treatment is warranted.

A) Ventricular tachycardia

On ECG it is recognizable as a regular broad complex tachycardia. The other important differential is supraventricular tachycardia with aberrancy. For the purpose of this guideline, all broad complex tachycardias should be treated as VT unless otherwise diagnosed by an expert cardiologist. This is because broad complex tachycardia is VT in 90% of the cases and in the setting of structural heart disease wide complex tachycardia is VT in 95% of cases.

Acute management of VT

In the hemodynamically unstable patient immediate cardioversion is recommended. Start with 150 J and increase to 200 J as may be required. Amiodarone can be used concomitantly to aid in cardioversion or to maintain sinus rhythm.

In the hemodynamically stable patient, beta blockers can be given intravenously or orally. Amiodarone can also be used at the dose of 200-400 mg thrice daily/every 8 hours.

Magnesium sulphate should be given to all patients with VT regardless of the magnesium level.

All cases of VT should be referred to a cardiologist for detailed evaluation. This will include coronary angiography and revascularization if appropriate, implantation of ICD or electrophysiology study with view to ablation.

Long term management of VT

This is dependent on the cause of the VT. In a structurally normal heart, the cause of VT is usually a channelopathy, and the treatment includes beta blockers and long acting calcium channel blockers e.g., verapamil.

In cases where structural heart disease is present, then treatment of structural heart disease is paramount. These diseases include cardiomyopathies, hypertrophic cardiomyopathies, ischemic heart disease and other infiltrative disorders.

In addition to medical therapies, most patient require ICD to prevent sudden death.

B) Torsades de Pointes' Ventricular Tachycardia

This is a specific form of polymorphic VT arising in association with a prolonged QT interval. The ECG reveals a continually changing axis over a sequence of 5 - 20 complexes and the ventricular rate is usually 200 - 250 bpm. The resting ECG has a QT interval of >0·5 s. There may also be prominent U waves.

The QT interval is measured from the onset of the QRS to the end of the T wave and should be corrected for heart rate. The corrected QT is easily available from online tools. The normal QT_c is <0·39 s in men, 0·44 s in women.

Common secondary causes are hypokalaemia, hypomagnesaemia, class Ia, Ic and III anti-arrhythmic drugs, digoxin, certain antihistamines, and antidepressants. The tachycardia often occurs in association with a bradycardia (e.g., sick sinus syndrome or AV block). These causes should be actively sought and reversed where possible.

The treatment for Torsades de Pointes' VT is magnesium infusion and overdrive pacing with a transvenous pacing wire if available.

C) Ventricular Fibrillation (VF) and Cardiac Arrest

VF is a life-threatening condition, usually presenting with cardiac arrest. The treatment is immediate defibrillation using an automatic AED or manual defibrillator. Hands on CPR should be ongoing before defibrillation is delivered. IV amiodarone 150mg should be considered for all patients after successful defibrillation.

In patients who have been successfully resuscitated from an out of hospital VF arrest, consideration should be given to immediate coronary angiography and revascularization if appropriate. This is essentially mandatory if the ECG suggests ischaemia if intervention is likely to affect outcome or if the biomarkers come out positive. For patients who are intubated,

immediate anaesthetic support is needed. Continued mechanical ventilatory support and hemodynamic support using adrenaline as the first choice and noradrenaline as the second choice.

All cases of cardiac arrest should follow the AHA recommended resuscitation guidelines. All physicians working in units dealing with heart rhythm disorders should be ACLS-certified.

8.4 Recommendations to Institutions that Offer Care for Patients with Arrhythmia

- All institutions should be equipped with an ECG machine.
- There should exist a link with a cardiologist to enhance diagnostic capability and management of patients with acute arrhythmia.
- There should exist a protocol for care for patients with arrhythmia including care pathways, care bundles and care teams to expedite care for patients with acute arrhythmia.
- Patients with acutely presenting arrhythmias should be evaluated in the acute room of the health facility, connected to a continuous ECG monitor, with access to resuscitation facilities including a defibrillator and resuscitation trolley and protocols in place for management of arrhythmia requiring mechanical and electrical interventions.
- There should be resuscitation teams with up-to-date training and resources in all facilities offering services to patients with arrhythmia.

The following tests should be considered on patients with arrhythmia:

Blood tests

- Complete blood count
- Renal function and electrolytes
- Blood glucose
- Blood cholesterol
- Thyroid function testing
- Extended electrolyte testing using calcium and magnesium
- Cardiac biomarkers specifically troponin and NT-pro BNP
- Coagulation profile including INR

Cardiovascular tests

- ECG
- Echocardiography
- Exercise stress ECG testing, stress echo or myocardiac perfusion scans
- Holter monitoring
- Cardiac MRI
- Electrophysiologic testing
- RF ablation

The following drugs should be available or accessible in all institutions:

- Beta blockers (Metoprolol oral and intravenous, esmolol, Bisoprolol, Carvedilol, Nebivolol, Propranolol)
- Verapamil (oral and IV)
- Diltiazem
- Amiodarone (oral and IV)

- Apixaban
- Dabigatran
- Rivaroxaban
- Warfarin
- Digoxin
- Ibutilide IV
- Flecainide IV and oral
- Sotalol
- Procainamide/lidocaine
- Propafenone
- Mexiletine

8.5 Cardiac Rhythm Disorders and Driving

There are no specific guidelines provided in Kenya.

The UK Driving Licence Authority (DVLA) has issued guidance on driving following arrhythmia and device therapy. These are summarised as below:

Table 8.1: DVLA Guidance on Driving Following Arrhythmia and Device Therapy

	GROUP 1 (Personal vehicles) ENTITLEMENT	**GROUP 2 (PSV and HGV) ENTITLEMENT**
ARRHYTHMIA • Sinoatrial disease • Significant atrio-ventricular conduction defect • Atrial flutter/fibrillation • Narrow or broad complex tachycardia (See also following Sections) NB: Transient Arrhythmias occurring during acute coronary syndromes do not require assessment under this Section.	• Driving must cease if the arrhythmia has caused or is likely to cause incapacity. • Driving may be permitted when underlying cause has been identified and controlled for at least 4/52.	• Disqualifies from driving if the arrhythmia has caused or is likely to cause incapacity. • Driving may be permitted when the arrhythmia is controlled for at least 3/12, provided that the LV ejection fraction is good (i.e. LVEF is > 40%), and there is no other disqualifying condition.
PACEMAKER IMPLANT • Includes box change	• Driving must cease for at least 1/52. • Driving may be permitted thereafter provided there is no other disqualifying condition.	• Disqualifies from driving for 6/52. • Re/licensing may be permitted thereafter provided that there is no other disqualifying condition.
ICD IMPLANT	See below section	Permanently bars
SUCCESSFUL CATHETER ABLATION	• Driving must cease for at least 2/7. • Driving may be permitted thereafter provided there is no other disqualifying condition.	• Following successful catheter ablation for an arrhythmia that has caused or would likely have caused incapacity, driving should cease for 6/52. Driving may recommence thereafter provided there is no other disqualifying condition. • When the arrhythmia has not caused nor would likely have caused incapacity, driving may recommence after 2/52 provided there is no other disqualifying condition.

PROPHYLACTIC ICD IMPLANT	• Asymptomatic individuals with high risk of significant arrhythmia. Driving should cease for 1/12. • Should the ICD subsequently deliver ATP and/or shock therapy (except during normal clinical testing) then the licensing criteria on the section below should be applied.	Permanently bars
ARVD AND ALLIED DISORDERS (See also arrhythmia, pacemaker and ICD sections)	• Asymptomatic - Driving may continue. • Symptomatic - Driving must cease if an arrhythmia has caused or is likely to cause incapacity. Re/licensing may be permitted when arrhythmia is controlled and there is no other disqualifying condition.	• Asymptomatic - Driving must cease but may be permitted following Specialist EP assessment provided that there is no other disqualifying condition. • Symptomatic - permanently bars
CRT **CRT-P** **CRT-D**	• Driving must cease for at least 1/52 following implantation. Driving may continue provided: There are no symptoms relevant to driving, there is no other disqualifying condition. • Driving may be permitted provided the ICD requirements are met. • There is no other disqualifying condition.	• Disqualifies from driving for 6/52 Following Implantation. Re/licensing may be permitted provided: The heart failure requirements are met. There is no other disqualifying condition. • Permanently bars

Physicians taking care of patients with devices should counsel them appropriately and this should be documented in the patient charts. It is important to consider patient education and welfare during these discussions.

9

9. ISCHAEMIC HEART DISEASE

Key messages

- Ischaemic heart disease (IHD) is a leading cause of heart failure.
- IHD is increasingly being recognized in Kenya as an important cause of cardiovascular disease due to increasing atherosclerotic risk factors attributed to epidemiologic transition.
- IHD has a wide spectrum of clinical presentations, from acute syndromes-ST- segment myocardial infarction (STEMI), non-ST-segment elevation myocardial infarction (NTEMI), and unstable angina to chronic coronary syndromes.
- Diagnostic evaluation with risk stratification using validated tools is key in making correct decisions on treatment strategies for optimal patient outcomes.
- Primary, secondary, and tertiary prevention interventions address control of established atherosclerotic risk factors, treatment of heart failure, use of devices and cardiac rehabilitation.

9.1 Introduction

Ischemic heart disease (IHD), also known as coronary heart disease (CHD) or coronary artery disease (CAD), is the eventual manifestation of myocardial dysfunction following gradual or sudden reduction of blood to the coronary arteries. Atherosclerotic mechanisms manifesting as plaques within the coronary arteries are the main cause of IHD. Other causes include coronary dissection, embolization of material through the coronary ostia, or even dysfunction at microvascular level.[1]

IHD is the most common cause of death of globally. In the USA almost one-third of adults above 35 years are affected by the disease.[2,3] In Kenya 4.6% of total deaths were caused by IHD in 2020 according to WHO and the age adjusted death rate from the disease is 72.70 per 100,000 of the population.[3]

9.2 Clinical Presentation of IHD

Patients with ischaemic heart disease can present acutely (acute coronary syndromes-ACS), or insidiously with symptoms of chest pain or dyspnoea over months to years (chronic coronary syndromes-CCS).

ACS results from acute vessel occlusion due to thrombus formation in atherosclerotic plaques whereas CCS results from progressive myocardial dysfunction due reduced tissue perfusion and myocardial cell dysfunction following long standing ischaemia.

i) Chronic Coronary Syndromes

Chronic coronary syndrome (CCS) is defined as myocardial ischaemia and cellular dysfunction due to progressive occlusion of the coronary artery or microvascular dysfunction causing symptoms of chest pain or dyspnoea commonly on exertion. Symptoms are relieved by rest or by inhaled or oral nitroglycerin. The term chronic coronary syndrome replaces the old term 'chronic stable angina". This stems from new evidence that myocardial dysfunction can result from both macrovascular and microvascular disease particularly in the setting of metabolic syndrome.[4]

The Canadian Cardiovascular Society Classification is usually used to grade angina as shown below.[5]

Table 9.1: Canadian Cardiovascular Society Classification of Angina

Class I	Angina with strenuous or prolonged exertion
Class II	Angina on walking or climbing stairs rapidly, walking/stair climbing after meals, during the first few hours after awakening, walking more than 2 blocks on level (~200 meters), or climbing more than one flight of ordinary stairs at a normal pace and conditions
Class III	Angina on walking 1 to 2 blocks (~100 to 200 meters) on level or climbing one flight of stairs at normal pace and conditions
Class IV	Angina at rest

II) Acute Coronary Syndrome (ACS)

This is a constellation of symptoms which defines cardiomyocyte necrosis following acute occlusion of coronary blood vessels that supply the myocardium. This can occur suddenly or over minutes to hours.

Acute coronary syndromes usually result from thrombotic occlusion or severe narrowing of the artery following plaque rupture.

III) Heart failure

Chronic ischemic heart disease may lead to heart failure due to myocardial necrosis, hibernation,[6] and/or scarring.

IV) Arrhythmia

Some patients may present with ventricular arrhythmias (ventricular tachycardia-VT/ventricular fibrillation-VF) due to scar formation in the myocardia or severe ischaemia. Less commonly they may present with supraventricular arrhythmia such as atrial fibrillation. VF usually signifies acute disease whereas VT signifies a scar in a previously infarcted territory.[7]

V) Cardiac arrest and sudden cardiac death

Patients with severe disease affecting the left main stem or severe disease with a single remaining vessel may experience sudden cardiac death. Sudden death can also result from arrhythmias.[8]

9.3 Diagnosis of IHD

A high index of suspicion for ischaemic heart disease is warranted from the clinician given the broad range of disease presentation. Patients with chest pain and suspected angina should have full history and examination performed as part of their initial evaluation. A comprehensive history should include all the cardiovascular risk factors including family history of premature coronary artery disease and sudden death.

9.3.1 Diagnosis of Chronic Coronary Syndromes

Chest pain and dyspnoea are the main presenting symptoms for chronic coronary syndromes.

The table below outlines the prediction tool developed by Diamond and Forrester to guide testing for persons with suspected CCS.

Table 9.2: Angina Risk Prediction Tool

Criteria						
1) Substernal chest pain, that is; 2) Reproducibly induced with exertion, and; 3) Relieved by rest or the use of nitroglycerin.						
Interpretation						
A: Typical angina-all 3 criteria present B: Atypical angina-2 criteria present C: Non-anginal chest pain-1 criteria present D: No criteria present						
Pre-test probability of coronary artery disease by age, sex, and symptoms						
Age	**Sex**	**A: Typical angina**	**B: Atypical angina**	**C: Non-anginal chest pain**	**D: No criteria present**	
30-39	Male	Intermediate	Intermediate	Low		
	Female	Intermediate	Very low	Very low		
40-49	Male	High	Intermediate	Intermediate		
	Female	Intermediate	Low	Very low		
50-59	Male	High	Intermediate	Intermediate		
	Female	Intermediate	Intermediate	Low		
60-69	Male	High	Intermediate	Intermediate		
	Female	High	Intermediate	Intermediate		
Action based on risk stratification						**Action**
Level of risk			**Action**			
Very low and low risk			Investigate for non-cardiac causes			

Intermediate risk	Perform/refer for stress testing/CT coronary angiogram	
High risk	Perform/refer for coronary angiogram	

The following dynamic stress tests should be performed under supervision by an experienced cardiologist:

- Exercise ECG
- Exercise stress echocardiogram
- Dobutamine stress echocardiogram
- Nuclear Myocardial perfusion

Patients that have negative tests should be evaluated for other causes of chest pain. Patients with borderline tests should be offered a CT coronary angiogram.[10]

Other tests for patients with IHD

The single most important non-laboratory test for patients with IHD is an ECG. The next most useful is an echocardiogram.

An echocardiogram is key is showing the left ventricular ejection fraction (LVEF) and left ventricular (LV) dimensions. Patients with acute coronary syndromes require an echocardiogram before leaving hospital to assess LV function. An echocardiogram is generally not recommended for the diagnosis of ACS as it lack sensitivity and specificity but can be used in patients as part of evaluation of chest pain differentials and for evaluation of complications of myocardial infarction (MI).

Patients with reduced ejection fraction (EF) and IHD are recommended to have complete revascularization as this can potentially improve LV function. Studies have showed that the best improvement in these patients is achieved through a coronary artery bypass graft (CABG).[11]

9.3.2 Diagnosis of Acute Coronary Syndromes

Acute IHD presents as acute coronary syndrome (ACS). The diagnosis of ACS is dependent on 3 variables: chest pain, ECG changes, and elevated cardiac biomarkers. These can be utilized to score the patient to guide therapy. The HEART score shown below has been validated in the emergency room to triage patients with chest pain or equivalent symptoms such as epigastric discomfort into low, intermediate, and high risk for major adverse cardiac events. Low risk patients can be discharged home for follow up by physicians with low risk of adverse events.

Table 9.3: HEART Score for Possible ACS

Parameter	Category	Points
History	Highly suspicious for cardiac origin	2
	Moderately suspicious	1
	Slightly/Non- suspicious	0
ECG	Significant ST depression	2
	Non-specific repolarization	1
	Normal	0
Age (Years)	≥65	2
	46-64	1
	≤45	0
Risk factors	≥3 risk factors or history of CAD	2
	1 or 2 risk factors	1
	No risk factors	0
Troponin levels	≥3× normal limit	2

	>1 to <3× normal limit	1
	≤ normal limit	0
Risk factors: DM, current/recent (1 month) smoker, HTN, hyperlipidaemia, family history of CAD, and obesity		
Interpretation and action		
HEART Score	Action	
0-3 (low risk)	Discharge home	
4-6 (intermediate risk)	Admit for observation	
>6 (high risk)	Perform/refer for invasive strategies	

I) Classification of ACS

- ST-Segment Elevation Myocardial Infarction: STEMI – ECG diagnostic with characteristic ST elevation in two contiguous leads.
- Non-ST-Elevation Myocardial Infarction: NSTEMI – The ECG is normal or non-diagnostic, but the troponin is elevated.
- Unstable angina – There are symptoms of chest pain and dynamic ECG changes and normal troponin.

II) Key Investigations for suspected ACS

Electrocardiogram

In patients with chest pain, the electrocardiogram (ECG) should be performed within 10 minutes of presentation. This includes interpretation of the ECG that should be documented.

If the ECG suggests ST-segment elevation myocardial infarction (STEMI), i.e., ST elevation in 2 contiguous leads, therapy should be commenced immediately with a view to reperfusion.

If the ECG is normal or non-diagnostic, it should be repeated in 30 minutes. Subsequently, it can be repeated if there is recurrent chest pain or discomfort. It is recommended that the ECG leads used to obtain the first ECG stay on the patient's chest for repeat ECG testing or if they cannot stay on then the site should be maked with skin marker to use the same site for easy and meaningful comparison. This allows observation of dynamic ECG changes that may be a clue to the diagnosis of unstable angina.

Biomarkers for ACS

The gold standard biomarker for the diagnosis of ACS is cardiac troponin. Most assays now use the highly sensitive troponin I and T (both of which have high sensitivity and specificity). The turn-around time for troponin should be capped at one hour to enable rapid turn-over for patients with chest pain.

Blood for troponin should be drawn immediately after the ECG is performed. It usually takes approximately 3 hours after the onset of symptoms before a rise in troponin can be detected in the peripheral blood.

It is recommended that all patients with suspected ACS should have troponin performed at the time of presentation, and if the initial test is negative and the patients still has suspicious symptoms, another test should be repeated in 4 hours.

A rise in troponin usually suggests a coronary cause of chest pain. A negative troponin in two serial tests and a normal ECG should trigger evaluation for non-cardiac causes of symptoms but where the index of suspicion remains high, non-invasive evaluation should be considered.

III) Differential Diagnosis of Acute Chest Pain

The table below outlines other possible diagnoses of acute chest pain and the suggested diagnostic approach.

Table 9.4: Differential Diagnosis for Acute Chest Pain in the ER

Diagnosis	History	Physical exam	Diagnostic tests
Aortic dissection	Tearing pain radiating to the back	New murmur, bruits,	• CXR • CT-angiogram • Echo
ACS	• Pressure-like pain radiating to the arms or face • Diaphoresis, • Dysponea • Presence of risk factors	Evidence of heart failure	• ECG • Biochemical markers (cardiac troponin)
Pulmonary embolism	• Sudden onset of pleuritic chest pain and dyspnoea • Risk for DVT	• Tachypnoea • Tachycardia • Features of DVT	• CXR • V/Q scan • CT pulmonary angiogram
Oesophageal rupture	• Constant severe retrosternal/ epigastric pain • History of inciting event	Mediastinal rub/crunch	CXR
Pneumothorax	• Pleuritic pain • Dyspnoea	Diminished breath sounds over affected hemi-thorax	CXR
Pneumonia	• Cough • Fever • Dyspnoea • Pleuritic pain	• Abnormal breath sounds • Fever • Hypoxia • Tachypnoea	CXR
Pericarditis	• Positional ache • Dyspnoea	Pericardial rub	• ECG • Sonogram • CXR
GI causes	• Associated abdominal symptoms • GERD	Abdominal tenderness, guarding	• Amylase • Lipase • KUB • Ultrasound
Musculoskeletal causes	Pain increased with minimal muscle movement	Chest wall tenderness to palpation	Normal

Adapted from Green G, Hill P. Approach to chest pain and possible myocardial ischemia. Emergency medicine: A comprehensive study guide. New York: McGraw Hill; 2000: 341-352

Treatment of IHD

Therapy for ischaemic heart disease is largely dependent on how the patient presents.

9.4. Treatment of Acute IHD

Acute IHD presents as ACS. This is usually STEMI, NSTEMI, or UA as defined previously.

9.4.1 Recommendations

A: To institutions that offer care for patients with ACS.

1. There should be clear point of contacts for patients and health care professionals where help can be obtained

immediately.

2. There should be ambulances that are appropriately equipped to support advanced cardiac life support (ACLS) care to patients with ACS.
3. The ambulances should be equipped with an ECG machine.
4. There should be a system that coordinates ambulances to enhance patient care.
5. The triage system in the hospital should identify chest pain as one of the symptoms whose care is expedited.
6. There should exist a link with cardiologist(s) to enhance diagnostic capability and management of patients with acute coronary syndromes.
7. There should exist a protocol for care for patients with ACS including care pathways, care bundles, and care teams to expedite care for patients with ACS.
8. There is need to have a collaborative effort that includes hospitals and cardiologists to improve care and outcomes for ACS patients.

B: In-hospital care of patients with ACS

1. Patients with ACS should be evaluated in the acute room of the health facility.
2. These patients should be connected to the ECG monitor and have their vitals assessed every 15 minutes.
3. There should be a resuscitation trolley in all hospitals that take care of patients with STEMI.
4. There should be resuscitation teams in all hospitals that take care of patients with STEMI.
5. ECG should be performed and interpreted within 10 minutes of arrival to the hospital.
6. ACS patients should be managed by the EMERGENCY team in consultation with an attending cardiologist.
7. The following tests should be performed on patients with ACS:
   i. Full blood count
   ii. Renal function and electrolytes
   iii. Random Blood Sugar
   iv. Lipid profile (random)
   v. SGPT (as statins are being given in the ER and liver functional status should be known)

9.4.2 Treatment Approach

A: STEMI

STEMI is considered a medical emergency.

The treatment for STEMI underscores the need for system preparedness, anticipation, and collaboration amongst different entities and institutions. Therefore, the patient must be identified early, diagnosis made swiftly, and treatment/transfer offered immediately.

The following are recommended for patients with STEMI1[4]

1. There should a care box for STEMI patients that consists of the following drugs:
   vi. Aspirin 300mg orally stat
   vii. Clopidogrel 300mg orally stat. The alternative is Ticagrelor 180mg orally stat
   viii. Enoxaparin 1mg/kg as a subcutaneous injection stat
   ix. Atorvastatin 80mg orally stat
2. Patient should be connected to ECG monitors immediately on arrival to the health facility.
3. Oxygen therapy should be considered for those patients with saturation of less than 92% at room air. Routine oxygen utilization is not recommended.
4. Intravenous access should be obtained as soon as possible once the patient is in the health facility.
5. For patients presenting within 12 hour of symptom onset, thrombolysis should be administered within 30

minutes of the diagnosis being made after consultation with the attending cardiologist.

6. If the facility has interventional capability (primary PCI) the recommended door-to-balloon time is 90 minutes.

STEMI should be treated in consultation with an interventional cardiologist. Where a cardiologist is not accessible, the above therapies should be administered without delay and transfer should be done to a facility with the capability for interventional therapy.

B) NSTEMI

Patients with NSTEMI will require the same initial treatment as patients with STEMI. However, they do not require thrombolysis as it has not been shown to be beneficial.

The following are recommendation for patients with NSTEMI1[4]

1. There should a care box for NSTEMI patients that consists of the following drugs:
   i. Aspirin 300mg orally as a stat dose
   ii. Clopidogrel 300mg orally as a stat dose
   iii. Enoxaparin 1mg/kg as a subcutaneous injection as a stat dose
   iv. Atorvastatin 80mg orally as a stat dose
2. Patient should be connected to ECG monitors immediately on arrival to the health facility.
3. Oxygen therapy should be considered to those patients with saturation of less than 92% at room. Routine oxygen utilization is not recommended.
4. Intravenous access should be obtained as soon as possible once the patient is in the health facility.
5. An attending cardiologist should be informed immediately to guide care in the patient.

Risk stratification of NSTEMI

This should be done early enough to guide need for invasive strategy.

Patients with the following criteria should be considered high risk and prioritized for PCI within 24 hours of presentation:

a) A confirmed diagnosis of NSTEMI
b) Dynamic ST-segment or T wave changes.
c) Transient ST-segment elevation.
d) A GRACE risk score >140.

C) Treatment of concurrent symptoms

Pain

- Morphine 2.5 to 5 mg given intravenously should be considered for patients with persistent chest pains. A pain scale should be used to assess efficacy of pain therapies during care.
- Nitroglycerin spray (one to two puffs of 400 mcg) should be considered for patients with anterior MI and persistent chest pain. Avoid in patients with hypotension (SBP <100 mmHg) and those with inferior infarcts.

Hypotension

- This should be anticipated.
- Start intravenous peripheral norepinephrine at a dose of 0.1 mcg/kg/minute up to a maximum of 1 mcg/kg/minute. Aim for mean arterial pressure (MAP) of 60 mmHg.

Hypertension

- Start intravenous nitroglycerin at 5-20 mcg/min and titrate to BP. Aim for normalization of blood pressure.

Hyperglycaemia

- Start an intravenous insulin infusion at 1-4 units per hour. Aim for a blood sugar level of ≤11 mmol/L.
- If diabetic ketoacidosis (DKA) is suspected, perform urinary ketones test and call a diabetologist for expert advice.

Nausea and vomiting

- Use intravenous metoclopramide or ondansetron in standard doses.

Bradycardia

- Administer atropine 0.6 mg stat and follow the ACLS bradycardia protocol.
- Placement of a temporary pacing wire should be considered immediately with the help of a cardiologist.

Tachycardia

- Follow the ACLS protocol for wide and narrow complex tachycardia.

Cardiac Arrest

- Follow the ACLS protocol as appropriate.

D) Revascularisation

All patients with ACS should be offered a coronary angiogram to enable revascularization. This has been shown to reduce mortality, recurrent events, and reduce length of hospital stay. Revascularization with PCI is commonly given in patients with STEMI and high risk NSTEMI. Coronary artery bypass grafting (CABG) should be considered in patients with left main disease, extensive and complex disease, and in those with diabetes and those with reduced EF.

E) Common complications of IHD

Complications	Sub types
Mechanical	Cardiogenic shock, free wall rupture, ventricular septum rupture, ventricular aneurysm, and acute mitral regurgitation
Electrical	Arrhythmias, AV blocks, and fascicular blocks
Inflammatory	Dressler syndrome
Ischemic	Post- infarction angina
Embolic	Mural thrombosis and systemic embolism

Modified from Moreno et al., 2017

Figure 9.1: Common Complications of IHD

F) Other Therapies

1. Cardiac rehabilitation – this is recommended for all patients post-acute coronary syndromes. This has been shown to reduce recurrent events and rehospitalization.
2. Smoking cessation – a smoking cessation program should be offered to all patients with the aim of helping all patients to quit smoking. Electronic cigarettes and vaping should not be offered as alternatives to cigarette use.

9.5 Treatment of Chronic Coronary Syndromes

The purpose of treatment for CCS is geared towards alleviation of symptoms and prevention of death.

Treatment is therefore dependent on making the correct diagnosis using coronary angiography and other physiologic assessments. Due to the complexity of chronic coronary syndromes, the differentiation between macrovascular and

microvascular disease is important.

Macrovascular disease includes patients with atherosclerotic stenosis and those with coronary vasospasm. Significant atherosclerosis is confirmed using functional tests such as stress echocardiogram, nuclear myocardial perfusion study, and a stress MRI or PET scan.

Coronary spasm can be confirmed in the catheterization laboratory during coronary angiography by performing an acetylcholine challenge/provocation test. Epicardial coronary spasms cause development of chest pain and ST changes on ECG during the procedure. The acetylcholine challenge can also be helpful in assessing microvascular spasm or dysfunction.

The following recommendations apply to patients with chronic coronary symptoms

1. Control of risk factors such as hypertension, diabetes, and dyslipidaemia
2. Medication:
    a. Statin
    b. Aspirin
    c. Short- and long-acting nitrates
    d. Beta blockers
    e. Ivabradine– for those with high heart rates (>70bpm) despite beta blocker use, or if beta blockers cannot be tolerated.
3. For those with persistent symptoms and particularly microvascular disease the following can be considered for symptom control.
    a. Nicorandil
    b. Ranolazine
    c. Trimetazidine

These patients should also undergo coronary angiography to confirm the diagnosis and determine the extent and severity of disease.

Medical therapy applies to all patients, and further treatment depends on severity of disease. This is an ongoing process that is guided by a cardiologist. Revascularization with percutaneous coronary intervention (PCI) is recommended to reduce symptoms. Those with left main disease, extensive disease, LV dysfunction or those with diabetes should be considered for CABG.

9.6 Secondary Prevention of IHD

Secondary prevention of IHD begins in the hospital. Measures that have been shown to be useful include:

1. Cardiac rehabilitation
2. Health education
    a. Physical activity: Thirty minutes of moderate intensity aerobic exercise at least five times per week is recommended.
    b. Dietary advise should be given to all patients with and without diabetes
    c. Medication adherence
    d. Tobacco cessation. See details in chapter 2: Prevention of CVD
3. Aggressive risk factors modification
    a. Blood pressure control: aim for BP < 130/85 mmHg. Avoid hypotension in patients with IHD. Medicine that can be utilised include ACEI/ARB and beta blockers particularly in patients with impaired LV dysfunction. Other anti-hypertensives may be utilized to optimize BP.

b. Diabetes control: aim for HbA1c <6.5%[15]
c. Body weight management: aim for normal BMI
d. Lipids: aim for LDL <2 mmol/L. This should be achieved with high intensity statins and, if necessary, addition of ezetimibe. Newly licensed PCSK9 inhibitors may play a role in patients that do not achieve this target despite statin/ezetimibe use.
e. Anti-platelet drugs: aspirin is recommended for all patients for secondary prevention of IHD. Patients that are intolerant to aspirin should be given clopidogrel.

4. Management of heart failure

It is recommended that patients with IHD who require treatment for heart failure should be followed up in specialized heart failure clinics.

5. Use of devices

Patients that survive acute myocardial infarction and have heart failure with a reduced ejection fraction may require primary prevention implantable cardioverter-defibrillators (ICDs).

9.7 Health Systems Recommendations for the Management of IHD

These guidelines come to fore at a time when competing interests of disease burden and resource allocation abound. The writers of the guidelines therefore felt there is a great need for system organization to optimize care and resource allocation. To do this the following recommendations are suggested to help health care organisations deliver the best care to their patients.

1. Shared resources:

Health institutions should plan to share resources to reduce pressure on existing resources as well as to concentrate expertise. Most benefit is achieved through having shared ambulances and ambulance systems, shared critical areas (HDU/ICU/CCU), catheterization laboratories, and diagnostic and rehabilitation centres. Systems of transfer can be put in place and health system exchanges optimized to improve care.

2. Shared manpower:

By sharing resources then sharing of manpower becomes easier. Therefore, experts will be located in given centres where patient care be optimized. These include physicians, nurses and other health care professionals.

3. Medical records:

By sharing health records using a secure and confidential platform, health care systems can optimise patient care and save meagre resources.

9.8 Screening for Asymptomatic IHD

Generally, there is no recommendation for blanket screening of people for occult IHD. However, there are some populations for whom screening for asymptomatic IHD is recommended:

1. People with abnormal ECG findings, particularly pathological Q-waves and ST-segment depression and have risk factors for CAD
2. People with diabetes
3. People with strong family history of IHD presenting with atypical symptoms
4. People with 3 or more cardiovascular risk factors who are due for major surgery
5. People over 50 years who are to undergo heart surgery or over 40 years and with two CVD risk factors that require

heart surgery e.g., mitral valve replacement

6. People being worked up for major organ transplant e.g. renal transplant, lung or liver transplant
7. People with heart failure of unclear aetiology may require screening for IHD
8. People with VT/VF
9. People who are resuscitated following cardiac arrest

9.9 Testing for Asymptomatic IHD

The ideal test chosen depends on the patient's primary diagnosis, the underlying comorbidities, and locally available resources. An experienced cardiologist should be involved in testing of these patients in view of the risk for missing disease and prescription of more expensive down- stream tests.

The following tests are recommended:

1. Exercise ECG
2. Exercise stress echocardiogram
3. Dobutamine stress echocardiogram
4. CT calcium score and CT coronary angiogram
5. Nuclear myocardial perfusion study
6. Cardiac MRI with gadolinium enhancement
7. Invasive coronary angiography

9.10 Cardiac Arrest in IHD

Many deaths occur early during the first few hours after STEMI due to ventricular fibrillation (VF). Since VF frequently occurs at an early stage, these deaths usually happen out of hospital. Therefore, it is crucial that all medical and paramedical personnel caring for persons with suspected myocardial infarction have access to defibrillation equipment and are trained in advanced cardiac life support. It is also vital that, at the point of first medical contact, ECG monitoring be immediately implemented in all patients with suspected myocardial infarction.

Care providers in ambulances and hospitals managing ACS patients should be ACLS certified. It is recommended for this guideline that ACLS re-certification should be performed every 2 years.

Hospitals taking care of ACS patients should put in place methods to ensure and facilitate the certification and re-certification of staff in basic life support (BLS) and ACLS through work plan schemes that should be freely available.

9.11 IHD in Special Populations

Female gender

Myocardial infarction remains a leading cause of death in women, who tend to present later than men. They also present more frequently with atypical symptoms. It is therefore imperative to maintain a high index of suspicion for myocardial infarction in women with potential symptoms of IHD.

Elderly

Elderly patients often present with atypical or mild symptoms, which may result in delayed or missed diagnoses of MI. They are also at particular risk of bleeding and other complications from acute therapies because of increased bleeding risk with age, reduction in renal function, and high prevalence of co-morbidities.

Kidney disease

Kidney dysfunction is present in approximately 30–40% of patients with ACS. It is associated with a worse prognosis and increased bleeding risk. In patients with known or anticipated reduction of kidney function, several antithrombotic agents should be either withheld or their doses reduced appropriately.

Diabetes

Diabetic patients are at higher risk of death and complications, but selection of antithrombotic therapies and reperfusion therapy is the same as in non-diabetics.

Hyperglycaemia on admission is common in patients with an ACS and is a powerful predictor of mortality and in-hospital complications. In the acute phase, it is reasonable to manage hyperglycaemia (i.e., maintain a blood glucose concentration ≤11.0 mmol/L). Hypoglycaemia must be avoided. This may require a dose-adjusted insulin infusion with monitoring of blood glucose levels in some patients.

Given the frequency of unrecognized diabetes and impaired glucose metabolism in STEMI patients, it is reasonable to measure HbA1c and fasting blood glucose in all patients without known diabetes who developed hyperglycaemia during the acute phase.

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10

10: VENOUS THROMBOEMBOLISM

Key Messages

- The diagnosis of VTE requires high clinical suspicion as many of the presenting symptoms are non-specific.
- Initial risk stratification should be performed in all patients with suspected or confirmed PE.
- In high-risk PE patients (i.e., haemodynamically unstable), systemic thrombolysis should be considered as the first choice of treatment with surgical embolectomy or catheter-assisted thrombolysis as options if thrombolysis fails/is contraindicated.
- Non-Vitamin K antagonist oral anticoagulants (NOACs) are recommended as the first choice for anticoagulation treatment in eligible patients. Vitamin-K antagonists are an alternative. Patients on treatment should be assessed and monitored for bleeding risk.
- All patients should receive at least 3 months of therapy; extended therapy can be considered depending on balance of risk factors for recurrence or bleeding.
- Low molecular weight heparin is the anticoagulant of choice in patients with cancer related thrombosis. Rivaroxaban or edoxaban are alternatives to LMWH except in gastric cancer due to increased bleeding risk.

10.1 Introduction

Venous thromboembolism (VTE) clinically presents as two serious medical conditions i.e. Deep Venous Thrombosis (DVT) and Pulmonary Embolism (PE). PE is almost invariably due to DVT. VTE is important because a missed diagnosis or delayed treatment can lead to death or debilitating long-term complications, including pulmonary hypertension and post-thrombotic syndrome [1]. Following symptomatic DVT, the incidence of severe post-thrombotic syndrome is 10% after 5 years but can be as high as 80% following pregnancy associated with VTE, mostly occurring within the first 2 years [2]. Chronic thromboembolic pulmonary hypertension (CTEPH) occurs in about 5% of patients with treated PE [2].

10.2 Epidemiology

Global data estimates the incidence of VTE in Europe and the USA to be approximately 1–2 per 1,000 person-years with variations within age, sex, race and medical conditions [3]. The rates are lower in Asia, at 0.2 per 1,000 person-years in South Korea for example [4]. The epidemiology of VTE in Africa is not well studied. According to a 2017 systematic review, the prevalence of deep vein thrombosis varied between 40% and 69.5% in medical patients and 2.4 to 9.6% in postoperative patient. It was estimated that at least one-quarter of patients who were at risk for VTE in Africa were not receiving prophylaxis [5]. In another review among post-operative patients, the case fatality rate of pulmonary embolism after surgery was 60% [6].

10.3 Aetiology/ Risk Factors

Virchow proposed three major pathophysiologic determinants of VTE including venous stasis, endothelial injury, and hypercoagulability. These mechanisms may fall under lifestyle-related conditions or inherited and acquired disorders [7].

VTE risk factors may be categorized as shown in the table below.

Table 10.1: VTE Risk Factors

Strong risk factors (Odds ratio >10)	Moderate risk factors (Odds ratio 2-9)	Weak risk factors (Odds ratio <2)
Fracture (hip or leg)	Arthroscopic knee surgery	Bed rest >3 days
Hospitalisation for HF or atrial fibrillation/flutter within past 3 months	Autoimmune diseases	Immobility due to sitting (e.g., prolonged car or air travel)
Hip or knee replacement	Blood transfusion	Increasing age
Major trauma	Central venous lines	Laparoscopic surgery (e.g., cholecystectomy)
MI within previous 3 months	Intravenous catheters and leads	Obesity
Previous VTE	Chemotherapy	Pregnancy/ antepartum
Spinal cord injury	Congestive heart failure or respiratory failure	Varicose veins
	Erythropoiesis-stimulating agents	Diabetes mellitus
	HRT (depends on formulation)	Arterial hypertension
	In vitro fertilization	
	Oral contraceptive therapy	
	Post-partum period	
	Infection-pneumonia, UTI, and HIV	
	Paralytic stroke	
	Superficial vein thrombosis	
	Thrombophilia	
VTE, venous thromboembolism; HF, heart failure, HRT, hormone replacement therapy; UTI, urinary tract infection; HIV, human immunodeficiency virus		

(Adapted from 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS) [7]

Additional risk factors include Coronavirus disease (COVID-19) infections. Thrombophilia or inherited causes of unprovoked DVT have mainly been studied in other populations, with few studies in our region. Factor V Leiden mutation is the most common hereditary thrombophilia, though it is rarely seen in non-white populations [8].

10.4 Diagnosis of DVT

Clinical signs and symptoms of DVT

DVT most commonly develops in the leg veins, but can occasionally also occur in the upper extremities, especially if there is an in-dwelling central venous catheter or a haemodialysis catheter resulting in upper extremity DVT (UEDVT) [2].

Common symptoms of proximal lower limb DVT include:

- Sudden onset of unilateral leg pain or tenderness of the thigh or calf
- Unilateral leg swelling (oedema)
- Skin that feels warm to the touch

Signs and symptoms are more severe with more extensive DVT, e.g., iliofemoral DVT.

Clinical Probability Testing in suspected DVT

There are many scoring systems to assist diagnosis, but a majority are difficult to implement. The Wells' Score is a simplified prediction tool for DVT.

Table 10.2: Simplified Wells' Score for Suspected DVT [2,12]

Clinical features	Score
Active cancer (treatment within last 6 months or on palliative care)	1 point
Paralysis, paresis, or recent plaster immobilization of leg	1 point
Recently bed-ridden for >3d or major surgery in last 12wks	1 point
Local tenderness along distribution of deep venous system	1 point
Entire leg swollen	1 point
Calf swelling >3cm compared with asymptomatic leg (measured 10cm below tibial tuberosity)	1 point
Pitting oedema (greater in the symptomatic leg)	1 point
Collateral superficial veins (non-varicose)	1 point
Previously documented DVT	1 point
Alternative diagnosis** at least as likely as DVT	-2 points
Note: In patients with symptoms in both legs, the more symptomatic leg is used ≥2 points = DVT likely: Perform ultrasound; if positive, treat as DVT. If ultrasound is unequivocal, do D-dimer test. If D-dimer positive and ultrasound negative, repeat ultrasound in 1 week. If both D-dimer and ultrasound negative, DVT excluded. <2 point = DVT unlikely: Perform D-dimer (where available). If negative, DVT excluded. If positive, proceed to ultra-sound (if ultrasound negative, DVT excluded; if positive, treat as DVT).	

**An alternative diagnosis may include: superficial venous thrombosis or phlebitis, post-thrombotic syndrome, lymphoedema, cellulitis, trauma, muscle strain or tear, leg swelling in paralyzed limb, venous insufficiency, oedema due to CCF or cirrhosis, external venous obstruction (e.g. due to tumour), lymphangitis or lymphedema, ruptured popliteal (Baker's) cyst, hematoma, or pseudoaneurysm in DVT

Imaging in DVT

The gold standard test for diagnosing lower or upper extremity DVT is venous compression ultrasonography (CUS). Failure to compress the vein is diagnostic of DVT [9].

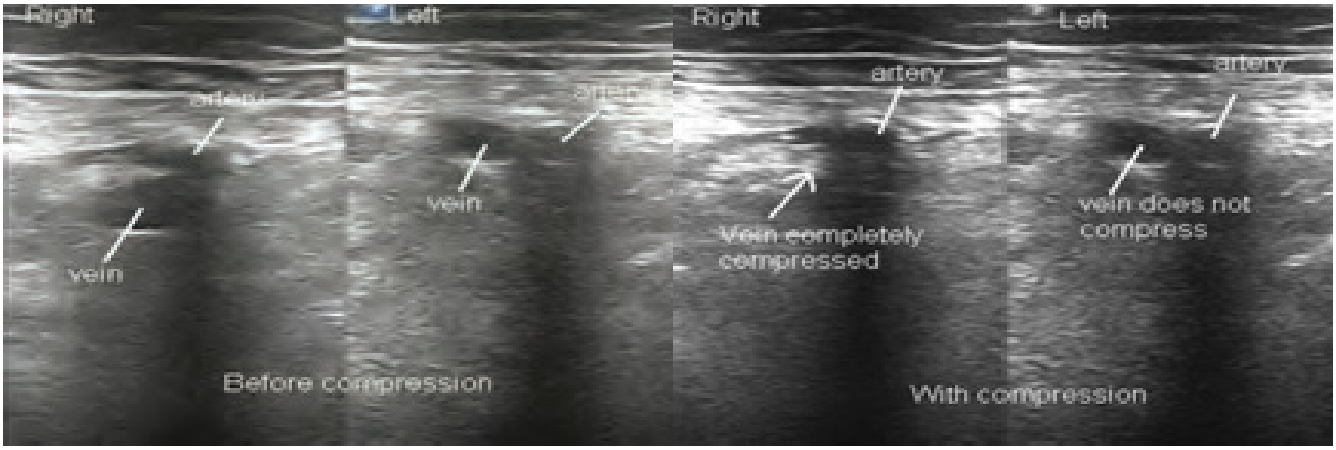

Figure 10.1. Ultrasonography images of femoral vessels before and with compression [10]

Alternative imaging using CT Venography (CTV) is usually reserved for imaging segments that are not easily assessed by CUS, e.g., pelvic veins, or subclavian vein DVT. CTV offers definite advantages over ultrasound when evaluating the pelvic veins or the inferior vena cava (IVC) and can detect concurrent medical conditions that cause pain and swelling [11]. CTV is expensive, not widely available, and requires the use of iodine contrast with radiation exposure.

Laboratory testing in DVT

Plasma D-dimer is a non-specific marker of fibrin lysis and may be elevated not only in VTE but also in many other conditions, including myocardial infarction, heart failure, infection, surgery, aortic dissection, and pregnancy. The D-dimer test is very useful in the evaluation of outpatients or casualty settings in patients with suspected VTE. If the D-dimer test is positive but CUS shows no evidence of proximal DVT, it is advised to repeat CUS in 7 days to rule out DVT [12].

Diagnostic algorithm for suspected DVT

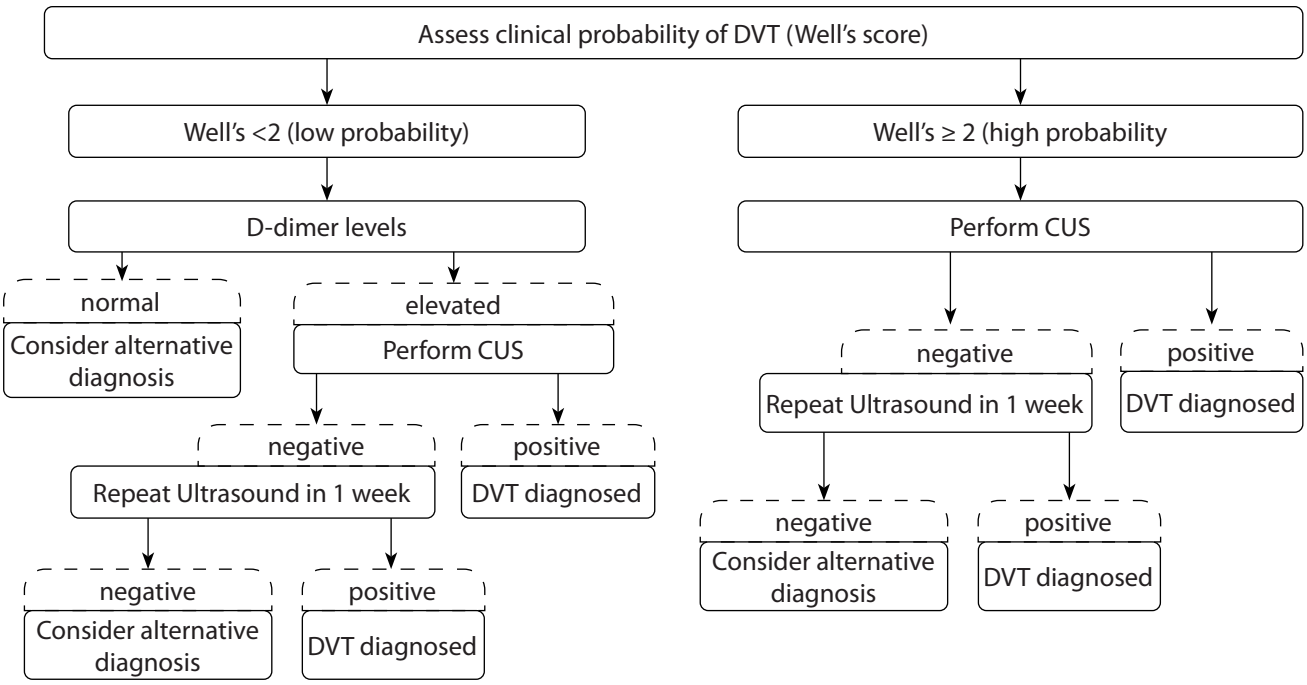

Figure 10.2: Algorithm for the Diagnosis of Suspected DVT

Source BMJ Evidence Centre [13].

10.5 Diagnosis of Acute Pulmonary Embolism

Clinical Presentation

The clinical presentation of acute PE may vary widely, and the signs and symptoms are often non-specific. Common features include dyspnoea, cyanosis, or fainting in massive acute PE. Large thrombi obstruct the pulmonary arterial tree and cause hemodynamic and gas exchange abnormalities, resulting in hypotension, hypoxemia, and increased right ventricular afterload. Clinical features may include the following:

- Unexplained sudden onset of dyspnoea
- Lightheaded sensation or syncope
- Pleuritic chest pain
- Pulse≥ 100 beats/minute
- Heart murmur of tricuspid regurgitation,
- loud P2
- Distended neck veins.

Assessment of clinical probability in acute PE

The combination of clinical findings and the use of prediction rules can help to classify patients with suspected PE into categories of probability that correspond to an increasing actual prevalence of confirmed PE on further testing [14].

Table 10.3: The revised Geneva clinical prediction rule for PE

Clinical Feature	Score
Previous PE or DVT	1
Pulse 75 to 94 bpm ≥95 beats/min	 1 2
Surgery or immobilization/fracture within the past 4 weeks	1
Haemoptysis	1
Active cancer	1
Unilateral lower limb pain	1
Pain on lower limb deep venous palpation and unilateral oedema	1
Age ≥65 years	1
Clinical Probability	
PE likely	≥3
PE unlikely 0-2	

(Adapted from 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS) [7].

Imaging in Acute PE

Multi-detector computed tomographic angiography (CT pulmonary angiography) is recommended in outpatients with an elevated plasma D-dimer and in patients with a high clinical probability of acute PE [15]. The CTPA is diagnostic for acute PE when it shows a thrombus in the pulmonary arterial tree. With regards to prognosis, a dilated right ventricle on CT imaging or echocardiography points to right ventricular dysfunction and increased severity of PE and carried a worse prognosis [16].

Laboratory testing in suspected Acute PE

Plasma D-dimer testing combined with clinical probability assessment should be carried out in patients with suspected acute PE in the absence of shock. D-dimer should not be measured in patients with a high clinical probability or hospitalized patients.

Prognostic assessment is recommended for patients without haemodynamic instability. Poor prognostic markers include high sensitivity troponin (preferred), B-type natriuretic peptide (BNP), N-terminal pro-B-type natriuretic peptide (NT-proBNP), and troponin (less sensitive than high-sensitivity troponin [17]. Patients with haemodynamic instability are already at high risk irrespective of other laboratory markers.

Predicting early mortality in acute PE

In patients with acute PE, it is important to consider their prognosis as certain patients carry a higher mortality risk and will need admission to critical care departments for monitoring and treatment. Other patients may have a very low risk of 30-day mortality, supporting admission to hospital in a general ward or even treatment at home with very close supervision [17].

The following features indicate higher 30-day mortality in acute PE:

- Shock
- Pulmonary Embolism Severity Index (PESI) Class [14]
- Signs of right ventricular dysfunction on echocardiography or CT imaging
- Elevated cardiac biomarkers.

10.6 Risk Factor Assessment in VTE

Imaging to detect occult malignancy

In patients with unprovoked VTE, routine clinical examination and sex-specific cancer screening are recommended.

Several studies have compared limited screening with more extensive cancer screening protocols including rectal examination, faecal occult blood testing, positron emission tomography (PET) imaging, and mammography and abdominopelvic CT scanning for women. Extensive screening diagnosed a higher number of malignancies compared with limited screening but there was no significant reduction in all-cause mortality or cancer-related mortality [18].

10.7 Prevention of Venous Thromboembolism

The use of VTE prophylaxis should be considered in all hospitalized patients but the implementation of mechanical or pharmacological measures is inconsistent in many institutions and among practitioners. It is recommended that health facilities have an admission policy that assesses VTE risk for all medical and surgical patients, to identify at-risk patients in whom VTE prophylaxis can commence. The risk of VTE persists after hospital discharge in many patients [19]. VTE mortality has been shown to rise between 10 - 35 days following hospital admission among acutely ill medical patients [20].

Pharmacological Thromboprophylaxis

Recommendations for hospitalized patients at risk of VTE include:

- Enoxaparin 40mg as a subcutaneous injection (SQ) once daily
- Unfractionated Heparin 5000 as a subcutaneous injection twice daily (12-hourly)
- Fondaparinux (where available) 2.5mg a subcutaneous injection once daily

Mechanical Thromboprophylaxis

Graduated compression stockings/Anti-embolism stockings and intermittent pneumatic compression devices (where available) should be considered for at-risk patients who are NOT candidates for pharmacological thromboprophylaxis due to the high risk of bleeding pre-operatively, intra-operatively, and post-operatively [21, 22].

Mechanical prophylaxis is effective when used in combination with early ambulation.

Standards for the use of anti-embolism stockings [21]

- Patients should have their legs measured and the correct size of stocking provided.
- Use anti-embolism stockings that provide graduated compression and produce a calf pressure of 14–15 mmHg.
- Encourage patients to wear their anti-embolism stockings day and night until they no longer have significantly reduced mobility.
- Remove anti-embolism stockings daily for hygiene purposes and to inspect skin condition.
- In patients with a significant reduction in mobility, poor skin integrity, or any sensory loss, inspect the skin two or three times per day, particularly over the heels and bony prominences.
- Discontinue the use of the stockings if there is marking, blistering, or discoloration of the skin, particularly over the heels and bony prominences, or if the patient experiences pain or discomfort. If suitable, offer intermittent pneumatic compression (IPC) device as an alternative.
- Avoid roll up of the stoking, a common happening, as it can present as a tourniquet and accelerate the DVT or can cause arterial insufficiency.

Standards for Intermittent Pneumatic COMPRESSION [22]

- Proper fitting of the device
- Compression pressure and cycling time: IPC pressure of 120–140mmHg applied to foot and calf with a one-second delay, and at a frequency of three to four impulses per minute [18].

Contraindications to mechanical prophylaxis [23]

- Peripheral artery disease, including a history of peripheral arterial bypass grafting.
- Severe peripheral neuropathy or other causes of sensory impairment
- Allergy to stocking material
- Massive leg oedema or pulmonary oedema from congestive cardiac failure
- Local skin or soft-tissue condition, including a recent skin graft, fragile skin, gangrene, severe dermatitis, and cellulitis.
- Extreme deformity of the leg, or unusual leg shape or size preventing correct fit
- Documented DVT.

10.8 VTE Treatment & Patient Management

10.8.1 Anticoagulation

Anticoagulation is the treatment foundation for patients with VTE. It is administered sequentially as follows:

- Initial anticoagulation in patients with acute DVT and PE.
- Long-term anticoagulation (usually up to 3 months)
- Extended- treatment (beyond 3 months in select patients)
- In patients with cerebral venous sinus thrombosis, anticoagulation therapy is recommended for at least the treatment phase (first 3 months) over no anticoagulant therapy.

Options of pharmacological agents include the following [11].

- Low Molecular Weight Heparin (LMWH)
- Unfractionated heparin (UH)
- Fondaparinux
- Warfarin
- Direct Oral Anti-Coagulants (DOACs)

Low Molecular Weight Heparin

- Dosing is based on weight and administered subcutaneously.
- Dose: Enoxaparin 1 mg/kg SQ twice daily.
- Renal Dosing: A dose reduction is recommended in patients with severe renal insufficiency (GFR < 30 ml/min): 1mg/kg SQ once daily.
- Advantages: no routine laboratory monitoring required.
- Safety: safe and effective as unfractionated heparin.
- Recommended over warfarin in cancer patients [24].

Fondaparinux

- A synthetic pentasaccharide that is safe for DVT and acute PE.
- Administered once daily according to weight and does not require routine monitoring or dose adjustment.
- Dosing
- Wt.<50kg- 5 mg OD x 5 days
- Wt.> 50-100kg: 7.5 mg OD X 5 days
- Wt. >100kg: 10mg OD X 5 days
- Fondaparinux should not be used in patients with renal impairment [25].

Unfractionated Heparin

- Give heparin 60IU/Kg IV bolus then infuse at a rate of 18 units/kg/hour. Check APTT at 6hr, aim for APTT of 60-85 seconds or APTT ratio of 1.5–2.5. Measure APTT daily or 10h after dose change [11, 19].
- Subcutaneous Regimen-17,500IU SQ twice daily.
- UFH is recommended in patients with a creatinine clearance <30 mL/min with dose adjustments based on the APTT [2].

NOTE: Parenteral anticoagulants (e.g., LMWH, fondaparinux, or UFH, in that order of preference) are used in the initial/acute phase of treatment during hospitalization. If planning to use Vitamin K antagonists (VKA) as long-term anticoagulation, warfarin can be started from day 1 while continuing unfractionated heparin until INR has reached the target therapeutic range or until day 5, as warfarin has an initial prothrombotic effect [11]. There is a risk of bleeding and thrombocytopenia when using heparin so monitoring the haemoglobin and platelet count is important when commencing therapy.

Vitamin K Antagonists (VKA) - Warfarin

- Recommended Starting Dose: 5 mg orally once daily.
- Initiate warfarin on day 1 or 2 of parenteral anticoagulation therapy. Do INR daily and adjust dose accordingly. Overlap warfarin and parenteral anticoagulant until desired INR is maintained for 24 hours, and then discontinue parenteral therapy.
- Typical maintenance dose: 2 to 10 mg orally once a day. Dosage must be individualized according to the patient's INR.
- Target INR: 2.5 (range: 2 to 3)
- Renal Dose: No dosage adjustment is necessary for patients with renal failure. However, some studies suggest lower warfarin doses in those with renal impairment [26].
- Important drug-drug interactions: Warfarin has interactions with many drugs including some antibiotics (anti-TBs), antifungals, antiretrovirals, cardiovascular drugs, corticosteroids, anticonvulsants, and contraceptives [2,11]. Consult with a pharmacist/pharmaceutical technologist before prescribing other medications that may alter the efficacy/potentiate the effects of warfarin.
- Contraindications: Peptic ulcers, bleeding disorders, severe hypertension, pregnancy. Use with caution in the elderly and those with past gastrointestinal bleeds [11].

- In patients with thrombosis and antiphospholipid syndrome being treated with anticoagulant therapy, adjusted-dose vitamin K antagonists (VKA) are recommended over direct oral anticoagulant therapy (DOAC) [27].
- It may be difficult to achieve stable INR levels in resource-limited settings and this may be related to drug-drug interactions, frequency of INR testing, and comorbidities. Close attention needs to be paid to achieving target anticoagulation levels in hospitalized patients. On admission in hospital and discharge, check the INR levels for patients with known VTE or an indication for VKA.
- Dietary restrictions: Warfarin has many food interactions. Consult a dietitian nutritionist as part of the initial patient counselling for warfarin therapy [28].

Direct Oral Anti-Coagulants (DOACs)

- Factor Xa inhibitors (rivaroxaban and apixaban) and direct thrombin inhibitors (dabigatran) are newer oral anticoagulants that offer the advantage of fixed dosing without the need for intense coagulation monitoring. Treatment for VTE can commence immediately with these drugs in patients with DVT or acute PE without the need for monitoring, though it is important to consider bleeding risk in all patients starting anticoagulation

Dose:

- Rivaroxaban 15 mg orally twice daily as the initial dose for 21 days followed by 20 mg once daily for the rest of the duration of treatment.
- **Dabigatran:** 150 mg orally twice daily after 5 days of parenteral therapy.
- **Apixaban:** 10 mg orally twice daily as initial dose for 7 days followed by 5mg twice daily for the rest of the duration of treatment. [29].

Thrombolytic therapy

Systemic thrombolytic therapy is recommended for high risk, haemodynamically unstable patients. Surgical embolectomy should be considered if these patients fail, or are not candidates for, thrombolytic therapy.

Catheter-directed thrombolysis should be reserved for high-risk patients in whom thrombolysis has failed or is contraindicated.

Rescue thrombolysis can be done for patients who are deteriorating despite adequate anticoagulation [30].

10.8.2 Duration of Anticoagulation Therapy in VTE

The importance of anticoagulation therapy in patients with VTE is to prevent a recurrence. VKAs are used in most cases, while LMWH is preferred in patients with VTE and active cancer. The DOACs have been utilized as an alternative to VKA for the long-term treatment of VTE [11].

Table 10.4 Recommendations for the Duration of Anticoagulation in VTE

Recommendations	Class[a]	Level[b]
Therapeutic anticoagulation for 3 months is recommended for all patients with PE [347].	I	A
Patients in whom discontinuation of anticoagulation after 3 months is recommended		
For patients with first PE/VTE secondary to a major transient/reversible risk factor, discontinuation of therapeutic oral anticoagulation is recommended after 3 months [331, 340, 341].	I	B
Patients in whom extension of anticoagulation beyond 3 months is recommended		
Oral anticoagulant treatment of indefinite duration is recommended for patients presenting with recurrent VTE (that is, with at least one previous episode of PE or DVT) not related to a major transient or reversible risk factor [358].	I	B
Oral anticoagulant treatment with a VKA for an indefinite period is recommended for patients with antiphospholipid antibody syndrome [359].	I	B
Patients in whom extension of anticoagulation beyond 3 months should be considered[c,d]		
Extended oral anticoagulation of indefinite duration should be considered for patients with a first episode of PE and no identifiable risk factor [330, 331, 347, 351-353].	IIa	A
Extended oral anticoagulation of indefinite duration should be considered for patients with a first episode of PE associated with a persistent risk factor other than antiphospholipid antibody syndrome [330, 352, 353].	IIa	C
Extended oral anticoagulation of indefinite duration should be considered for patients with a first episode of PE associated with a minor transient or reversible risk factor [330, 331, 352].	IIa	C
NOAC dose in extended anticoagulatione		
If extended oral anticoagulation is decided after PE in a patient without cancer, a reduced dose of the NOACS apixaban (2.5 mg b.i.d.) or rivaroxaban (10 mg o.d.) should be considered IIa after 6 months of therapeutic anticoagulation [352, 353].	IIa	A
Extended treatment with alternative antithrombotic agents		
In patients who refuse to take or are unable to tolerate any form of oral anticoagulants, aspirin or sulodexide may be considered for extended VTE prophylaxis [355-357].	IIb	B
Follow-up of the patient under anticoagulation		
In patients who receive extended anticoagulation, it is recommended that their drug tolerance and adherence, hepatic and renal function, and bleeding risk be reassessed at regular intervals [259].	I	C

b.i.d.: bis in die (twice a day); DVT: deep vein thrombosis; NOAC(s): non-vitamin K antagonist oral anticoagulant(s); o.d.: omni die (once a day); PE: pulmonary embolism; VKA: vitamin K antagonist; VTE: venous thromboembolism. Class of recommendation. Level of evidence. "The patient's bleeding risk should be assessed (see supplementary table 14 for prediction models) to identify and treat modifiable bleeding risk factors, and it may influence decision-making on the duration and regimen/dose of anticoagulant treatment. "Refer to supplementary table 9 for therapeutic decisions in specific clinical situations. If dabigatran or edoxaban is chosen for extended anticoagulation after PE, the dose should remain unchanged, as reduced-dose regimens were not investigated in dedicated extension trials [313, 350]. 'Especially for patients receiving NOACs.

Source:. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS). Eur Respir J 2019; in press [https://doi.org/10.1183/13993003.01647-2019][7].

10.8.3 Antidotes to Anticoagulants

1. UFH overdose: stop the infusion. If there is bleeding, administer protamine sulphate in consultation with a physician.
2. Warfarin: Stop warfarin. Give prothrombin complex concentrate 50units/kg (where available) in consultation with a physician. If unavailable, give Fresh Frozen Plasma (FFP) (15mL/kg). Also, give 5–10mg vitamin K IV slowly.
3. Dabigatran: give idarucimab (a monoclonal antibody that reverses the anticoagulation caused by dabigatran). It does not stop bleeding, however.
4. Rivaroxaban and apixaban: andexanet alpha given intravenously.

10.8.4 Important Considerations

- Monitoring of bleeding: take note of gastrointestinal, brain, skin, and urological bleeding.
- Dosing, especially in renal disease
- Special groups-Pregnancy, HIV, elderly and children, sickle cell disease (refer to appropriate experts)
- Precaution for drug interactions
- Follow-up- with regards to the efficacy of anticoagulation and recurrence of VTE
- In patients with acute DVT of the leg, the use of an inferior vena cava (IVC) filter in addition to anticoagulants is not recommended.

10.8.5 Practice Recommendations

- Thrombo-prophylaxis assessment in patients with medical and surgical conditions
- Anticoagulation monitoring- multidisciplinary anticoagulation clinics with designated staff e.g., anticoagulation nurses and pharmaceutical technologists
- Strengthening of Research and Health Information Systems concerning VTE.
- Training of specialists in thrombosis and haemostasis

10.9 Venous Thromboembolism in Pregnancy

10.9.1 Epidemiology

Though infrequent, VTE complicates about 1.2 of every 1000 deliveries. It is a leading cause of maternal morbidity and mortality. Increased risk persists until 12 weeks postpartum, with the greatest risk in the first 6 weeks after delivery. The incidence of VTE is similar in antepartum and postpartum periods, but the postpartum period is shorter so has a higher daily VTE risk [31]).

10.9.2 Diagnosis

For pregnant women with suspected DVT, it is recommended that additional investigations including serial compression ultrasound or magnetic resonance venography (MR-V), be undertaken, compared with no further investigations, following an initial negative ultrasound with imaging of the iliac veins [32].

10.9.3 Treatment

In acute VTE, treatment with LMWH is recommended, either once-daily or twice-daily dosing.
In acute PE with life-threatening hemodynamic instability, systemic thrombolysis is advised in addition to anticoagulant therapy.

For low-risk acute VTE initial outpatient therapy over hospital admission is recommended

For pregnant women receiving therapeutic-dose LMWH for VTE, scheduled delivery with prior discontinuation of anticoagulant therapy is recommended [2].

Table 10.5: Choice of Anticoagulation in Pregnancy

Anticoagulant	Acceptability in Pregnancy	Comments
LMWH	Yes	• Does not cross the placenta. • LMWH preferred over UFH due to better maternal safety profile (likely lower risk of HIT, reduced bone mineral density).
UFH	Yes	• Does not cross the placenta
Fondaparinux	Not preferred	• Reported to cross the placenta in small amounts. • Clinical experience with fondaparinux is very limited.
Vitamin K Antagonist (VKA)	No	• Crosses the placenta. • Potential for teratogenicity, pregnancy loss, foetal bleeding, neurodevelopmental deficits
Direct Oral Anticoagulants	No	• Dabigatran and Xa inhibitors likely cross the placenta. • Reproductive effects in humans are unknown

For breastfeeding women who have an indication for anticoagulation, use of UFH, LMWH, warfarin, acenocoumarol, fondaparinux, or danaparoid is recommended as safe options [33].

For breastfeeding women who have an indication for anticoagulation use of direct-acting oral anticoagulants is not recommended [29].

Table 10.6: Choice of Anticoagulants in Lactation [34]

Anticoagulant	Acceptability in Breastfeeding	Comments
UFH	Yes	• Does not pass into breast milk due to large size and negative charge
LMWH	Yes	• Excreted into breast milk in small amounts, but limited bioavailability so unlikely to be absorbed by newborn.
Non-lipophilic VKA	Yes	• Non-lipophilic VKAs (warfarin, acenocoumarol) unlikely to be secreted in breast milk; small studies showing no detectable levels
Rivaroxaban	No	• Case reports suggesting low excretion of rivaroxaban into breast milk (estimated relative infant dose < 2%), but limited experience. • A paucity of data on all direct oral anticoagulants, including rivaroxaban

For women not already receiving long-term anticoagulant therapy who have a history of VTE, the following recommendations are suggested:

Table 10.7: VTE Prophylaxis in Pregnancy and Breastfeeding [34].

Prior VTE history	Antepartum Prophylaxis	Postpartum Prophylaxis
Unprovoked VTE	Yes	Yes
Provoked VTE, Hormonal risk factor	Yes	Yes
Provoked VTE, Non-Hormonal risk factor	No**	Yes

10.10 Cancer-Associated Thrombosis

Cancer is recognized as one of the strongest risk factors for venous thromboembolism; thromboembolism is known to be the joint second highest cause of death in cancer patients after cancer progression itself [35].

The risk of cancer-associated thrombosis is multi-factorial and can be divided into:

- Cancer-specific risk factors including cancer type and cancer cell biology.
- Treatment-related risk factors such as type of chemotherapy (e.g., Lenalidomide) or surgical interventions.
- Patient-related risk factors such as age, thrombophilia, laboratory parameters such as platelet count, and modifiable factors like smoking and obesity.

10.10.1 Thromboprophylaxis in Cancer: Risk Assessment of VTE

Using known risk factors, risk assessment tools can be used to stratify patients into risk groups. Patients at higher risk of VTE should be targeted for thromboprophylaxis.

An example of a risk scoring tool is the Khorana score [36].

Table 10.8 The KHORANA Score [36]

Patient characteristic	Risk score
Site of cancer	
• Very high risk (stomach, pancreas)	2
• High risk (lung, lymphoma, gynaecological, bladder, testicular)	1
Pre-chemotherapeutic platelet count ≥350 × 10^9/L	1
Haemoglobin concentration <100 g/L or use of erythropoiesis-stimulating agents	1
Pre-chemotherapeutic leucocyte count >11 × 10^9/L	1
Body mass index ≥35 kg/m^2	1

Interpretation:

Thrombosis rate per 2·5 months (%)		
Low score	0	0·3–0·8
Intermediate score	1–2	1·8–2
High score	>2	6·7–7·1

10.10.2 Treatment of VTE in Cancer

- For patients who are diagnosed with VTE with active cancer or recently treated cancer, the choice of drugs includes low molecular weight heparin, apixaban, rivaroxaban, or fondaparinux [37].
- Patients with gastrointestinal cancer are at an increased bleeding risk with non-vitamin K antagonist oral anticoagulants (DOACs) [24].
- It is recommended that anticoagulation should be continued for a minimum of 6 months for VTE in cancer. After treatment of the acute VTE for 6 months, the patient should be assessed to determine whether it is appropriate to discontinue anticoagulation. If the patient still has active cancer, secondary prophylaxis with ongoing anticoagulation at treatment or the prophylactic dose may be necessary.
- If the patient is having recurrent VTE despite therapeutic anticoagulation, please consult with a Haematologist.

10.11 COVID-19 and Thrombosis

10.11.1 COVID-19 and Hypercoagulability

COVID-19 has been associated with inflammation and a prothrombotic state, with increases in fibrin, fibrin degradation products, fibrinogen, and D-dimers [38].

Several studies have reported varying incidences of venous thromboembolism (VTE) in patients with COVID-19 [11].

Several haematologic changes have been reported in COVID-19 infection.

Table 10.9: Haematological changes in COVID-19 and their clinical significance

Parameter	Trend in COVID-19	Clinical Significance
Platelets	20-30% have platelets 100-150	Not clearly associated with mortality
Lymphocytes	Often moderate to severe lymphopenia 75-83% have ALC < 1.5	Severe lymphopenia (ALC < 0.5) and LDH elevation often seen in critical illness
PT (prothrombin time)	Mild prolongations (15-16 sec)	Prognostic (some association with mortality)
D-Dimer	Persistent, marked elevations (4-6x ULN) often seen in severe COVID	Prognostic (associated with mortality)
Fibrinogen	Typically elevated until late in disease course	Reductions can be seen late (10-14 days) into admission

Bhatraju PK, et al. NEM. 2020,0(0):null. doi:10.1056/NEJMoa2004500; Guan W, et al. NE.M. 2020;0(0):null doi:10.1056/NEJMoa2002032 Targ Y-W, et al.J Cli Microbiol. April 2020. doi:10.1128/JCM.00512-20; Fan BE, et al. Amer J Hematol. n/a(n/a). doi:10.1002/ajn.25774

10.11.2 Evaluation and Management of COVID-19 Associated Hypercoagulability

Table 10.10: Evaluation and Management of COVID-19-associated Hypercoagulability

Evaluations and Monitoring	
Inpatient	• Daily PT, aPTT, fibrinogen, D-dimer; frequency may be reduced depending on acuity and trend in values. • Diagnostic imaging studies if feasible for clinically suspected DVT or PE; consult PERT. • Alternative evaluations if standard imaging studies are not feasible
Outpatient	• Routine coagulation testing is not required
Management	
Abnormal Coagulation Studies	• Use for prognostic information and level of care. • Do not intervene solely based on coagulation abnormalities
VTE Prophylaxis	• Prophylactic dosing preferred over higher dosing in most inpatients, including those in the ICU. • Dose adjustments may be made for increased body weight or decreased kidney function. • LMWH is generally preferred over other anticoagulants. • Thromboprophylaxis is generally not continued following discharge, with rare exceptions. • Thromboprophylaxis is generally not used in outpatients, with rare exceptions.

VTE Treatment	• Therapeutic (full dose) anticoagulation for documented VTE or high suspicion for VTE. • Initiate in hospital per standard protocols. • Continue treatment for at least 3 months. • Reserve fibrinolytic agents (e.g., tPA) for limb-threatening DVT, massive PE, acute stroke, or acute MI; consult PERT or stroke team.
Clotting in vascular catheters or extracorporeal circuits	• Therapeutic (full-dose) anticoagulation • Standard protocols for continuous renal replacement therapy or ECMO
Bleeding	• Similar to individuals without COVID-19 • Transfusions for anaemia or thrombocytopenia • Anticoagulant reversal and/or discontinuation for anticoagulant-associated bleeding • Specific treatments (e.g., factor replacement) for underlying bleeding disorders • Avoid antifibrinolytic agents in individuals with acute decompensated DIC

COVID-19, coronavirus disease of 2019; PT, prothrombin time; aPTT, activated partial thromboplastin clotting time; DVT, deep venous thrombosis; PE, pulmonary embolism; PERT, Pulmonary Embolism Response Team; VTE, venous thromboembolism; ICU, intensive care unit; LMWH, low molecular weight heparin; tPA, tissue-type plasminogen activator; MI, myocardial infarction; ECMO, extracorporeal membrane oxygenation; DIC, disseminated intravascular coagulation.

10.11.3 Summary of Anticoagulation in Covid-19

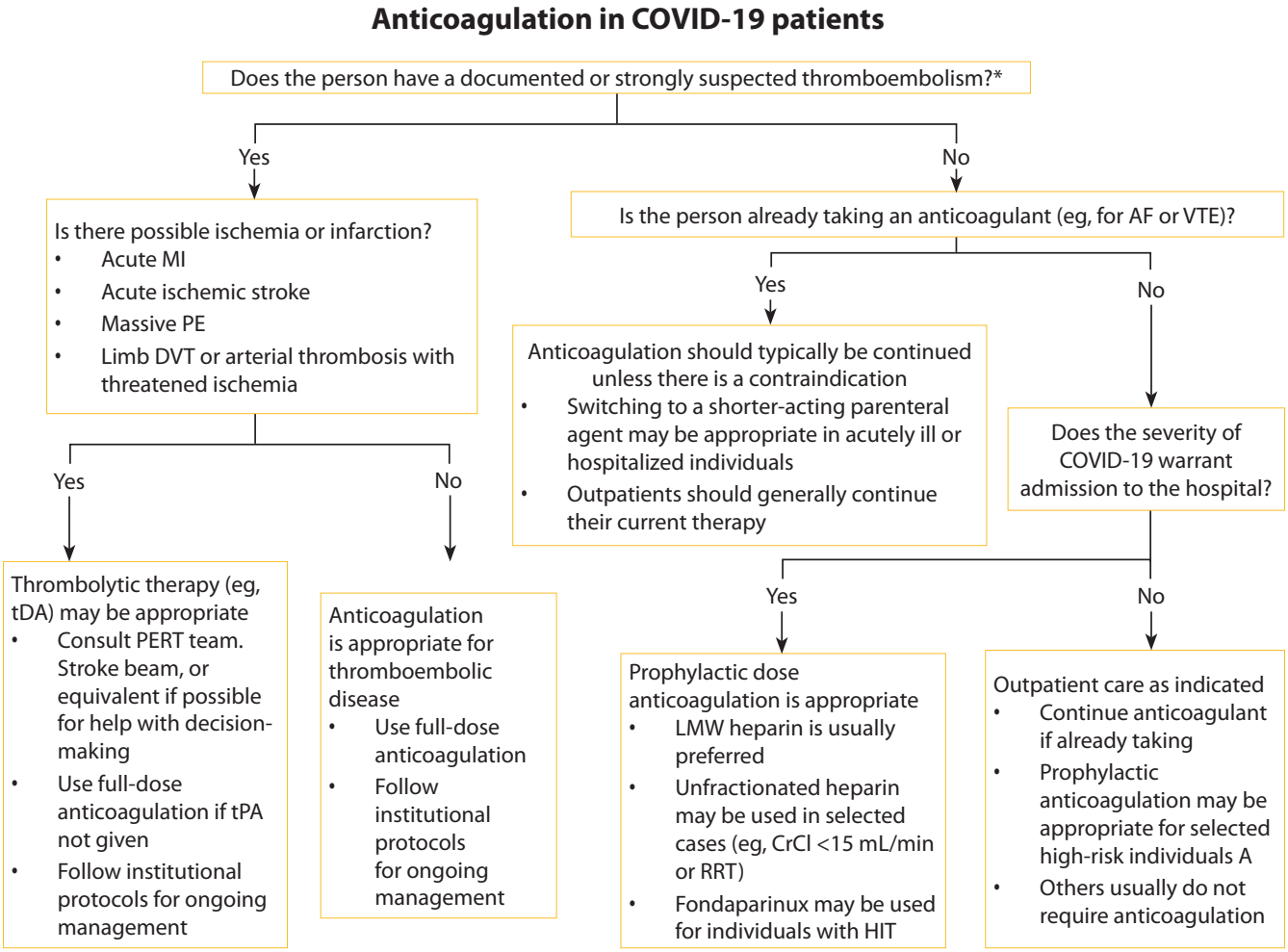

Figure 10.3: Summary of Anticoagulation in Covid-19

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11

11. STROKE

Key Messages

- Consider stroke in anyone who presents with acute and sudden neurological deficits.
- TIME IS BRAIN. Permanent damage to brain tissue occurs very quickly. To minimize the level of disability following stroke, treatment must be initiated as soon as possible.
- FAST: simplified criteria for assessment of suspected stroke:
    - FACE-has their mouth drooped?
    - ARM-can they lift both arms?
    - SPEECH
    - TIME-time is critical-get to hospital fast!
- The initial assessment should be done within 10 minutes of arrival to an emergency facility, with timely organisation for referral to a facility capable of handling stroke as needed.
- Management of cardiovascular risk factors (e.g., hypertension, dyslipidaemia) is important in primary prevention of stroke.
- Secondary prevention is key to prevent recurrent strokes.
- A long-term care plan after stroke including psychological support and rehabilitation should be availed for patients.

11.1 Introduction

Definitions

Stroke: An ACUTE or SUDDEN (i.e., rapidly developing) onset of neurological deficit due to a vascular cause.

Transient Ischemic Attack (TIA): Stroke symptoms that resolve rapidly, usually within 1-24 hours, with no evidence of infarction.

11.2 Epidemiology

Stroke is the second-leading cause of death and the third leading cause of both death and disability in the world. The with more death and disability in lower income countries compared to higher income countries. In 2019, there were approximately 12.2 million new cases of stroke, with an estimated 6.5 million deaths attributed to stroke (1).

Studies in Kenya have demonstrated hospital prevalence of stroke of 0.6% in a referral hospital in Western Kenya, 3.0% in an urban private hospital in Nairobi, and 7.1% in a rural hospital in Eastern Kenya. Stroke mortality in Kenya is high even in tertiary settings (2).

11.3 Classification of Stroke

There are two main types of strokes: ischaemic and haemorrhagic.

Ischaemic stroke[3]

Approximately 80-87% of strokes are from ischaemic infarction caused by thrombotic or embolic cerebrovascular occlusion. These may result from thrombosis in a brain artery, embolus from the heart or from major arteries like the carotid artery.

Ischaemic stroke is further classified as acute or chronic.

Haemorrhagic stroke[3]

This results from a weakened vessel that ruptures or due to defects in coagulation leading to bleeding into the surrounding brain. The blood accumulates and compresses the surrounding brain tissue. The bleeding may be intra-parenchymal (within the brain) or in the subarachnoid space, and may spill into the ventricular space.

Intraparenchymal haemorrhage accounts for about 10% of strokes, while subarachnoid haemorrhage makes up ~3%.

Haemorrhagic stroke may be:

- Primary (Intraparenchymal and subarachnoid)
- Haemorrhagic transformation of ischaemic stroke

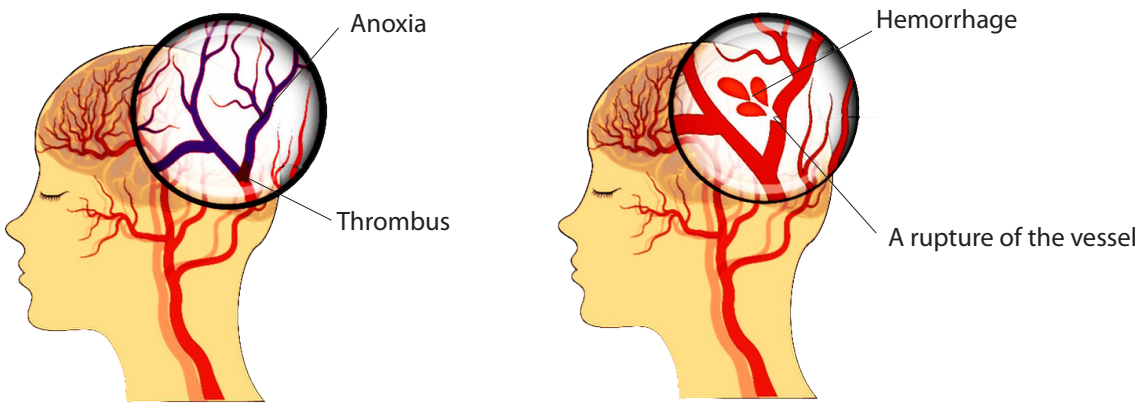


Figure 11.1: Illustration demonstrating the main types of stroke

Source: Shutterstock © 2013-2021

11.4 Risk factors for Stroke

Table 11.1: Risk factors for stroke

Modifiable risk factors that account for most strokes are:
• Hypertension-associated with ~50% of all strokes • Obesity • Physical inactivity-regular exercise reduces several stroke risk factors including hypertension and diabetes (See Prevention of ASCVD: Physical Activity and Weight Management) • Poor diet • Smoking tobacco, including passive exposure to tobacco smoke
Other risk factors:
• Advanced age • Race-risk for stroke in higher in black and Hispanic people • Sex: males are more likely to get a stroke at younger ages, but women have a higher lifetime risk as they tend to live longer • Family history and genetics-stroke in a first degree relative especially at a young age increased the risk • Previous stroke or transient ischaemic attack (TIA) • Diabetes mellitus • Cardiac disease • Valvular heart disease • Heart failure • Coronary artery disease • Arrhythmias, e.g, atrial fibrillation • Unhealthy lifestyle habits: excessive alcohol use, illicit drug use (cocaine, other sympathomimetic drugs), • High cholesterol • Use of oral contraceptive pills or hormone replacement therapy • Hypertension in pregnancy-eclampsia and pre-eclampsia • Other medical conditions such as sleep apnoea, kidney disease, disorders of coagulation, sickle cell disease • Anticoagulant or antithrombotic therapy • Ateriovenous malformations, aneurysms, and other vascular malformations-increase risk of bleeding • Vasculitis due to autoimmune disease or viral infections such as HIV infection • Other implicated factors: anxiety, depression, high levels of stress; residence or working in areas with air pollution.

The Stroke Riskometer™ app from the World Stroke Organisation can be used to assess stroke risk (https://www.strokeriskometer.com/).

11.5 Prevention

Primary stroke prevention refers to the treatment of individuals with no history of stroke but at increased risk of developing it.

Secondary stroke prevention refers to the treatment of individuals who have already had a stroke or transient ischemic attack.

11.5.1 Primary Prevention of Stroke

Risk-reduction measures in primary stroke prevention include:

- Optimise treatment for diabetes, hypertension, obesity, and dyslipidaemia.
- Mitigate behavioural risk factors e.g., tobacco use, alcohol use, physical inactivity, unhealthy diet.
- Screen for hypertension, obesity, diabetes, dyslipidaemia in the community and refer cases to health facilities for care.

Refer to chapters on Prevention of ASCVD, Hypertension, and Dyslipidaemia for more details.

11.5.2 Secondary Prevention of Stroke

Preventing recurrent stroke is crucial to minimize damage to brain tissue and therefore degree of disability.

Secondary prevention can be summarized by the mnemonic A, B, C, D, E, as follows (6):

A. Antiaggregants (aspirin, clopidogrel, extended-release dipyridamole, ticlopidine) and anticoagulants (apixaban, dabigatran, edoxaban, rivaroxaban, warfarin)
B. Blood pressure–lowering medications
C. Cigarette smoking cessation, cholesterol-lowering drugs, carotid revascularization
D. Diet
E. Exercise

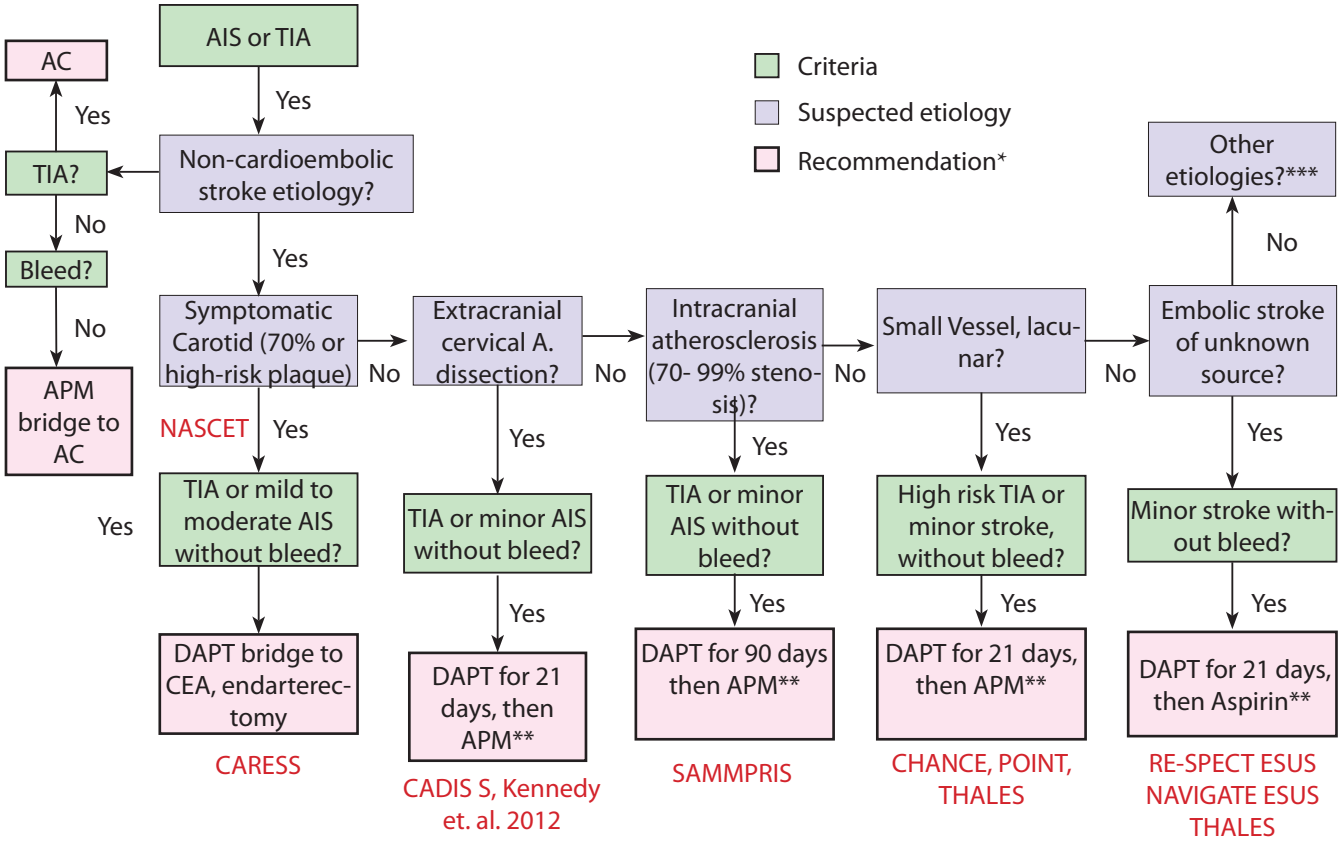


Figure 11.2: Flow Diagram Decision Tree on Medical Management for Secondary Stroke Prevention

A clinical decision tree regarding medical management for secondary stroke prevention based on initial acute stroke presentation and suspected aetiology of stroke following consideration of tPA or thrombectomy. Relevant guiding studies have been included.

Abbreviations: AC anticoagulation, AIS acute ischemic stroke, APM antiplatelet monotherapy, CEA carotid endarterectomy, DAPT dual antiplatelet therapy, TIA transient ischemic attack.

*Recommendations assume the patient did not receive tPA or thrombectomy.

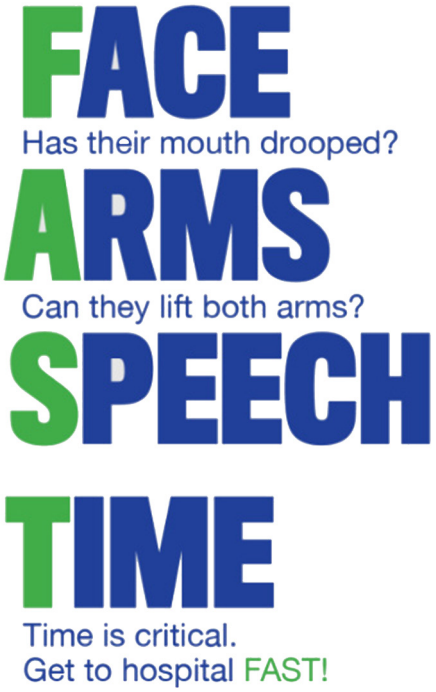
**Consider weight-based aspirin dosing (325 mg daily for patients weighing >70 kg) when aspirin monotherapy is indicated for secondary stroke prevention.

***Secondary prevention strategies of other ischemic stroke aetiologies (i.e., paradoxical embolus, vasculitis, Moyamoya disease) as well as ischemic strokes that fall outside the criteria in the above table are beyond the scope of these guidelines, and the reader is encouraged to discuss with a specialist cardiologist and/or neurologist.

11.6 Diagnosis

Diagnosis is made by history and clinical findings (FAST) supported by a CT scan of the brain.

FAST is a simplified criteria for detecting stroke:



Consider stroke in any patient presenting with ACUTE and SUDDEN neurologic deficit:

- Abrupt onset of limb weakness
- Hemi-sensory disturbance
- Visual disturbance
- Abnormal speech
- Facial droop
- Abnormal gait or posture
- Dizziness and loss of balance
- Sudden decrease in level of consciousness

Although such symptoms can occur alone, they are more likely to occur in combination.

JoinTriage App

Standard assessment tools as shown are used to improve the speed and accuracy of diagnosis in patients with suspected stroke, although there is a small risk of wrong diagnosis. The aim of using these tools is to minimize delay in initiating treatment (5). Available from https://www.world-stroke.org/

11.7 Management of Stroke

11.7.1 Hyper-Acute Management of Stroke

Emergency medical services should be redesigned to facilitate rapid recognition, assessment, and access to specialist stroke services according to the following timelines:

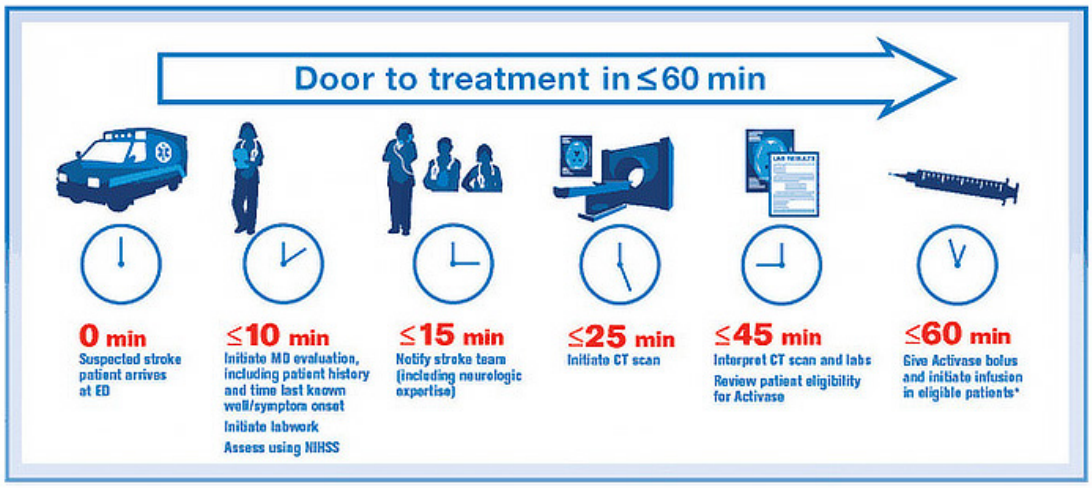


Figure 11.3: Recommended timelines in emergency management of stroke[9]

11.7.2 Initial Emergency Assessment

Time is Brain

This is a popular phrase that calls for urgent action when managing stroke. Permanent damage to brain tissue occurs very quickly and therefore to minimize the level of disability following stroke, treatment must be initiated as soon as possible.

The initial assessment should be done within 10 minutes of arrival to an emergency facility:

- Assessment of the ABCs, take vitals - BP, temperature, pulses
- General examination: Examination of the head and neck may reveal signs of trauma or seizure activity (e.g., contusions, tongue lacerations), carotid disease (bruits), and jugular venous distention.
- Cardiac examination focuses on identifying concurrent myocardial ischemia, valvular conditions, irregular rhythm, or congestive heart failure.
- Respiratory examination
- Neurological examination: Confirming the presence of a stroke syndrome.

- Distinguishing stroke from stroke mimics
- Establishing a baseline, should the patient's condition improve or deteriorate
- Establishing stroke severity, using a structured neurologic exam and score (e.g.National Institutes of Health Stroke Scale [NIHSS]) to assist in prognosis and therapeutic selection.
    - See: https://www.stroke.nih.gov/documents/NIH_Stroke_Scale_508C.pdf for NIHSS stroke scoring.

World Stroke Organisation Decision-making Flowchart[5]

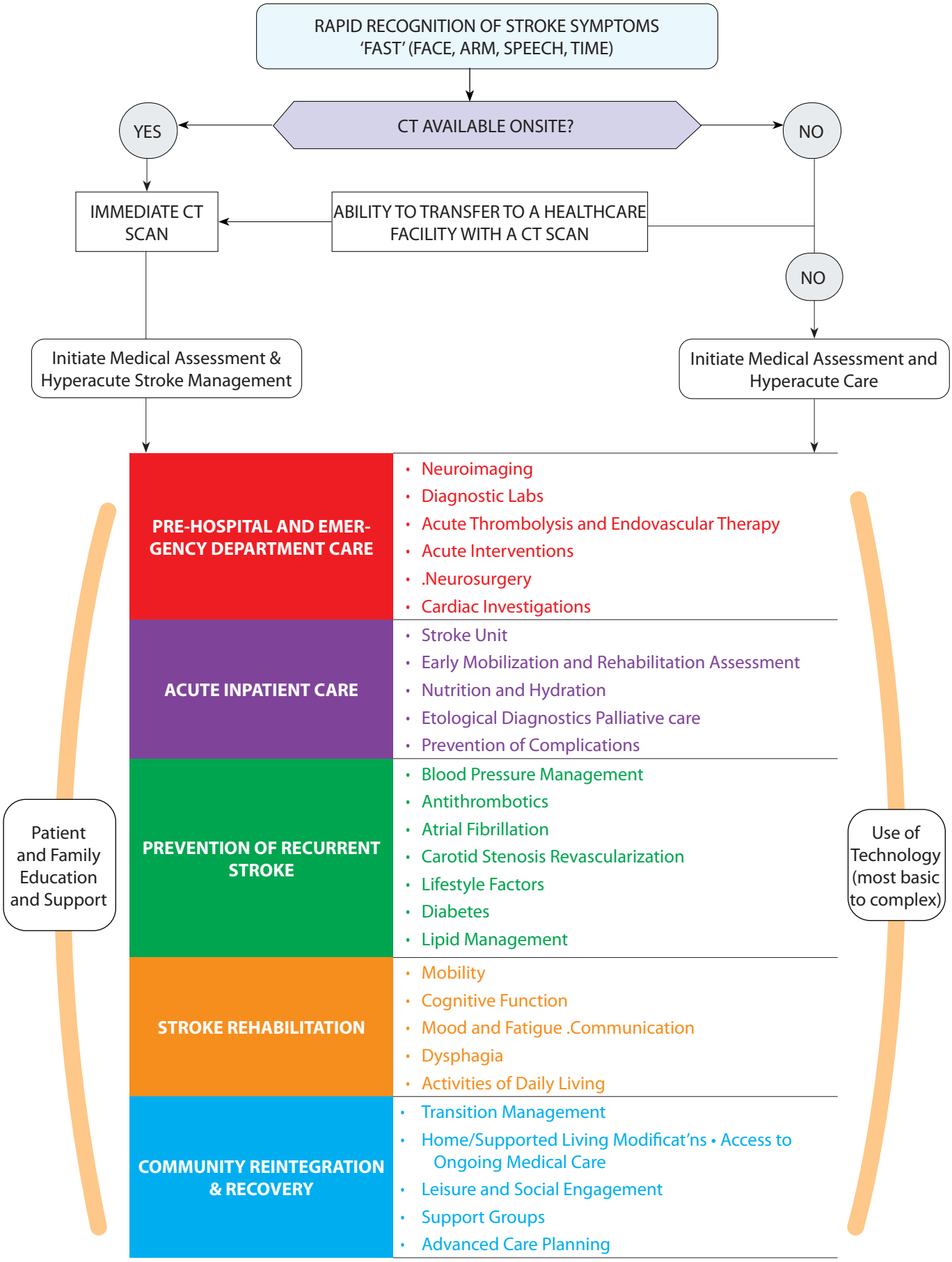


Figure 11.4: World Stroke Organisation Decision-making Flowchart

11.7.3 Initial supportive care

Table 11.2: Recommended Initial Supportive Care

Step by Step Procedure
1.Manage ABCs-routine airway, breathing, and circulation assessments
2. Monitor blood pressure and other vital signs every 15 min for the first hour and hourly thereafter. Obtain actual patient weight, do not use estimated weight.
3. Gain large bore intravenous access-14 to 18G IV cannula 4. Oxygen (as required, keep O_2 saturation >94%) 5.If temp >38ºC, give paracetamol and look for source of infection 6. Assess for and correct hypoglycaemia or hyperglycaemia 7.Take blood sample for lab analysis: CBC, UEC, troponin (coagulation profile if known to have end-stage renal disease or on anticoagulants) 8.Maintain nil per oral (NPO) until stroke swallow assessment done. If fails insert a nasogastric tube to prevent aspiration 8. Get CT scan of the brain as soon as possible, ideally reported within 45 minutes of symptom onset 9. Admit patient or organise for referral to closest appropriate facility capable of treating hyper-acute stroke 10. Alert receiving Hospital/Emergency Department

11.7.4 Blood Pressure in the Acute Stroke Patient

If the patient is a potential candidate for thrombolysis, initiate interventions to control BP immediately.

Hypotension is uncommon in acute ischaemic stroke. If present, it should be corrected to maintain adequate systemic perfusion and support organ function.

Patient otherwise eligible for emergency reperfusion therapy except that BP is >185/110 mm Hg:

- Labetalol 10–20 mg intravenously (IV) over 1–2 min, may repeat 1 time; or
- Nicardipine 5 mg/h IV, titrate up by 2.5 mg/h every 5–15 min, maximum 15 mg/hour; or
- Clevidipine 1–2 mg/h IV, titrate by doubling the dose every 2–5 min; maximum 21 mg/hour;
- While agents that are easier to titrate are preferred, other agents (e.g., hydralazine, enalapril) may also be considered depending on availability.

If systolic BP >180–230 mm Hg or diastolic BP >105–120 mm Hg:

- Labetalol 10 mg IV followed by continuous IV infusion 2–8 mg/min; or
- Nicardipine 5 mg/h IV, titrate up to desired effect by 2.5 mg/h every 5–15 min, maximum 15 mg/h; or
- Clevidipine 1–2 mg/h IV, titrate by doubling the dose every 2–5 min; maximum 21 mg/h

If BP not controlled despite above measure or diastolic BP >140 mmHg:

- Consider IV sodium nitroprusside: 0.3 mcg/kg/min, not to exceed 10 mcg/kg/min; continuous BP monitoring is required during the infusion.

For primary intracranial haemorrhage (ICH):

- Target systolic BP is 140 mmHg. Use agents above.

Things to avoid:

- Do not drop blood pressures drastically in acute ischaemic stroke unless the patient meets the parameters shown above. Hypoperfusion can lead to extension and worsening of the stroke.
- Do not use sublingual captopril and/or nifedipine as it may cause a precipitous fall in BP causing watershed extension of ischemia.
- Do not initiate LMWH for thromboprophylaxis in the first 48 hours in AIS.
- Do not use prophylactic anti-epileptic medication. Only prescribe if patient is known to have seizures, or has presented with seizure(s).

11.7.5 Medical Management of Stroke

Table 11.3: Medical management of stroke

Thrombolysis	1. Give intravenous thrombolysis (IVT) as soon as possible with no delays, and do not wait for improvement first. 2. IVT is given as alteplase 0.9 mg/kg (maximum dose 90 mg) a. 10% of the dose given as a bolus over 1 min and the remaining 90% as infusion over one hour. 3. Tenecteplase (single IV bolus of 0.25 mg/kg, maximum 25 mg) is an alternative to alteplase 4. After thrombolysis: measure BP (aim <185/110 mmHg) and perform NIHSS at least hourly for first 24 hours. 5. Intra-arterial thrombolysis is not recommended
Endovascular mechanical thrombectomy	1. For patients with NIHSS >6, obtain CT angiography in addition to CT brain 2. If there is a large-vessel occlusion of middle, anterior or posterior circulation in the M1, A1 or P1 vessels, transfer patient as an emergency to a centre with an appropriately trained, qualified and accredited neuro-intervention specialist. 3. Interventional cardiologists can be upskilled through specialised training to provide this service
Antiplatelet Agents	1. Aspirin 300mg should be started immediately where thrombolysis is not available/ indicated. a. Do not give less than 24 hours after thrombolysis b. Repeat CT head scan to ensure there is no post-thrombolysis bleed. 2. Dual antiplatelet therapy is ONLY recommended in patients with minor strokes i.e. NIHSS score <5 instead of thrombolysis
Anticoagulants	Anticoagulant therapy is recommended for cardio-embolic events. (Refer to chapter on Ischaemic Heart Disease for details.) Use the 1-3-6-12 rule for starting anticoagulation after an AIS: • 1 day for TIA • 3 days for small stroke • 6 days for moderate-sized stroke • 12 days for large/malignant strokes
Statins	Statins should be prescribed to patients who have had an ischaemic stroke, irrespective of cholesterol level: atorvastatin 80mg nocte.

11.7.6 Management of Haemorrhagic Stroke

- The treatment and management of patients with ICH is very similar to that of AIS.
- The main difference is that coagulopathy should be reversed, and blood pressure should be targeted to 140mmHg systolic within the first 24 hours and maintained as such for two weeks.
- Sub-arachnoid haemorrhages are best managed by the neuro-surgical team and should be transferred under their care for specific management.

11.7.7 Treatment of Comorbid Conditions

May include the following:

- Reduce fever
- Correct hypotension/significant hypertension
- Correct hypoxia
- Correct hypoglycaemia
- Manage cardiac arrhythmias
- Manage myocardial ischemia

11.8 Inpatient Supportive Care

1. Mobilise early to prevent complications such as pneumonia, deep vein thrombosis, pulmonary embolism, and pressure sores.
2. Nutrition and Hydration
   a. Assess ability to swallow by performing a water swallowing test at the bed side. Patients able to swallow are encouraged to feed orally. Patients not able to swallow should have a nasogastric tube inserted for feeding and oral medication where necessary.
   b. Dehydration is a potential cause of deep vein thrombosis after stroke. Hydration is sustained orally for those able to swallow or intravenously for those unable to swallow. Hydration status is monitored by maintenance of an input-output chart.
   c. Bowel management to avoid constipation and faecal impaction or diarrhoea is required from the outset.
3. Infection Prevention
   a. Pneumonia, which is most likely to occur in seriously affected, immobile patients and those who are unable to cough, is an important cause of death after stroke.
   b. Protect the airway and carry out suctioning as required to lower the risk of aspiration.
   c. Treat nausea and vomiting to lower the risk of aspiration pneumonia.
   d. Enrol chest physiotherapy if needed from the outset or any point during admission.
   e. Exercise and encouragement to take deep breaths to lessen the development of atelectasis.
   f. Monitor vital signs for fever and tachypnoea and treat for pneumonia upon diagnosis.
4. Deep Vein Thrombosis and Pulmonary Embolism Prevention
   a. The risk of deep vein thrombosis is highest among immobilized and older patients with severe stroke.
   b. Symptomatic deep vein thrombosis also slows recovery and rehabilitation after stroke.
   c. Pulmonary emboli generally arise from venous thrombi that develop in a paralyzed lower extremity or pelvis.
   d. Thromboembolic deterrent stockings are NOT recommended for DVT prophylaxis.
   e. Pneumatic compression devices should be used instead especially in the first 72 hours of AIS and during the management of ICH.
   f. In AIS – prophylactic LMWH can be commenced if there is no suggestion of haemorrhagic transformation from day 3.

11.9 Management of Stroke-Specific Complications

11.9.1 Cerebral Oedema

These are more common in large cerebral or cerebellar infarctions. Frank hypodensity on head CT within the first 6 hours, involvement of one third or more of the MCA territory, early midline shift, and MRI stroke volume >80mL are useful in predicting cerebral oedema. Serial head CT scans in the first 2 days are useful in assessing oedema.

Bridging therapies to consider while waiting for decompressive hemicraniectomy:

- Mannitol 0.5 to 1g/kg twice or thrice daily, and/or
- Hypertonic saline ≥3% with 6-hourly sodium level checks, target window 145-150mmol/L.
- Use of brief moderate hyperventilation (PCO2 target, 30–34 mm Hg)
- Do NOT use hypothermia, barbiturates, or corticosteroids.

Neurosurgical decompression/intervention:

- Use a decrease in level of consciousness as selection criteria.
- In patients who deteriorate neurologically within 48 hours from oedema associated with unilateral MCA infarctions despite medical therapy, request for decompressive craniectomy with dural expansion.

- Decompressive suboccipital craniectomy with dural expansion should be performed in patients with cerebellar infarction causing neurological deterioration from brainstem compression despite maximal medical therapy.
- Ventriculostomy is recommended in the treatment of obstructive hydrocephalus after cerebellar infarction.

11.10 Long-TERM CARE

1. Psychosocial support
2. Providing information and support: Information should be offered to patients and carers in a variety of formats, including easy access in the living environment. Caregivers should be offered ongoing practical information and training individualised for the needs of the person for whom they are caring for.
   - Clinical care referral for investigations and/or further management
   - Rehabilitation in terms of feeding, toileting, walking, writing, etc
3. Assessment of degree of dependency: Once a patient has been admitted, the use of standard impairment scales such as the modified Rankin Score (mRS) can be predictive of the degree of dependency and length of hospital stay.
4. Other components of long-term care should be applied as part of the management plan depending on the individual needs of the patient. These include:
   - Pain management
   - Physiotherapy
   - Occupational therapy
   - Speech therapy
   - Psychotherapy
   - Nutritional support
   - Palliative care

11.11 Management of Stroke at Different Levels of care

Table 10.4: Management of Stroke at Different Levels of Care

Level of Service Delivery	Action Taken
Community level	Refer to nearest facility with basic emergency services
Level 2 – Dispensary	Basic emergency – ABCs Detection and emergency care Refer to specialist or county referral
Level 3 – Health centres	Basic emergency – ABCs Detection and emergency care Refer to specialist or county referral
Level 4 – sub county hospital	Basic emergency – ABCs Diagnosis and initiation of treatment Refer to specialist or county referral if necessary
Level 5 – County Referral Hospital	Basic emergency – ABCs Diagnosis and initiation of treatment Definitive management Rehabilitation and palliation Training
Level 6 – National Referral Hospital	Rehabilitation and Palliation Training Research

11.12 Referral Criteria

- Rapidly deteriorating Glasgow Coma Scale (GCS) or GCS of 8 or below
- Onset of symptoms < 4.5 hours for all AIS for possible thrombolysis to a capable centre
- Onset of symptoms <24 hours and large vessel occlusion suspected/confirmed therefore candidate for endovascular mechanical thrombectomy
- Deranged UECs
- If unable to carry out basic lab tests or to obtain brain CT scan
- If unable to manage comorbid conditions
- CT scan evidence of neurosurgical intervention: brain oedema or increased intracranial pressure, subdural haemorrhage or subarachnoid haemorrhage
- Rare causes of strokes

11.13 Recommendations for Health System Strengthening

Certain interventions have been shown to be effective:

- Education programmes to improve the general public's recognition of symptoms of stroke.
- Training paramedics to diagnose stroke more accurately and decrease time to hospital transfer.
- Urgent ambulance transfer.
- Training emergency and hospital medical staff in acute stroke care, including triage, nursing, swallow assessment, chest management, and neuro-intervention.
- Multifaceted interventions (including telemedicine systems and tele-radiology).
- Re-organisation of hospital systems to allow for dedicated stroke management teams through a spoke-and-hub model.
- Development of dedicated 'stroke units' in central county or referral hospitals In a resource constraint set up, a section of the general ward can be dedicated for stroke patients only. Dedicated stroke care in such units is known to significantly improve patient outcomes.
- Development of, with adequate numbers of appropriately trained staff in, specialised in-patient and outpatient neuro-rehabilitation, including physiotherapy, occupational therapy, cognitive rehabilitation, and speech/ swallow therapy.

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12

12. PULMONARY HYPERTENSION

Key Messages

- Pulmonary hypertension is a result of diverse group of diseases causing elevated pressure in the pulmonary tree and is frequently associated with right heart.
- Echocardiography and right heart catheterization are key to diagnostic evaluation together with other tests to establish or rule out secondary causes.
- Groups 1 and 4 (WHO Classification) pulmonary hypertension have established treatment by either medical and surgical modalities.
- The disease carries an overall poor prognosis.

12.1 Introduction

Pulmonary hypertension (PH) denotes a hemodynamic and pathophysiological condition that can occur in several different clinical contexts in both children and adults. The high pulmonary pressures increase resistance at the pulmonary vascular bed, thus causing the right ventricle to contract with much more energy. This puts a strain on the right ventricle, and over time the heart begins to fail and can lead to death.

12.2 Epidemiology

Data from Africa on PH is limited, yet mortality remains high at 12-35%.[1,2] Data from the Pan African Pulmonary Hypertension Cohort (PAPUCO) study showed 69% of PH due to left heart disease; 16% with pulmonary arterial hypertension (PAH), 12% due to lung disease and/or hypoxia; 2% with chronic thromboembolic PH and 16% with unclear/multifactorial PH.[1]

A 2017 systematic review and meta-analysis by Bigna et al, showed that the prevalence of PH in adults in Africa varied widely across different populations: approximately 10% in people presenting with cardiac complaints; 11% in HIV-infected people; 33% in patients with heart failure; 23% in people on haemodialysis; 13% in patients with rheumatic heart disease; 37% in patients with sickle cell disease; 63% in patients with chronic obstructive disease; 25% in patients with systemic lupus erythematosus; 69% in patients with cardiac surgery and 7% in patients with systemic sclerosis.[3]

In Kenya, over half of pregnant mothers with rheumatic heart disease at a national referral hospital in western part of the country had PH.[4] In another study, and about one in five children with adenoid/adenotonsillar hypertrophy at another national referral hospital in Nairobi had PH.[5]

12.3 Definition

PH is defined as an elevated mean pulmonary pressure (mPAP) >20 mmHg during right heart catheterization (RHC). The normal mPAP at rest is approximately 14.0 ± 3.3 mmHg.[6]

12.4 Classification

PH is sub-classified on the basis of pulmonary arterial wedge pressure (PAWP) and the pulmonary vascular resistance (PVR) into:

- Pre-capillary PH (as seen in pulmonary arterial hypertension)
- Isolated post-capillary PH
- Combined pre-and-post-capillary PH

PVR is calculated as the transpulmonary gradient (TPG: mPAP-PAWP) divided by the cardiac output (CO). PVR is usually 1-2 Wood units (WU).[6]

Table 12.1: Haemodynamic Definitions of Pulmonary Hypertension.

Classification	Mean pulmonary artery pressure	Pulmonary arterial wedge pressure	Pulmonary vascular resistance
Pre-capillary PH	>20 mmHg	≤15 mmHg	>2 WU
Isolated post-capillary PH (IpcPH)	>20 mmHg	>15 mmHg	≤2 WU
Combined pre-and post-capillary PH (CpcPH	>20 mmHg	>15 mmHg	>2 WU

Exercise PH	mPAP/CO slope between rest and exercise >3 mmHg/L/min		

Adapted from the 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension

PH can also be classified based on conditions associated with similar pathophysiological mechanisms, clinical presentation, haemodynamic characteristics, and therapeutic management.

Table 12.2: Clinical Classification of Pulmonary Hypertension

Group 1: Pulmonary arterial hypertension (PAH)
1.1 Idiopathic
1.1.1 Non-responders at vasoreactivity testing#
1.1.2 Acute responders at vasoreactivity testing#
1.2 Heritable
1.3 Associated with drug- and toxins
1.4 Associated with:
1.4.1 Connective tissue disease
1.4.2 HIV infection
1.4.3 Portal hypertension
1.4.4 Congenital heart disease
1.4.5 Schistosomiasis
1.5 PAH with features of venous/capillaries (pulmonary veno-occlusive disease/pulmonary capillary haemangiomatosis) involvement
1.6 Persistent PH of the newborn
Group 2: PH associated with left heart disease
2.1 Heart failure:
2.1.1 with preserved left ventricular ejection fraction
2.1.2 with reduced or mildly reduced left ventricular ejection fraction
2.2 Valvular heart disease
2.3 Congenital/acquired cardiovascular conditions leading to post-capillary PH
Group 3 PH associated with lung diseases and/or hypoxia
3.1 Obstructive lung disease or emphysema
3.2 Restrictive lung disease
3.3 Other lung disease with mixed restrictive/obstructive pattern
3.4 Hypoventilation syndromes
3.5 Hypoxia without lung disease (e.g., high altitude)
3.6 Developmental lung disorders
Group 4: PH due to pulmonary artery obstructions
4.1 Chronic thromboembolic PH (CTEPH)

4.2 Other pulmonary artery obstructions: sarcoma (high or intermediate grade) or angiosarcoma; other malignant tumours (e.g., renal carcinoma, uterine carcinoma, germ cell tumours of the testis, other tumours); non-malignant tumours (e.g., uterine leiomyoma), arteritis without connective tissue disease, congenital pulmonary stenoses, and hydatidosis
Group 5: PH with unclear and/or multifactorial mechanisms
5.1 Haematological disorders: including inherited and acquired chronic haemolytic anaemia and chronic myeloproliferative disorders
5.2 Systemic disorders: including sarcoidosis, pulmonary Langerhans cell histiocytosis and neurofibromatosis type 1
5.3 Metabolic disorders: including glycogen storage diseases and Gaucher disease
5.4 Chronic renal failure with or without haemodialysis
5.5 Pulmonary tumour thrombotic microangiopathy
5.6 Fibrosing mediastinitis

[#]Inhaled nitric oxide (10-20ppm), inhaled iloprost or intravenous epoprostenol, are recommended for performing vasoreactivity testing

[a]Patients with heritable PAH or PAH associated with drugs and toxins might be acute responders.

[b]Left ventricular ejection fraction for HF with reduced ejection fraction: ≤40%; for HF with mildly reduced ejection fraction: 41–49%

12.5 Diagnosis

The goals of performing a diagnostic evaluation in PH is to:

1. Confirm the diagnosis and fast track referral of patients with severe PH
2. Identify underlying diseases and comorbidities to ensure proper classification, risk assessment and treatment.[8]

Diagnosis of PH in children is often missed because the symptoms are often subtle and mimic other more common cardio-respiratory conditions e.g., asthma. Additionally, young children are not able to report their symptoms reliably or perform an exercise test. Similarly in adults, the diagnosis of PH is often delayed 2-3 years from symptom onset and should be considered in all patients with relevant symptoms. Particular attention should be paid to patients with increased risk of development of PAH (hereditary predisposition, congenital heart disease, connective tissue disease especially scleroderma, HIV, or portal hypertension) and suspect chronic thrombo-embolism PH of disability after previous acute pulmonary embolism. Hence diagnosis relies heavily on parental observations for children, and overall good clinical acumen. (Figure 1)

12.5.1 History

The symptoms of PH are nonspecific and are triggered at the beginning by exertion. They occur due to inability of the right ventricle to increase cardiac output with exercise. These include:

- Dyspnoea on exertion
- Fatigue and rapid exhaustion
- Dyspnoea when bending forward (bendopnea)
- Palpitations
- Haemoptysis
- Exercise-induced abdominal distension and nausea
- Weight gain due to fluid retention
- Syncope (during or shortly after physical exertion)

Rare symptoms due to pulmonary artery dilatation include:

- Exertional chest pain –> dynamic compression of the left main coronary artery
- Hoarseness (dysphonia) –> compression of the left recurrent laryngeal nerve (cardiovocal or Ortner's syndrome)
- Shortness of breath, wheezing, cough, lower respiratory tract infection, atelectasis –> compression of the bronchi

The patient history should include information on putative risk factors such as:

1. Family history of PH
2. Use of weight loss agents/drugs and toxins
3. Underlying disease: connective tissue disease, liver disease, HIV infection, chronic lung disease, left-sided heart disease, etc
4. Previous episodes of venous thromboembolism

The functional level in patients with PAH is indicated as WHO class I-IV (Similar to NYHA classification of heart failure).

Table 12.3: World Health Organization (WHO) Functional Assessment

Class I	Patients with PH but without resulting limitation of physical activity. Ordinary physical activity does not cause undue dyspnoea or fatigue, chest pain, or near syncope.
Class II	Patients with PH resulting in slight limitation of physical activity. Comfortable at rest; ordinary physical activity causes undue dyspnoea or fatigue, chest pain, or near syncope.
Class III	Patients with PH resulting in marked limitation of physical activity. Comfortable at rest; less than ordinary activity causes undue dyspnoea or fatigue, chest pain, or near syncope.
Class IV	Patients with PH with inability to carry out any physical activity without symptoms. These patients manifest signs of right-heart failure. Dyspnoea and/or fatigue may even be present at rest. Discomfort is increased by any physical activity

12.5.2 Physical Examination

A. Signs of PH

- Central, peripheral, or mixed cyanosis
- Accentuated pulmonary component of the second heart sound (loud P2)
- RV third heart sound
- Systolic murmur of tricuspid regurgitation
- Diastolic murmur of pulmonary regurgitation

A. Signs of RV backward failure

- Distended and pulsating jugular veins
- Abdominal distension
- Hepatomegaly
- Ascites
- Peripheral oedema

A. Signs of RV forward failure

- Peripheral cyanosis (blue lips and tips)
- Dizziness
- Pallor

- Cool extremities
- Prolonged capillary refill

A. Signs pointing towards underlying cause of PH

- Digital clubbing: cyanotic CHD, fibrotic lung disease, bronchiectasis, PVOD, or liver disease
- Differential clubbing/cyanosis: PDA/Eisenmenger's syndrome
- Auscultatory findings (crackles or wheezing, murmurs): lung or heart disease
- Deep venous thrombosis or venous insufficiency.
- Telangiectasia: hereditary haemorrhagic telangiectasia or systemic sclerosis
- Sclerodactyly, Raynaud's phenomenon, digital ulceration, gastro-oesophageal reflux disease: systemic sclerosis

12.5.3 Investigations

These include:

1. 12-lead electrocardiogram

- Signs of right atrial enlargement (P >0.25 mV in lead II)
- Right axis deviation (QRS axis >90° or indeterminable)
- RV hypertrophy (R/S in I,with R>0.5mV in V1; R in V1 + S in lead V5>1 mV)
- Right bundle branch block: complete or incomplete (qR or rSR patterns in V1)
- RV strain pattern (ST depression/T-wave inversion in the right precordial V1–4 and inferior II, III, aVF leads) -> present in advanced PH
- Prolonged QT interval (unspecific) –> independent predictor of mortality

2. Chest radiograph

2.1 Signs of PH

- Right heart enlargement
- PA enlargement
- Pruning of the peripheral vessels
- 'Water-bottle' shape of cardiac silhouette –> may be present with advanced RV failure and moderate pericardial effusion

2.2 Signs of left heart disease/pulmonary congestion

- Central airspace opacification
- Interlobular septal thickening 'Kerley B' lines
- Pleural effusions
- Left atrial enlargement (including splayed carina)
- Left ventricular dilatation

2.3 Signs of lung disease

- Flattening of the diaphragm (COPD/emphysema)
- Hyperlucency (COPD/emphysema)
- Lung volume loss (fibrotic lung disease)
- Reticular opacification (fibrotic lung disease)

3. Transthoracic echocardiography

3.1 Verifying pulmonary hypertension

A peak systolic tricuspid regurgitation velocity of <2.8, 2.9-3.4 and >3.4 m/s indicate low, intermediate, and high probability

of PH respectively, but identification of other echo PH signs is mandatory which include (Adapted from the ESC/ERS Guidelines):

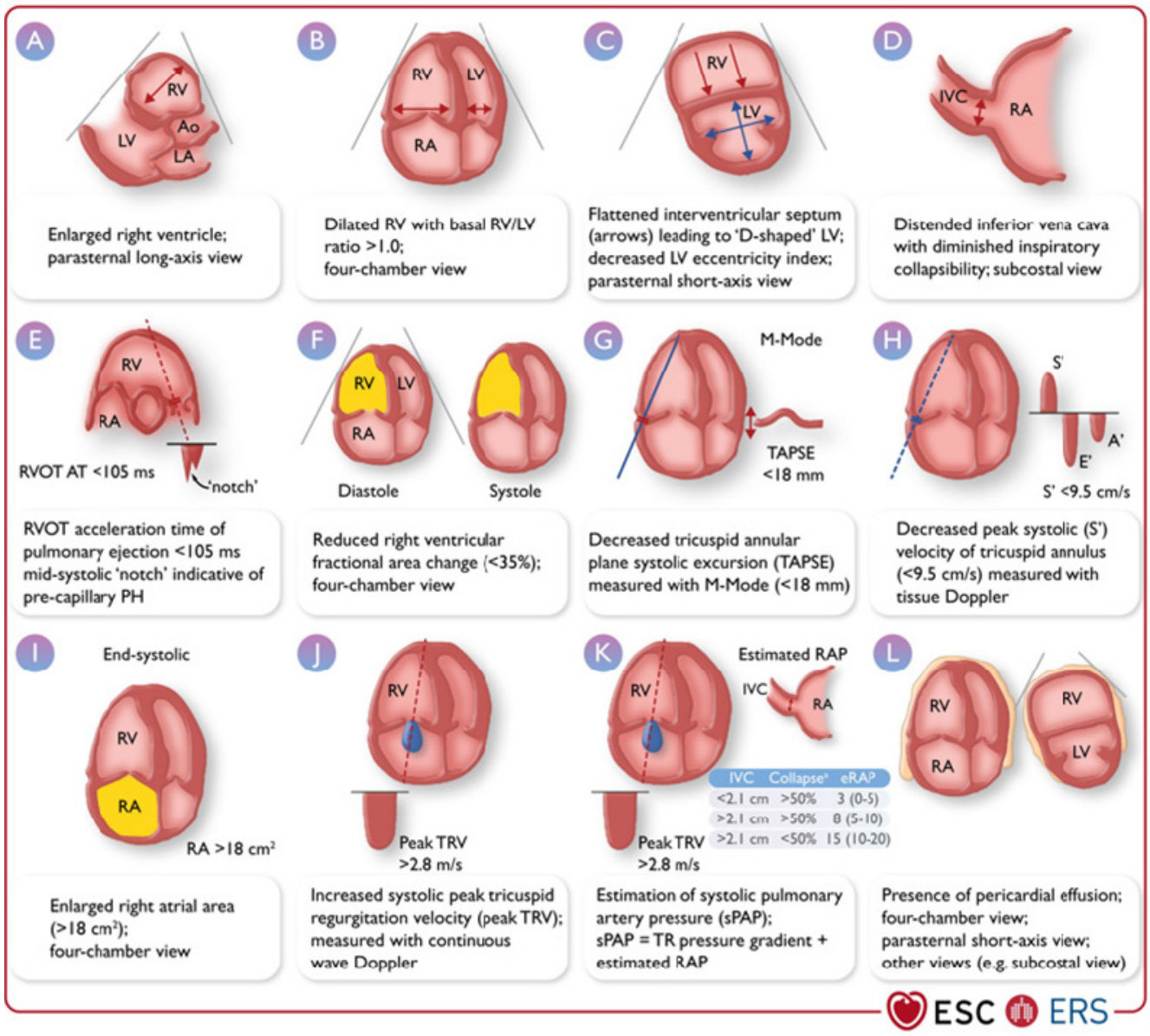

Figure 12.1: Echo findings in PH (Courtesy of ESC/ERS Guideline for PH 2022, copyright)[6]

a. Right ventricle:

- Dilatation (RV is > LV in apical 4-chamber image - RV/LV basal diameter/area ratio >1.0) See B in Figure 12.1 above.
- RVH (wall thickness > 5 mm) – sign of chronic PH
- Reduced RV systolic function (TAPSE ≤ 1.8 cm) See G, Fig 12.1
- Deviation of the interventricular or interatrial septum to the left

b. Pulmonary artery:

- Dilatation (> 25 mm) – parasternal short-axis – also larger than Aorta
- Abbreviated pulmonary arterial acceleration time (< 105 ms and/or mid-systolic "notch") See E, Figure 12.1
- Pulmonary valve regurgitation with increased early regurgitation (> 2.2 m/s)

c. Right atrium:

- Dilated to (> 18 cm2) – apical 4-chamber See I, Figure 12.1
- Dilatation of IVC - See D, Figure 12.1

d. Pericardium:

- A minor pericardial effusion is often seen.

3.2 Determining the type of pulmonary hypertension

Echocardiography effectively assesses left-sided heart disease (LHD). A dilated left atrium (LA) may be a sign of underlying diastolic LV dysfunction/hypertensive heart disease which is a frequent cause of PH in the elderly. 2D-echo may also assess the presence of congenital defects with shunts (possibly supplemented with contrast echo, TEE, cardiac CT or cardiac MRI). Sinus venosus-ASD, partial abnormal pulmonary venous return can be easily missed on 2D-echo examination.

4. **Blood tests**
    - N-terminal pro-Brain Natriuretic Peptide (NT-proBNP) and BNP correlate with myocardial dysfunction, provide prognostic information at diagnosis and during follow-up and have been incorporated into risk scores[9]
    - Relevant tests to rule out/in secondary causes of PH including HIV, hypercoagulability, and connective tissue disease.
5. **Pulmonary function tests and arterial blood gases**
    - These are to screen for chronic lung disease
6. **6-minute walk test (6MWT)**
    - Quantifies functional capacity.
    - Can be performed in children who can walk and follow instructions, usually aged 3 years and above (see nomograms)
    - Children are usually able to work longer distances than their adult counterparts of the same functional classification.
7. **Overnight oximetry/Polysomnography**
    - To screen for upper airway obstruction and hypoventilation
8. **Chest HRCT scan**
    - To identify features of lung disease e.g., interstitial lung disease (ground glass opacities), bronchiectasis (increased broncho-arterial ratio) etc. or features pointing towards the presence of PVOD/PCH (centrilobular ground glass opacities, septal lines and lymphadenopathy)
9. **CT pulmonary angiography**
    - to identify to LE and CTEPH, but a normal study does not rule out CTEPH
10. **Ventilation/perfusion scan**
    - In the absence of parenchymal lung disease, a normal study rules out CTEPH.
11. **Liver ultrasound**
    - Carried out in suspected portal hypertension
12. **Right-sided cardiac catheterization**
    - Gold standard for diagnostic confirmation of PH. It is indicated:
        - To make the diagnosis of PH definitively and to determine the hemodynamic type of PH (see Table 12.1)
        - To determine the severity of the disease
    - To test the vascular reactivity of the pulmonary circuit (see Table 12.2: Group 1.5)

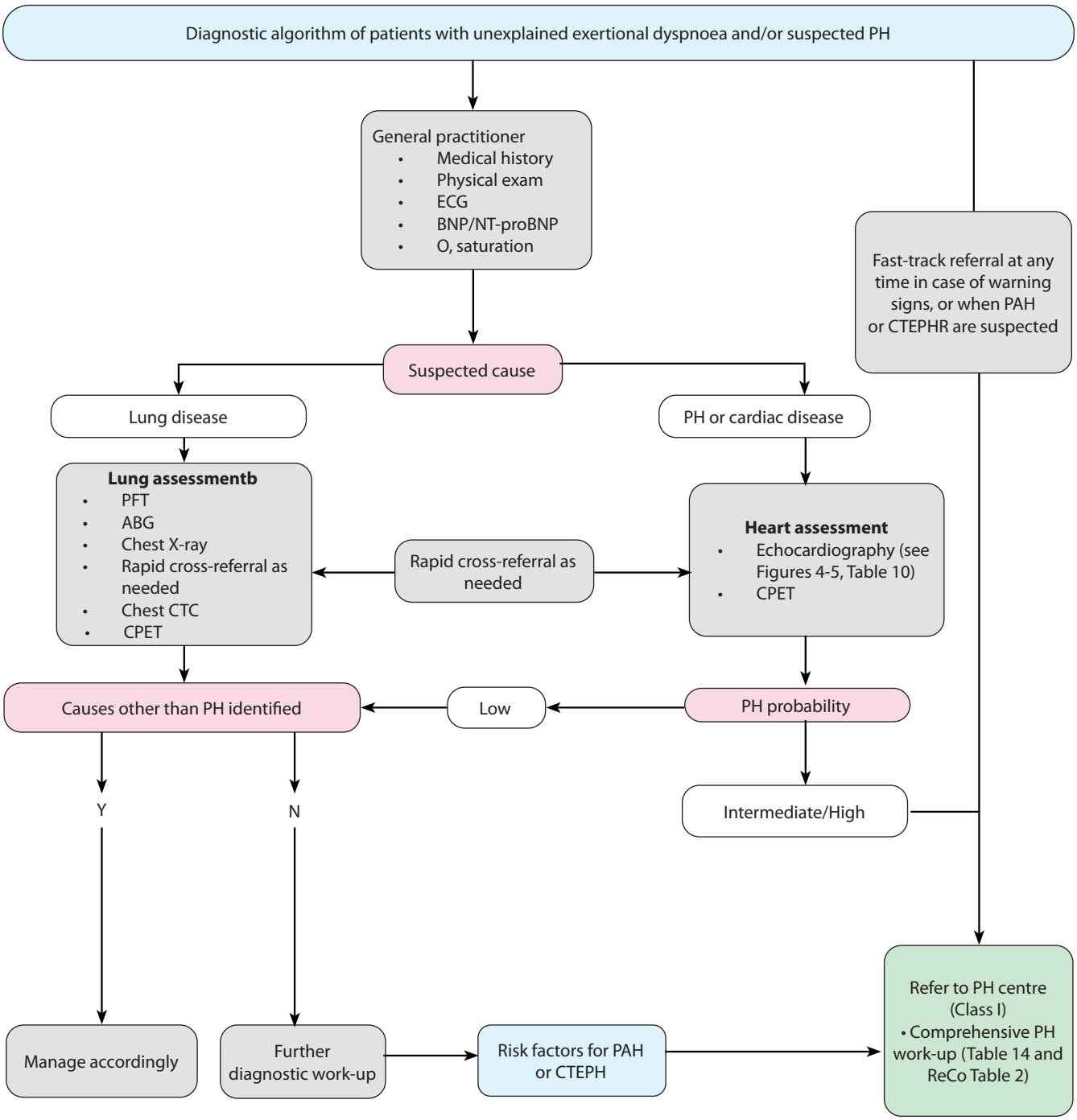

Figure 12.2: Diagnostic Algorithm for Pulmonary Hypertension

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12.6 Prognosis

The natural history of PH is characterized by gradually increasing lung vessel resistance and RV dysfunction. The prognosis is closely correlated to the degree of RV dysfunction. A Kenyan study in an adult population suggested a 2-year mortality of 34.1%.[8]

Untreated, the prognosis for IPAH is poor with survival after 1, 3 and 5 years around 70%, 50% and 35% respectively.[1]

For the individual patient with PAH, the following parameters indicate a poor prognosis:[6]

a) Low WHO functional (III-IV)

b) RV systolic dysfunction assessment by echo (TAPSE <1.5mm)

c) Pericardial effusion on 2D-echocardiography

d) RAP >15 mmHg, CI < 2.0 l/min/m2, absence of significant vasoreactivity to inhaled NO by right-sided cardiac catheterization

e) Increased BNP > 180 pg/ml, NT-proBNP > 1400 pg/ml

Table 12.4: Comprehensive risk assessment in pulmonary arterial hypertension (three-strata model)

Determinants of prognosis (estimated 1-year mortality)	Low risk (<5%)	Intermediate risk (5-20%)	High risk (>20%)
Clinical observations and modifiable variables			
Signs of right HF	Absent	Absent	Present
Progression of symptoms and clinical manifestations	No	Slow	Rapid
Syncope	No	Occasional syncope	Repeated syncope
WHO-FC	I, II	III	IV
6MWD	>440 m	165-440 m	<165 m
CPET	Peak VO2>15 mL/min/kg (>65% pred.) VENCO2 slope <36	Peak VO2 11-15 mL/min/kg (35-65% pred.) VENCO2 slope 36-44	Peak VO2 <11 mL/min/kg (<35% pred.) VENCO2 slope >44
Biomarkers: BNP or NT-proBNP	BNP <50 ng/L NT-proBNP <300 ng/L	BNP 50–800 ng/L NT-proBNP 300-1100 ng/L	BNP >800 ng/L NT-proBNP >1100 ng/L
Echocardiography	RA area <18 cm2 TAPSE/SPAP>0.32 mm/mmHg No pericardial effusion	RA area 18-26 cm2 TAPSE/SPAP 0.19-0.32 mm/mmHg Minimal pericardial effusion	RA area >26 cm2 TAPSE/SPAP<0.19 mm/mmHg Moderate or large pericardial effusion
CMRI	RVEF >54% SVI >40 mL/m^2 RVESVI <42 mL/m^2	RVEF 37-54% SVI 26-40 mL/m2 RVESVI 42-54 mL/m2	RVEF <37% SVI <26 mL/m2 RVESVI >54 mL/m2
Haemodynamics	RAP <8 mmHg CI ≥2.5 L/min/m2 SVI >38 mL/m2 SvO2>65%	RAP 8-14 mmHg CI 2.0-2.4 U/min/m2 SVI 31-38 mL/m2 SvO2 60-65%	RAP >14 mmHg CI <2.0 L/min/m2 SVI <31 mL/m2 SvO2 <60%

Courtesy of ESC Guideline for PH 2022 (Copyright).

12.7 Referral to highly specialized units

Patients with PH (tricuspid valve > 40 mmHg) and/or other echocardiographic signs of PH) with symptoms deemed to be caused by PH should be referred to a specialized centre for definitive diagnosis, which will often include right-sided cardiac catheterization.

Patients with PH which is well explained based on pulmonary disease or left-sided heart disease usually do not require referral to a highly specialized unit, but this should be considered if there is uncertainty about the cause (type of PH) or about the severity, e.g., if it is out of proportion with the underlying disease.

Specific pharmacological treatment for PAH is initiated and reviewed at the highly specialized centre. Once the patient is stable, the referring centre can be included in the reviewing the patient peripherally.

Patients with PAH, WHO class III-IV and failure of specific pharmacological agents should ideally be assessed for lung transplantation, which however, is currently not available in Kenya.

Patients suspected to have CTEPH (segmental and/or lobular) in WHO function class II-IV are eligible for examination for

surgical pulmonary endarterectomy (PEA) or balloon pulmonary angioplasty (BPA).

Patients suspected of PAH due to congenital heart disease should be referred to a specialist in congenital heart disease for further ascertainment of possible treatment or palliation.

We recommendation to have a National pulmonary hypertension centre equipped with specialist who will carry out advanced evaluation and perform advanced treatment/interventions including BPA, lung transplants.

12.8 General Recommendations

Physical exercise is recommended within symptom limits. Rehabilitation can improve patients' functional status. Strenuous physical activity accompanied by severe shortness of breath, dizziness or chest pain is discouraged.

As a rule of thumb, pregnancy is contraindicated in PH. Termination of pregnancy is advised to preserve the life of the mother.

WHO-Class II-III PH patients usually tolerate air flight without any problems. Oxygen can be offered by contacting flight attendants. WHO-class IV PH patients should be accompanied by a doctor if flying.

PH increases the risk of general anaesthesia and surgery.

Vaccination against influenza and pneumococcal pneumonia is recommended.

12.9 Pharmacological Treatment

12.9.1 General

1. **Anticoagulation:**
    a. Lifelong treatment for CTEPH. Warfarin is preferred.
    b. There is little experience with DOACs.
2. **Diuretics:**
    a. In right-sided cardiac congestion and right heart failure with peripheral edema and/or ascites.
    b. Loop diuretics are recommended.
3. **Oxygen:**
    a. Significant hypoxemia is quite rare in PAH, but frequently in PH in chronic lung disease.
    b. Should be treated with continuous oxygen (ambulatory oxygen) if oxygen saturation is < 86% to mitigate against hypoxic pulmonary vasoconstriction.
4. **Iron deficiency treatment:**
    a. Indicated in the presence or absence of anaemia.
    b. In severe iron deficiency anaemia <8 g/dl, parenteral iron therapy is indicated.

12.9.2 Specific Pharmacological Treatment of PAH (Group 1)

1. **Calcium antagonists (CCB)**

- Indicated when significant reversibility has been demonstrated by a RHC pulmonary vasodilatation test with nitric oxide.
- Non-Dihydropyridine calcium antagonists (Diltiazem and Verapamil).Reasses response after 4 months
- Patients with PAH and absent vasoreactivity are at increased risk of hemodynamic collapse when treated with calcium antagonists due to negative inotropic effect and systemic vasodilatation.

2. **Prostanoids**

- Epoprostenol (synthetic prostacycline) may be used when available to treat PAH patients in WHO function classes III-IV. Due to short half-life (0.5-3 min), continuous infusion in a central venous catheter via portable infusion pump is necessary.
- Their side effects include catheter infection/sepsis, vasodilatation, hypotension, tachycardia, flushing, headache, nausea, vomiting, colic and jaw pain.
- Iloprost has a longer half-life of 30 minutes and fewer side effects from the systemic vasculature due to pulmonary selectivity.
- Treprostinil is a prostanoid with a longer half-life than both epoprostenol and iloprost which can be used as continuous subcutaneous or intravenous infusion.
- Selexipag is an orally active IP prostacycline receptor agonist that reduces disease progression and hospitalization in PAH. It is also effective in PAH patients who are already being treated with endothelin receptor antagonists or PDE-5 inhibitors but have not shown additional efficacy by already instigating double treatment with endothelin receptor antagonists and PDE-5 inhibitors at the primary endpoint, pulmonary vascular resistance.

3. Endothelin receptor antagonists

- Endothelin induces vasoconstriction and cell proliferation in the pulmonary circuit.
- Bosentan is a competitive blocker of endothelin ETA- and ETB-receptors. It improves symptoms, haemodynamics, and prognosis for PAH patients in WHO function class II-IV.
  - Reversible elevation of liver transaminases occurs in 10%. Treatment requires regular monitoring of liver function tests.
  - Other side effects include flushing, weight gain, fluid retention, oedema, decrease in haemoglobin, inhibition of hormonal contraception, teratogenicity, and possibly male infertility.
- Macitentan is an oral combined ETA- and ETB-blocker that improves symptoms and prognosis at PAH (WHO function class II-IV). It is less liver-toxic than bosentan and has fewer interactions.
- Ambrisentan is a selective blocker of endothelin ETA-receptors. Administered orally. Can be used to treat PAH patients in WHO functional classes II-IV. Ambrisentan has no liver toxicity and fewer interactions than bosentan.

4. Stimulators of the sGC-NO-cGMP system

- PDE-5 inhibitors (sildenafil, tadalafil) potentiate the action of endogenous nitric oxide (NO) in the pulmonary vasculature. NO induces vasorelaxation and inhibition of cell proliferation in the pulmonary arteries.
- They improve symptoms and haemodynamics in WHO Class II-III PAH patients.
- Side effects include headaches and visual disturbances.
- Riociguat is a stimulator of soluble guanylate cyclase (sGC) that mimics the action of NO and increases cGMP in, among other things, the smooth muscle cells of pulmonary arteries. It improves symptoms and prognosis at PAH and CTEPH (WHO function class II-IV). Administered orally.
- Nitrates are contra-indicated with the use of the above drugs to the risk of catastrophic hypotension

12.9.3 Treatment Targets And Monitoring

The effect of the medical treatment targeting PAH is assessed in the individual patients with WHO function class, 6MWT, echocardiography and haemodynamics (RHC). Patients are sought to achieve WHO function class I-II, a 6MWT > 400 m and absence of RV failure.

12.9.4 Combination Therapy

- There is potential for additive beneficial effects by combining specific pharmacological agents for PAH with different mechanisms of action (ET blocker, PDE-5 inhibitor/sGC stimulator, prostanoid). Up to 3 drugs may be combined in group I PH.
- Specific PAH pharmacological agents for PH group 2 and 3:

- There is no evidence of beneficial efficacy of specific PAH agents in groups II and III PH.

- Treatment of CTEPH (PH Group 4):
  - First line treatment is surgical pulmonary endarterectomy.
  - CTEPH patients who are inoperable, or who have significant PH after pulmonary endarterectomy can often be offered Balloon Pulmonary Angioplasty (BPA).
  - Riociguat is shown to improve symptoms and functioning in this patient group.

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13

13: PERICARDIAL DISEASES

Key Messages

- Pericardial diseases are still important causes of heart failure in Kenya. Tuberculosis is the commonest cause of clinically significant pericardial effusions.
- Clinical presentation is common via 3 syndromes: dry pericarditis, effusive disease, and constriction.
- Echocardiography and Electrography is key to diagnosis, other relevant tests should be done based on suspected aetiology.
- Medical and surgical treatment of established disease together with management of underlying causes is highly effective.
- Congenital and malignant disorders of the pericardium are rare but should be suspected in patients with atypical presentation of recurrent disease.

13.1 Introduction

Pericardial disease is a pathological process involving the pericardium. The pericardium is a sac that surrounds the heart and its major blood vessels, consisting of two layers - a visceral layer and a parietal layer (1). The two layers form a (pericardial) cavity, which contains fluid to lubricate the moving heart. The pericardium has other multiple functions, including anchoring the heart to the mediastinum and surrounding structures, protection against infection, and diastolic coupling of the ventricular pressures during cardiac relaxation.

The incidence of acute pericarditis varies widely in Africa ranging from 2 to 11.3% among patients admitted in a hospital for cardiovascular diseases. It has been shown to affect mostly young male population of ages between 26 and 42 years, and tuberculosis as the most frequent etiology from 33 to 69.5% in sub-Saharan Africa (2). Pericardial diseases are an important cause of heart failure syndrome in Kenya (3), though with decreasing incidence due to improvements in living conditions and control of other diseases like HIV infection that predisposes to several pericardial diseases (4). These diseases may be either primary or secondary (associated with multi-systemic conditions). They can take one of the following specific syndromes:

1. Pericarditis
2. Pericardial effusion with /without tamponade
3. Constrictive Pericarditis
4. Pericardial tumours

13.2 Pericarditis

Pericarditis is inflammation of the pericardium and is commonly associated with the other pericardial syndromes, especially pericardial effusion.
It may be acute (<4-6 weeks), persistent (4-6 weeks to 3 months) or chronic (more than 3 months) (2)

Common causes of pericarditis are outlined in the table below:

Table 13.1: Causes of Pericarditis

Condition	Estimated incidence (%) [a]
Idiopathic	85-90
Infectious	
Viral Bacterial Tuberculous Fungal Parasites	1-2 1-2 4 Rare Rare
Neoplastic disease	7
Systemic autoimmune disease	3-5
After cardiotomy or thoracic surgery	Rare (<1)
Aortic dissection	Rare (<1)
Chest wall trauma	Rare (<1)
Chest wall irradiation	Rare (<1)
Adverse drug reaction	Rare (<1)
Acute myocardial infarction	5-20b
Myocarditis	30b
Uremia	
Before dialysis	5
After initiation of dialysis	13

13.2.1 Clinical Presentation

- Sudden onset of chest pain, worsened by taking deep breaths and relieved by leaning forward. It is often in the middle or left side of the chest, there may be pain in one or both shoulders, and it may mimic a heart attack (6).
- Fever
- Weakness
- Difficulty in breathing
- Cough
- Palpitations

13.3 Acute Pericarditis

Acute pericarditis can be either viral e.g., enteroviruses and herpesviruses, or idiopathic.

a) Diagnostic criteria

Two of the following features: (6)

a) Chest Pain-typically sharp, pleuritic, and improved by sitting & leaning forward. (Positive in up to 90%)
b) Pericardial rub (seen in 33%)
c) Consistent ECG charge (60%), typically new diffuse ST elevation or PR segment depression.
d) Pericardial effusion on echocardiogram (new or worsening)

Supporting Evidence:

i) Elevated inflammatory markers (ESR, CRP, WBC)
ii) Consistent Cardiac MRI findings (delayed gadolinium enhancement)
iii) Elevated Cardiac troponins suggesting Myocardial involvement.

b) Investigations

- CXR –Usually normal unless pericardial effusion >300mL is present.
- Transthoracic echocardiogram
- Inflammatory makes –CRP, creatinine kinase (CK), troponins;
  - also consider ESR, WBC counts
- Chest CT Scan
- Cardiac MRI
- Specific tests for suspected aetiology:
  - sputum studies,
  - HIV test,
  - urinary lipoarabinomannan (LAM),
  - Liver function tests (LFTs),
  - Urea, electrolytes, and creatinine (UECs,)
  - pericardial fluid adenosine deaminase (ADA).

c) Complications

Pericardial effusion with progression to hemodynamic significance (cardiac tamponade)

- Recurrent disease
- Constrictive pericarditis

d) Risk factors for complications

- High-grade fever >38o c
- Subacute course

- Large pericardial effusion on ECHO (≥ 2cm in diastole)
- Cardiac tamponade
- Others:
    - Myopericarditis
    - Immunosuppression
    - Trauma
    - History of anticoagulant use.

e) Treatment of Viral /idiopathic acute pericarditis

- ASA 750-1000mg q8h x 1-2/52 followed by a gentle taper (250-500mg/week)

OR

- Ibuprofen 600mg q8 x1/52 followed by a slow taper (200-400mg week)

Plus

- Colchicine 0.5mg od if < 70kg and BD if >70kg for a period of three months for the initial episode. When added as an adjunct therapy, it reduces symptoms and rate of recurrence. No tapering is required.
- Glucocorticoids: should be considered only if NSAIDS are contraindicated, or if there is nonresponse.
- Prednisone 0.25-0.5 mg/day is recommended until symptoms improve then tapper accordingly. (7, 8, 9)

13.4 Treatment of Tuberculous Pericarditis

TB is the most important aetiology of pericarditis in Sub-Saharan Africa (4). Unfortunately, diagnosis of this specific disease may be challenging due to low sensitivity of most of the available diagnostic tests. Consider using the Tygerberg score (10) in defining probable disease. The Tygerberg score is a validated clinical decision tool that can facilitate the diagnosis of TB pericarditis in resource-limited settings.

Table 13.2: The Tygerberg Score

The Tygerberg score
• Weight loss (1 point) • Night sweats (1 point) • Fever (2 points) • Serum globulin >40 g/L (3 points) • Blood leukocyte count <10 × 109/l (3 points) A total score of 6 or more is highly suggestive that tuberculosis is the cause of the pericarditis.

The Investigation of the Management of Pericarditis (IMPI) trial which recruited participants from Kenya employed the Tygerberg tool in recruitment and defined the role of steroids as adjunct therapy in the management of TB pericarditis (11), (12).

Confirmed or probable cases should be started on standard TB therapy as per the Kenyan National Guidelines on TB management plus steroids unless in the presence of HIV infection because they increase the risk of developing HIV-associated malignancies. The recommended choice of steroid is prednisolone for 6 weeks dosed as follows: 120mg OD for the first week, 90mg OD in the second week,60mg OD for third week, 30mg OD for fourth week, 15mg OD for the fifth week and 5mg OD for the final week (11), (12).

13.5 Treatment of Recurrent Pericarditis

This is defined as recurrent disease after four weeks or longer after demonstrated remission.(13), (14). The rate of recurrence is 15 to 30% following viral or idiopathic pericarditis, with the risk increasing to 50% if colchicine is not used. Such cases are best referred to a specialist (cardiologist) for further evaluation. Treatment options available following negative evaluation include the use of similar drugs like those for acute episodes and the addition of immunosuppressants like azathioprine, methotrexate.

13.6 Pericardial Effusions

This refers to accumulation of fluid in the pericardial space, to the extent that it may be appreciated by standard imaging modalities, such as radiography and ultrasonography.

Table 13.3: Classification of pericardial effusion

Onset	Acute Subacute Chronic (>3 months)
Size	Mild <10 mm Moderate 10-20mm Large >20 mm
Distribution	Circumferential Loculated
Composition	Transudate Exudate

(Adopted from ESC Guidelines for the diagnosis and management of pericardial diseases, 2015)

Diagnostic evaluation of suspected pericardial effusion is similar to dry pericarditis with the addition of fluid aspiration for biochemistries: glucose, protein, LDH.

- Additionally, pericardial biopsy is recommended for definitive diagnosis as well as a urinary LAM in the presence of HIV infection.
- If the patient is in cardiac tamponade: Therapeutic pericardiocentesis by a specialist is an emergency in addition to treating the primary cause.

13.7 Constrictive Pericarditis

Acute pericarditis or pericardial effusion may progress to constriction in their natural history, especially if not recognized early or not treated appropriately. As part of the pathogenesis, they may progress to effusive constrictive form and peri-myocarditis, a period where myocardial involvement may cause left ventricular dysfunction.

Constrictive pericarditis should be suspected whenever a diagnosis of right sided heart failure and impaired diastolic filling is demonstrated bu echocardiography, CT, CMR or cardiac catheterization (15). The main differential diagnosis is restrictive cardiomyopathy, and a referral to a cardiologist level is necessary for definitive diagnosis and management.

Treatment of constrictive pericarditis assumes a multi-disciplinary approach, and pericardiotomy offers the definitive treatment. Early diagnosis may respond to Anti TBs combined with adjunctive steroids if it is of tuberculous aetiology (4).

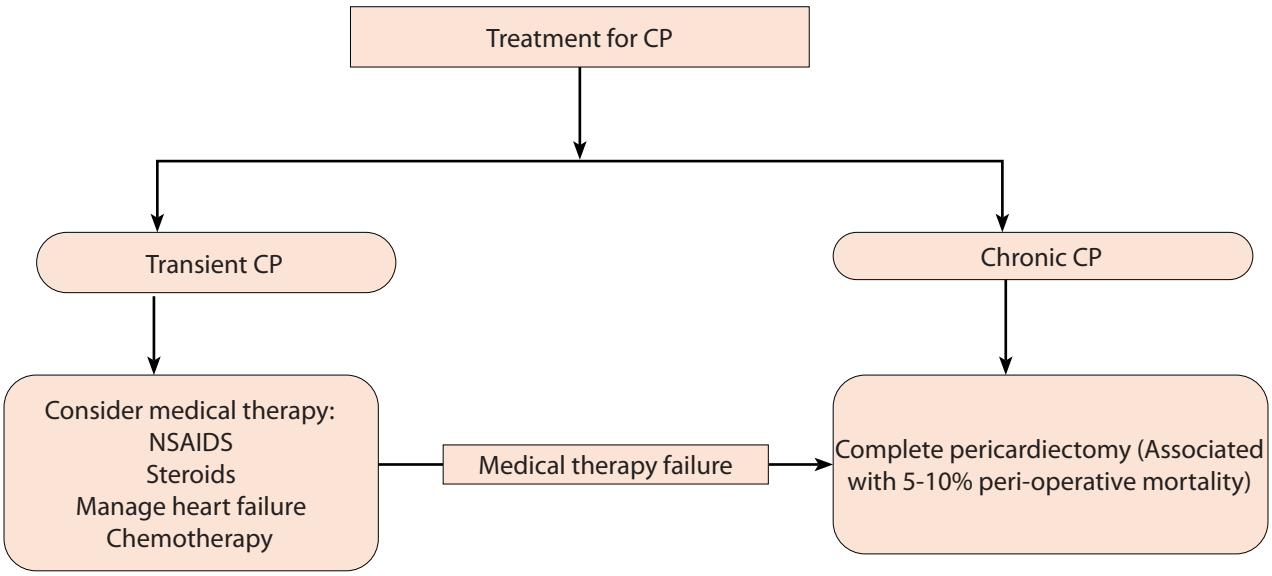

Figure 13.1: Management algorithm for constrictive pericarditis

13.8 Congenital Disorders of the Pericardium

Congenital disorders of the pericardium are exceedingly rare with a reported incidence of 1 in 10, 000. However, the true prevalence may be underestimated as most patients are asymptomatic, and diagnosis is generally incidental (16). Familial occurrence is rare. Associated cardiac abnormalities include (30-50%): atrial septal defects (ASDs): sinus venosus, patent ductus arteriosus (PDAs), mitral valve disease, Tetralogy of Fallot (TOF), and partial anomalous pulmonary venous drainage. Occasionally, they may be part of cardiac insolvent of multisystemic syndromes such as Marfan syndrome, pectus excavatum, diaphragmatic hernia and VATER syndrome (vertebral defects, anal atresia, tracheoesophageal fistula, and radial and renal dysplasia).

Notable congenital abnormalities of the pericardium include complete absence, partial absence, and pericardial cysts. They are usually asymptomatic. but occasionally patients may present with nonspecific chest complaints and sudden cardiac death (especially in partial absence due to herniation).

Standard cardiac imaging including CXR, echocardiogram, and Chest CT are diagnostic Surgery is usually indicated for symptom relief, especially for cysts or partial absence of the pericardium.

13.9 Pericardial Tumours

Pericardial tumours are usually diagnosed incidentally at imaging or in association with new effusion (17).

They may be primary (rare), or more commonly, metastatic (breast, lung, malignant melanoma, lymphomas) and may be the causes of refractory pericardial effusions. The significance of the pericardium in neoplastic processes is linked to the development of pericardial effusion and infiltration of the myocardium with consequent heart failure.

Multimodality diagnostic imaging, with chest CT scan being the initial test in many centres, should be instituted, followed by referral to specialty centre.

Pericardiocentesis with cytology of the associated pericardial fluid, and biopsy of the mass, should be considered as well.

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14

14. CARDIOVASCULAR DISEASE IN DIABETES

Key Messages

- CVD is a major complication of diabetes mellitus (DM)
- Left Ventricular Hypertrophy (LVH) is a characteristic of hypertensive and/or diabetic heart disease, which is an important cause of heart failure in Africa
- People with Type 2 diabetes (T2DM) have high prevalence of hypertension, dyslipidaemia, and obesity, which contribute to high rates of CVD

14.1 Introduction

CVD is a major complication of diabetes mellitus (DM) and causes premature death(2) . About 65% of people with DM die from heart disease and stroke (2). Adults with DM are 2-4 times more likely to have heart disease or suffer a stroke than people without diabetes (2). Hyperglycaemia in adults with diabetes increases the risk for myocardial infarction, stroke, angina, and coronary artery disease. People with Type 2 diabetes (T2DM) have high prevalence of hypertension, dyslipidaemia, and obesity, which contribute to high rates of CVD (3). Smoking doubles the risk of CVD in people with diabetes (2).

14.2 Mechanisms of Developing CVD in the Diabetes Setting

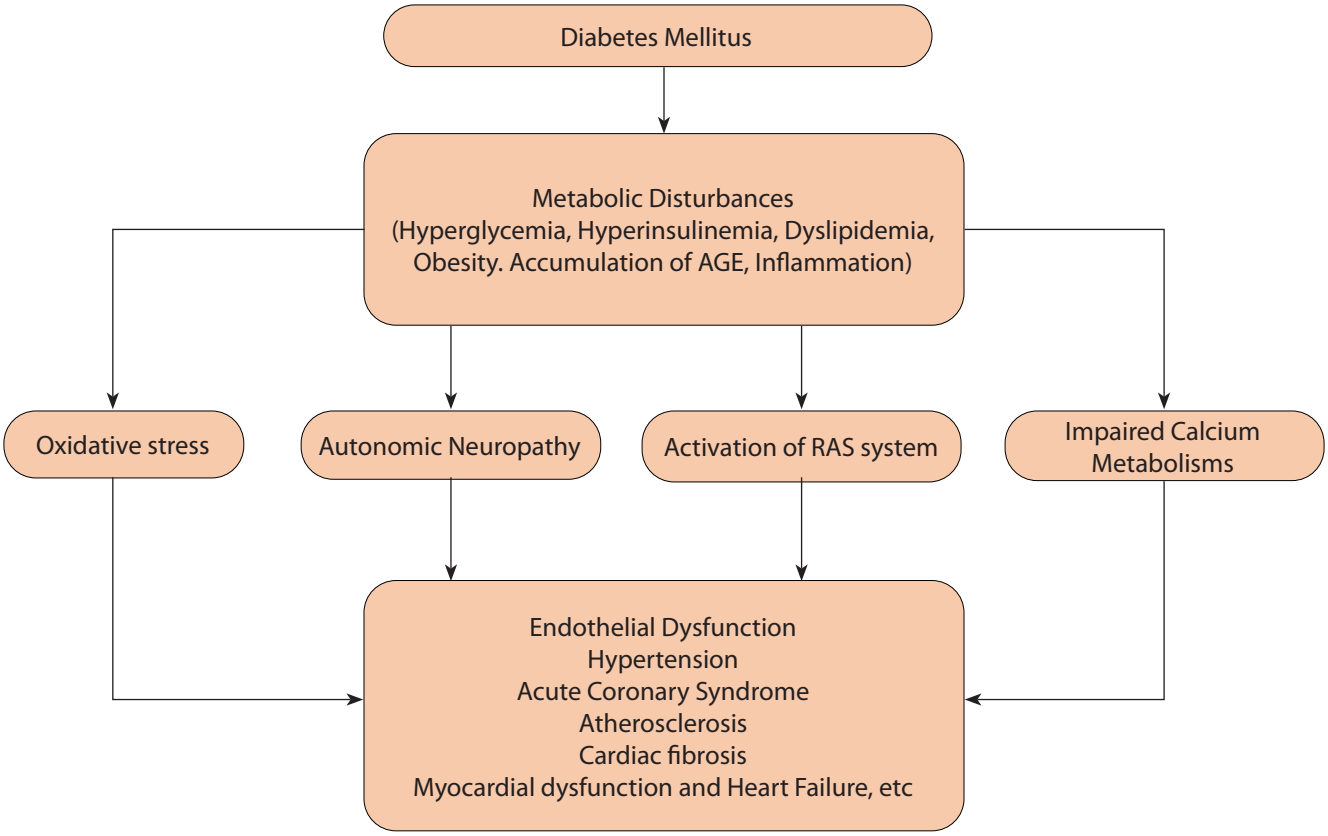

Figure 14.1: Mechanisms of CVD Development in Diabetes

Diabetes affects the heart and the blood vessels. The pathogenesis of CVD in Type 2 Diabetes is related to multiple pathways including epigenetic, genetic, and inflammatory (Keating ST Plutzky 2016: Epigenetic changes in diabetes and CVD). Atherosclerosis and cardiac remodelling contribute to the changes in the heart and vessels. Left Ventricular Hypertrophy (LVH) is a characteristic of hypertensive and/or diabetic heart disease, which is an important cause of heart failure in Africa. LVH is associated with susceptibility to atherothrombosis and therefore stroke or CAD, increased albuminuria, and therefore chronic kidney disease - a marker of microvascular disease and endothelial dysfunction.

The most common cardiovascular conditions found in DM patients are:

- Hypertension
- Heart Disease –LVH, Coronary Artery Disease, Heart Failure
- Stroke

Heart failure is a common initial manifestation of CVD in patients with T2DM and may present with either reduced or preserved ejection fraction.

Table 14.1: The Risk Factors for Developing Heart Failure in T2DM

Cardiac risk factors	• Ischaemic heart disease • Myocardial infarction • Hypertension • Valvular heart disease • Arrhythmias
Non-cardiac risk factors	• Age • Chronic kidney disease • Increased body mass index • Longer duration of diabetes • Smoking • Alcohol excess

14.3 Principles of Management of CVD in Diabetes Melllitus

The management of CVD in diabetes follows the principles outlined in the previous sections of this guideline; however, treatment of hypertension in diabetes varies, and is further expounded in the following sections.

14.3.1 Management of Hypertension in Diabetes Mellitus

All persons whether hypertensive or not should be counselled on the following at each visit:

- Lifestyle modifications (physical exercise, diet, and weight loss) and setting health goals
- Diet should be low in sodium, rich in vegetables and fruits, and use of low-fat dairy products (DASH diet)
- Alcohol consumption and tobacco cessation

Determine blood pressure in people with T2DM at every visit, using standard techniques (measure with a well calibrated BP machine and with the right-sized cuff with the patient seated after 5 minutes).

Table 14.2: Hypertension Treatment Target for Various Categories of Diabetic Patients[6]

Hypertension treatment in patients with diabetes mellitus		
	BP levels	
	SBP	**DBP**
Treatment indication	≥140 mmHg	≥ 90 mmHg
Treatment targets	<140 mmHg	< 90 mmHg
Hypertension treatment in diabetic patients with established cardiovascular disease		
	BP levels	
	SBP	**DBP**
Treatment indication	≥140 mmHg	≥ 90 mmHg
Treatment targets	<140 mmHg	< 90 mmHg
Hypertension treatment in patients with diabetes, and renal impairment (serum creatinine >133µmol/L), GFR <60 and microalbuminuria)		
	BP levels	
	SBP	**DBP**
Treatment indication	≥140 mmHg	≥ 90 mmHg
Treatment targets	<140 mmHg	< 90 mmHg

Pharmacologic Management of Hypertension

- Pharmacologic management should be considered in all patients with diabetes and a documented sustained blood pressure of above 140/90 mmHg. Lifestyle modification should be developed in all patients with diabetes and/or hypertension.
- Individualize hypertensive therapy to achieve good control.
- Multiple agents are frequently required. Fixed dose combinations should be used when BP are stable and response to individual agents is known.
- Monitor serum creatinine and potassium once a year and more frequently if there is evidence of renal impairment.

Note the potential problems with certain anti-hypertensives:

- Diuretics in large doses inhibit insulin release.
- Beta-blockers may blunt or mask symptoms of hypoglycaemia and exacerbate peripheral vascular disease.
- Dyslipidaemias may be worsened by beta blockers and diuretics.
- Impotence and postural hypotension may be precipitated or aggravated by alpha blockers and centrally acting agents (e.g., methyldopa).
- Angiotensin converting enzyme (ACE) inhibitors may induce hyperkalaemia, renal failure, and a persistent cough.

> Avoid sublingual antihypertensives and hydralazine that have the potential to dramatically and catastrophically reduce blood pressure which can cause renal injury.

14.4 Multifaceted Management Approach

A multifaceted approach to management is essential to achieve of good outcomes in care for CVD in DM.
This approach includes:

- Optimisation of healthy behaviour
- Blood glucose, blood pressure, and lipid control
- Use of vascular protection mechanisms as outlined below.

Table 14.3: Multi-faceted Vascular Protection Checklist

Acronym	Parameter	Remarks
A	HbA1c	Optimal glycaemic control (usually ≤7%)
B	BP	Optimal blood pressure control (<130/80 mmHg)
C	Cholesterol	LDL-C ≤1.8 mmol/L or lower if tolerated
D	Drugs to protect the heart (regard-less of baseline BP or LDL-C)	A – ACEi or ARB S – Statin A – ASA if indicated. No benefit to routine use in DM. Prescribe if established CVD or with additional CV risk factors (Age over 40, HTN, Dyslipidaemia) (3,4) SGLT2i or GLP1-RA in diabetic patients at high risk or established CVD or CKD
E	Exercise/Eating healthily	Regular physical activity, achieve and maintain healthy body weight
S	Smoking cessation	

HbA1c, glycated haemoglobin; BP, blood pressure; LDL-C, low-density lipoprotein cholesterol; ACEi, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; ASA, acetylsalicylic acid (aspirin); DM, diabetes mellitus; CV, cardiovascular; CVD, cardiovascular disease; HTN, hypertension; SGLT2i, sodium-glucose cotransporter-2 inhibitor; GLP1-RA, glucagon-like peptide 1 receptor agonist; CKD, chronic kidney disease.

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15

15. CARDIOVASCULAR DISEASE IN PEOPLE LIVING WITH HIV/AIDS

Key Messages

- Cardiovascular disease has become a major cause of morbidity in persons living with HIV/AIDS (PLHIV). The risk of CVD is higher in PLHIV than in the non-infected persons.
- Early identification and management of CVD risk factors is important to reduce the burden of disease in this population.
- Lifestyle interventions such as heathier diet, physical activity, smoking and alcohol cessation should be recommended for every PLHIV.
- The potential for drug-drug interactions is high and should be checked at every visit.

15.1 Introduction

The prevalence of HIV/AIDS in Kenya has continued to fall over the last few years owing to effective control measures adopted by the government and other stakeholders. Data from the National AIDS Control Council showed that as at 2021, the prevalence of HIV infection was 4.3%, down from 5.9% in 2016, with approximately 1.43 million people living with HIV. The disease burden was higher in females with a prevalence of 5.5% while that in males stood at 2.9%.[1]

15.2 Epidemiology

Cardiovascular diseases, particularly coronary heart disease (CHD), have become a major cause of mortality among PLHIV who respond well to ART in the developed countries.[2] Multiple observational cohort studies have demonstrated elevated rates of acute myocardial infarction or coronary heart disease (CHD) in HIV-infected versus control patients, with an approximately 1.5 to 2-fold increase in relative risk. This cardiovascular risk persists even in patients on suppressive antiretroviral therapy, with CVD significantly impacting the long-term health of this group. HIV-infected patients have been shown to have an increased risk of stroke and cerebrovascular endpoints in comparison to control cohorts. The risk of MI is also increased ~1.5-fold relative to HIV-uninfected persons.[3,4]

A recent study in Western Kenya reported 44% rate of obesity and 70% rate of dyslipidaemia among PLHIV (7). Therefore, proper control of the modifiable risk factors and detection and treatment of cardiovascular diseases among the PLHIV could greatly lessen the burden.

Hypertension, on the other hand, is one of the commonest non-communicable diseases (NCDs) globally and is a leading cause of preventable and reversible cardiovascular disease morbidity (such as myocardial infarction, heart failure, stroke, and chronic kidney disease) and mortality.[6] According to the STEPwise survey on NCDs 2015, one in four adults in Kenya has elevated blood pressure (BP).[7]

HIV infection increased the risk for both acute and chronic kidney disease. CKD has been associated with in increased progression to AIDS, greater risk for CVD, and increased mortality, even with effective ART. Kidney disease in HIV is caused by a combination of various factors including direct effects of the virus on the kidney, genetic factors, opportunistic infections, co-infections such as hepatitis C virus, toxicity from medication used to treat opportunistic infections as well as ARVs, and comorbidities such as diabetes and hypertension. The ageing of PLHIV due to ART also contributes to the increasing incidence of CKD. [8]

HIV and other chronic diseases require health systems that support chronic care and adherence. Consideration should be given for integrating their management in the health facility.

15.3 Pathophysiology of CVD (Hypertension, CKD, Heart failure) in HIV

HIV infection and antiretroviral therapy together or independently pose a great risk to development of cardiovascular disease. HIV causes persistent inflammation, viraemia and immune activation. ART may increase risk through dyslipidaemia and other metabolic events (especially protease inhibitors (PIs)) while abacavir (ABC) may increase short term cardiovascular risk. The ageing population of HIV-infected persons also increases the risk of CVD.[3,4]

The prevalence of smoking among the HIV infected is 2 to 3 times higher than that of the general population. Previous history of heart disease, increased age and cigarette smoking are the strongest predictors of developing CVD among those infected in HV.[3,4]

There is increasing evidence that the burden of hypertension is higher in HIV infection compared to the general population.[3] Both HIV and elevated BP are amenable to screening for early identification and treatment to prevent end-organ damage and, if absent, lifestyle modification for prevention.

HIV, human immunodeficiency virus; HTN, hypertension; CVD, cardiovascular disease; CKD, chronic kidney disease; ART, antiretroviral therapy

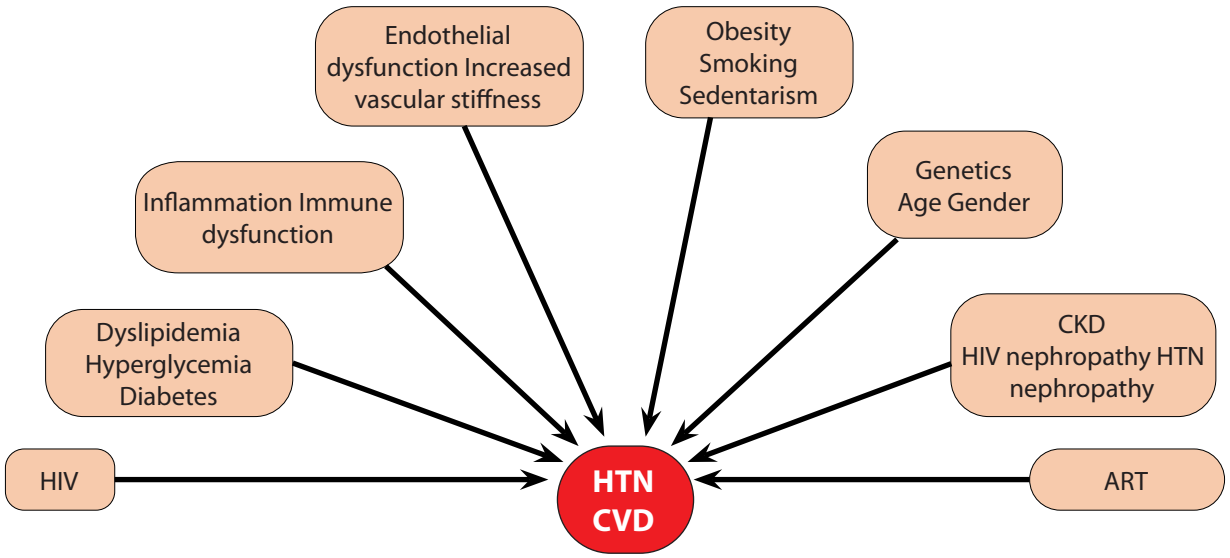

Figure 15.1: Interaction Between HIV and HTN

From: Amado Costa L, Almeida AG. Cardiovascular disease associated with human immunodeficiency virus: A review. Revista Portuguesa de Cardiologia (English Edition). 2015;34(7):479-91.[9] Used under a Creative Commons license available at https://creativecommons.org/licenses/by-nc-nd/4.0/

15.4 Recommended investigations for diagnosis and follow-up for CVD in PLHIV

Table 15.1: Baseline Investigations for CVD Risk Factors in Patients with HIV (already on treatment)

Test category	Recommended tests
HIV specific	• Viral load (HIV-1 RNA) • CD4 cell count • Serum Cryptococcal Antigen (sCrAg)
Others (HIV-related)	• Haemoglobin • Urinalysis (protein and glucose baseline then annually on TDF) • TB screening • Creatinine (baseline then annually on TDF) • Plasma lipid profile (baseline, then annually) • HBsAg (baseline) • PDT for pregnancy status (at every clinic visit) • RPR (syphilis serology baseline then annually for those at risk) • Hepatitis B test • Glucose (baseline then annually) • HCV (for those who inject drugs) • Cervical cancer screening
Dyslipidaemia	• Fasting lipid profile (total cholesterol, LDL cholesterol, triglycerides)

Hypertension	• Urinalysis (urine dipstick for protein, blood, and sugar) • Random blood sugar (finger prick) • Electrocardiogram (ECG)
Chronic Kidney disease	• Urinalysis • Creatinine

HIV, human immunodeficiency virus; RNA, ribonucleic acid; TDF, tenofovir disoproxil fumarate; TB, tuberculosis; HBsAg, hepatitis B surface antigen; PDT, pregnancy test; RPR, rapid plasma reagin; HCV, hepatitis C virus; LDL, low-density lipoprotein.

15.5 Treatment and Prevention of CVD in HIV

Data on CVD management tailored to HIV-infected patients are unfortunately limited and recommendations for management are largely reliant on guidelines and data from the general population.

15.5.1 Lifestyle Modification

This is recommended for the initial step of prevention and management for cardiovascular diseases and should be integrated into routine HIV treatment and prevention.

15.5.2 Dyslipidaemia

Table 15.2: Screening, Diagnosis, and Initial Management of Dyslipidaemia in PLHIV

Screening
• Fasting lipid profile should be evaluated at baseline for all PLHIV, then annually if baseline screening is normal
Diagnosis
• Dyslipidaemia is defined as high fasting total cholesterol (>5.2 mmol/L), LDL (>3.4 mmol/L) or triglycerides (>2.2 mmol/L)
Management

• Lifestyle modification for 3-6 months
• If the patient is on an ARV known to cause or exacerbate dyslipidaemia (primarily LPV/r & EFV) then consider a single-drug substitution to a more lipid-friendly drug (such as from LPV/r or EFV to ATV/r or DTG) as the treatment of choice before adding a lipid-lowering drug. Rule out treatment failure before making single-drug substitutions.
• If does not meet treatment target with lifestyle modifications then add drugs:
  • Atorvastatin: starting dose of 10 mg once daily (maximum dose 20 mg if patient is on a ritonavir-boosted protease inhibitor (PI/r); maximum dose 80 mg once daily if not on a PI/r)
  • Allow at least 3 months before repeating the fasting lipid profile and titrating statin dose
• Once targets achieved can monitor lipids every 6-12 months

PLHIV, persons living with HIV; LDL, low-density lipoprotein; ARV, antiretroviral; LPV/r, ritonavir-boosted lopinavir; EFV, efavirenz; ATV/r, ritonavir-boosted atazanavir; DTG, dolutegravir.

15.5.3 Chronic kidney disease

Table 15.3: CKD Screening, Diagnosis, and Management among PLHIV

Screening
• Urinalysis (for protein) and serum creatinine should be evaluated at baseline for all PLHIV
Diagnosis
• Impaired renal function is defined as creatinine clearance (CrCl) <90 ml/min, or dipstick proteinuria ≥1 • Abnormal results should be repeated to confirm diagnosis
Management
• Management depends on the cause of the renal impairment; additional investigations and/or specialist consultation may be required. • Treat dehydration promptly and aggressively • If on TDF-containing regimen, substitute with another ARV if CrCl<50 ml/min, with the exception of patients with HBV/HIV co-infection (see chart below from the Kenya HIV Prevention and Treatment Guidelines 2022). • Avoid nephrotoxic drugs e.g., aminoglycosides, non-steroidal anti-inflammatory drugs (NSAIDS) • Evaluate for and treat hypertension. • All NRTIs except ABC require dose adjustments for renal impairment, depending on the severity. • NNRTIs, PIs, and INSTIs do not require dose adjustments for impaired renal function

CKD, chronic kidney disease; PLHIV, persons living with HIV; TDF, tenofovir disoproxil fumarate; ARV, antiretroviral; HBV, hepatitis B virus; HIV, human immunodeficiency virus; NRTIs, nucleoside reverse transcriptase inhibitors; ABC, abacavir; NNRTIs, non-nucleoside reverse transcriptase inhibitors; PIs, protease inhibitors; INSTIs, integrase strand transfer inhibitors.

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Table 15.4: Dose Adjustment of TDF and 3TC in Patients with Impaired Renal Function

Drug	**Creatinine clearance (ml/min)**			**Haemodialysis**
	50-80	**30-49**	**10-29**	
TDF 33 mg/g granules (=1scoop)	245 mg (7.5 scoops of granules or 245mg film-coated tablet) granules) once daily	132 mg (4 scoops of of granules) once daily	65 mg (2 scoops of of granules) once daily	16.5 mg (0.5 scoop) after each 4 hr session of dialysis
TDF 300 mg	Unchanged: 300 mg 300 mg once daily	300 mg every 48hrs	300 mg every 72 to 96 hours (twice weekly). For patients getting hemodialysis, administer once weekly after completion of dialysis sessions [2]	
3TC 300mg	Unchanged: 300 mg once daily or 150 mg BD	150 mg once daily	150 mg once daily	50 mg first dose, 25 mg once daily

1. Patients with impaired renal function in whom the benefits of continued use of TDF outweighs the risks (such as in the management of HIV/HBV co-infection) should be managed with input from a specialist in internal/paediatric or renal medicine
2. Assuming 3 haemodialysis sessions per week, each of approximately 4 hours duration or after 12 hours cumulative haemodialysis

15.5.4 Hypertension

Screening, diagnosis, and initial management of hypertension in PLHIV is similar to that in the general population, except for a few considerations as outlined in the table below. This should follow the standard classification of hypertension as outlined earlier in these guidelines.

Table 15.5: Screening, Diagnosis, and Initial Management of Hypertension in PLHIV

BP level	Recommended Drug Therapy	Precautions
Stage 1 • SBP 130-139 and DBP 80-89 mmHg; not responsive to lifestyle modification	• Start on long acting CCB; review patient after 2 weeks* and adjust dose every 4-6 weeks depending on BP control. • If BP goal not achieved after 8 weeks, add a thiazide diuretic. • Thiazides may also be used as initial monotherapy and a CCB added later	• Metabolism of CCBs is induced by EFV or NVP, blunting antihypertensive effect. Higher starting doses may be required. Monitor closely for response. • PIs (such as LPV/r or ATV/r) inhibit metabolism of CCBs. Monitor closely for excessive reduction in BP* and reduce the dose of CCB accordingly. • ACEi and thiazide diuretics do not have significant interactions with ARVs.
Stage 2 • SBP >140 and/or DBP 90mmHg	• Start with combination therapy such as a long acting CCB plus a thiazide diuretic. • Alternative options include ACEi and a thiazide diuretic or long acting CCB and an ACEI. • ARBs can be used if/when the ACEis are not tolerated.	
Hypertensive urgency: • SBP >180 mmHg and/or DBP >110 mmHg but with no evidence of target organ damage	• Start with combination therapy such as a long acting CCB plus a thiazide diuretic. • Alternative options include ACEi and a thiazide diuretic or long acting CCB and an ACEI. • ARBs can be used if/when the ACEis are not tolerated. • Emphasize need for compliance to medication; close follow-up advisable. Refere to the section on Hypertension in this guidelines for additional management protocols.	
Hypertensive emergency: Markedly elevated BP (SBP >180 mmHg and/or DBP >110 mmHg) and end organ damage	• These should be referred for admission as they require urgent intervention. • Refer to the section on hypertension in these guidelines (Chapter 2) for additional management protocols	

* Patients on PIs (e.g. LPV/r or ATV/r) may experience oedema, dizziness, fatigue and orthostatic hypotension within the first week of initiation of CCB therapy

PLHIV, persons living with HIV; BP, blood pressure; SBP, systolic blood pressure, DBP, diastolic blood pressure; CCB, calcium channel blocker; EFV, efavirenz; NVP, nevirapine; PIs, protease inhibitors; LPV/r, ritonavir-boosted lopinavir; ATV/r, ritonavir-boosted atazanavir; ACEi, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blockers; ARV, antiretroviral.

15.6 ARVs Commonly Used in Kenya

Below are some of the ARV drugs commonly used in Kenya. For further information refer to the Kenya HIV Prevention and Treatment Guidelines 2022.

Table 15.6: Classes of ARV Drugs Commonly Used in Kenya

Class	Examples
Nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs)	• Lamivudine (3TC) • Tenofovir (TDF) • Abacavir (ABC) • Zidovudine (AZT)
Non-nucleoside reverse transcriptase inhibitors (NNRTIs)	• Efavirenz (EFV) • Nevirapine (NVP)
Protease Inhibitors (PIs)	• Atazanavir (ATV) • Lopinavir (LPV) • Ritonavir (RTV) • Darunavir (DRV)
Integrase strand transfer inhibitors (INSTI)	• Raltegravir (RAL) • Dolutegravir (DTG)

15.7 Potential Drug-drug Interactions

Table 15.7: Potential Drug Interactions Between Antihypertensive and ARV Drugs

Antihypertensive class	Potential interactions with ARV drugs	Corrective measures/ Precautions
A, Angiotensin-converting enzyme inhibitors (ACEIs): e.g., enalapril, lisinopril, perindopril, and ramipril	None with NRTIs, NNRTIs, or PIs	None
A, Angiotensin II receptor blockers (ARBs): e.g., Losartan, Telmisartan, and Candesartan	Telmisartan, Candesartan: none with PIs, NNRTIs, or NRTIs Losartan: Potential interactions with all PIs, NNRTIs and Zidovudine; none with other NRTIs	Net effect of Losartan interactions: difficult to predict.
B, Beta blockers: e.g., atenolol, carvedilol, and propranolol	Atenolol: Potential interactions with Atazanavir, Lopinavir, and Ritonavir; none with Saquinavir.	Potential increase in B-blocker effect. Careful dose† adjustment and ECG where indicated.
C, Calcium channel blockers (CCBs): e.g., Nifedipine, Amlodipine and Felodipine	Potential interaction with all NNRTIs. • Metabolism of CCBs is induced by EFV or NVP, blunting antihypertensive effect. No interaction with NRTIs	Higher starting doses may be required. Monitor closely for response and adjust dose according to BP readings.
	Potential interaction with all PIs: PIs (e.g., LPV/r or ATV/r) inhibit metabolism of CCBs.	Monitor closely for excessive reduction in BP and reduce the dose of CCB accordingly.
D, Diuretics: e.g., Bendroflumethiazide; HCTZ, Indapamide. Furosemide and Spironolactone	No significant interactions with PIs, NNRTIs, or NRTIs Indapamide: Potential interactions with Lamivudine and Tenofovir. No interactions with other NRTIs, PIs and NRTIs. Spironolactone: No interactions with PIs, NNRTIs and NRTIs.	No effect on all the listed diuretics except Indapamide (levels may fluctuate). Adjust dose if necessary
Z, Others: Alpha blockers: Methyldopa, Hydralazine	No potential interactions with any PIs, NRTIs, or NNRTIs.	None

ARV, antiretroviral; NRTI, nucleoside/nucleotide reverse transcriptase inhibitor; NNRTI, non-nucleotide reverse transcriptase inhibitors; PI, protease inhibitor; ECG, electrocardiogram; LPV/r, ritonavir-boosted lopinavir; ATV/r, ritonavir-boosted atazanavir; HCTZ, hydrochlorothiazide.

Dose†: for adjustments refer to the hypertension treatment protocol.

Listed drugs in bold: commonly used in Kenya/HHA project sites.

Similar precautions are indicated in patients using post-exposure prophylaxis (PEP) and pre-exposure prophylaxis (PrEP)

Consult the Kenya HIV Prevention and Treatment Guidelines 2022 Edition for further information.[10]

> Patients with HTN and TB and/or Diabetes should be referred to a facility with capacity to monitor and manage potential drug interactions.

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16

16. CARDIOVASCULAR DISEASE IN CHRONIC KIDNEY DISEASE

Key Messages

- Cardiovascular disease (CVD) mortality accounts for ~40-50% of all deaths in advanced chronic kidney disease (CKD).
- CKD is one of the strongest risk factors for development of CVD. This risk increases as CKD progresses.
- Traditional and emerging risk factors for CVD are common in CKD.
- CKD modifies the clinical presentation of many forms of CVD, and decreases the utility of some biomarkers (e.g., cardiac natriuretic peptides) and evidence based therapies
- Dosing modifications for kidney dysfunction may be necessary for some drugs.

16.1 Definition

Chronic kidney disease is defined as abnormalities of kidney structure or function, present for >3 months, with implications for health. It encompasses all degrees of decreased kidney function, from damaged to at risk through mild, moderate, and severe chronic kidney failure. The classification is based on Cause, GFR category (G1-G5), and Albuminuria category (A1-A3), abbreviated as CGA. Kidney disease is ascertained by the presence of albuminuria, defined as albumin-to-creatinine ratio >30 mg/g (1).

16.2 Introduction

When compared with the general population, patients with chronic kidney disease (CKD) are at a higher risk of developing cardiovascular disease and its complications, with the commonest conditions being ischemic heart disease, congestive heart failure, arrhythmias (commonly atrial fibrillation) and peripheral vascular disease (1). About 50% of all patients with CKD stage 4 to 5 have CVD, and cardiovascular mortality accounts for ≈40% to 50% of all deaths in patients with advanced CKD (stage 4) as well as end-stage kidney disease (stage 5), compared with 26% in controls with normal kidney function. The risk of developing CVD in patients with CKD surpasses the risk of reaching end-stage kidney disease, and therefore, CKD must be considered one of the strongest risk factors for the development of CVD (2). Several measures directed at preventing the progression of CKD can have impact on CVD prevention as well. Accurate recording of traditional cardiovascular risk factors and co-morbid cardiovascular disease will enable adjustment for case-mix in analysis of patient outcomes.

Progression of CKD by GFR and Albuminuria Categories				**Albuminuria categories Description and range**		
				A1	**A2**	**A3**
				Normal to mildly increased	Moderately increased	Severely increased
				-30 m/y <3 mg/ mmol	30-299 m/ 3-29 mg/mol	300 mg/g 30 mg/mmol
GFR categories (ml/min 1.73m²) Description and range	G1	Normal to high	≥90			
	G2	Mildly decreased	60-90			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	15			

Green: low risk (if no other markers of kidney diseases, no CKD): Yellow: moderately increased risk: Orange: high riak: Red, very high risk

Figure 16.1: Classification and Prognosis of Chronic Kidney Disease (CKD) from 2012 KDIGO (Kidney Disease Improving Global Outcomes) Guidelines.

(Source: KDIGO)

16.3 Economic and Public Health Burden

CKD is an important contributor to both morbidity and mortality in Kenya. There is no robust data on prevalence of CKD in Kenya though studies have been done for its prevalence in specific disease conditions like HIV, rheumatoid arthritis, diabetes, and heart failure (3-5). According to the Global Burden of Disease 2020, CKD has an estimated annual mortality rate of 3.5 per 100,000 people, healthy years lost due to disability (YLD) at 163.5 per 100,000 people while the years of life lost due to premature mortality from the condition is 133.5 per 100,000 population 2013 (6). The global prevalence of CKD is estimated at (13.4%, 95% CI 11.7–15.1%) (7) while that in the African continent at (15.8%, 95% CI 12.1–19.9%)

(8). The global prevalence of CKD has been shown to disproportionately impact low and middle-income countries where both prevalence and deaths attributable to CKD are significantly higher (9).

These countries experience limited access to renal replacement therapy (dialysis or kidney transplantation) leading to premature deaths among people with CKD who develop ESRD (10). Even for those who receive the renal replacement therapy, the financial burden that it inflicts is often catastrophic and poses far-reaching implications for individuals and their families. Cardiovascular disease has been found to complicate approximately 10% of stable CKD patients (11) and contribute to at least 50% of deaths in patients with end-stage renal disease (12). Even with the best treatment, patients with CKD still exhibit a dramatically reduced life expectancy, with a loss of 25 years of life at advanced stages compared with individuals with normal kidney function (11). CKD has a major economic impact on individuals, their families and health care systems, especially the advanced stages, and cardiovascular disease compounds this effect, especially because CVD is the leading cause of hospitalization in CKD patients (5).

16.4 Etiology and Risk Factors

The reasons for the increasing incidence and prevalence of advanced CKD include aging populations, increasing prevalence of type 2 diabetes and hypertension, glomerulonephritis with an attendant low detection rate and therapeutic inertia in the early stages of CKD (6). Other risk factors are genetics, family history, gender, increasing age, smoking and nephrotoxins (12).

16.5 Pathophysiology

Traditional risk factors for CVD such as increasing age, dyslipidaemia, hypertension, diabetes, smoking, and obesity are the same risk factors for CKD, hence they are common in CKD patients. In addition, other risk factors are more common in CKD patients as compared to the general population and include albuminuria, anaemia, hyperparathyroidism, metabolic bone disease, malnutrition, hyperhomocystinaemia, inflammation, endothelial dysfunction, and oxidative stress (14).

In addition to the established risk factors, development of CVD in CKD can occur due to mechanisms by which the kidney releases hormones, enzymes, and cytokines in response to kidney injury or kidney insufficiency, which leads to characteristic changes in the vasculature (Tan). CKD-associated mediators as well as hemodynamic alterations also contribute to cardiac damage in these patients (14). The relationship between aforementioned two set of factors (traditional vs non-traditional CVD risk factors) are illustrated in the figure below.

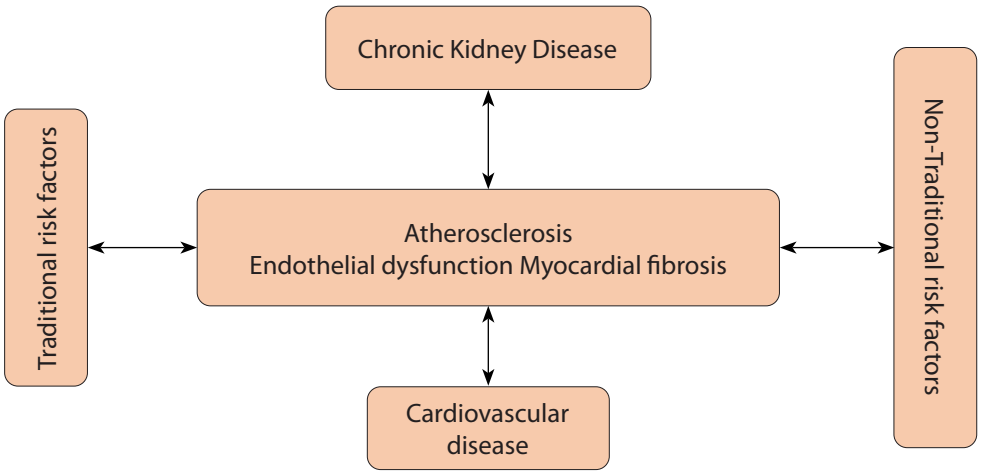
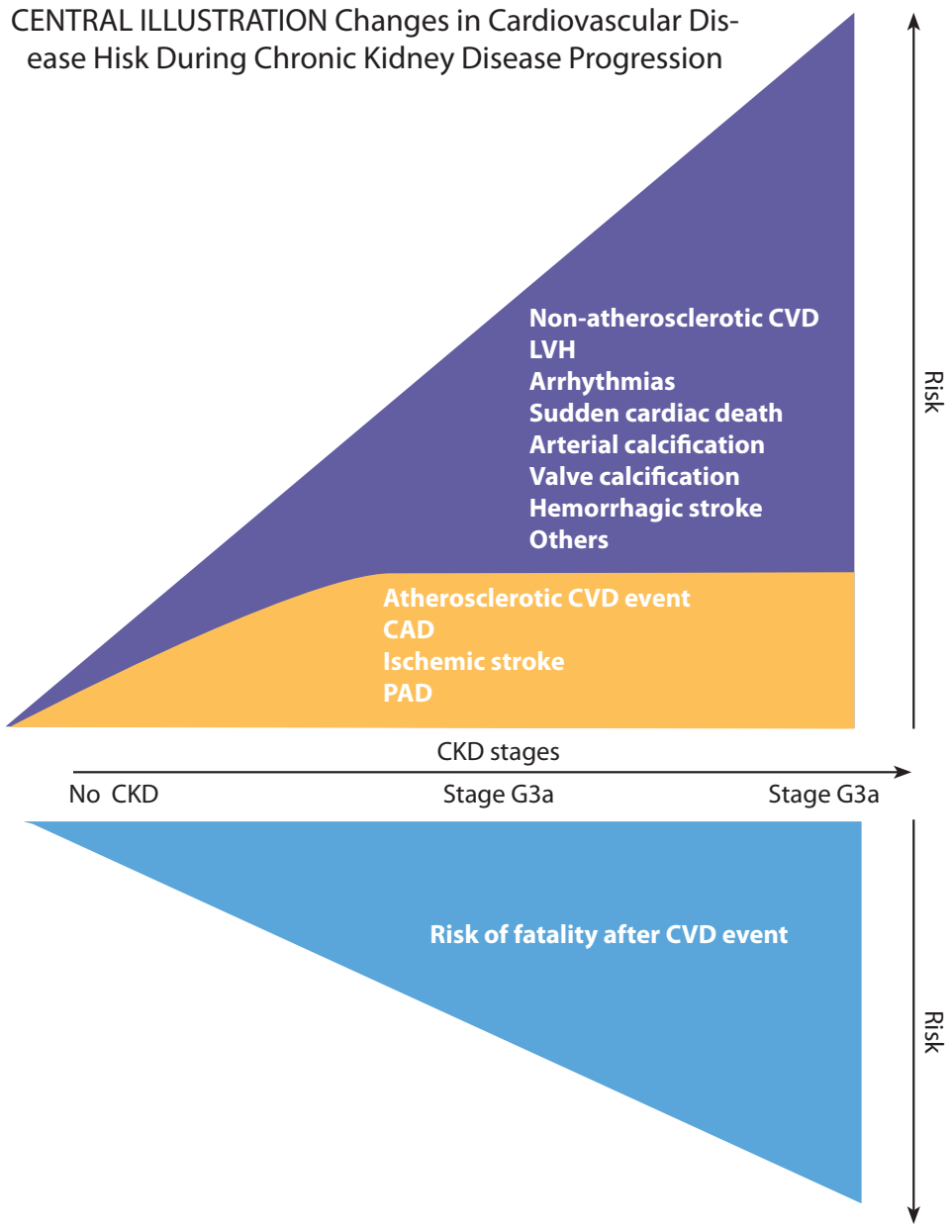


Figure 16.2: Interaction of CVD Risk Factors.

(Source: Heart Asia. 2016; 8(2): 56–61).

16.6 Important Considerations in Management

Diagnosis requires high index of suspicion since the classic triad of ischæmic symptoms, elevated cardiac biomarkers and ECG changes may be absent in CKD patients, data on diagnostic modalities is sparse since mostly CKD patients are excluded from trials and diagnostic tests have low negative predictive value due to the relatively high prevalence of CVD in CKD patients (6) CKD modifies the clinical presentation and cardinal symptoms of coronary artery disease. Fewer CKD patients with acute coronary syndrome present with typical chest pain symptoms compared to those with normal kidney function, while there is an increased incidence of sudden cardiac death among these patients (15). Cardiac biomarkers such as troponins and N-terminal pro B-type natriuretic peptide are frequently raised in CKD, limiting their specificity for cardiac abnormality (16).



Samak, M.J. et al. J Am Coll Cardiol. 2019;74(14):1823-38.

Cardiovascular diseases (CVD) event (upper triangle), contributions of atherosclerotic CVD (yellow) nonatherosclerotic CVD (purple), andrisk of fatality after CVD event (blue). Reproduced with permission from Wanner et. al (10). CAD = coronary artery disease LVH =ventricular hypertrophy.

Figure 16.3: Changing CVD Risk with Progressive CKD

(Source: Sarnak, M.J. et al. J Am Coll Cardiol. 2019;74(14):1823–38.)

During evaluation of CKD patients, history and risk factor assessment of the following conditions to be established:

- Angina and myocardial infarction
- Previous coronary angioplasty or coronary artery bypass grafting
- Stroke and transient ischaemic attack
- Previous carotid artery surgery or angioplasty
- Peripheral vascular disease or previous intervention
- Cardiac failure
- Arrhythmias (supraventricular and ventricular)
- Diabetes

16.7 Treatment

a) CKD and hypertension

- Lower systolic blood pressure to a range of 130 to 139 mm Hg in patients with diabetic or nondiabetic CKD.
- Adherence to non-pharmacological measures as in the general population like salt restriction, physical activity, weight loss and reduction of alcohol consumption.
- Renin-angiotensin-aldosterone inhibitors are first-line agents for therapy.

b) CKD and Diabetes

- HBA1c targets should be individualized, and side effects such as hypoglycaemia should be avoided.
- Preferential use of SGLT2 and GLP-1 receptor agonists to be considered in patients with type 2 diabetes at high cardiovascular risk.

c) CKD and Heart Failure

- For patients with HFrEF (left ventricular EF <40%), therapy with an ACE or ARB or even better with ARNI and β-blockers is recommended as first-line therapy. RAAS blockers have been shown to reduce morbidity and mortality in numerous large randomized trials.
- There is now evidence for use of SGLT2 inhibitors (empagliflozin and dapagliflozin) for all ranges of heart failure (with or without diabetes) in patients with eGFR>30ml/min/1.73m2
- Spironolactone and eplerenone improve the prognosis of patients with HFrEF, and this therapy is effective in patients with HF and CKD stages 1 to 3. MRAs are contraindicated in advanced CKD (stage 4-5) due to risk of hyperkalaemia although novel therapeutic strategies with potassium binders may provide an additional option for patients with hyperkalaemia.
- Diuretics are indicated at all stages to reduce the risk of decompensation even though there is no mortality benefit.
- Ivabradine may be considered once maximally tolerated β-blocker therapy is in place.
- Antiplatelet therapy
- Antiplatelet therapy is well established to reduce cardiovascular risk, but in CKD, the prognostic benefit is less clear. Aspirin to be considered for secondary prevention but not primary prevention of vascular disease in renal failure.
- Statins
    - Cardiovascular benefit of lipid-lowering therapies is attenuated in subjects with low glomerular filtration rate and limited/absent in patients with end-stage renal disease on haemodialysis. Statins are beneficial in early CKD.

d) Sudden Cardiac death

- Increased risk of sudden cardiac death due to volume and sudden electrolyte shifts after dialysis as well as volume overload and electrolyte disturbance.
- Benefits of slow dialysis, low potassium dialysate. ICD benefit is questionable.

e) Valvular heart disease (VHD)

- Clinical presentation of VHD has significant overlap with CKD leading to under-diagnosis of the later.
- Control of volume status may prevent the progression of VHD.
- Interventions based on specific valve disease are recommended.

f) Stroke

- Low dose antiplatelet therapy for both primary and secondary prevention
- Statins are indicated just as for non CKD patients
- CKD patients are at a higher risk of bleeding on antiplatelet therapy.

g) Atrial Fibrillation

- Warfarin for those at high risk for stroke based on risk assessment (those with CHF, previous stroke, LVH, hypertension)
- DOAC preferred to warfarin in patients with mild to moderate CKD, and may be used in advanced CKD
- In stage 4, apixaban, rivaroxaban and edoxaban may be used with caution in a reduced dose, whereas dabigatran is contraindicated.
- Risk stratification excluded ESRD patients hence it is best to avoid warfarin in these patients.

H) Peripheral Arterial Disease

Therapies for PAD mirror those for patients without CKD.

16.8 Prevention

Table 16.1: Targeting Risk Factors for Prevention of CVD in CKD

Targeting Risk Factors for prevention of CVD in CKD		
Risk factors for CVD in CKD	Specific aspects/treatment options compared with the non-CKD population	
Traditional		
Hypertension	Optimal target for blood pressure	
Dyslipidaemia	Characteristic lipid pattern of hypertriglyceridemia and HDL cholesterol levels – to be reduced	
Smoking	Cessation	
Hyperglycaemia	Intensive glucose control beneficial to avoid microvascular complications	
Increased proteinuria	RAS blockade	

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17

17. CARDIOVASCULAR DISEASE IN ATHLETES AND SPORTS CARDIOLOGY

Key Messages

- Regular physical activity, including systematic exercise, is associated with reduced cardiovascular and all-cause mortality.
- Intense exercise may lead to sports-related adverse cardiovascular outcomes in persons with underlying cardiovascular disease, especially in older persons.
- Experts support pre-participation cardiovascular screening to detect disorders associated with sudden cardiac death.
- Risk stratification prior to an exercise prescription is recommended. The exercise prescription should be reviewed and updated as necessary.
- Regular and long-term participation in exercise (minimum of 4 hours per week) is associated with unique changes in the electrocardiogram and echocardiogram which are considered normal physiological adaptations to regular exercise and do not require further evaluation. Skill is needed to differentiate these from pathological findings.
- Athletes or other individuals with cardiac disease or risk factors for sudden cardiac death who wish to take part in regular exercise need to be evaluated by a cardiologist.

17.1 Introduction

Regular physical activity (PA), including systematic exercise, is an important component of therapy for most CVDs and is associated with reduced cardiovascular (CV) and all-cause mortality.[1] Promotion of regular physical activity and exercise is even more important given that there is an increasing trend towards a sedentary lifestyle and a rising prevalence of obesity and associated CVD.

Despite the substantial health benefits provided by regular PA, intense exercise may paradoxically act as a trigger for life-threatening ventricular arrhythmias (VAs) in the presence of underlying CVD. Indeed, sudden cardiac death (SCD) is the leading cause of sports and exercise-related mortality in athletes.[1]

Sports cardiology is a relatively novel and emerging sub-speciality, therefore the evidence base for the natural history of disease progression or risk of death during intensive exercise and competitive sport among individuals with CVD is relatively sparse. This is reflected by the fact that many recommendations from most societies are reliant on the wisdom and experience of the consensus group rather than on large prospective studies. Pre-participation CV screening aimed at the detection of disorders associated with SCD is universally supported by major medical societies.[2] However, the best method for CV screening of young competitive athletes (<35 years old) remains controversial, and limited data are available to guide recommendations in master athletes (≥35 years old).[2]

17.2 Definitions

Athlete: an individual of young or adult age, either amateur or professional, who is engaged in regular exercise training and participates in official sports competition. A recreational athlete engages in sports for pleasure and as a leisure-time activity. On the other hand, a competitive athlete is a highly trained individual who participates in an organized team or individual sport that requires regular competition against others as a central component, places a high premium on excellence and achievement, and requires some form of systematic (and usually intense) training.

Master athletes are individuals aged 35 years or more who participate in regular exercise, training, or competition. In this group of individuals coronary artery disease is more prevalent and the leading cause of sports related adverse cardiovascular events.

Sudden cardiac arrest (SCA) is defined as an unexpected collapse due to a cardiac cause in which cardiopulmonary resuscitation (CPR) and/or defibrillation is provided in an individual regardless of the survival outcome.

Sudden cardiac death (SCD) is defined as an abrupt unexpected death due to a cardiac cause, or a sudden death in a structurally normal heart at autopsy with no other explanation for death and a history consistent with cardiac related death (i.e., requiring cardiac resuscitation).

17.3 Physiology

Top-level training is often associated with morphological changes in the heart, including increases in left ventricular (LV) chamber size, wall thickness, and mass. This constellation of adaptive changes induced by training is referred to as "athlete's heart." It is important for medical practitioners who are involved in the medical care of athletes to be cognisant of these features. Compared to non-athletes, athletes have 15–20% greater LV wall thickness and 10–15% greater LV size.

Left atrial (LA) dilation is also a physiological adaptation in trained athletes. Studies have reported a 20% increase in LA dimensions (M-mode transverse dimension) and indexed LA volume. The increased LA size can be explained by concomitant LV cavity enlargement and volume overload. Although not completely understood, LA remodelling may be one of the mechanisms associated with supraventricular arrhythmias in athletes.

Due to its unusual shape, which makes it more difficult to image, the effects of exercise on right ventricular (RV) structure have not been as well studies as those of the LV. The RV also enlarges in response to continuous exercise training, supporting the concept of balanced biventricular enlargement. MRI studies have confirmed greater RV dimensions in athletes compared to non-athletes, mainly in those involved in endurance activities.

17.4 ECG changes in Athletes

Regular and long-term participation in exercise (minimum of 4 hours per week) is associated with unique electrical manifestations that reflect enlarged cardiac chamber size and increased vagal tone. These electrocardiogram (ECG) findings in athletes are considered normal physiological adaptations to regular exercise and do not require further evaluation.

Accurate ECG interpretation in athletes requires adequate training and an attention to detail to distinguish physiological ECG findings from abnormal ECG findings that might indicate the presence of cardiac pathology. Cardiac adaptation and remodelling from regular athletic training produce common ECG alterations that could be mistaken as abnormal. Whether performed for screening or diagnostic purposes, it is critical that physicians responsible for the cardiovascular care of athletes be guided by ECG interpretation standards that improve disease detection and limit false-positive results.

We recommend use of the international criteria for ECG interpretation in athletes: consensus statement published in 2017.[6] This classifies ECG findings into normal, borderline, and abnormal. Any abnormal findings, or two or more borderline findings on the ECG should prompt referral for further evaluation. A summary of these findings is detailed in figure 1 below. It is recommended that all physicians involved in management of cardiovascular conditions in athletes and screening should familiarize themselves with these criteria.

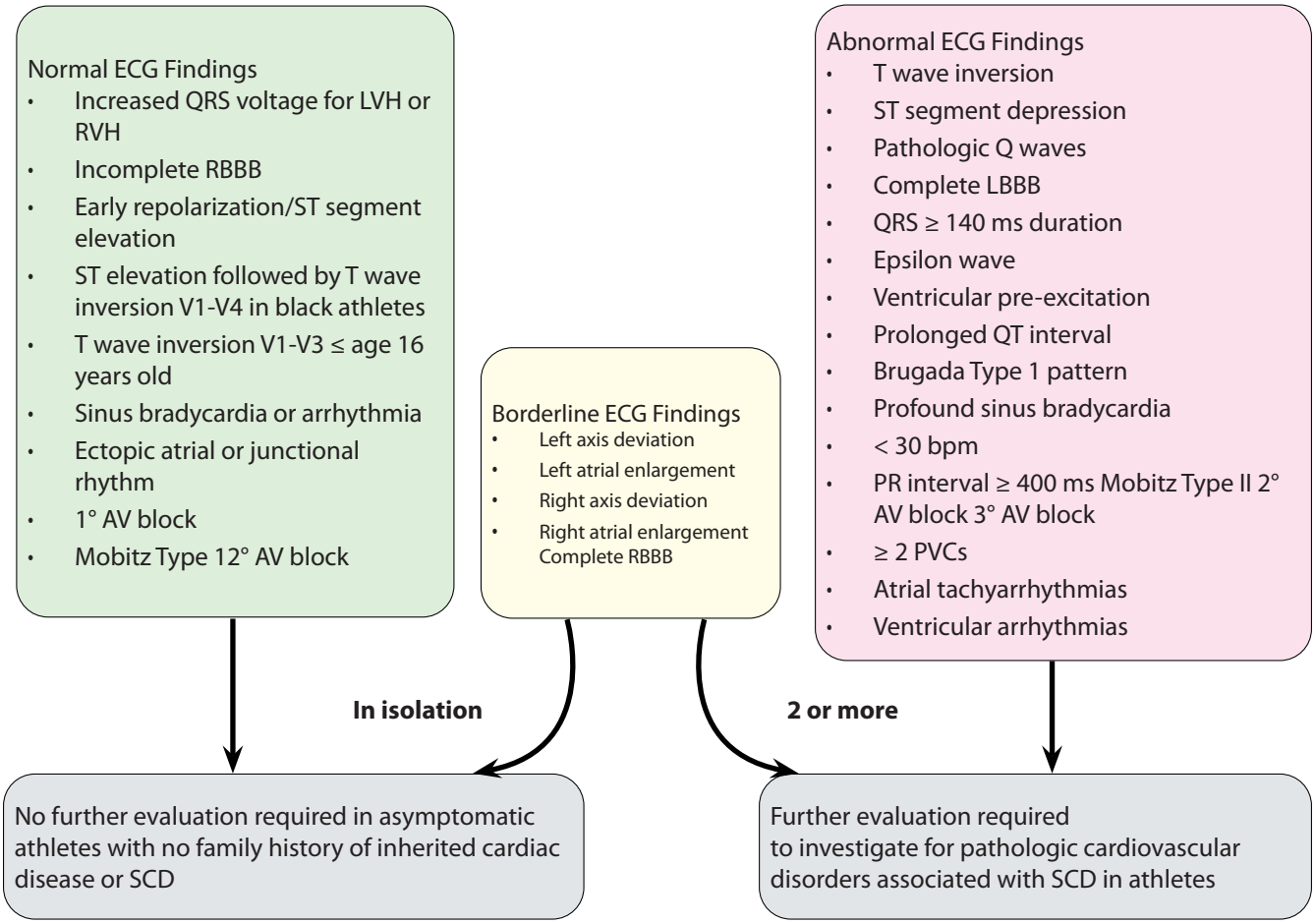


Figure 17.1: International Consensus Standards for ECG Interpretation in Athletes[6]

17.5 Sudden Death in the Athlete

Current estimates of the incidence of SCD in competitive athletes range from almost 1 in a million to 1 in 5000 athletes per year. Differences in current estimates are largely due to inconsistent study methodology and heterogeneous population comparisons. The true incidence is however often underestimated due to underreporting and incomplete case ascertainment. No African data is available on this matter.

Western studies suggest that incidence rates are consistently higher in male athletes than in female athletes, with a relative risk ranging from 3: 1 to 9: 1 (male: female). Black athletes of African Caribbean descent also have a higher risk than white athletes. In US college athletes, males had a higher risk than females (1 in 38 000 vs. 1 in 122 000), and black athletes had a 3.2 times higher risk than white athletes (1 in 21 000 vs. 1 in 68 000).

Screening strategies must be tailored to the target population and the specific disorders with highest risk. SCD in young athletes is caused by a variety of structural and electrical disorders of the heart, including cardiomyopathies, ion channel disorders, coronary anomalies, and acquired cardiac conditions. In adult and senior athletes, atherosclerotic CAD is the primary condition leading to major adverse cardiovascular events (MACE).

17.5.1 Conditions Associated with Sudden Death

SCD in young athletes is usually caused by a genetic or congenital structural cardiac disorder. However, autopsy-negative sudden unexplained death (AN-SUD), also referred to as sudden arrhythmic death syndrome, is reported on post-mortem examination in up to 44% of presumed SCD cases depending on the study population.

In apparently healthy young athletes, the prevalence of cardiac disorders associated with SCD is approximately 0.3%, and this figure is supported by multiple studies using non-invasive evaluation tools to detect cardiac disorders at elevated risk of SCD. In athletes >35 years of age, more than 80% of all SCD is due to atherosclerotic CAD, and vigorous physical exertion is associated with an increased risk of AMI and SCD.

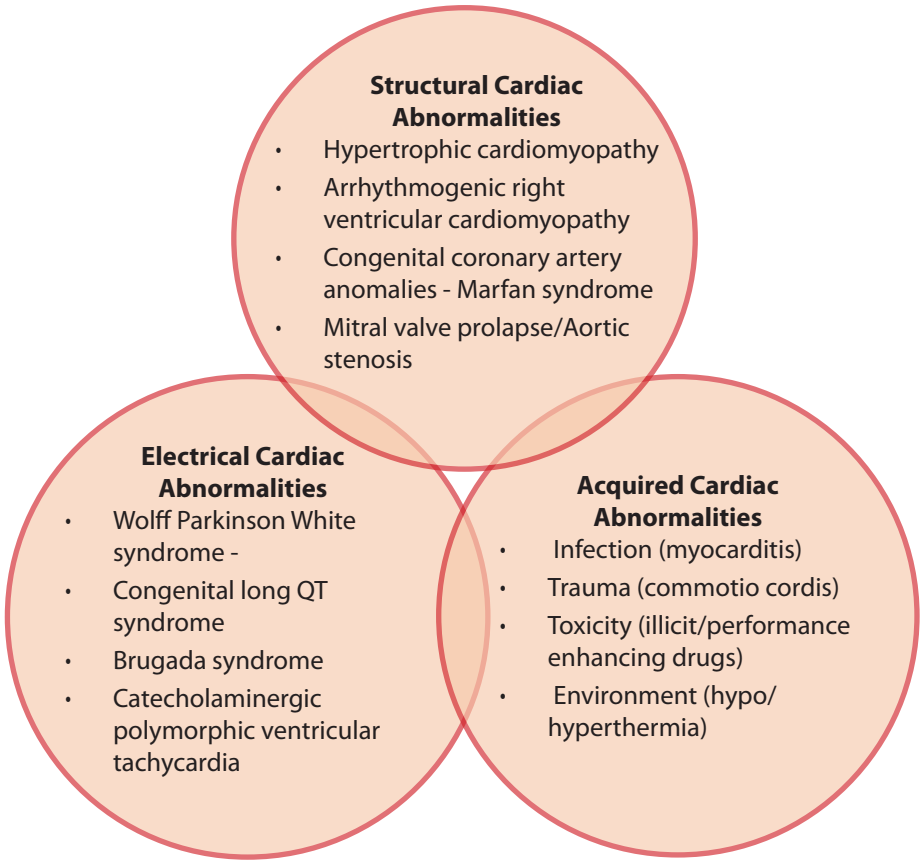


Figure 17.2: Cardiovascular Reasons for Sudden Cardiac Death in Athletes.[7]

17.6 Preparticipation Screening

Preparticipation screening is a controversial subject. Most experts believe that early detection of potentially lethal disorders in athletes can decrease CV morbidity and mortality through risk stratification, disease-specific interventions, and/or exercise modifications. CV screening by history and physical examination or by electrocardiogram (ECG) presents unique challenges and limitations and may not be feasible for all individuals planning to engage in sports.

For professional and elite athletes, most societies recommend preparticipation screening. The AHA 14-point questionnaire is a structured screening tool which may be utilized for initial screening of these individuals. Individuals who have a positive screen should be referred to a cardiologist for further evaluation.

Table 17.1: The American Heart Association 14-point screening questionnaire for conditions associated with SCD[2]

The 14-Element AHA Cardiovascular Screening Checklist for Congenital and Genetic Heart Disease

Personal history		
Yes	**No**	
☐	☐	1. Chest pain/discomfort/tightness/pressure related to exertion
☐	☐	2. Unexplained syncope/near-syncope*
☐	☐	3. Excessive exertional and unexplained dyspnea/fatigue or palpitations, associated with exercise
☐	☐	4. Prior recognition of a heart murmur
☐	☐	5. Elevated systemic blood pressure
☐	☐	6. Prior restriction from participation in sports
☐	☐	7. Prior testing for the heart, ordered by a physician
Family history		
Yes	**No**	
☐	☐	8. Premature death (sudden and unexpected, or otherwise) before age 50 attributable to heart disease in ≥1 relative
☐	☐	9. Disability from heart disease in close relative <50 y of age
☐	☐	10. Hypertrophic or dilated cardiomyopathy, long-QT syndrome, or other ion channelopathies, Marfan syndrome, or clinically significant arrhythmias; specific knowledge of certain cardiac conditions in family members
Physical Examination		
Yes	**No**	
☐	☐	11. Heart murmur**
☐	☐	12. Femoral pulses to exclude aortic coarctation
☐	☐	13. Physical stigmata of Marfan syndrome
☐	☐	14. Brachial artery blood pressure (sitting position)***

- *Judged not to be of neurocardiogenic (vasovagal) origin; of particular concern when occurring during or after physical exertion.
- **Refers to heart murmurs judged likely to be organic and unlikely to be innocent; auscultation should be performed with the patient in both the supine and standing positions (or with Valsalva manoeuvre), specifically to identify murmurs of dynamic left ventricular outflow tract obstruction.
- ***Preferably taken in both arms.

In CV screening studies in which experienced clinicians use contemporary ECG interpretation standards, ECG screening outperforms history and physical examination in all statistical measures of performance. A screening ECG may discover undiagnosed cardiomyopathies and primary electrical disorders in athletes. A baseline ECG should be performed in professional athletes and interpreted according to the criteria described above.

While echocardiography may identify additional structural disorders, there is insufficient evidence to recommend an echocardiogram for universal routine screening. Exercise testing may also be useful to evaluate the blood pressure (BP) response to exercise, the occurrence of exercise-induced arrhythmias, and to assess symptoms or physical performance and its relation to exercise training.

We recommend that professional athletes should undergo an annual medical screen, where the AHA 14-point questionnaire and a 12 lead ECG are employed to screen for conditions associated with sudden cardiac death.

17.7 Referral and Follow-up

Individuals who have a positive pre-participation screen and individuals who are diagnosed to have cardiac conditions associated with sudden cardiac death should be referred for further evaluation and follow-up by a cardiologist or physician trained in sports medicine. Risk assessment should be performed for such individuals and decision about the safety of engaging in sporting activities determined. Shared decision making involving the patient, their family and cardiologist is encouraged, and the underlying condition, level of participation, risk and need for further treatment taken into consideration.

Athletes who have been diagnosed with a cardiac condition, or conditions associated with SCD and who wish to continue participating in sporting activities of any level should have regular follow-up by a cardiologist. In the sections that follow specific conditions associated with SCD are discussed in some detail and general guidance on participation and management is given.

17.8 Sports Participation in Patients with Cardiovascular Conditions

Exercise has a positive effect on several risk factors for atherosclerosis. Regular exercise reduces the risk of many adverse health outcomes irrespective of age, sex, ethnicity, or the presence of comorbidities. Indeed, there is a dose-effect relationship between exercise and CV all-cause mortality, with a 20-30% reduction in adverse events compared with sedentary individuals.

In keeping with other society guidelines, we recommend that healthy adults of all ages should perform a minimum of 150 min of moderate intensity endurance exercise training over 5 days or 75 min of vigorous exercise per week over 3 days.

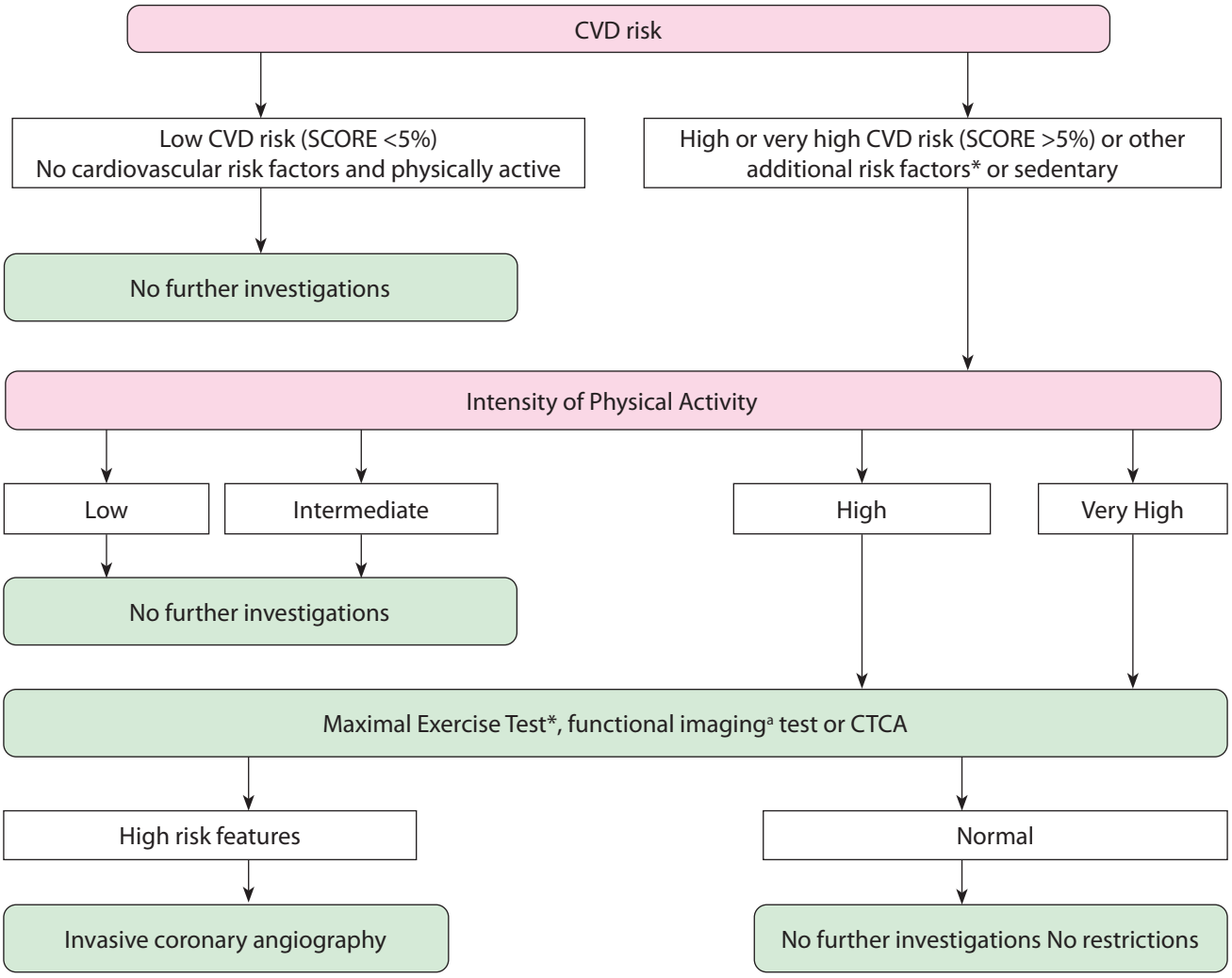
Patients with cardiovascular risk factors

While exercise is also beneficial in patients with established CVD, the risk associated with vigorous exercise and sports in these individuals is increased. Importantly, CVD may be subclinical and unrecognized; therefore, consideration should be given to preparticipation assessment of risk in individuals with a higher likelihood of CVD.[1]

Assessment of the individual likelihood of subclinical CVD may be performed by calculating the patient's cardiovascular risk through established risk scores such as the WHO and SCORE risk charts (See chapter on Prevention of ASCVD in these guidelines for more information on the risk charts) and considering individual risk factors such as very high total cholesterol and low-density lipoprotein (LDL), diabetes mellitus, or a strong family history of CVD. Based on this assessment the individual CV risk can be categorized from low to very high risk.

Sedentary individuals and individuals at high or very high risk may engage in low-intensity exercise without further evaluation. Sedentary individuals and/or those at high or very high-risk planning to undertake high-intensity exercise as

well as selected individuals planning to undertake moderate-intensity exercise should undergo a physical examination, 12-lead ECG, and exercise stress test. The aim of the exercise test is to identify prognostically important CAD and to assess the presence of exercise-induced arrhythmias. Individuals with symptoms, abnormal findings on physical examination, abnormal ECG, or abnormal exercise test should be investigated further. The figure below proposes an algorithm for evaluation of these individuals.



Proposed algorithm for cardiovascular assessment in asymptomatic individuals aged >35-years-old with risk factors for cardiovascular disease and possible subclinical chronic coronary syndrome before engaging in sports. *Consider functional test or CCTA if exercise stress test is equivocal or the ECG is uninterpretable. "See text for examples of functional imaging. "Single-photon emission computed tomography: area of ischaemia ≥10% of the left ventricular myocardium, stress echocardiography. 23 of 16 segments with stress-induced hypokinesia or akinesia, stress cardiovascular magnetic resonance. >2 of 16 seg- ments with stress perfusion defects or ≥3 dobutamine-induced dysfunctional segments; coronary computed tomography angiography (CCTA): three-vessel disease with proximal stenoses; left main disease; proximal left anterior descending disease.110 CVD = cardiovascular disease; ECG = electrocardiogram; SCORE=Systematic Coronary Risk Evaluation.

Figure 17.3: Proposed algorithm for cardiovascular risk assessment in 'master athletes' Pelliccia A, Sharma S, Gati S, Bäck M, Börjesson M, Caselli S, et al. 2020 ESC Guidelines on sports cardiology and exercise in patients with cardiovascular disease: The Task Force on sports cardiology and exercise in patients with cardiovascular disease of the European Society of Cardiology (ESC). European heart journal. 2020;42(1):17-96.1

If investigations are normal, there should be no restrictions to sports participation. All individuals should, however, be thoroughly informed that development of symptoms during exercise should prompt reassessment. While a normal exercise test and a high exercise capacity is associated with a good prognosis, the test has limited sensitivity in diagnosing mild to moderate obstructive CAD.

17.8.1 Hypertension

Hypertensive individuals should participate in at least 30 min of moderate-intense dynamic aerobic exercise (walking, jogging, cycling, or swimming) for 5-7 days per week. Such exercise intervention is associated with a mean reduction in SBP of 7 mmHg and DBP of 5 mmHg.

If high-intensity sports participation is desired, a pre-participation CV assessment is warranted to identify athletes with exercise induced symptoms, excessive BP response to exercise, and the presence of end organ damage. Individuals with symptoms suggestive of CAD require further assessment and optimization of medical therapy before participation in sports.

When BP is uncontrolled, temporary restriction from competitive sports is recommended, with the possible exception of skill sports e.g., golfing while using a golf cart, bowling. In individuals with a high-risk profile, including those with end organ damage [(LV) hypertrophy, diastolic dysfunction, ultrasound evidence of arterial wall thickening or atherosclerotic plaque, hypertensive retinopathy, increased serum creatinine and/or microalbuminuria] in whom BP is controlled, participation in all competitive sports is possible, except for the most intensive power disciplines such as discus/javelin throwing, shot-putting, and weightlifting.

17.8.2 Coronary Disease

Atherosclerotic CAD is the predominant cause of exercise-related (Ex-R) cardiac events including acute coronary syndrome (ACS), acute myocardial infarction (AMI), and SCA in individuals with established chronic coronary syndrome (CCS), or SCD as a primary presentation in individuals >35 years of age. In addition to atherosclerotic CAD, other entities, including an anomalous origin of a coronary artery (AOCA), myocardial bridge (MB) and spontaneous coronary artery dissection (SCAD) are also associated with myocardial ischaemia, and potentially with Ex-R SCD.

Physical inactivity is a risk factor for CAD, but somewhat paradoxically, vigorous physical exertion transiently increases the risk for AMI and SCD. Overall, the benefits of regular exercise greatly outweigh the Ex-R risk, even in individuals with CCS.

Individuals at risk of CAD and asymptomatic individuals in whom CAD is detected at screening should have aggressive management of risk factors for atherosclerosis. Considering the benefits of exercise on primary and secondary prevention of CCS, individuals with risk factors should be restricted from competitive sport only when there is substantial risk of an adverse event, as indicated by functional tests, or when there is evidence of disease progression during serial evaluations. Exercise recommendations should be individually tailored based on the intensity of the exercise and the sporting discipline.

Individuals with long-standing CCS who do not show any abnormalities on a maximal exercise test or functional imaging test, or have unimpaired LV function, may be considered as low risk for an exercise induced adverse event. Such individuals may engage in all competitive sports on an individual basis.

Individuals with inducible ischaemia during functional testing, despite adequate treatment, should undergo coronary angiography; those with high-risk lesions on coronary angiography should have revascularization prior to considering high-intensity exercise programmes or competitive sport.

When ischaemia cannot be treated despite adequate therapy, including revascularization, the individual should be restricted from competitive sports, apart from individually recommended low-intensity skill sports. Such individuals may

engage in regular recreational exercise of low and moderate intensity provided risk factors and symptoms are treated adequately and there is regular clinical surveillance.

Individuals with CAD should receive conventional antithrombotic treatment for secondary prevention, according to published guidelines for the general population. Individuals taking dual antiplatelet agents should avoid sports with bodily collision, especially when they are combined with oral anticoagulants, due to the risk of haemorrhage.

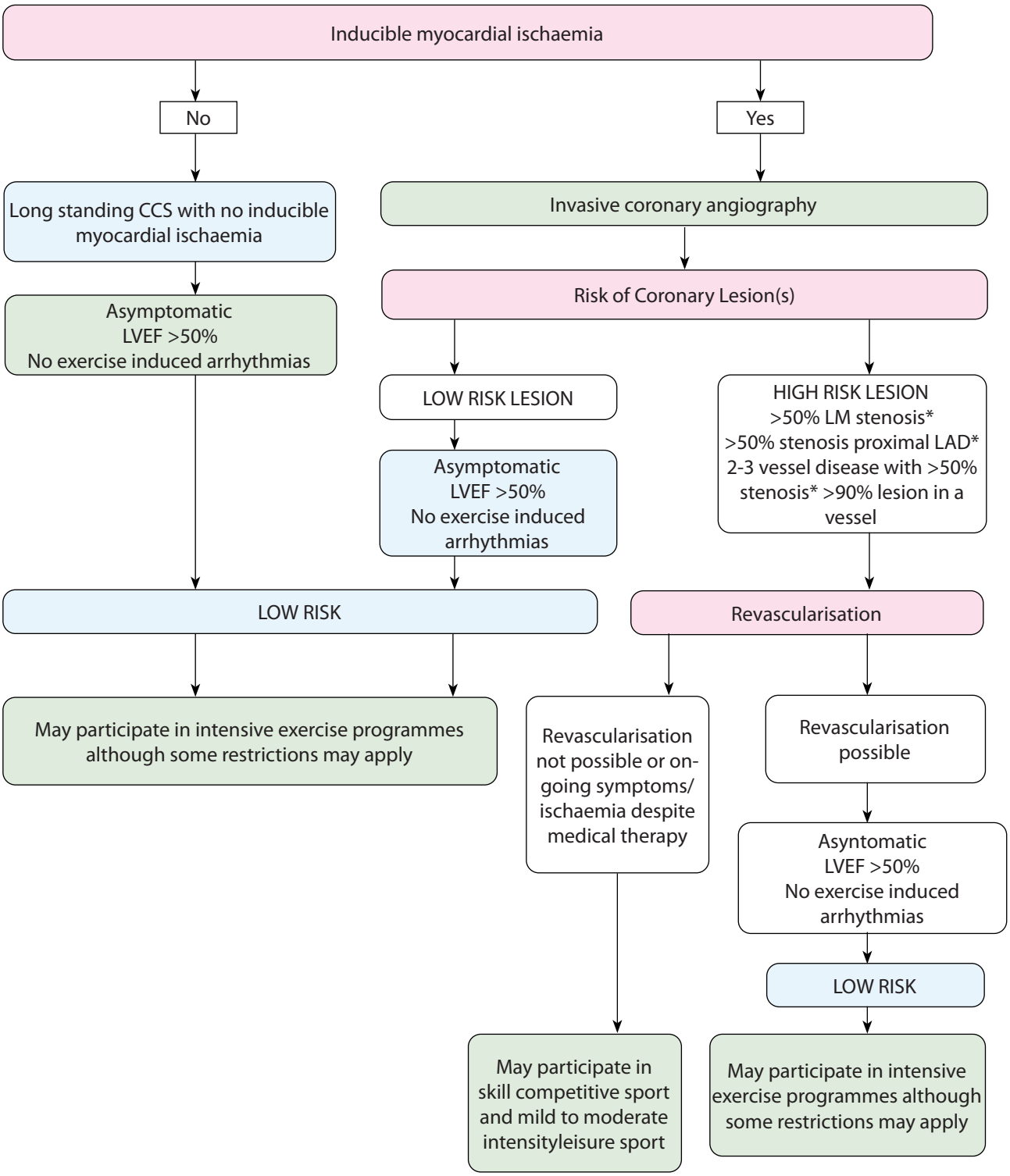


Figure 17.4: Recommendations for sports participation in individuals with established coronary artery disease

Pelliccia A, Sharma S, Gati S, Bäck M, Börjesson M, Caselli S, et al. 2020 ESC Guidelines on sports cardiology and exercise in patients with cardiovascular disease: The Task Force on sports cardiology and exercise in patients with cardiovascular disease of the European Society of Cardiology (ESC). European heart journal. 2020;42(1):17-96.[1]

17.8.3 Hypertrophic Cardiomyopathy

The diagnosis of hypertrophic cardiomyopathy (HCM) is based on the presence of unexplained LV hypertrophy, defined as a maximum end-diastolic wall thickness ≥15 mm, in any myocardial segment on echocardiography, CMR, or CT imaging. HCM may also be considered in individuals with a lesser degree of LV hypertrophy (wall thickness ≥13 mm) in the context of a family history of definite HCM or a positive genetic test.

A systematic approach is required when assessing an individual with HCM who requests exercise advice. The baseline evaluation should include a comprehensive personal and family history with consideration of the age of the individual and years of exercise prior to diagnosis, assessment of the severity of the HCM phenotype, and the presence of any conventional risk factors for SCD/SCA. In older patients with HCM, the physician should review the presence of cardiac comorbidities such as hypertension and ischaemic heart disease, which may confer a worse prognosis in HCM.

The presence of symptoms attributed to HCM should prompt more conservative exercise recommendations. Individuals with a history of cardiac arrest or unheralded syncope and individuals with exercise-induced symptoms should be advised to engage in low-intensity recreational sports only. Further assessment of risk can be carried out using echocardiography, ambulatory ECG monitoring and exercise testing.

In relation to risk stratification for SCD the clinician should assess the following echocardiographic indices:

(i) LV wall thickness
(ii) LV outflow tract (LVOT) gradient
(iii) left atrial diameter

All individuals should have the LVOT gradient assessed at rest, during the Valsalva manoeuvre, on standing suddenly, and after light exercise on the spot, such as repeated squats. By convention, LVOT obstruction is defined as a peak pressure gradient ≥30 mmHg at rest or during physiological provocation. A gradient ≥50 mmHg is haemodynamically important. Exercise stress echocardiography should be considered in individuals with exertional symptoms who have resting systolic anterior motion of the mitral valve leaflets but who do not reveal LVOT obstruction or show only mild to moderate LVOT obstruction with the aforementioned manoeuvres.

Asymptomatic non-sustained ventricular tachycardia (NSVT) on ambulatory ECG confers considerable risk of SCD in individuals ≤35 years.

Exercise testing should be part of the routine evaluation to assess functional capacity in an individual with HCM who intends to exercise. In addition, an abnormal BP response to exercise defined as <20 mmHg increase in SBP from baseline, or exercise induced hypotension and the presence of exercise-induced symptoms or arrhythmias are markers of high risk and should result in more conservative exercise recommendation.

The ESC risk score for HCM is a useful tool for risk stratification and uses seven variables (age, syncope, family history of SCD from HCM, maximal LV wall thickness, left atrial diameter, LV outflow obstruction, NSVT) to assess the risk of SCD of patients with HCM and should be considered.[11]

Table 17.2: Factors Associated with Sudden Cardiac Death in Adult Patients with HCM

Risk factor	Comment
Age	• Risk factors that appear to be more important in younger patients include non-sustained ventricular tachycardia, severe LVH, unexplained syncope
Non-sustained ventricular tachycardia (NSVT)	• Defined as ≥3 consecutive ventricular beats as ≥120 beats/min lasting <30 seconds and is an independent predictor of SCD. • NSVT occurring during or immediately after exercise is very rare but it may be associated with a very high risk of SCD.

Maximum LV wall thickness	• Maximum wall thickness of ≥30 mm as measured on TTE has the highest risk of SCD. • There are few data in patients with extreme hypertrophy (≥35 mm)
Family history of sudden cardiac death at a young age	• Clinically significant when ≥1 first-degree relatives have died suddenly aged <40 years, or when SCD has occurred in a first-degree relative at any age with an established diagnosis of HCM
Syncope	• Non-neurocardiogenic syncope for which there is no explanation despite investigation is associated with an increased risk of SCD
Left atrial diameter	• There are data showing a positive association between LA size and SCD, but not LA area or volume. • Measurement of LA size is also important in assessing the risk of AF.
LV outflow tract obstruction	• A significant association between LVTO and SCD risk has been reported, but there are no data on the impact of treatment on SCD, or on the importance of provocable LVOTO on prognosis

AF, atrial fibrillation; HCM, hypertrophic cardiomyopathy; LA, left atrium; LV, left ventricular; LVH, left ventricular hypertrophy; LVOTO, left ventricular outflow tract obstruction; NSVT, non-sustained ventricular tachycardia; SCD, sudden cardiac death; TTE, transthoracic echocardiogram

Adapted from Arbelo E, Protonotarios A, Gimeno JR, Arbustini E, Barriales-Villa R, Basso C, et al. 2023 ESC Guidelines for the management of cardiomyopathies: Developed by the task force on the management of cardiomyopathies of the European Society of Cardiology (ESC). European heart journal. 2023;44(37):3503-626.[11]

On completion of the baseline evaluation, the physician should consider:

I. the presence of symptoms;
II. ESC risk score;
III. presence of resting or inducible LVOT obstruction during exercise;
IV. the haemodynamic (BP) response to exercise; and
V. the presence of resting or exercise-induced arrhythmias before recommending the appropriate form and intensity of exercise.

For the purposes of these guidelines the risk of SCD is defined as low if <4%, moderate if between ≥4% and <6%, and high if ≥6% in 5 years.[11]

Participation in high-intensity exercise/competitive sports, if desired, may be considered for individuals who do not have any markers of increased risk following expert assessment. For individuals who have any markers of increased risk, participation in low- or moderate-intensity recreational exercise, if desired, may be considered. However, participation in high-intensity exercise (including recreational and competitive sports) is not recommended.

Annual follow-up is recommended for most individuals with HCM who exercise on a regular basis. More frequent (6-monthly) follow up should be considered in adolescent individuals and young adults whose phenotype, and therefore risk of SCD, may still be evolving and who are more vulnerable to exercise-related SCD. Follow-up evaluation should focus on assessment of disease progression and risk stratification.

17.8.4 Heart Failure

Most of the evidence regarding exercise in chronic heart failure (HF) is derived from studies implementing exercise training programmes that are considered safe and highly recommended in stable patients. These studies have demonstrated a significant improvement in exercise tolerance and quality of life and a modest effect on all-cause and HF-specific mortality and hospitalisation.

Exercise intervention should only be initiated in a clinically stable individual after medical therapy for HF has been

optimized, i.e., those showing no physical signs and symptoms suggestive of worsening heart function.

Table 17.3 Key components before commencing an exercise programme and sports participation

Exclude contraindications to exercise	• Hypo- or hypertension at rest or during exercise • Unstable cardiac disease • Deteriorating symptoms of heart failure • Myocardial ischaemia despite therapy-exercise may however be permitted up to ischaemic threshold. • Severe and sub-opitmally treated pulmonary disease
Perform a baseline assessment	• Thorough cardiological evaluation • HF severity (biomarkers, echocardiography) • Exercise test to extablish functional capacity, lookf for exercise-induced arryythmias or haemodynamic instability.
Optimise medical therapy	• All patients should be treated according to current guidelines. • Cardiac devices should be implanted when required.

Asymptomatic individuals with preserved (≥50%) EF (HFpEF) or with mid-range (≥40-49%) EF (HFmrEF) who are optimally treated may be eligible to participate in some competitive sports in the absence of exercise-induced arrhythmias or exercise-induced hypotension. In such cases, a progressive increase in exercise dose is recommended. The duration of this process is dependent upon the functional capacity and perceived symptoms. Some restrictions may apply to high-intensity endurance, mixed, and power sports with high demands, especially in older patients.

Asymptomatic patients with HFrEF who are optimally treated may only be considered safe to perform specific low-intensity skill sports at a competitive level. Higher-risk patients including those who are sub-optimally treated, those that remain in NYHA II or III despite optimal therapy, and those with exercise induced arrhythmias or exercise-induced hypotension should not participate in competitive sports, particularly those sports with moderate to high cardiopulmonary strain during training or competition.

17.8.5 Arrhythmias

When individuals with known arrhythmias or with a potentially arrhythmogenic condition want to engage in sports activity, three principal questions should guide management:

1) is there an increased risk for life-threatening arrhythmias?
2) how does one control symptoms due to arrhythmias, during sports, but also at rest?
3) what is the impact of sports on the natural progression of the arrhythmogenic condition?

The general view on the association between sports and arrhythmias is that exercise sets the stage for an arrhythmia in the context of an underlying and pre-existing condition, be it structural, electrical, inherited, or acquired. Conceptually, all the structural and functional cardiac adaptations to regular intensive exercise may contribute to the development of arrhythmias, at the atrial, nodal, and ventricular level.

General guidelines for different arrhythmic conditions are detailed in the table below.

Table 17.4: General Guidelines for the Management of Various Arrhythmic Conditions and Sports Participation

Arrhythmic condition	Guidance
Atrial Fibrillation (AF)	Regular physical activity is recommended to prevent AF. Evaluation and management of structural heart disease, thyroid dysfunction, alcohol or drug abuse, or other primary causes of AF is recommended before engaging in sports.

Paroxysmal SVT and Pre-excitation	Participation in all sports activities is recommended in individuals PSVT without preexcitation. Ablation of the accessory pathway is recommended in competitive and recreational athletes with pre-excitation and documented arrhythmia. In competitive/professional athletes with asymptomatic pre-excitation, an EP study is recommended to evaluate the risk for sudden death.
PVCs and NSVT	In exercising individuals with ≥2 PVCs on a baseline ECG or documented NSVT thorough evaluation (including a detailed family history) and Holter monitoring, 12-lead ECG, exercise test, and suitable imaging is recommended to exclude underlying structural or arrhythmogenic conditions is recommended. It is recommended that all competitive and leisure-time sports activities are permitted, with periodic re-evaluation in individuals without familial or structural underlying disease.
Long QT syndrome	It is recommended that all exercising individuals with LQTS with prior symptoms or prolonged QTc be on therapy with beta-blockers at target dose. It is recommended that exercising individuals with LQTS should avoid QT prolonging drugs and electrolyte imbalance such as hypokalaemia and hypomagnesaemia. Participation in high-intensity recreational and competitive sports, even when on beta-blockers, is not recommended in individuals with a QTc >500 ms or a genetically confirmed LQTS with a QTc ≥470 ms in men or ≥480 ms in women. Participation in competitive sports (with or without ICD) is not recommended in individuals with LQTS and prior cardiac arrest or arrhythmic syncope.
Brugada Syndrome (BrS)	ICD implantation is recommended in patients with BrS with episodes of arrhythmic syncope and/or aborted SCD. Following implantation of an ICD, resumption of leisure or competitive sports should be considered after shared decision making in individuals who have not experienced recurrent arrhythmias over 3 months after ICD implantation. Prescription of drugs that may aggravate BrS, electrolyte abnormalities, and sports practice that increases core temperature >39C are not recommended in individuals with overt BrS or phenotypically negative mutation carriers.
Patients with devices	In the first weeks after device implantation, sports activities that increase the risk of lead dislocation (e.g., strong upper extremity movements) should be avoided. For all patients with cardiac devices (PM, cardiac resynchronization therapy, and ICD), sports activities associated with a risk of chest trauma should be avoided. Shared decision making should be considered during decisions relating to continuation of intensive or competitive sports participation in individuals with an ICD, considering the effect of sports on the underlying substrate, the fact that intensive sports will trigger more appropriate and inappropriate shocks, the psychological impact of shocks on the athlete/patient

AF, atrial fibrillation; ECG, electrocardiogram; ICD, implantable cardioverter defribrillator; LQTS, long QT syndrome; NSVT, non-sustained ventricular tachycardia; PM, pacemaker; PVC, premature ventricular complexes; SCD, ; SVT, supraventricular tachycardia; QTc, corrected QT interval

17.8.6 Congenital Heart Disease

For adults with CHD (ACHD) regular exercise is and exercise participation should be discussed at every patient encounter. However, CHD represents a spectrum of conditions with widely varying physiological consequences.

Individualized assessment is essential before advising on sports participation. This requires detailed understanding of the congenital heart defect, its physiological consequences, and the effect of surgical or transcatheter intervention. Athletes with CHD include those with minor unoperated lesions and palliated and repaired CHD. Some athletes will be diagnosed with CHD for the first time during pre-participation screening.

The assessment and follow-up of these individuals should be carried out by a cardiologist with training in congenital heart disease. There is considerable variation in the haemodynamic consequences and prognosis of different CHD lesions. Furthermore, the consequences of any individual lesion can vary hugely between individuals.

Regular structured exercise is safe and effective therapy for most patients with CHD. This is true for most diagnostic groups, including symptomatic patients, and includes aerobic and strength-based exercise. Exercise intolerance in CHD is a strong predictor of both outcome and SCD.

The following five baseline parameters should be evaluated:

(1) Ventricular function

- Assessment of ventricular function can usually be achieved using echocardiography. The aim is to establish whether function is reduced (EF < 55%), and if so, is it mild (45 - 55%), moderate (30 - 45%), or severe (<30%). This is used for baseline assessment and subsequent monitoring of the effects of exercise training.

(2) Pulmonary artery pressure

- Pulmonary hypertension (PH) is diagnosed when the mean pulmonary arterial pressure (PAP) is >20 mmHg. PH may occur in the context of a chronic left-to-right shunt (e.g., atrial septal defect, ventricular septal defect, patent ductus arteriosus) that allows unrestricted volume/pressure overload. Eventually this can result in supra-normal PAP with reversal of shunting and elevated pulmonary vascular resistance (Eisenmenger syndrome).
- An increased RV afterload limits the ability to increase cardiac output by increasing stroke volume and can impair LV function through disruption of normal RV-LV interaction.

(3) Aortic assessment

- Many CHD patients are at risk of aortic dilatation, in particular, patients with tetralogy of Fallot, coarctation of the aorta, and syndromes such as 22q11 microdeletion and Turner syndrome.
- Athletes have mildly increased aortic dimensions in comparison to sedentary controls, but it is not known if this has a cumulative effect in CHD athletes with aortic dilatation. The presence of ascending aorta dilatation should lead to assessment for coarctation of the aorta as this can be associated with severe coarctation, which may be missed on clinical assessment but may cause severe exercise-related hypertension.

(4) Arrhythmia assessment

- Arrhythmias are responsible for 25% of CHD hospital admissions. Over 80% are atrial but life-threatening ventricular arrythmias can occur. Independent risk factors include increasing age, male gender, double outlet right ventricle, atrioventricular septal defect, HF, obstructive sleep apnoea, transposition of the great arteries, congenitally corrected transposition, and tetralogy of Fallot.
- Assessment of CHD athlete should include a symptom history with evaluation of palpitations, presyncope and syncope, particularly during exercise. Arrhythmias may be the first sign of underlying haemodynamic deterioration and new-onset arrhythmias should lead to a full haemodynamic assessment.

(5) Assessment of saturations/lung function

- CHD athletes should be assessed for the potential of an underlying intracardiac right to left shunt. This can be

assessed using pulse oximetry, but a resting saturation >95% does not exclude exercise related central cyanosis, and exercise assessment is essential. The potential for a pulmonary cause of cyanosis must be considered and lung function should be assessed as part of a cardiopulmonary exercise test. Even after surgical correction of the cardiac defect there may be residual intracardiac shunting.

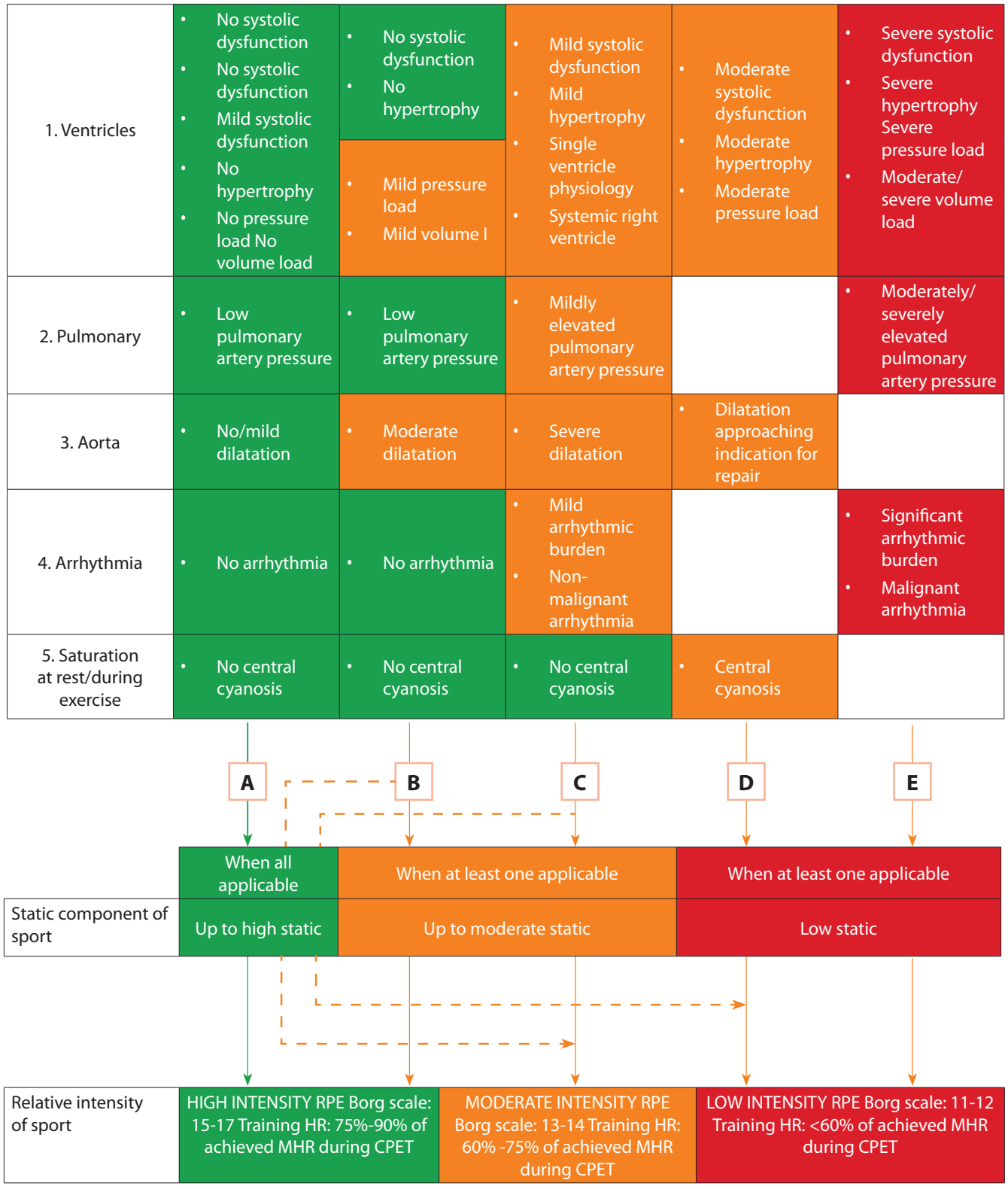


Figure 17.5: A recommended approach to preparticipation assessment and intensity of recommended activities[1]

(Source: Pelliccia A, Sharma S, Gati S, Bäck M, Börjesson M, Caselli S, et al. 2020 ESC Guidelines on sports cardiology and exercise in patients with cardiovascular disease: The Task Force on sports cardiology and exercise in patients with cardiovascular disease of the European Society of Cardiology (ESC). European heart journal. 2020;42(1):17-96.[1]

Table 17. 5 The Borg Rating of Perceived Exertion Scale

Score	Level of exertion
6	No exertion at all
7	
7.5	Extremely light
8	
9	Very light (for most healthy people, this is equivalent to walking slowly at one's own pace).
10	
11	Light
12	
13	Somewhat hard. Most healthy persons can however continue with the activity
14	
15	Hard
16	
17	Very hard. Most people can continue but must push themselves beyond the feeling of being very fatigued.
18	
19	Extremely hard. Individuals would describe is as the hardest exercise they have ever experienced.
20	Maximal exertion

Copyright Gunnar Borg

17.8.7 Valvular Heart Disease

Valvular heart disease affects approximately 12% of young exercising individuals in the general population. Reports on the natural history of valvular heart disease in athletes are sparse; however, there is a theoretical possibility that a large stroke volume, coupled with vigorous mechanical contractions of the heart, and an increased chronotropic state induced by exercise may accelerate valve dysfunction. The ensuing effects on chronic stenotic or regurgitant lesions may cause compensatory cardiac hypertrophy, impaired ventricular function, myocardial ischaemia, cardiac arrhythmias, and possibly SCD.

All individuals should be assessed with a clinical history, physical examination, ECG, echocardiography, and exercise stress test.

Asymptomatic individuals with mild to moderate valvular dysfunction who have preserved ventricular function and show good functional capacity without exercise-inducible myocardial ischaemia, abnormal haemodynamic response, or arrhythmias are considered to be at low risk and may participate in all sports. Indeed, mild valvular regurgitation (mostly tricuspid and pulmonary) are common among trained athletes and likely represent a feature of the athlete's heart.

Conversely, individuals with exertional symptoms, moderate or severe valvular dysfunction, left or right ventricular dysfunction, pulmonary hypertension, and exercise-induced cardiac arrhythmias or abnormal haemodynamic response are considered to be at high risk and should be considered for invasive intervention. These patients should refrain from competitive sports until they undergo definitive management. Specific valve lesions are discussed in greater detail in the chapter on valvular heart disease in these guidelines.

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18

18. CARDIOVASCULAR DISEASE AMONG THE ELDERLY

Key Messages

- Elderly people are at a higher risk of developing cardiovascular disease. CVD is associated with higher mortality in this age group.
- Management of CVD in the elderly must take into consideration the presence of comorbidities, organ deficiencies and impaired cognitive abilities to direct their own health care.
- Treatment should be titrated carefully.
- Drug toxicities and drug-drug interactions are common and should be monitored closely.

18.1 Introduction

Adults above 65 years of age currently constitute about 2.7% of the total Kenyan population as of early 2017, or 1, 285, 585 persons (1). Elderly people are at a higher risk of developing cardiovascular disease (2), and this is associated with higher rates of mortality among this age bracket. Management of cardiovascular disease among elderly persons has to incorporate special considerations due to presence of comorbidities, organ deficiencies and impaired cognitive abilities to direct their own health care.

18.2 Epidemiology

The mortality from cardiovascular disease in elderly people above 60 years in Kenya ranges from 346.3 per 100,000 in those between 60-65 years to 4264.6 per 100,000 in those; above 80 years, with a combined 122.8 years lost to disability (YLD) per 100,000 population (3). The main risk factors for the elderly population include high systolic blood pressure/ wide pulse pressure, dietary patterns, high body mass index, air pollution and tobacco smoke. The leading causes of cardiovascular morbidity and mortality in this age group include ischemic heart disease, stroke and hypertensive heart disease(3). Management of the risk factors has a major role in reducing the burden of cardiovascular disease among older people globally.

18.3 Pathophysiology

Progressive arteriolosclerosis and associated atherosclerosis work in tandem increase the risk posed by hypertension and diabetes in the elderly. There is increased calcification in the plaque contributing to plaque vulnerability. The aorta and great vessels experience progressive stiffening and intimal medial weakening predisposing these patients to aortopathy.

Table 18.1: Age Associated Changes and Cardiovascular Disease in Older People

Organ	Age-associated changes	Cardiovascular disease
Vasculature	Increased intimal (wall) thickness	Systolic hypertension Early atherosclerosis
	Arterial stiffening	Coronary artery obstruction Systolic hypertension Left ventricular wall thickening Stroke Atherosclerosis
	Increased pulse pressure	Peripheral artery obstruction
	Increased pulse wave velocity	Carotid artery obstruction
Atria	Increased left atrial size	Atrial fibrillation
	Atrial premature complexes	
Sinus node	Decreased maximal heart rate	Sinus node dysfunction
	Decreased heart rate variability	
Atrioventricular node	Increased conduction time	Heart block
Valves	Sclerosis, calcification	Stenosis, regurgitation
Ventricle	Increased left ventricular wall tension	Left ventricular hypertrophy
	Prolonged myocardial contraction	Heart failure
	Prolonged early diastolic filling rate	
	Decreased maximal cardiac output	
	Right bundle branch block	
	Ventricular premature complexes	Ventricular tachycardia, fibrillation
	Increased cardiovascular reserve	Heart failure

18.4 Common Comorbidities

Older adults not only have coronary risk factors and coronary artery disease but are also at a higher risk of cerebrovascular disease, peripheral artery disease, congestive heart failure, chronic kidney disease, atrial fibrillation, chronic obstructive pulmonary disease, arthritis, dyslipidaemia, hypertension and diabetes [5].

18.4.1 Special Considerations in Management of Hypertension

1. Careful monitoring of treatment since drug toxicities are common.
2. Slow, careful titration of medications (go low and slow).
3. Avoid atenolol in adults over 60 years of age, unless they have coronary artery disease.
4. Avoid short-acting calcium channel blockers, e.g., sublingual nifedipine
5. Compelling indications for hypertension treatment are outlined in the table below:

Table 18.2: Compelling Indications for Antihypertensive Medications in the Elderly Patient

Compelling Indication	Recommendation
Congestive Heart Failure	Use ACE Inhibitors or ARB's as first-line agents. B-blockers are also beneficial.
Myocardial Infarction	Beta-blockers and/or ACE inhibitors (or ARB's) should be considered as first-line agents. If an anti-anginal drug is necessary, the use of calcium channel blockers can be considered.
Nephropathy	Use ACE inhibitors (or ARB's) when the serum creatinine is greater than 1.5 mg/dL or the 24-hour urine protein is greater than 1 gram.
Gout	Avoid thiazide diuretics in patients with gout.
Hyperlipidaemia	Use calcium channel blockers or ACE inhibitors
Erectile dysfunction	Use chlorthalidone with caution.
Hyperglycemia	Use Beta blockers and thiazide diuretics with caution and monitor

18.5 Treatment cut-offs and targets:

Table 18.3: Hypertension Treatment Indications and Targets

Hypertension treatment in the elderly patient over 80 years		
	BP levels	
	SBP	DBP
Treatment indication	≥150 mmHg	≥90 mmHg
Treatment targets	<150 mmHg	<90 mmHg

Hypertension treatment in the elderly patient 60-79 years		
	BP levels	
	SBP	DBP
Treatment indication	≥140 mmHg	≥90 mmHg
Treatment targets	<140 mmHg	<90 mmHg

Hypertension treatment in the elderly patient over 60 years, with diabetes		
	BP levels	
	SBP	DBP
Treatment indication	≥135 mmHg	≥85 mmHg
Treatment targets	<135 mmHg	<85 mmHg

18.6 Preventive therapy

Table 18.4: Indications for Statins and Anticoagulants in Patients Above 60 Years of Age

Treatment	Indications	Remarks
Statins	1. Patients with atherosclerotic CVD 2. Patients with LDL cholesterol above 190mg/dL 3. Diabetic patients between 40-75 years 4. Estimated 10-year risk of CVD of 7.5% or higher	No evidence of benefit for patients over 75 years
Anticoagulant therapy	Secondary prevention: Patients with atrial fibrillation, left ventricular thrombus, cerebral embolism, venous embolism, pulmonary embolism	Anticoagulation and antiplatelets should be used with caution in those >75 years of age

18.7 Treatment Approach for Heart Failure in the Elderly

Use the DEFEAT (12) mnemonic:

- **D**iagnosis: careful history taking can enable one to make a clinical diagnosis of heart failure in the elderly
- **E**tiology: It is important to determine the underlying aetiology of the heart failure
- **F**luid volume: by careful examination of the external jugular veins in all visits
- **E**jection FrAction: should be assessed to guide therapy
- **T**herapy: When ejection fraction cannot be determined, all heart failure in the elderly should be managed as systolic heart failure with an ACE inhibitor, beta blocker and aldosterone antagonists for advanced heart failure. Diuretics should be used judiciously to achieve euvolemia.

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19

19. CARDIO-ONCOLOGY

Key Messages

- Cardio-oncology is a new field of practice in cardiology that focuses on the detection, monitoring, and treatment of cardiovascular disease occurring as an effect of a cancer as well as the side effect of different chemotherapy agents and radiotherapy used in its treatment.
- Cardio-oncology practice is relatively new in Kenya and therefore cardio-oncology services will in many circumstances be offered by Cardiologists, Oncologists, Physicians, and other allied health workers trained to treat oncology patients. There is a need to train specialists in this field and offer courses to other health workers who are involved in the treatment of these patients.
- Optimal care to patients with cancer undergoing treatment requires a multidisciplinary approach and is recommended throughout the whole process of treatment and at follow-up post treatment.

19.1 Introduction

Cardio-oncology focuses on the detection, monitoring, and treatment of cardiovascular disease (CVD) occurring as a result of cancer or as side effects of chemotherapeutic agents and radiotherapy. These treatment modalities predominantly cause myocardial dysfunction, a major cause of morbidity and mortality in this population of patients (1)

Cancer treatment-related cardiotoxicity (CTR-CVT) refers to damage to the heart and/or cardiovascular system (including heart valves and vessels) that can occur during or after cancer treatment. Cardiotoxicity symptoms during cancer treatment can lead to interruption or stopping of treatment, reducing its effectiveness.

Advances in cancer diagnostic capacity and availability of potent chemotherapy agents coupled with improved access to radiotherapy has led to an increase in the numbers of cancer survivors and the consequent need to develop the means and capacity to take care of these patients during and after chemotherapy.

CVD and cancer share common modifiable and non-modifiable risk factors. The focus in cardio-oncology is to allow patients with cancer to receive the best possible cancer treatments safely, minimizing cancer therapy related cardiovascular toxicity across the entire continuum of cancer care.

For every individual patient being initiated on cancer therapies, the cardio-oncology team should identify and treat CV risk factors (CVRF) and pre-existing CVDs and define an appropriate prevention and surveillance plan for early identification and appropriate management of potential CV complications (2).

Whereas patients who have completed cancer treatment require co-ordination of long-term follow-up and treatment, those on long-term cancer therapies with CV toxicity risk require continued surveillance until the treatment is finished (3)

19.2 General Principles of Cardio-oncology

The severity, duration, and type of manifestation of CTR-CVT vary by type of malignancy and cancer treatment and hence the need to risk stratify and grade patients into low, moderate, high, and very high risk of CV complications prior to starting treatment.

The high-risk indicators of cardiac dysfunction in adult cancer survivors include: (1)

- Use of high-dose anthracyclines (doxorubicin ≥250 mg/m2, epirubicin ≥600 mg/m2) or the use of low-dose anthracyclines (doxorubicin ≤ 250 mg/m2 and epirubicin ≤600 mg/m2) accompanied with smoking
- Hypertension
- Diabetes
- Obesity
- Age over 60 years[1]

The grading of cancer-related cardiac dysfunction is shown in the table below.

Table 19.1: Grading of Cancer Related Cardiac Dysfunction

Severity Level Criteria	
Symptomatic CTRCD	
Very severe	HF requiring ionotropic or mechanical circulatory support or consideration of transplantation
Severe	HP hospitalisation
Moderate	Need for outpatient intensification of diuretic and HF therapy
Mild	Mild HF symptoms, no intesification of therapy required
Asymptomatic CTRCD	

Severe	New LVEF <40%
Moderate	New LVEF reduction by ≥ 10 percentage points to an LVEF of 40-49% OR New LVEF reduction by <10% to an LVEF of 40-49% and either new relative decrease in GLS by >15% from baseline or new rise in cardiac biomarkers
Mild	LVEF≥50% and new relative decline in GLS>15% from baseline and/or new rise in cardiac biomarkers

(Adapted from Oxford University Press)

19.2.1 Cancer Therapy-related Cardiovascular Toxicity Spectrum

The spectrum of CTR-CVT include: [3]

- Cardiomyopathy and heart failure (HF)
- Myocarditis
- Vascular toxicities
- Hypertension
- Cardiac arrhythmias QT interval (QTc) prolongation
- Pericardial and valvular heart diseases (VHDs)

19.2.2 Cardiovascular Toxicity Risk Stratification Before Anticancer Therapy

The optimal time to consider CVD prevention strategies in patients with cancer is at cancer diagnosis and prior to the initiation of cancer treatment [1]

This enables the oncology team to consider CV risk while making cancer treatment choices, educating patients regarding their CV risk, personalizing CV surveillance and follow-up strategies, and making appropriate referrals of high-risk patients to cardio-oncology services. These strategies are needed to mitigate CVD risk and improve the adherence to effective cancer treatments and overall survival. The choice of the cardiac tests (electrocardiogram [ECG], biomarkers, and imaging) should be individualized based on CV risk and the planned cancer treatments.[3]

19.2.3 General Approach to Cardiovascular Toxicity Risk in Patients with Cancer

Pre-treatment CTR-CVT risk assessment should incorporate the patient's multiple risk factors to determine patient-specific risk based on various validated tools. Baseline risk assessment should be considered by the treating oncology or haematology team for all patients diagnosed with cancer who are scheduled to receive a cancer treatment identified to have a clinically significant level of CRT-CVT, or by a cardiologist if appropriate.

Based on the baseline risk assessment (see Table 14.1 above): (3)

- High risk and very high-risk patients: referral to a cardiologist is recommended to institute strategies to mitigate risk.
- Moderate risk patients-: closer cardiac monitoring, strict management of traditional CVRF. Selected moderate-risk patients may also benefit from a cardio-oncology referral.
- Low-risk patients- follow up within the oncology programme with appropriate referral to cardio-oncology if a CTR-CVT emerges or new or uncontrolled CVRF appear.

A careful clinical history and physical examination is recommended as part of the baseline risk assessment. Oncology patients can be divided into two groups with respect to the presence or absence of pre-existing CVD. Primary prevention strategy can be considered in patients without previous CVD or CTR-CVT while secondary prevention includes interventions in patients with prior or active CVD or previous CTR-CVT (3).

- The traditional risk factors for CVD should be looked for and where present, the efficacy of treatment and control of these modifiable risk factors should be determined to ensure optimal control during cancer therapy.
- A family history of premature CVD should be considered because genetic abnormalities associated with CVD may predispose patients with cancer to a higher risk of CTR-CVT.
- Lifestyle factors such as smoking, alcohol consumption, sedentary lifestyle, exposure to pollution, and frailty are important shared risk factors for both cancer and CVD.
- Information on prior history of cancer, cardiotoxic cancer therapies, and their respective doses should be collected. Patients should be asked about typical cardiac symptoms, which can guide clinical examination and investigations.
- Physical examination should document vital signs and look for potential indicators of undiagnosed CVD such as HF, pericardial disease, VHD, and arrhythmias.[3]

19.3 Clinical presentation

Majority of patients may remain asymptomatic or only have subtle cardiac symptoms, therefore calling for careful surveillance especially in the context of high CV risk burden or agents known to cause significant. Possible presentations include:

- Chest pains as a symptom for coronary or pericardial disease may occur in those who have undergone radiation therapy.
- Leg pains and claudication may occur in peripheral vascular bed disease.
- Normal to overt features of HF depending on the degree of myocardial damage
- Cardiogenic shock with the need for inotropic support in patients presenting late in the progression of the disease, with attendant grave prognosis.
- Takotsubo syndrome (TTS) in some patients

19 3.1 Screening

Electrocardiogram (ECG)

A baseline 12-lead ECG to provide clues to underlying CVD.

- ECG evidence of chamber enlargement, conduction abnormalities, arrhythmias, ischaemia, or prior myocardial infarction (MI), and low voltages should be interpreted in the clinical context.
- A baseline ECG is recommended prior to starting a cancer treatment known to cause QTc prolongation.
- When baseline QTc prolongation is recognized, the correction of reversible causes and the identification of genetic conditions that prolong QT is recommended [(3)].
- Cardiac serum biomarkers
- Help in baseline CV risk stratification.
- Allow identification of those who may benefit from cardioprotective therapy.
- Baseline measurements are required if the degree of change in the biomarkers is to be used to identify subclinical cardiac injury during cancer treatment [(3).]
- Recommended tests include cardiac troponin (cTn) I or T and natriuretic peptides (NP) (e.g.B-type natriuretic peptide [BNP] or N-terminal pro-BNP [NT-proBNP])
- Relevant in cancer therapies including anthracyclines, human epidermal receptor 2 (HER2)-targeted therapies, vascular endothelial growth factor (VEGF) inhibitors (VEGFi), proteasome inhibitors (PI), immune checkpoint inhibitors (ICI), chimeric antigen receptor T cell (CAR-T) and tumour-infiltrating lymphocytes (TIL) therapies.

19.3.2 Cardiovascular Imaging

CV imaging has an important role in identifying patients with subclinical CVD, determining the degree of pre-existing cardiac comorbidity prior to decisions regarding cancer therapy, and serves as a reference for identification of changes during treatment and long-term follow-up.

- Transthoracic echocardiography (TTE) -preferred imaging technique for baseline risk stratification as it provides quantitative assessment of LV and right ventricular (RV) function, chamber dilation, LV hypertrophy, regional wall motion abnormalities, diastolic function, VHD, pulmonary arterial pressure (PAP), and pericardial disease, which may influence the therapeutic decision.[3]
- Three-dimensional (3D) echocardiography -preferred echocardiography modality for the assessment of LVEF and cardiac volumes. Modified two-dimensional (2D) assessment using Simpson's biplane method is recommended when 3D Echo is not feasible.
- Global longitudinal Strain (GLS) with speckle tracking – has better sensitivity in picking mild disease but requires expertise. It should be considered as part of TTE assessment for all cancer patients.
- CMR –to be considered in subjects with poor-quality echocardiography windows.

TTE with LVEF and GLS is recommended at baseline in all patients evaluated with cancer before cardiotoxic treatment initiation to stratify CTR-CVT risk and to identify significant changes during treatment (3)

TTE with LVEF and GLS is recommended in secondary prevention setting or patients with symptoms or signs of pre-existing CVD, to obtain baseline assessment as in the primary prevention setting and to determine the severity of the underlying CVD (3)..

19.3.3 Cardiovascular Risk Evaluation Before Cancer Surgery

Pre-operative CV risk stratification to identify and provide appropriate management and surveillance of the potential risk factors is recommended.

The peri-operative cardiac complications are determined by patient-related risk factors, the tumour type, concomitant cancer therapies, and the expected surgical risk.

Special considerations include:

1. Patients with previous significant or symptomatic CVD
2. Patients at high and very high CV toxicity risk, according to baseline HFA-ICOS risk assessment tools, when adjuvant (post-surgery) cancer treatment is planned
3. Patients who have received neoadjuvant cancer therapy that is potentially cardiotoxic3

19.4 Genetic Testing

Routine genetic testing prior to initiation of cancer therapy is not currently recommended. In the future, a personalized genetic approach may help define individual susceptibility to CVD in patients with cancer and more research is required.[3]

19.5 Prevention and monitoring of cardiovascular complications during cancer therapy

19.5.1 General Principles

CTR-CVT risk may vary according to cancer type and stage, anticancer drugs, doses, and underlying comorbidities. Certain therapy combinations (drug-drug or drug-radiation) may have a synergistically toxic effect on the heart, possibly

depending on the timing of these therapies (sequential or concomitant) and previous co-morbidities.

- Optimize lifestyle CVRF, smoking cessation, restricting alcohol consumption to a maximum of 100g per week, and maintaining adequate physical activity.
- Optimal treatment of CVRF like arterial hypertension, DM, and dyslipidaemia, and underlying CVD and modifiable comorbidities.
- Reduce the use of drugs that may interfere with cancer therapies to the essential and actively monitor their CV side effects and drug–drug interactions.
- Electrolyte imbalances such as hypokalaemia and hypomagnesaemia should be corrected.

19.5.2 Primary Prevention Strategies

Primary prevention of CTR-CVT aims to avoid or minimize the development of CV damage due to therapy in patients without CVD.

- Use of neuro-hormonal therapies with RAAS blockers, beta-blockers, and mineralocorticoid receptor antagonists during anthracycline chemotherapy (with or without subsequent trastuzumab treatment) to reduce the risk of significant LVEF decline.
- Reducing anthracycline-related toxicity by adjusting the infusion time and dose intensity.
- Use of Dexrazoxane and liposomal anthracyclines in patients with high and very high CTRCD risk or who have already received high cumulative anthracyclines doses.
- For patients on radiotherapy, minimize the mean heart dose (MHD) either by shaping the dose distribution (intensity-modulated RT) or by using respiratory management (gating or breath-hold)
- Proton therapy in RT to further decrease exposure to surrounding healthy organs.
- MDT where RT only has a consolidating role, and the risk of RT-induced CV injury is very to consider the risk/benefit of RT.

19.5.3 Secondary Prevention Strategies

Secondary prevention refers to interventions in patients with pre-existing CVD, including prior CTR-CVT, and new emerging CTR-CVT during cancer therapy.

- Optimal management of CVD and comorbidities before and during cancer therapy as discussed in previous sections.
- Regular clinical assessments, physical examinations, and CV investigations (including 12-lead ECG, TTE with GLS, and cardiac biomarkers) with the frequency of surveillance guided by baseline risk and the emergence of new CTR-CVT.

19.5.4 Cardiovascular Surveillance During Cancer Therapies

A careful clinical evaluation and physical examination is recommended during cancer treatment to detect early signs and symptoms of CTR-CVT. Early recognition of asymptomatic CTRCD allows use of cardioprotective therapy before there is a significant decline in LVEF, which may or may not be reversible, and decreases the risk of interruptions in cancer therapy.

- ECG monitoring is required in patients at risk of cardiac arrhythmias according to specific drug protocols.
- NP and cTn for CTRCD screening and diagnosis to guide therapy.
- Use of advanced echocardiography (TTE including 3D-LVEF and GLS assessment) and CMR to facilitate early diagnosis and management of CTR-CVT. The frequency of cardiac imaging during therapy should be adapted according to the estimated baseline risk and the expected CTR-CVT manifestation but should be performed at any time if patients present with new cardiac symptoms.

19.6 Diagnosis And Management

In patients who develop CTRCD, a multidisciplinary team (MDT) is recommended to guide clinical decisions.[3]

19.6.1 Anthracycline Chemotherapy-Related Cardiac Dysfunction

- CTRCD during anthracycline chemotherapy may present clinically or be detected in asymptomatic patients during surveillance. The diagnosis includes new CV symptoms, new abnormalities in cardiac function on CV imaging, and/or new increases in cardiac bio- markers.
- Guideline-based HF therapy is recommended in patients who develop symptomatic CTRCD or asymptomatic moderate or severe CTRCD during anthracycline chemotherapy.
- The use of an ACE-I/ ARB or angiotensin receptor–neprilysin inhibitor, a beta-blocker, a sodium glucose co-transporter 2 inhibitor, and a mineralocorticoid receptor antagonist is recommended.

19.6.2 Human Epidermal Receptor 2-Targeted Therapy-Related Cardiac Dysfunction

- The diagnosis of HER2-targeted therapy-related CTRCD can be made using the combination of new CV symptoms, imaging, and biomarkers.
- Patients may present with symptomatic CTRCD or may be asymptomatic.
- Early treatment of symptomatic and asymptomatic severe CTRCD (LVEF,40%) is recommended to prevent worsening HF, particularly when targeted cancer therapy is continued.
- Temporary interruption is recommended in patients who develop moderate or severe symptomatic CTRCD or severe asymptomatic CTRCD (LVEF 40%)
- In patients with asymptomatic moderate CTRCD (LVEF 40–49%), HER2-targeted treatment should be continued, and cardioprotective therapy (ACE-I/ARB and beta-blockers) is recommended with frequent cardiac monitoring.
- In patients with asymptomatic mild CTRCD (LVEF ≥ 50% with a significant new GLS reduction and/or cardiac biomarker increase), continuing HER2-targeted treatment is recommended and cardioprotective therapy (ACE-I/ ARB and/or beta-blockers) should be considered.

19.6.3 Immune Checkpoint Inhibitor-Associated Myocarditis and Non-Inflammatory Heart Failure

- Myocarditis is a severe complication of ICI with a high fatality rate that most frequently develops during the first 12 weeks of treatment.1
- Other ICI-related CV toxicities include dyslipidaemia, ACS, vasculitis, AV block, supraventricular and ventricular arrhythmias, sudden death, TTS, non-inflammatory LVD, pericarditis, pericardial effusion, and ischaemic stroke, with higher risks for myocarditis and dyslipidaemia.
- TTE and CMR are recommended in all patients with suspected ICI-associated myocarditis.
- The diagnosis of ICI-associated myocarditis is initially based on the presence of symptoms, a new increase in troponin (associated with either CV symptoms or non-CV immuno-related adverse events), and new ECG abnormalities (AV or intraventricular conduction disorders, bradycardia, tachyarrhythmias).
- Treatment with high-dose methylprednisolone should be promptly initiated in haemodynamically unstable patients (including those with ventricular arrhythmias [VA] or complete AV block) while awaiting further confirmatory testing.
- Where there is paucity of response to steroids, use of other immunosuppressive drugs, such as infliximab, mycophenolate mofetil, and anti-thymocyte globulin, may be necessary.

19.6.4 Chimeric Antigen Receptor T Cell and Tumour-Infiltrating Lymphocytes Therapies and Heart Dysfunction

- CV complications related to CAR-T represent around 20% of adverse events and are associated with high mortality rates.
- The most common CV complications are arrhythmias (77.6%), including QTc prolongation, ventricular arrhythmias, and AF; HF (14.3%); and MI and VTE (0.5%).
- A resting 12-lead ECG, continuous ECG monitoring, TTE, and cTn and NP are recommended.
- Admission to ICU is recommended in severe cases.

19.6.5 Heart Failure During Haematopoietic Stem Cell Transplantation

- CV complications during HSCT include congestive HF, arterial events, cardiac tamponade, and rhythm disturbances (AF, atrial flutter, and supraventricular tachycardia),
- Treatment should be as per specific relevant guidelines. There is limited data on effective therapies, though ACE-I and beta-blockers may be used.
- Outpatient and home-based exercise and education programmes instituted after HSCT can improve exercise capacity and quality of life, and the role of exercise prehabilitation prior to HSCT is being investigated.[3]

19.6.6 Takotsubo Syndrome (TTS) and Cancer

The prevalence of malignant diseases is high in patients with TTS and is a risk factor for worse outcomes. Malignancy itself, some cancer treatments (5-FU, ICI, VEGFi), and the stress associated with the diagnosis, investigations, and treatment are recognized triggers or predisposing factors for TTS.

- Diagnosis using general TTS criteria is recommended.
- Investigations in a patient with cancer with suspected TTS should include clinical examination, ECG, TTE, cardiac biomarkers (cTn and NP), and CMR.
- Cardiac imaging studies should be performed as early as possible when the diagnosis is suspected as LVD can be transient, and if significant LVD is detected then repeat imaging to confirm recovery is recommended.
- Interruption of the culprit cancer drug in patients with TTS is recommended.
- QT-prolonging drugs should be avoided.
- In cases of ICI-associated TTS, the role of immunosuppression is unknown.
- If myocardial inflammation is present in a TTS pattern on CMR, i.v. methylprednisolone is recommended given the overlap between ICI-induced TTS and ICI-induced myocarditis.[3]

19.6.7. Coronary Artery Disease

A) Acute coronary syndromes

Patients with cancer are at increased risk of CAD because of shared CVRFs and CV toxicity of cancer therapy compounded by a cancer-induced pro-inflammatory and prothrombotic state.

- Diagnosis of ACS is based on symptoms, an early 12-lead ECG, and serial measurements of hs-cTn for patients presenting with possible non-ST-segment elevation ACS (NSTE-ACS).
- Clinical presentation can be atypical or masked by cancer or therapy-related side effects; therefore, diagnostic suspicion should be increased in patients at high CV risk or treated with vascular cardiotoxic therapies.
- Management of ACS can be challenging because of frailty, increased bleeding risk, thrombocytopaenia, increased thrombotic risk, and the possible need for future surgery/interventions.
- Cancer treatment should be temporarily interrupted, and initiation of appropriate anti-ischaemic and

antithrombotic treatment are indicated, in the absence of contraindications.

- Any cancer drug associated with thrombosis and MI should be stopped. Restarting cancer drugs associated with acute thrombosis and MI after ACS should occur only after a MDT discussion but therapies not associated with MI can be restarted once revascularization, where indicated, has been completed and the patient is stabilized on ACS medical therapy without complications.[3]

B) Chronic coronary syndromes

Several cancer treatments are associated with an increased risk of stable angina and chronic coronary syndromes (CCS).

- 5-FU and capecitabine can precipitate effort angina in some cases.
- Platinum-containing chemotherapy-induced ischaemia usually occurs after one of the first three cycles and in patients with underlying CAD.

The management of CCS is like that in patients without cancer in accordance with guideline recommendations. The decisions regarding coronary revascularization should be undertaken by an MDT that includes cardio-oncology, intervention, and oncology specialists.[3]

19.6.8 Valvular Heart Disease

New or worsening VHD may be related to coexisting conditions like CTRCD, ACS, PH, endocarditis, cardiac tumours, and mechanical prosthetic valve thrombosis. Pre-existing severe VHD is associated with an increased risk of CTRCD, and may also pose a risk for cancer surgery outcomes.

- In patients with mechanical prosthetic valves, the risk of thrombosis vs. bleeding should be carefully balanced during chemotherapy treatment.
- In patients with severe VHD diagnosed at baseline assessment, an MDT is required before cancer therapy to decide the best treatment option.
- Patients with cancer suspected of new or worsening VHD, such as dyspnoea or a new cardiac murmur, or those with fever and positive blood cultures, should be screened for endocarditis and managed according to existing guidelines.

19.6.9 Cardiac Arrhythmias

Cardiac arrhythmias have been observed with chemotherapeutic drugs include atrial fibrillation, long corrected QT interval, ventricular arrhythmias and bradyarrhythmias.

- Treatment of cancer therapy-induced arrhythmias should follow available guidelines and when inevitable, the offending drug should be withdrawn, and an alternative used instead.

19.6.10 Arterial Hypertension

Causes of arterial hypertension in patients with cancer include:

- Cancer drugs (e.g., VEGFi, second and third-generation BCR-ABL TKI, brigatinib, ibrutinib, fluoropyrimidines, cisplatin, abiraterone, bicalutamide, enzalutamide)
- non-cancer drugs (e.g., corticosteroids, non-steroidal anti-inflammatory drugs)
- other factors including stress, pain, excessive alcohol consumption, renal impairment, untreated sleep apnoea, obesity, and reduced exercise.

In all patients with cancer with new hypertension assessment, correction of these other factors is important before considering interruption of a cancer treatment. Untreated hypertension is a confirmed risk factor of HF during treatment

with anthracyclines, Ibrutinib, and VEGFi [5].

- Treatment of hypertension with ACE-I or ARB as first-line therapy is recommended to reduce the risk of CTRCD.
- Combination therapy with an ACE-I or ARB and a dihydropyridine CCB is recommended when systolic BP ≥ 160 mmHg and diastolic BP ≥ 100 mmHg due to the more rapid onset of BP control with the combination compared with ACE-I/ARB monotherapy.
- In severe hypertension (systolic BP ≥ 180 mmHg or diastolic BP ≥ 110 mmHg), any cancer therapy associated with hypertension should be deferred or temporarily withheld until the BP is controlled [3].

19.7 Follow-up

19.7.1 Cardiovascular Evaluation During The First Year After Cardiotoxic Anticancer Therapy

End-of-cancer therapy CV risk assessment covers the first 12 months after the last cardiotoxic cancer treatment [3].

The timing of the first CV assessment after cardiotoxic cancer treatment will depend on:

- The risk defined by baseline CV assessment
- The type of cancer therapy
- Whether or not CTR-CVT was diagnosed during treatment.

In asymptomatic high-risk patients, echocardiography and cardiac serum biomarkers are recommended at 3 and 12 months after completion of cancer therapy.

In asymptomatic moderate-risk patients, echocardiography and cardiac serum biomarkers should be considered within 12 months after completion of cancer therapy.

In asymptomatic low-risk patients, echocardiography and cardiac serum biomarkers may be considered within 12 months after completion of cancer therapy.

All patients started on CV therapies (ACE-I/ARB/angiotensin receptor-neprilysin inhibitors, beta-blockers, mineralocorticoid receptor antagonists, sodium-glucose co-transporter 2 inhibitors, antihypertensive medications, antiarrhythmic medications, antiplatelet therapies, statins) for any CTR-CVT (especially CTRCD) should have a clinical assessment, ECG, echocardiography, and cardiac serum biomarkers (if LV systolic dysfunction/HF is a potential risk) at 3, 6, and 12 months after completing cancer treatment.

An MDT-based approach to palliative and end-of-life care for patients with cancer with HF or other CTR-CVT should be focused on symptom relief.[3]

19.7.2 Management of Cancer Therapy-Related Cardiac Dysfunction at the End-of-therapy Assessment

Cardioprotective medications initiated during cancer therapy to treat CTRCD should be reviewed at end-of-therapy and in selected patients with asymptomatic mild or moderate CTRCD who have fully recovered with normal TTE and cardiac serum biomarkers.

A trial of weaning off CV medication should be considered after MDT discussion.

This should be considered especially after asymptomatic mild or moderate CTRCD secondary to trastuzumab, particularly in younger otherwise healthy HER2+ breast cancer survivors with no exposure to anthracycline chemotherapy.

Further assessment of cardiac function with TTE and cardiac serum biomarkers is recommended following withdrawal of CV medication in patients with previous CTRCD to ensure cardiac function remains normal.

Continuing long-term CV medication is generally recommended in patients with moderate and severe symptomatic or severe asymptomatic CTRCD due to the high rate of recurrent HF. Long-term treatment is also recommended in CS with mild or moderate CTRCD who fail to recover normal LV function at their end of therapy assessment.[3]

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20. CARDIAC REHABILITATION

Key Messages

- Cardiac rehabilitation helps improve the physical, social, psychological, and vocational function of people with cardiovascular disease through exercise training and lifestyle modification.
- CR requires multi-disciplinary team comprising doctors, nurses, physiotherapists, nutritionists, and mental health specialists for successful implementation.
- The treatment plan for every patient should be individualized.

20.1 Introduction

Cardiac rehabilitation (CR) is a medically supervised comprehensive exercise, education and behaviour modification program that helps improve the physical and psychological health and well-being of people who have cardiovascular diseases (CVDs).[1]

The goal of CR is to enable the individual to improve their physical, social, psychological, and vocational functioning through exercise training and lifestyle modification. Lifestyle modification interventions involve reduction of CVD risk factors such as blood sugar control, smoking cessation, lipid lowering, consumption of heart-healthy foods, blood pressure (BP) control, weight loss and increasing physical activity.

The American College of Cardiology (ACC) and American Heart Association (AHA) class 1 Guideline recommendations for CR referral include patient with myocardial infarction (MI), coronary artery bypass graft (CABG), heart failure (HF), peripheral arterial disease (PAD), chronic stable angina and CVD prevention in women.[2]

CR among patients with CVD disease has been shown to:[3]

- Improve heart failure symptoms.
- Support faster recovery after a heart attack or heart surgery.
- Reduce hospital readmissions, and death related to cardiovascular disease.
- Reduce symptoms of coronary artery disease (CAD) and non-fatal MI.
- Address CVD risk factors such as obesity, hypertension, diabetes, hyperlipidaemia, sedentary lifestyle, and depression
- Improve adherence to preventive medication.
- Support adaptation of healthy lifestyle changes including a heart healthy diet, physical activity, tobacco cessation, limiting alcohol intake and learning how to manage stress.
- Improve overall patient health and quality of life.
- Improve the ability of the patient to return to work.

20.2 Phases of Cardiac Rehabilitation

CR programs are delivered in 4 phases:[4]

- **Phase I:** Inpatients rehabilitation (admission period): This is done during admission and involves ambulation in the ward as well as sensitization of the patient on the CR programs and what to expect after discharge.
- **Phase II:** Early out-patient rehabilitation: This begins immediately after discharge and is usually done in a hospital setting or a dedicated CR centre. It is physician supervised and conducted by a multi-disciplinary team with cardiac monitoring. In some instances, part of this can be done in the home setting. Most guideline recommend at least 3 sessions per week. The duration of this phase may vary depending on the resources available however the more sessions the patients receive the greater the benefits.5 Patients should also remain exercise on non-CR days.
- **Phase III:** late out-patient phase (variable duration) – This is home-based CR where the patient independently continues with the program with periodic follow-up.
- **Phase IV:** preventive phase – Aims to sustain activity levels and lifestyle modifications. This phase should have a starting date but not a finishing one, the patient will choose an activity of their choice, carrying out the program at least 3 times a week throughout one's lifetime.

The specific elements covered during the inpatient and outpatient phases of a CR program are outlined in the figure below:

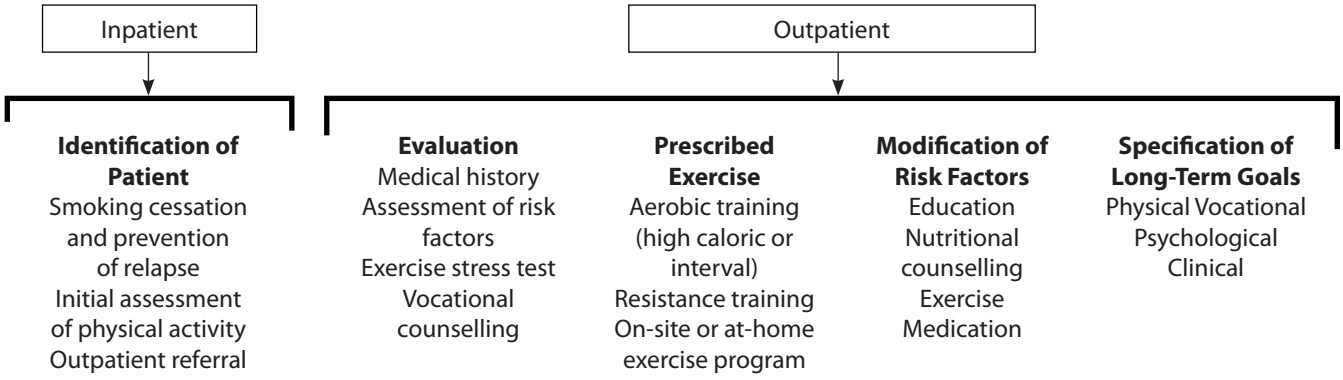

Figure 20.1: Components of cardiac rehabilitation[6]

Source: Ades PA. Cardiac Rehabilitation and Secondary Prevention of Coronary Heart Disease. New England Journal of Medicine. 2001;345(12):892-902. Copyright © 2001, Massachusetts Medical Society

20.3 Indications for Cardiac Rehabilitation

People of all ages, ethnic backgrounds and sexes can benefit from CR. It improves overall health and prevents development of CVDs and even death. The treatment should be tailored to meet individual patient needs in order to improve overall health and lower the CVD risk.

CR should be offered to the following patients:

- Coronary Heart Disease
  - After myocardial infarction
  - After revascularization
  - Stable Angina
- Other cardiac conditions
  - Chronic Heart Failure
  - Peripheral Artery Disease
  - Valvular Heart Disease
  - Congenital Heart Disease
  - Cardiac Transplant
- Healthy individuals
  - High CV risk (hypertensive, diabetic)

20.4 Components of Cardiac Rehabilitation Services

The core components of a rehabilitation program include:

- Prescribed exercise to safely improve cardiovascular fitness
- Education, lifestyle modification and management of the following risk factors:
  - Smoking cessation
  - Lipid management
  - Blood pressure control
  - Controlling diabetes
  - Weight loss

- Increasing physical activity
- Eating a heart-healthy diet
- Alcohol moderation

- Psychosocial counselling
- Audit and evaluation

20.5 The Cardiac Rehabilitation Team

Cardiac rehabilitation involves a long-term commitment from the patient and a team of healthcare providers.

To successfully delivery the above components, the CR team is multi-disciplinary comprising doctors, nurses, physiotherapists, nutritionists, and mental health specialists.

A team approach is an important part of cardiac rehabilitation. The team composition can be tailored to the human resources available as long as safety of the patient and integrity of the program is maintained.

The CR team members required will depend on the CR Phase. Table 1 below summarizes some of the team members needed for each phase.

Table 20.1: Recommended CR team members for each CR phase[8]

CR Phase	Staff
Phase 1	Exercise physiologist/physiotherapist/Nurse
Phase 2	Cardiologist/physician/Medical Officer Nurse Exercise physiologist/physiotherapists Nutritionists/dietitians Psychologist
Phase 3	Exercise physiologist/physiotherapist/Nurse

20.5.1 Roles and Competencies of CR Team Members

The table below summarizes some of the roles the respective team members will carry out in the CR program.

Table 20.2: Roles and Competencies of the CR Team

Team member	Competency/role
Cardiologist/ physician /Medical Officer	• History, risk factor assessment, basic tests • Interpret laboratory results • Physical examination • Develop the individualized treatment plan (ITP) for the patient • Patient outcome assessment (pre-post assessments)
Nurse	• Implement the Individualized treatment plan • Lifestyle modification (nutrition counselling, weight management counselling and monitoring) • BP/lipids/blood sugar monitoring (assess compliance to medication and management plan) • Referral to diabetes educator/dietician/nutritionist as required • Measure and report outcomes of glucose control and episodes of hyperglycemia and hypoglycemia • Assess for tobacco use and provide behavioral and medical interventions to promote cessation • Measure and report outcomes of tobacco cessation at the conclusion of the program

Exercise physiologist/ Physiotherapist	• Risk stratify each patient depending on their conditions • Carry out exercise capacity assessment • Assess physical and metabolic requirements for activities of daily living, occupational, and recreational activities • Assist patients in setting realistic incremental goals for future physical activity • Develop an individualized, safe, and effective exercise prescription, including modes, intensity, duration, frequency, and progression for both aerobic exercises and resistance exercises • Skin preparation and electrode placement for exercise ECG telemetry monitoring • Apply communication/behavioral strategies that will improve compliance with regular physical activity recommendations • Measure and report outcomes for exercise training at the conclusion of rehabilitation • Recognition of life-threatening cardiac arrhythmias, myocardial ischemia or infarction, hypoxemia, hypotension, hypoglycemia, and other signs and symptoms of exercise intolerance
Nutritionist	• Dietary assessment • Assess anthropometric parameters (body mass index (BMI), waist circumference • Agree with patient on goals • Preparation of dietary plan
Psychologist	• Screening and assessment for psychological distress, especially depression, anxiety, anger, or hostility; social isolation; marital/family distress; sexual dysfunction; and substance abuse • Appropriate referrals for psychiatric or psychological care when needs are recognized as beyond the scope of usual care • Individual and group education and counselling interventions that address stress management and coping strategies • Measure and report outcomes of psychosocial management at the conclusion of the program

20.6 Equipment Required for Cardiac Rehabilitation

The following equipment is required for Phase 2 CR:

Table 20.3: Basis Equipment Required for Phase 2 CR centre:

Equipment	Quantity
Automated External Defibrillator	2
Oxygen cylinder and regulator	1
Treadmills	1
Ergometers	2
Free weights	Assorted
Exercise Mats	10
Weighing scales	2
BP machines	2
Pulse oximeters	2
Pedometers	10
ECG machine	1

20.7 Patient Referral

There should be a coordinated patient referral and recruitment process to ensure all eligible patients are identified and invited to participate. Referral should be initiated either during the in-patients stay or within 24 hours of discharge. Prior to discharge, all eligible hospitalized patients should be encouraged by health professionals to attend and complete CR.[10] Contact details for patients referred should be provided to the CR team who will contact the patients within 3 days to review their progress and discuss enrolment.

When selecting a suitable location to set up the CR program, consider the following factors:

- Location of the services
- Access by potential patients
- Anticipated workload
- Holding capacity for equipment
- Safety of the patients

20.8 Initial Assessment and Patient Preparation

20.8.1 Phase 1 Cardiac Rehabilitation (Inpatient)

Once an eligible patient has been identified in the ward, they should be visited by a member of the CR team at least once before discharge during which the following are done:

- Review the chart
- Risk stratify the patient
- Explain to the patient about the CR program
- Assist the patient to ambulate and reassure them (monitor their HR and BP)
- Give them realistic physical activity targets and what they should watch out for
- Identify their risk factors
- Refer the patient to a CR program of their convenience

20.8.2 Phase 2 Cardiac Rehabilitation (Outpatient)

Patients may self-refer or be referred to cardiac CR by their providing clinician during a clinic visit or while in the hospital recovering from a heart problem. CR activities will vary depending on the patient's condition. Overall, patients may work with the rehab team for 3 months or longer as needed. The length of time patients' needs to continue CR depends on the underlying cardiovascular disease. The initial assessment involves taking a comprehensive history and physical examination.

20.8.3 History

Before patients start cardiac rehab, the rehab team will assess patient. This includes taking a medical history and doing a physical exam and tests. The rehab practitioner will ask about previous heart problems, heart surgery, and any heart-related symptoms. He or she also will ask whether the patient has had medical procedures or other health problems (such as diabetes or kidney disease) as well as what medication the patient is taking (including over-the-counter medicines and dietary supplements). Lifestyle risk factors are also identified (exposure to tobacco, alcohol intake, diet, physical activity status). Medical risk management is also assessed (control of BP, lipids, glucose, and adherence to medication).

For diabetic patients it is recommended to establish how the patient checks their blood sugar level, and how often and whether they have experienced any hypoglycaemic episodes.

Assess the quality of life and psychosocial health. This involves assessment psychosocial health (anxiety, depression, illness perception, social support, psychological stress, sexual wellbeing, and quality of life).

20.8.4 Physical Exam and Diagnostic Testing

It is recommended that before initiation of cardiac CR, a patient should have a physical exam to evaluate overall health, including your heart rate, blood pressure, reflexes, and breathing. Patients should have a baseline ECG done prior to CR to establish baseline heart rhythm and electrocardiographic deflections. A baseline exercise capacity test using a treadmill or stationary bike is useful to determine baseline fitness level and exercise capacity. As guided by the clinical evaluation some patients will require further cardiovascular imaging and testing to evaluate cardiac function, valvular/obstructive lesions and to risk stratify rehabilitation participants.

20.8.5 Risk Stratification

Table 20.4: Risk stratification of patients undergoing CR

It is important to risk stratify all patients accessing CR services. This will assist with determining how much supervision is required.

Patient is at HIGH RISK IF ANY ONE OR MORE of the following factors are present:

- Left ventricular ejection fraction <40%
- Survivor of cardiac arrest or sudden death
- Complex ventricular dysrhythmias (ventricular tachycardia, frequent (>6/min) multiform PVCs) at rest or with exercise
- MI or cardiac surgery complicated by cardiogenic shock, CHF, and/or signs/symptoms of post-procedure ischemia
- Abnormal haemodynamics with exercise, especially flat or decreasing systolic blood pressure or chronotropic incompetence with increasing workload
- Significant silent ischemia (ST depression 3mm or greater without symptom) with exercise or in recovery
- Signs/symptoms including angina pectoris, dizziness, light-headedness or dyspnoea at low levels of exercise (<5.0 metabolic equivalents of task-METs§) or in recovery
- Maximal functional capacity less than 5.0 METs
- Clinically significant depression or depressive symptoms

Patient is at LOW RISK if ALL of the following are present:

- Left ventricular ejection fraction >50%
- No resting or exercise-induced complex dysrhythmias
- Uncomplicated MI, CABG, angioplasty, atherectomy, or stent:
- Absence or CHF or signs/symptoms indicating post-event ischemia
- Normal hemodynamic and ECG responses with exercise and in recovery
- Asymptomatic with exercise or in recovery, including absence of angina
- Maximal functional capacity at least 7.0 METs
- Absence of clinical depression or depressive symptoms

Patient is at MODERATE RISK if they meet neither High Risk nor Low Risk standards:

- Left ventricular ejection fraction = 40-50%
- Signs/symptoms including angina at "moderate" levels or exercise (60-75% of maximal functional capacity) or in recovery
- Mild to moderate silent ischemia (ST depression less than 2mm) with exercise or in recovery

*If measured functional capacity is not available this variable can be excluded from the risk stratification process
§MET: the metabolic equivalent of task is the ratio of the working metabolic rate to the resting metabolic rate.

AACVPR Stratification Algorithm for Risk of Event

20.8.6 Develop an Individualised Treatment Plan

After the initial assessment, an Individualized Treatment Plan (ITP) is developed. This is written plan tailored to each individual patient and includes the following elements:

Description of individual diagnosis

- Risk stratification
- Services to be provided including type, amount, frequency and duration
- Patient goals

The plan should be reviewed every 30 days.

Table 20.5: Components of an Individualized Treatment Plan

Component	Details
Biodata	Name, age, sex
Diagnosis	Describe the diagnosis and comorbidities
History and physical examination	Comprehensive history and physical examination
Risk Stratification	See Table above
Exercise prescription/training	• Exercise testing (Maximal exercise test or Sub-maximal exercise test (6-minute walk test) • Exercise type (aerobic and strength) • Exercise mode (treadmill, arm bike, cross-trainer etc.) • Exercise frequency (days per week) • Exercise duration (minutes per session) • Exercise intensity (MET (metabolic equivalent) level, target heart rate, rating of perceived exertion, Rate of Perceived Dyspnoea (RPD) scales
Risk factor modification and treatment goals	• Tobacco addiction/cessation counselling • Weight loss counselling • Diabetes management • BP management • Lipid management • Nutrition education • Physical activity counselling
Psychosocial assessment	• Evaluation of the individuals mental and emotional functioning • Family and home situation • Depression, anxiety, social isolation • Stress management

Adapted from AACVPR

20.9 Delivery of the Core Components

20.9.1 Health Behaviour Change Education

The goal is for the patient to adopt health behaviours to prevent and control CVDs. To facilitate behaviour, change, the following should be taken into consideration:

- Use proven behaviour change interventions such as motivational interviewing techniques
- Support the clients to make informed choices by providing information and education
- Address any myths and misconceptions

- Support the patient to make goals and explore potential barriers
- Regular follow up and assessment
- Support patient to identify someone to support them and if possible, this person should be allowed to accompany the client
- Education give should be culturally sensitive and tailored to the needs identified during the initial assessment

The education given should increase knowledge and understanding of the risk factors. The CR team should prepare and schedule delivery of education content in the following areas:

- Signs and symptoms of cardiac conditions and risk factors
- Physical activity
- Healthy eating
- Weight management
- Tobacco cessation
- Self-management of BP, lipids, and glucose
- Psychological and emotional self-management
- Resuming and maintaining sexual relations
- Surgical interventions and devices

20.9.2 Lifestyle Risk Factor Management

A) Physical activity and exercise

Exercise capacity assessment

Assessment of exercise capacity is the initial step which provides valuable information to guide preparation of the exercise prescription. The assessment method used depends on the clinical risk of the patients, resources and expertise available.

The methods available for exercise capacity assessment include:

1. **Maximal Test**

The is involves subjecting the patient to graduated exercise until the patient experiences signs/symptoms of cardiovascular compromise, limiting symptom or volition exhaustion. The have a risk of adverse events so they required 12-lead ECG and BP monitoring, trained personnel and a medical doctor to supervise. This test is therefore not commonly used in most clinical settings and is reserved for tertiary hospitals with adequate resources and expertise.

Maximal Tests are recommended for high-risk patients (decompensated heart failure, uncontrolled arrhythmias or angina at rest or with minimal exertion. It is also recommended for patients who wish to participate in a high intensity exercise programme.

2. **Sub-maximal Test**

The is the recommended test as it is easily administered and is less likely to cause adverse events, does not require medical supervision and ECG monitoring. The submaximal tests are pegged on the age-predicted Heart Rate (HR) <85% or a Rate of Perceived Exertion (RPE) <15 (Borg scale of 6-20).

The most commonly used sub-maximal test is the six-minute walk test.[12]

SIX-MINUTE WALK TEST (6MWT)[13-18]

The six-minute walk test is the commonly recommended submaximal test. It is a self-paced walking test suited for hospital and community setting. It is preferable done on a straight 30-meter track although this can be adapted or shortened as needed. The objective is to walk as far as possible within 6 minutes.
During the test, the following are monitored:

- Heart rate
- Blood pressure
- Oxygen saturation
- Perceived exertion (using the Rating of Perceived Exertion (RPE) – Borg scale)
- Symptom

Equipment required:

- Recording form
- RPE – Borg scale (see figure below)
- Pulse oximeter
- Stop-watch or timer
- Chairs (depending on patient's condition or risk)
- Sphygmomanometer and stethoscope (or automated BP machine) for BP assessment
- Portable oxygen if required

Instructions to the patient:

- They should not talk during the test unless there is a problem
- They can slow down or stop as needed. If they stop, they have the option of resting on a chair, check their SpO2 and HR and ask why they stopped. Keep the stop watch running.
- Once they complete, they should remain in the clinical area for at least 15 minutes if there are no complications.

The following should be recorded before and after 6 minutes:

- RPE
- BP
- HR
- SPO_2
- Recovery time

Meaningful change in 6MWT can be measured in 2 ways:

1. Absolute change (25meters is considered significant)
2. Percentage change (post-program distance-pre-program distance x 100).

NOTE: Two 6MWT are recommended during the initial assessment with 25 minutes recovery in between due to the learning curve. However, a single measurement is also acceptable.

(Affix patient label here)	
Patient ID:	
Family name:	
Given name(s):	
Date of birth:	
Sex:	☐ M ☐ F ☐ I

Six Minute Walk Test (6MWT) recording form

☐ Medical history checked
☐ Medical clearance provided for the patient to participate in exercise testing

Contraindications to 6MWT:

☐ Resting heart rate > 120 beats/min after 10 minutes rest (relative contraindication)
☐ Systolic blood pressure > 180 mm Hg +/- diastolic blood pressure > 100 mm Hg (relative contraindication)
☐ Resting SpO2 <35% on room air or on prescribed level of supplemental oxygen
☐ Physical disability preventing safe performance
☐ No contraindications identified

6MWT 1						Date:	Time:
Supplemental Oxygen						**Mobility Aid**	
Time mins	**BP**	**SpO_2**	**HR**	**RPE**	**Distance walked**	**Rests/comments**	
Rest							
1							
2							
3							
4							
5							
6							
Recovery 1							
2							

Total distance: _____ **Symptom recovery:** _____ **HR recovery:** _____

Limiting factor: _____

Was test terminated? ☐ No ☐ Yes If yes: when?

6MWT Termination Criteria: ☐ Chest pain or angina-like symptoms ☐ Heart rate > Predicted HR max. ☐ Evolving mental confusion, light-headedness or incoordination ☐ Physical or verbal severe fatigue	☐ Intolerable dyspnoea, unrelieved by rest ☐ Persistent SpO2 <85% (Note: pending clinical presentation) ☐ Abnormal gait pattern (leg cramps, staggering, ataxia) ☐ Other clinically warranted reason

Rating of Perceived exertion: Borg scales[19]
The Rating of Perceived Exertion (RPE) is used to monitor and prescribe exercise intensity. Individuals are able to rate their level if exertion during exercise testing and exercise.

The original Borg scales was developed by Gunnar Borg and has a range from 6-20. It correlates with the HR. It is particularly useful when the HR is not an accurate measure of intensity for example when the patient sis on a beta blocker.

RATING OF PERCEIVED EXERTION (RPE)
BORG'S RPE 6 - 20 SCALE

6 No exertion at all
7 Extremely light
8
9 Very light10
11 Light
12
13 Somewhat hard
14
15 Hard (heavy)
16
17 Very hard
18
19 Extremely hard
20 Maximal exerrtion

Borg RPE Scale ©Gunnar Borg, 1970 1984, 1985, 1998

Exercise Prescription

- The prescription and progression are dependent on the exercise capacity assessment.
- The patients should be advised on the activities of daily living (ADL). The tailored activity and exercise plan should increase physical fitness and decrease sedentary behaviour.
- The activity and exercise plan should be created together with the patient taking in to account their comorbidities, physical and psychosocial capabilities.
- An exercise prescription includes aerobic exercise, resistance exercises (muscle-strengthening activities), warmup and cooling down components.

Aerobic exercises

- Should always be accompanied by 5 – 10 minutes warm-up and cool-down.
- Select an activity the individual enjoys and tolerates
- Exercise intensity for patients with CVD or HF should be based on perceived exertion rather than HR because cardiac medications can affect the HR.
- For home-based or virtual programs, reduce the intensity slightly
- The exercise is prescribed using the FITTP principle: Frequency, Intensity, Type, Time, Progression
- A standard Aerobic Exercise Prescription for CR is as shown below:[12, 20, 21]

Table 20.6: A standard Aerobic Exercise Prescription for CR

Parameter	Description
Frequency	At least 3 days/week (6-7) days/week
Intensity	RPE 12 – 16 (on a 6 – 20 scale) Patient should remain asymptomatic Talk test: Patients should be able to maintain a comfortable conversation
Type	Continuous rhythmic activities involving major muscle groups: walking, treadmill, cycle ergometer, rower, elliptical trainers, stair climbing
Time	20 – 60 minutes
Progression	• Review progression each session • Increase progression each week • Increase only 1 component of FITT per session • Increase duration followed by intensity and frequency • Increase aerobic exercise by 1-5min per session • Increase intensity by 5-10%

Resistance exercises

These should begin 2 months after an acute Myocardial infarction and upper body exercises 12 weeks after cardiac surgery via sternotomy.

This should be prescribed as follows :[21]

Table 20.7: Resistance Exercises

Parameter	Description
Frequency	2 times a week
Intensity	Upper body: 30 – 70% of one-repetition maximum (1RM)* Lower body: 40 – 80% of one-repetition maximum (1RM)* 2-3 sets per muscle group (begin with 1 set) 12 – 15 repetition per set (begin with 8 – 10)
Type	Target to carry out 8 – 10 different exercises targeting different muscle groups to include: • Biceps • Tricep • Lower back • Upper back • Abdominal • Quadriceps • Hamstrings • Calf muscles

**Maximum weight a person can lift just once in a particular muscle group*

Contraindications to exercise training[7]

Although there are numerous benefits to lifestyle changes made during rehab with few risks, exercise training as part of cardiac rehab might not be safe for all patients. However, the patient can still benefit from other parts of the cardiac rehab program. The absolute contraindications are scenarios where physical exercise has a potential risk.

Cardiac related	Other
• Unstable angina • Advanced heart failure • Hight blood pressure • Left ventricular outflow tract obstruction • Grade 2 and 3 AV block • Myocarditis • Acute pericarditis • Severe valvular disease • Ventricular arrhythmias	• Aortic dissection • Acute thrombophlebitis • Pulmonary or systemic embolism • Severe psychological disorders • Severe mobility limitations

B) Healthy eating and body composition[10]

The rehabilitation team should guide patients to make dietary adjustments and follow a heart healthy diet including planning meals that are low in unhealthy fats and sodium and meet their caloric needs. The goal is to assist the patient to make healthy choices to reduce total cardiovascular and improve body composition.

A qualified nutritionist should delivery this component. The activities here should include:

- Baseline assessment of dietary habits
- Measurement of weight, BMI and waist circumference
- Address misconceptions about nutrition dieting and weight

- Deliver personalized dietary advise that is sensitive to their culture, needs and capabilities
- Offer patients with co-morbidities tailored dietary advice
- Support weight management (weight gain for debilitated patients, weight loss or weight maintenance)
- Refer for medical or surgical weight management specialists as appropriate
- For specific cardioprotective dietary recommendations, refer to the chapter of CVD prevention (include page number).

C) Tobacco cessation[10]

- Staff delivering this component should be appropriately trained. Activities in this component include:
- Assess current or past tobacco use. This includes if they are a current user (use of any tobacco product within the past 30 days), former user, past quit attempts and exposure to second hand smoke
- For current users, assess frequency and quantity.
- Assess motivation to quit and nicotine dependence. In addition, assess psychological co-morbidities like depression and tobacco use by others at home
- At the first assessment, advise client to quit and develop a quit plan. Consider use of pharmacological support and provide follow-up counselling
- Patient preference is a priority regarding the choice of aids in tobacco cessation such as long and short acting nicotine replacement therapy
- The goal is complete cessation of all forms of tobacco use (tobacco chewing)
- Assess progress at every visit
- Encourage quit attempts in partners/spouses/friends/children to prevent relapse
- Refer to the guideline for further information

20.10 Psychosocial Health

Every patient should be assessed for psychological, psychosocial and sexual health and wellbeing as ineffective management can lead to poor health outcomes. This assessment should be done by qualified, skilled, and competent staff.

Assessment should include:

- Psychological assessment for anxiety and depression (use an appropriate tool such as the Hospital Anxiety and Depression Scale (HADS)
- Quality of Life (use an appropriate toll such as Minnesota Living with Heart failure (MLWHF),
- Psychological stressors
- Illness perceptions and self-efficacy for behaviour change
- Social support
- Alcohol and substance misuse
- Sexual health

The patient should be made to understand how their psychological state, illness perceptions, stress levels and improved stress management can affect their physical health.

The CR team can assist the patient to deal with the normal range of emotional stress. Patients with clinical levels of anxiety and depression may need to be referred to trained psychological practitioners if the CR team does not have this capacity.

Patients with alcohol or substance misuse should be referred appropriately.

Sexual health issues can negatively impact the quality of life and psychological wellbeing. Concerns raised should be addressed through counselling and medical management as appropriate. Patients with complex and/or long-standing sexual issues should be referred appropriately.

20.11 Medical Risk Management

The CR team should be appropriately qualified, skilled, and competent to support medical risk management. Guidelines for medical risk factor management (BP, lipids, and glucose) should be availed to the CR team.

Assessment should include:

- Measurement BP, lipids, glucose, heart rate and rhythm
- Current medication use (dose and adherence)
- Patient's beliefs about medication (this affects adherence)
- Sexual activity
- Determine treatment targets for each patient as per the guidelines. Monitor BP, glucose and lipids regularly and up titrate medications as per the guidelines. Titration of medication should be either directly through independent prescribing by a member of the CR team or agreed protocols or through liaison with an appropriate health professional.
- Refer patients with erectile dysfunction for further management.

20.12 Long-Term Strategies

a) Patient responsibilities

The goal of the CR program is to enable the patient to develop self-management skills and to take ownership of their healthy. The client should be encouraged to join a local support group, community exercise or weight management group and should be referred for tobacco cessation services as appropriate. Online or technology-based applications or tools and other self-monitoring resources can be availed to the patient.

b) System responsibilities

After completion of the program, conduct a formal assessment of lifestyle risk factors (physical activity, diet, tobacco use) psychological and psychosocial health status, medical risk factors (BP, lipids, glucose), use of cardioprotective therapies and long-term goals. This assessment should be given to their primary physician and other health providers involved in their care.

Support the patient to plan and implement self-management strategies so they can continue minimizing their risk of CVD progression.

20.13 Monitor Outcomes

CR Outcomes should be monitored at both individual and program level. These outcomes include:

- Tobacco use (proportion that received intervention for quitting or relapse, proportion who quit/relapsed)
- Improvement in functional capacity at completion of CR (6mwt improved by >10%, GTX improved by >15% or Peak MET level improved by 40%)
- Improvement in depression at completion of CR – Improve by one MIDC – Minimal Clinical Important Difference)
- Optimal BP control at completion of CR
- Enrolment in CR
- Adherence to CR

20.14 Models of Service Delivery

Traditionally, CR was delivered primarily in-person. Newer and more innovative delivery models have emerged such as virtual approaches (remote) or a combination of in-person and remote (hybrid). Virtual/remote approached deploy technologies such as telephone, internet, video, mobile applications and wearables.

CR can also be delivered either one-on-one or in a group.

It is still unknown which of these models is the most optimal or the specific sub-set of patients who can benefit from the different models.

An individualized approach is recommended and programs should strive to provide options that will optimize participation within the available resources.

20.15 Risks and Complications

Most of the complications arise due to inappropriate prescription of exercise levels and inadequate surveillance.

The most serious complications are ventricular fibrillation, myocardial infarction and sudden death. These can occur during or after exercise and therefore adequate surveillance is needed during and at least 15 minutes after physical training.[7]

Other serious complications include:[7]

- Angina pectoris
- Hypertension
- Vasovagal syncope
- Dyspnoea
- Papillary muscle dysfunction
- ECG changes: ST segment elevation/depression, supraventricular ectopic beats, ventricular ectopic heats, atrioventricular block

Patients should be informed of these risks and involved in decision making to participate in cardiac rehabilitation. Informed consent should be obtained from all patients prior to commencing the program.

It is important that all staff are trained and prepared to manage common medical emergencies. Medical emergency equipment and supplies (such as defibrillator/AED, portable oxygen) should be available in the cardiac rehabilitation department. Medical emergency management policies and procedures must be available to manage the patient from onset of signs and symptoms until the emergency is resolved (i.e., hospital admission, transfer to the Emergency Department, discharge home, resolution of symptoms etc,).

All staff working in the CR unit should have training in Advanced Cardiac Life Support (ACLS).

20.16 Organization of Services at County Level

Table 20.8: Recommended organization of CR services at county level

Level of facility	Services	Personnel
Level 3	Phase II and III Cardiac rehabilitation	• Nurse • Physiotherapist
Level 4 Hospital	Phase I, II and III Cardiac Rehabilitation services	• Medical doctor • Nurse • Trained physiotherapist • Nutritionist • Psychologist
Level 5 and 6	Phase 1, II and III rehabilitation services	• Cardiologist/Physician Nurse • Trained physiotherapist • Nutritionist • Psychologist

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21

21. PALLIATIVE CARE

Key Messages

- The goal of palliative care is to optimize quality of life by addressing physical, spiritual and psychological needs, providing caregiver/family support and advanced care planning
- Effective pain control is central to palliative care using both pharmacological and non-pharmacological measures.
- Pain and difficulty in breathing are two of the most frequent and serious symptoms experienced by patients in need of palliative care
- Basic palliative care should be initiated by the clinical care team with the support of specialists who come in to address refractory symptoms and advanced care planning.

21.1 Introduction

The purpose of this section is to provide background on the importance of palliative care as it pertains to patients with advanced cardiovascular disease and stroke and their families.

Palliative care, defined as patient- and family-centred care that optimizes health-related quality of life by anticipating, preventing, and treating suffering, should be integrated into the care of all patients with advanced cardiovascular disease and stroke early in the disease trajectory.[1] Palliative care focuses on communication, shared decision making about treatment options, advance care planning, and attention to physical, emotional, spiritual, and psychological distress with inclusion of the patient's family and care system in assessment and management.

21.2 Epidemiology

Each year, an estimated 40 million people are in need of palliative care; 78% of them people live in low- and middle-income countries.[2]

Approximately, 38.5% of adults with cardiovascular diseases require palliative care.[3] According to the World Health Organization, only about 14% of people who need palliative care worldwide currently receive it.

The Kenya Health Facility Assessment conducted in 2018 revealed that availability of palliative care services in Kenya was low with only 3% of health facilities offering the services.[2]

Patients with advanced CVD are faced with long-term challenges which burden the patient and their families. Patients with advanced heart failure experience poor quality of life because of depression, anxiety, social impairment, physical disability, deterioration of health, complex treatment regimens and distressing symptoms. Advanced treatments such as heart transplant are also accompanied by risks.

21.3 Benefits of Palliative Care

Palliative care is an essential health benefit that is central to high-quality overall care. Integrating palliative care in the management of patients with advanced CVD and stroke may provide the following benefits:

- Improved patient and caregiver understanding of disease, treatment, and prognosis
- Improved treatment of symptoms and relief of suffering
- Shared decision making based on patient values, preferences, and goals
- Enhanced patient-clinician communication
- Individualized advance care planning based on benefits, risks, and burdens of care
- Improved patient and caregiver outcomes
- Improved preparation for end-of-life and associated care
- Bereavement support

21.4 Cardiovascular Conditions Requiring Palliative Care

- Patients with advanced CVDs and stroke often have long-term challenges and burdens facing them and their families. Whereas a majority of chronic cardiovascular conditions begin acutely, they often require lifelong treatment to slow progression as there is rarely a permanent cure. The common conditions that may require palliative care include:
- Advanced heart failure: These patients often experience poor Health Related Quality of Life (HRQOL) including anxiety, depression, social impairment, physical disability, due to debilitating symptoms (dyspnoea, orthopnoea, fatigue, weakness, anorexia), deteriorating health and complex care regimens such as heart transplantation or Mechanical Circulatory support (MCS).

- Heart Transplant patients or patients on Mechanical Circulatory support (MCS): These treatments are associated with serious complications
- Stroke: patients report lower HRQOL due to altered physical and cognitive abilities, language impairment, depression and emotional lability.
- Patients with advanced age and multiple comorbidities
- Patients with chronic angina
- Patients with frailty or dementia for whom implantable cardioverter-defibrillator is considered.

21.5 Provision of Palliative Care Services

21.5.1 Palliative Care Plan

Palliative care should be provided by a multidisciplinary team and should be integrated into the care of all patients with advanced CVDs and Stroke. A patient should have a detailed holistic assessment and care plan developed by a clinician with the required knowledge and skills in collaboration with the patient and family in order of priority.

Basic palliative care can be provided by clinicians without specialized training. This included management of symptoms (dyspnoea, pain, oedema, depression and anxiety) and care planning (prognosis, goals of care, values, preferences). Palliative care specialists are required to provide advanced treatment in the event of refractory symptoms, complex depression, complex anxiety and spiritual distress. In addition, the specialists will provide advanced care planning where there is complex prognosis, patient-clinician conflict, family conflicts of disagreements in the goals of care.[4]

Effective pain control is central to palliative care using both pharmacological and non-pharmacological measures.

The plan should ensure patients and their caregivers understand the illness, prognosis and treatment options. The approach should embrace shared decision making between the patients and providers.

21.5.2 Pharmacological Measures

Pain and difficulty in breathing are two of the most frequent and serious symptoms experienced by patients in need of palliative care.[5]Controlling such symptoms at an early stage is an ethical duty to relieve suffering and to respect a person's dignity. The WHO analgesic ladder[6] is used for all types of pain including nociceptive and neuropathic pain and should be used as the standard approach to the management of pain.

Opioids are essential for managing the pain as well as alleviate other common distressing physical symptoms including breathlessness. Uncontrolled pain may elevate the blood pressure, pulse rate, adrenaline, and cortisol serum levels by simultaneously stimulating the sympathetic autonomic nervous system. These physiologic responses may cause hazardous stress on the CV system producing coronary spasms. Provide treatment regimen that normalizes blood pressure and pulse rate and use long acting around the clock opioids to prevent angina.

21.5.3 Non-Pharmacological Measures

Spiritual Care:

Involves being a compassionate presence to patients even as they suffer. It recognizes that emotional and spiritual healing can take place even though a physical cure is impossible. Areas of life that can generate spiritual peace or spiritual distress to patients include a relationship with God/Creator/Higher Being, with self, with others, and with the world around them.

End of life care (EoLC)

End-of-life care for patients with advanced CVD often involves decisions to stop or deactivate devices, including implantable cardioverter-defibrillators and Left Ventricular Assisting Devices (LVAD). Before deactivating cardiac devices, patients and family members need to understand the patient's condition and care options and have clear knowledge of what will happen if the device is stopped (e.g., anticipated death). Protocols need to be in place to guide nurses and physicians as devices are withdrawn. Conflicts that may arise in connection with these decision processes may be referred to institutional ethics committees.

Symptom control

CVD and Stroke patients and families need to be prepared for what to expect near the end of life. Care is focused on the prevention and management of distressing symptoms, with a focus on pain, dyspnoea, and anxiety. The goal of care is to support a peaceful death for the patient and to provide support for the family. Hospice care offers in-home visits, access to requisite medications and equipment, inpatient hospice care, and relief and support for family members. Assessment for the cause and severity of the symptoms (physical, psychological, social, and spiritual), treatment of reversible causes and initiation of disease/symptom-specific medicines such as non-drug measures and involvement of the patient and family on the management plan is recommended.

Grief and bereavement

The World Health Organization guidelines [7]identify the patient's family as requiring support in bereavement. Because caregivers may experience depression, major depressive disorder, complicated or prolonged grief, or even posttraumatic stress disorder, the period after a patient's death remains an important part of the illness experience. Hospice services offer bereavement care for up to 1 year after the death of a patient (sometimes longer for paediatric patients). It is essential that providers who had supportive relationships with the deceased patient and his or her family members develop systems for supporting surviving family members during their bereavement.

21.6 Special Considerations

21.6.1 HF and Palliative Care

In patients with HF, palliative should be provided to improve quality of life. Palliative care is specifically indicated for patients with 1) refractory symptoms 2) major medical decisions 3) multimorbidity, frail or cognitive impairment.[8]

It is recommended that palliative care, including necessary education of patients and families about QOL, prognosis, risk of death (including sudden cardiac death) despite ongoing active treatment, goals and efficacy of therapeutic plans, and discussions of hospice or end-of-life care and wishes (including explicit discussion of defibrillator deactivation) should be integrated early in the course of the disease.

21.6.2 Heart Transplant (HT)

HT candidates will benefit from palliative care consultation during the evaluation for transplantation, at listing, and postoperatively. Palliative care is relevant for patients being considered for HT because these patients have needs for advance care planning and are likely to have needs for symptom palliation and family support.

21.6.3 Mechanical Circulatory Support (MCS) and Palliative Care

Except for emergency situations, prospective MCS patients should meet with palliative care providers before MCS implantation to assist them with the decision-making process and to help with their perioperative management. Patients and family members may be asked to make decisions about turning the MCS device off, which often raises ethical and

spiritual issues for patients and their caregivers. Hospice can be particularly helpful for this patient population, but hospice providers may require specific training on how to care for patients with MCS. For all these reasons, it is preferable for MCS programs to work collaboratively with palliative care teams and for these palliative care teams to assist with the transition to hospice when appropriate.

21.6.4 Stroke and Palliative Care

The palliative care needs will depend on the stage (acute versus chronic). During the acute stage, the care will revolve around decision making during the uncertainty and managing terminal symptoms for those who succumb in the acute stage. For those in the chronic and recovery stage, the needs include adapting to the cognitive and functional deficits, managing physical (spasticity, pain) and psychological symptoms (anxiety, depression) during the course of rehabilitation.[1]

21.7 Paediatric Palliative Care (0-16 years)

Palliative care for children is the active total care of the child's body, mind, and spirit, and involves giving support to the family. It begins when illness is diagnosed and continues regardless of whether a child receives treatment directed at the disease. Health providers must evaluate and alleviate a child's physical, psychological, spiritual, and social distress.

Paediatric pain control

- Pain assessment tools should be age appropriate (Refer to Annex 8, National Palliative Care Guidelines – 2013).
- Aspirin is contraindicated in children less than 12 years.
- Dosages shall be calculated in kilogram per body weight (Annex 7, National Palliative Care Guidelines)

Special needs for children

- Special needs shall be identified through comprehensive assessment and addressed holistically.
- Children shall be involved in decisions about their own care. Appropriate information according to age shall be communicated in clear and simple language at their pace
- Children shall be allowed to lead a normal life that includes access to education within the limitation of their illness. School teachers, community members including other children shall be encouraged to support and deal sensitively with the affected child
- Recreation activities shall be encouraged like play activities, drawings, poems or songs.
- Palliative care providers shall take into consideration the needs of orphans and vulnerable children and shall refer them to appropriate services for care and support

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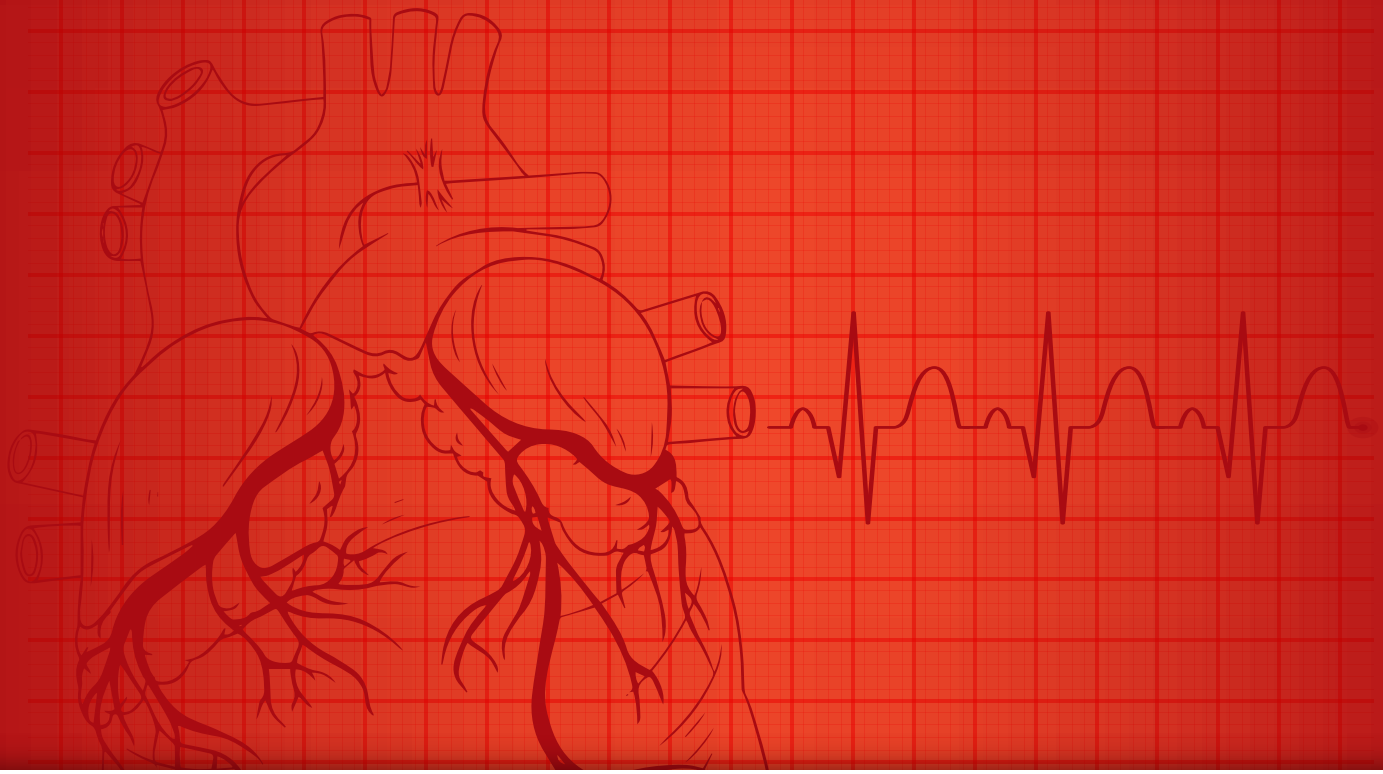

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