CARDIOVASCULAR DISEASE UPDATE 2021

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TABLE OF CONTENTS

PREFACE

It gives me immense pleasure to write this introductory note on our "Cardiovascular Disease Update 2021" on behalf of Cardiac Society of Nepal.

This update/handbook was conceptualized almost a few years back to bring about uniformity and ensure a standardized level of care for cardiovascular diseases in the country. I strongly believe that this update will help in exactly ensuring the above, and be of great assistance and benefit to all physicians and surgeons who are involved in treating cardiovascular disease in any part or corner of our country. We are confident that this will also be helpful to our medical students, residents and trainees in understanding the spectrum of cardiovascular disease - its clinical manifestation, diagnosis and treatment. It has been a great learning experience for me individually while reviewing this update.

The chapters in this compilation have been concisely written explaining on subjects from congenital heart disease to valvular heart disease with a great focus on rheumatic heart disease. It also describes the treatment of coronary artery disease – Myocardial infarction taking in to consideration our medical services in our country, such as the accessibility to a catheterization lab and surgery. It will help readers understand disease such as heart failure, cardiac tumors and protocol for treatment of aortic diseases. Chapters have been compiled to even include carotid and peripheral vascular diseases so as to ensure a more holistic understanding of the entire spectrum of cardiovascular disease.

I would like to congratulate and acknowledge all our authors who have contributed to this update. This handbook serves as a perfect example on how our members and Cardiac Society of Nepal can have a positive impact to medical education and medical sciences in our country. I would like to thank our editors for their tireless efforts, and in their repetitive and meticulous reviews done both individually and collectively, scrutinizing each chapter in detail to finally ensure a valuable handbook. I would like to acknowledge our Past Presidents Dr. Bhagawan Koirala and Dr. Deewakar Sharma for conceptualizing and pushing this task in the initial phase and editors for their tireless efforts to compile, and lead this undertaking to its publication.

I am sure this will be of great benefit to our medical fraternity in our country.

Bijoy G Rajbanshi
President
Cardiac Society of Nepal.

UNIT - I

Evaluation of Common Cardiovascular Conditions

I. 1. SYNCOPE

Syncope is defined as a symptom that presents with an abrupt, transient, complete loss of consciousness, associated with inability to maintain postural tone, with rapid and spontaneous recovery. The presumed mechanism is global cerebral hypoperfusion.

Syncope may be sometimes confused with clinical features of other causes of loss of consciousness, such as seizure, antecedent head trauma or apparent loss of consciousness (i.e. pseudo syncope).

Loss of Consciousness: A cognitive state in which one lacks awareness of oneself and one's situation, with an inability to respond to stimuli.

Pre syncope (near syncope): The symptoms that appear before syncope. These symptoms could include extreme lightheadedness, visual sensations such as 'tunnel vision' and variable degrees of altered consciousness without complete loss of consciousness. Presyncope could progress to syncope or it could abort without syncope.

Transient loss of consciousness: Self limited loss of consciousness can be divided into syncope and non syncope conditions. Non syncope conditions include but are not limited to seizures, hypoglycemia, metabolic conditions, drug or alcohol intoxication and concussion due to trauma. The underlying mechanism of syncope is presumed to be cerebral hypoperfusion, whereas non-syncope conditions are attributed to different mechanisms.

Cardiac Syncope: Syncope caused by bradycardia, tachycardia, or hypotension due to low cardiac index, blood

flow obstruction, vasodilation or acute vascular dissection.

Non-Cardiac Syncope: Syncope due to non-cardiac causes, such as reflex syncope, volume depletion, dehydration, and blood loss.

Reflex (neurally mediated) syncope: Syncope due to a reflex that causes vasodilation, bradycardia, or both.

Vasovagal Syncope (VVS): The most common form of reflex syncope mediated by the vasovagal reflex.

1) May occur with upright posture (standing or seated), with emotional stress, pain.
2) Typically is characterized by diaphoresis, warmth, nausea, and pallor.
3) Is often followed by fatigue.

Risk assessment and initial treatment:

There is significant importance of risk stratification in the initial evaluation of patients with suspected syncope. Numerous factors have been shown to independently predict poor outcomes, including age >60 years, male, palpitations preceding syncope and abnormal ECG. Some diagnostic criteria at initial evaluation can be listed as:

Non cardiac cause:

VVS is diagnosed if syncope is precipitated by emotional distress or orthostatic stress and is associated with typical prodrome.

Situational syncope is diagnosed if the syncope occurs during or immediately after specific triggers.

Orthostatic syncope is diagnosed when it occurs after standing up and there is documentation of Orthostatic hypotension.

Cardiac Cause

Arrhythmia related syncope is diagnosed by ECG when there is:

- Persistent sinus bradycardia<40 bpm in awake or repetitive sinus pauses >3 Sec.

- Mobitz type II or third degree AV block
- Alternating left and right bundle branch block
- VT or rapid paroxysmal SVT
- Non-sustained episodes of polymorphic VT and long or short QT interval
- Pacemaker or ICD malfunction with cardiac pauses

Cardiac ischemia related syncope is diagnosed when syncope presents with ECG evidence of acute ischemia with or without myocardial infarction.

Cardiovascular syncope is diagnosed when syncope presents in patients with prolapsing atrial myxoma, severe aortic stenosis, pulmonary hypertension, pulmonary embolus, or acute aortic dissection.

After the initial evaluation, hospital admission is indicated in patients with serious medical issues, while patients with intermediate risk may benefit from further investigations in the emergency department. Outpatient treatment is typically appropriate in patients with reflex mediated syncope.

Diagnosis

The differentiation between syncope and non-syncope conditions can be difficult sometimes. The following questions should be answered:

- Was LOC complete?
- Was LOC transient with rapid onset and short duration?
- Did the patient recover spontaneously, completely and without sequelae?
- Did the patient lose postural tone?

If the answers to these questions are positive, the episode has a high likelihood of being syncope. If the answer to one or more of these is negative, exclude other forms of LOC before proceeding with syncope evaluation. A **thorough history and physical examination** should be conducted and an **Electrocardiogram** is often helpful for determining etiology. **Transthoracic echocardiography** can be useful in selected patients presenting with syncope if structural

heart disease is suspected. **Exercise Stress testing** can be useful to establish the cause of syncope in selected patients who experience syncope or pre syncope during exertion. **Cardiac monitors** can be used in patients with syncope. The choice of a specific cardiac monitor should be determined on the basis of the frequency and nature of syncope events. To evaluate selected ambulatory patients with syncope of suspected arrhythmic etiology external cardiac monitoring such as **holter monitor**, **external loop monitor** can be useful. In selected patients, **Implantable loop recorders** can be considered.

Coronary angiogram should be carried out in suspected myocardial ischemia or infarction and to rule out ischemia driven arrhythmias.

If the diagnosis is still unclear, further testing should be selected at the clinician's discretion.

Treatment

The principal goals of treatment for patients with syncope are to prolong survival, limit physical injuries, and prevent recurrences. The general framework of treatment is based on risk stratification and specific mechanisms when possible.

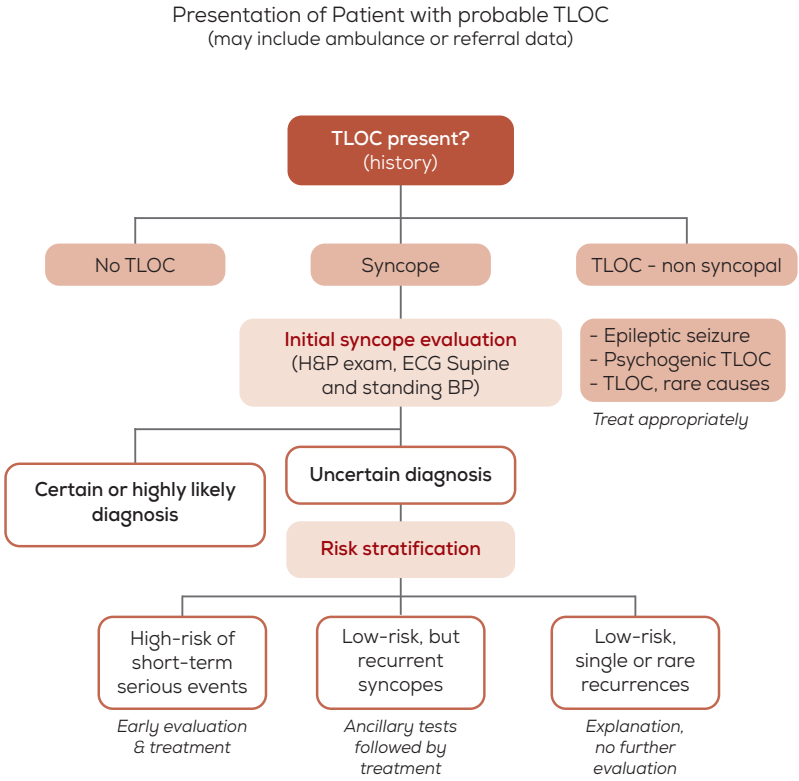


Figure 1: Flow diagram for the initial evaluation and risk stratification of patients with syncope. BP = blood pressure; ECG = electrocardiogram; H&P exam = =history and physical examination; TLOC = Transient loss of consciousness.

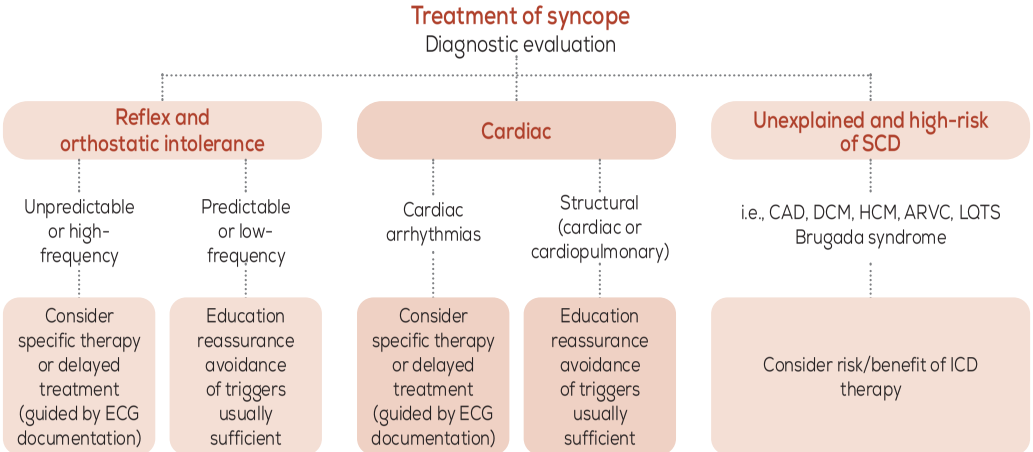


Figure 2: General framework of treatment is based on risk stratification and the identification of specific mechanisms when possible, ARVC = arrhymogenic right ventricular cardiomyopathy; CAD = coronary artery; DCM = dilated cardiomyopathy; ECG = electrocardiographic; HCM = hypertropic cardiomyopathy; ICD = implantable cardioverter defibrillator; LQTS = long QT syndrome; SCD = sudden cardiac death.

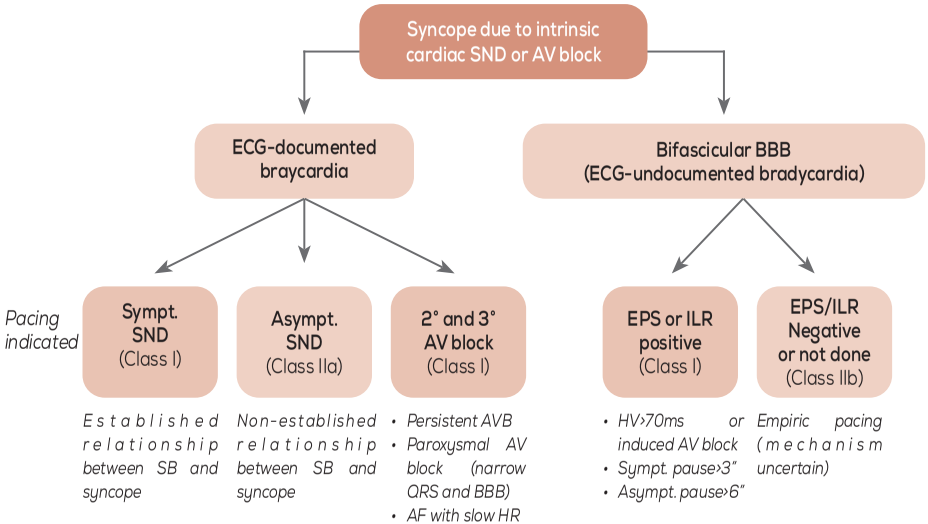
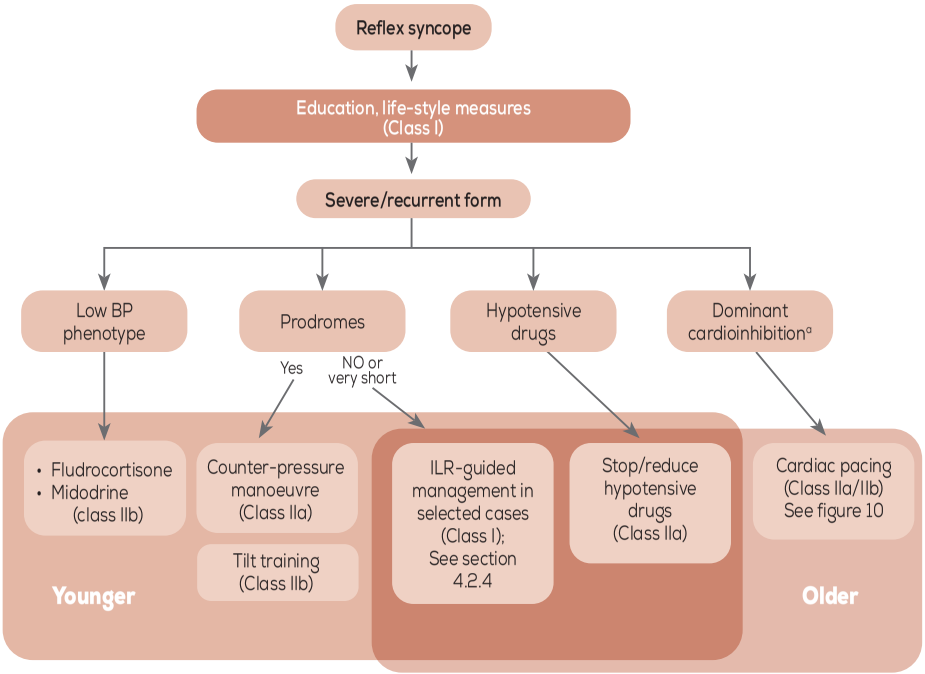


Figure 3: Summary of indications for pacing in patients with syncope due to intrinsic cardiac bradycardia. AV = atrioventricular; BBB = bundle branch block; ECG electrocardiogram; EPS = electrophysiological study; HR = heart rate; ILR = implantable loop recoreder; SB sinus bradycardia; SND = sinus node dysfunction; sympt. = symptomatic.


Reflex syncope
Education, life-style measures (Class I)
Severe/recurrent form
Low BP phenotype
Prodromes
Hypotensive drugs
Dominant cardioinhibition[a]
Yes
NO or very short
• Fludrocortisone
• Midodrine (class IIb)
Counter-pressure manoeuvre (Class IIa)
Tilt training (Class IIb)
ILR-guided management in selected cases (Class I); See section 4.2.4
Stop/reduce hypotensive drugs (Class IIa)
Cardiac pacing (Class IIa/IIb) See figure 10
Younger
Older

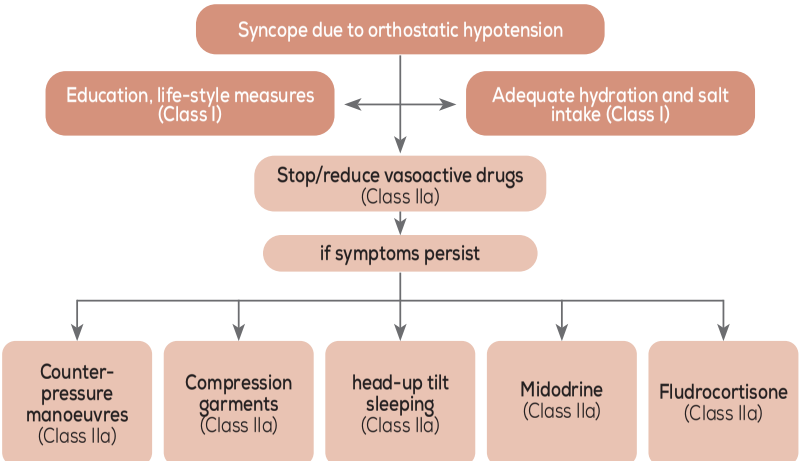


Figure 4: Schematic practical guide for the treatment of orthostatic hypotension.

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I. 2. APPROACH TO CHEST PAIN

Chest pain is a common cardinal symptom of cardiac disease but it can also be present due to non-cardiac causes. It is the most common reason for visit to the emergency department for seeking medical care. The common causes of chest pain are :

1. **Cardiac:** Angina, Unstable Angina, Acute Myocardial Infarction, Pericarditis, Mitral valve prolapse
2. **Vascular:** Aortic dissection, Pulmonary embolism, Pulmonary hypertension
3. **Pulmonary:** Pneumonia, Pleuritis, spontaneous pneumothorax
4. **Gastrointestinal:** Esophageal reflux, esophageal spasm, peptic ulcer, pancreatitis, Mallory-Weiss tear
5. **Musculoskeletal:** costochondritis (Tietze's syndrome), rib fracture, Bornholm disease
6. **Neurological:** Herpes zoster
7. **Psychological:** Panic disorder

The common causes of Acute chest pain and key features as mentioned in Table 1.

Table 1. Common Cause of Acute Chest Pain and their Key features

System	Diagnosis	Symptoms	Key features
Cardiac	Angina	Retrosternal chest pressure, burning, or heaviness; radiating occasionally to the neck, jaw, epigastrium, shoulders, left arm	Precipitated by exercise, cold weather, or emotional stress; duration of 2-10 min
	Rest or unstable angina	Same as angina but severe	Same as angina, but may be more severe Typically <20 min; lower tolerance for exertion; crescendo pattern
	Acute myocardial infarction	Same as angina, but may be more severe	Sudden onset, usually lasting ≥30 min; often associated with shortness of breath, weakness, nausea, vomiting
	Pericarditis	Sharp, pleuritic pain aggravated by changes in position; highly variable duration	Pericardial friction rub
Vascular	Aortic dissection	Excruciating, ripping pain of sudden onset in the anterior aspect of the chest, often radiating to the back	Marked severity of unrelenting pain; usually occurs in the setting of hypertension or underlying connective tissue disorder such as Marfan syndrome
	Pulmonary embolism	Sudden onset of dyspnea and pain, usually pleuritic with pulmonary infarction	Dyspnea, tachypnea, tachycardia, signs of right-sided heart failure
	Pulmonary hypertension	Substernal chest pressure, exacerbated by exertion	Pain associated with dyspnea and signs of pulmonary hypertension

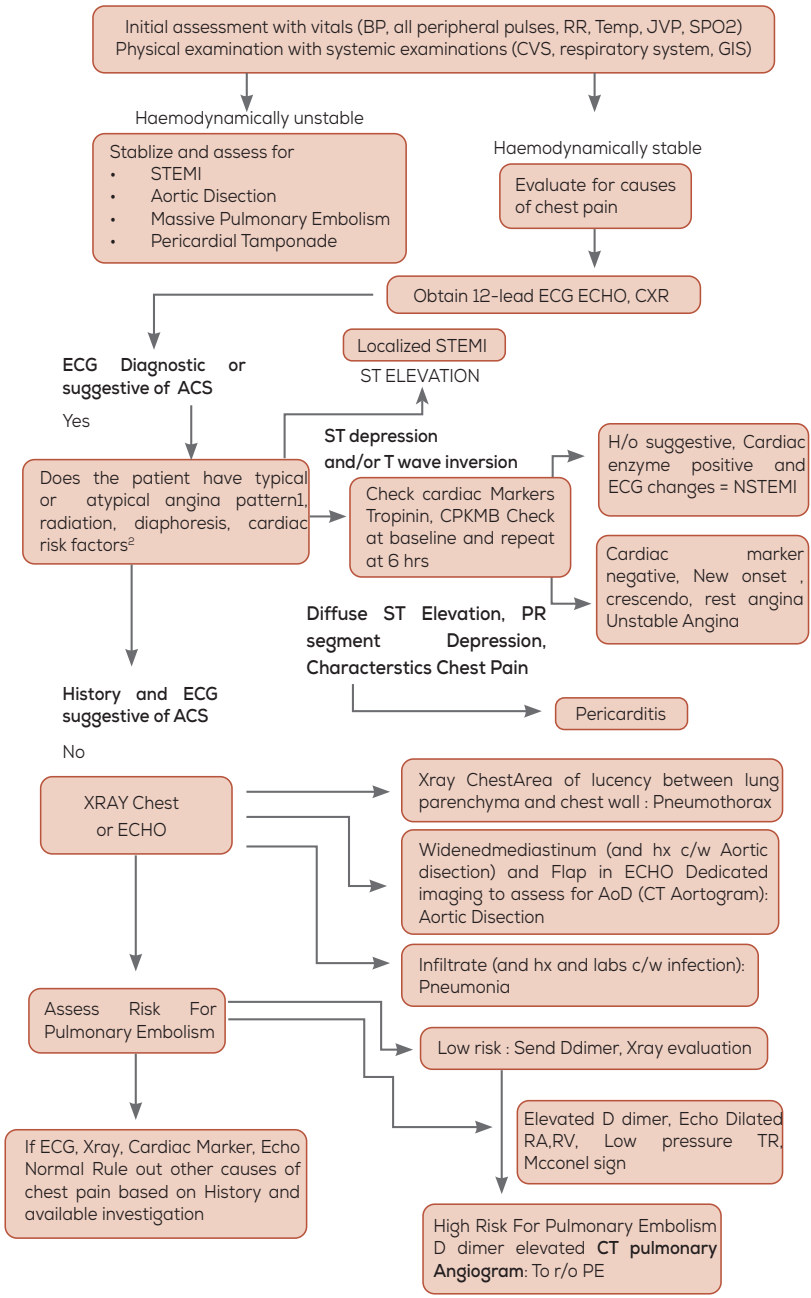
Pulmonary	Pleuritis and/or pneumonia	Pleuritic pain, usually brief, over the involved area	Pain pleuritic and lateral to the midline, associated with dyspnea
	Tracheobronchitis	Burning discomfort in the midline Midline location,	associated with coughing
	Spontaneous pneumothorax	Sudden onset of unilateral pleuritic pain, with dyspne	Abrupt onset of dyspnea and pain
Gastrointestinal	Esophageal reflux	Burning substernal and epigastric discomfort, 10-60 min in duration	Aggravated by a large meal and postprandial recumbency; relieved by antacid
	Peptic ulcer	Prolonged epigastric or substernal burning	Relieved by antacid or food
	Gallbladder disease	Prolonged epigastric or right upper quadrant pain	Unprovoked or following a meal
	Pancreatitis	Prolonged, intense epigastric and substernal pain	Risk factors, including alcohol, hypertriglyceridemia, medications
Musculoskeletal	Costochondritis	Sudden onset of intense fleeting pain	May be reproduced by pressure over the affected joint swelling and inflammation over the costochondral joint
	Trauma or strain	Constant pain	Reproduced by palpation or movement of the chest wall or arm
	Cervical disc disease	Sudden onset of fleeting pain	May be reproduced with movement of the neck
Infectious	Herpes zoster	Prolonged burning pain in a dermatomal distribution	Vesicular rash, dermatomal distribution
Psychological	Panic disorder	Chest tightness or aching, often accompanied dyspnea and lasting 30 min or more, unrelated to exertion or movement	Patient may have other evidence of an emotional disorder

Approach To chest Pain:

The evaluation of the patient with chest discomfort must address a series of issues related to prognosis and immediate management. The clinician must focus first on identifying patients who require aggressive interventions to diagnose or manage potentially life-threatening conditions, including acute ischemic heart disease, acute aortic dissection, pulmonary embolism, and tension pneumothorax. Before a definite diagnosis, high priority should be given to:

1. *Clinical stability:* Does the patient need immediate treatment for actual or impending circulatory collapse or respiratory insufficiency?
2. *Immediate prognosis:* If the patient is currently clinically stable, what is the risk that a life-threatening condition such as ACS, PE, or aortic dissection exists?
3. *Safety of triage options:* If the risk for a life-threatening condition is low, is it safe to discharge the patient for outpatient management, or should further testing or observation to guide management be undertaken?

Patient presents with chest pain



I. 3. ASSESSMENT OF CARDIAC RISK IN NON CARDIAC SURGERY

The main purpose of perioperative cardiac risk evaluation involves answering few basic questions.

- What are the underlying cardiac risk factors which a patient might have before he undergoes noncardiac surgery?
- Will such cardiac evaluation change the management of the patient?
- Will it defer surgery altogether in favor of resolving the patient's cardiac disease and hence reducing perioperative mortality?
- What will be the course of management in the postoperative period?

Perioperative Cardiac evaluation–A Systematic Approach

Before we go into the details of perioperative cardiac evaluation, it is important to know the different categories of non-cardiac procedures. It is recommended to approach in stepwise manner as below:

Step 1. The urgency of the surgical procedure should be assessed. In emergent cases, patient- or surgery-specific factors dictate the strategy and do not allow further cardiac testing or treatment.

Step 2. In non emergent surgery, if the patient is unstable and has active cardiac conditions, this condition should be clarified and treated appropriately before surgery. Examples are ***unstable coronary syndromes, decompensated heart failure, severe arrhythmias, and symptomatic valvular disease.*** Stabilization usually leads to cancellation or delay

of the surgical procedure. Treatment options should be discussed by a multidisciplinary expert team.

Step 3. In cardiac-stable patients, determine the risk of the surgical procedure (Table 1). If the estimated 30-day cardiac risk of the procedure in cardiac stable patients is low (<1%), it is unlikely that test results will influence management and it would be appropriate to proceed with the planned surgical procedure. The physician can identify risk factors and provide recommendations on lifestyle and medical therapy to improve long-term outcome, as per present guidelines.

Initiation of a beta-blocker regimen may be considered prior to surgery in patients with known IHD or myocardial ischemia. Treatment should ideally be initiated between 30 day and a minimum of 2 days before surgery and should be continued post-operatively. Beta-blockade should be started with a low dose, slowly up-titrated and tailored to achieve a resting heart rate of between 60 and 70 bpm with systolic blood pressure >100 mm Hg. In patients with heart failure with reduced ejection fraction, ACEIs (or ARBs in patients intolerant of ACEIs) should be considered before surgery. In patients undergoing vascular surgery, initiation of statin therapy should be considered. Discontinuation of aspirin should be considered in those patients in whom homeostasis is difficult to control during surgery.

Step 4. Consider the functional capacity of the patient. (Table 2). If an asymptomatic or cardiac-stable patient has moderate or good functional capacity (>4 METs), perioperative management is unlikely to be changed on the basis of test results, irrespective of the planned surgical procedure. Even in the presence of clinical risk factors, it is appropriate to refer the patient for surgery. The recommendations for medication are the same as in Step 3.

Step 5. In patients with a moderate or poor functional capacity(≤4 METs), consider the risk of the surgical procedure, as outlined in Table 1. Patients scheduled for intermediate-risk surgery can proceed for surgery. In addition to the suggestions above, in patients with one or more clinical risk factors (Table 3), a pre-operative baseline

ECG is recommended to monitor changes during the surgical procedure. It is recommended to use 'revised cardiac risk index' in our context to calculate clinical risk factors.

Step 6. In patients scheduled for high-risk surgery, consider non-invasive testing in patients with more than two clinical risk factors (Table 3). Non-invasive testing can also be considered before any surgical procedure for patient counseling, or change of perioperative management in relation to type of surgery and anesthesia technique. Risk factors can be identified and medical therapy optimized as in Step 3.

Step 7. Interpretation of non-invasive stress test results: patients without stress-induced ischemia—or with mild-to moderate ischemia can proceed to the planned surgical procedure. In patients with extensive stress-induced ischemia, individualized perioperative management is recommended, taking into consideration the potential benefit of the proposed surgical procedure, weighed against the predicted adverse outcome. Also, the effect of medical therapy and/or coronary revascularization must be assessed, not only for immediate postoperative outcome, but also for long-term follow-up. In patients referred for percutaneous coronary artery intervention, the initiation and duration of antiplatelet therapy will interfere with the planned surgical procedure.

Table 1: Surgical Risk Estimate According to Type of Surgery or Intervention*

Low Risk: <1 %	Intermediate Risk: 1–5 %	High Risk: >5 %
Breast	Endovascular aneurysm	Aortic
Dental	Head and neck	Major vascular
Endocrine (thyroid)	Renal transplant	Duodeno-pancreatic
Eye	Intrathoracic (non-major)	Liver resection
Carotid (asymptomatic)	Major orthopaedic	Oesophagectomy
Minor gynaecology	Major neurology	Bowel perforation repair
Minor orthopaedic	Major gynaecological	Adrenal resection
Minor urology (TURP)	Major urology	Cystectomy
Reconstructive	Intraperitoneal (splenectomy, cholecystectomy)	Lung or liver transplant
Superficial	Carotid (symptomatic)	Pneumonectomy

Ann Surg 2012;255:696–702.

Table 2: Daily activities and associated value of metabolic equivalents.

Can take care of self, such as eat, dress, or use the toilet	1 MET
Can walk up a flight of steps or a hill or walk on level ground at 3 to 4 mph	4 METs
Can do heavy work around the house, such as scrubbing floors or lifting or moving heavy furniture, or climb two flights of stairs	4-10 METs
Can participate in strenuous sports such as swimming, singles tennis, football, basketball, and skiing	> 10 METs

Table 3: Revised Cardiac Risk Index*

1.	History of ischemic heart disease
2.	History of congestive heart failure
3.	History of cerebrovascular disease (stroke or transient ischemic attack)
4.	History of diabetes requiring preoperative insulin use
5.	Chronic kidney disease (creatinine > 2 mg/dL)
6.	Undergoing suprainguinal vascular, intraperitoneal, or intrathoracic surgery

*Risk for cardiac death, nonfatal myocardial infarction, and nonfatal cardiac arrest: 0 predictors = 0.4%, 1 predictor = 0.9%, 2 predictors = 6.6%, ≥3 predictors = >11% *Circulation 1999;100:1043–1049*

Summary

- Every patient should undergo thorough and detailed history and clinical examination.
- Patients who require emergency non-cardiac surgery should be taken up for surgery at the earliest. Diligent clinical assessment regarding any cardiac disorder should be made.
- Patients requiring low risk surgeries may go for surgery in absence of active cardiac conditions without any further work-up.
- Patients with active or acute cardiac conditions like symptomatic severe valvular stenosis or regurgitation, acute coronary syndrome, uncontrolled heart failure or uncontrolled rhythm disorder should be referred for detailed cardiac evaluation prior to elective non-cardiac surgery.

It should be noted, however, that we cannot predict all the acute cardiac events in perioperative period by any means.

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I. 4. ACUTE PULMONARY EDEMA: DIAGNOSIS AND MANAGEMENT

Introduction:

Acute pulmonary edema is a medical emergency which is due to excess fluid accumulation in lungs.

Classification:

It can be divided into non-cardiogenic and cardiogenic pulmonary edema.

Non-cardiogenic pulmonary edema is a distinct clinical syndrome associated with diffuse filling of the alveolar spaces in the absence of elevated pulmonary capillary wedge pressure. The causes of non-cardiogenic pulmonary edema are: 1) Lymphatic obstruction causing decreased drainage from interstitium, 2) Excess volume administration, 3) Decreased oncotic pressure e.g.: low albumin state and, 4) Damage to the lung itself.

Cardiogenic pulmonary edema is most often a result of acute decompensated heart failure (ADHF). "Flash" pulmonary edema is a term that is used to describe a particularly dramatic form of cardiogenic alveolar pulmonary edema and is often related to a sudden rise in left-sided intracardiac filling pressures in the setting of hypertensive emergency, acute ischemia, new onset tachyarrhythmia, bilateral renal artery stenosis, or obstructive valvular disease.

In this section, we will be discussing about the cardiogenic pulmonary edema.

Causes:

Cardiogenic pulmonary edema is due to increase in pulmonary capillary wedge pressure and ineffective

pumping or filling capacity of the heart. The causes can be

1. Congestive Heart failure (CHF) either diastolic or systolic
2. Valvular heart disease: Acute valve syndromes and Progressive valve disease
3. Arrythmias
4. Myocarditis
5. Coronary artery disease: Acute coronary syndrome, Myocardial infarction/ischemia, Ventricular septal rupture
6. Cardiomyopathic states: Hypertrophic cardiomyopathy, Dilated cardiomyopathy, Tachycardia induced cardiomyopathy, Stress (Takotsubo) cardiomyopathy
7. Poorly controlled hypertension
8. Bilateral renal artery stenosis

Pathophysiology:
The primary etiologic factor is a rapid and acute increase in left ventricular filling pressures and left atrial pressure. The net result is filtration of protein-poor liquid across the pulmonary endothelium into the pulmonary interstitium and alveolar spaces, leading to decreased diffusing capacity, hypoxia, and shortness of breath.

Clinical Manifestations:
Most patients presenting with ADHF have known chronic HF and may or may not have had a prior episode of decompensation. In many patients with chronic HF, symptoms have gradually worsened over the preceding days and weeks but have not been sufficient for the patient to seek medical attention. In a minority of patients, an episode of ADHF may be the first presentation of HF.

The symptoms include dyspnea, cough, pink frothy sputum, anxiety and chest discomfort. Physical examination includes tachypnea, tachycardia, rales, rhonchi, wheezing and presence of S3, S4, cool extremities and skin mottling in later stages. The chest radiograph may show cardiomegaly, upper zone redistribution of blood flow, interstitial edema (with ill-defined vessels, peribronchial cuffing, and interlobular septal thickening), and alveolar edema (with perihilar and lower-lobe airspace filling, with the periphery generally spared in the mid and upper lung zones).

The natriuretic peptides, brain natriuretic peptide (BNP) and N-terminal pro-brain natriuretic peptide (NT-pro-BNP), are the biomarker for evaluation of acute dyspnoea. Other tests include assessment of renal function, calculation of estimated glomerular filtration rate, blood urea nitrogen (BUN). Electrocardiogram (ECG) is useful in patients with symptoms suggestive of ischemia and to detect cardiac arrhythmias. Echocardiogram is the single most useful test in investigation of the cause of the pulmonary edema.

Management:

Urgent/Emergent Care:

The initial goal is to expeditiously establish the diagnosis, treat life-threatening abnormalities, initiate therapies to rapidly provide symptom relief, and identify the cause and precipitating triggers.

Oxygen administration: In patients with severe hypoxia (oxygen saturation [SPO2] <90%). Noninvasive ventilation (NIV) with continuous positive airway pressure (CPAP) or noninvasive intermittent positive-pressure ventilation (NIPPV) or mechanical ventilation with endotracheal intubation may be required in patients who don't improve with oxygen therapy..

Morphine: useful in patients with severe anxiety or distress but should be used cautiously or avoided, especially in the presence of hypotension, bradycardia, advanced atrioventricular block, or CO2 retention.

Intravenous loop diuretics: are the most frequently administered pharmacologic agents. Initial therapy typically consists of a bolus injection with a dose between 1 and 2.5 times the patient's oral loop diuretic dose for patients on chronic diuretic therapy.

Intravenous vasodilators (e.g., nitroglycerin) are indicated in patients with systolic blood pressure more than 110mmHg.

Intravenous Inotropes are indicated in patients with shock.

Antibiotics are indicated if the infection is the precipitating factor.

Hospital Care:

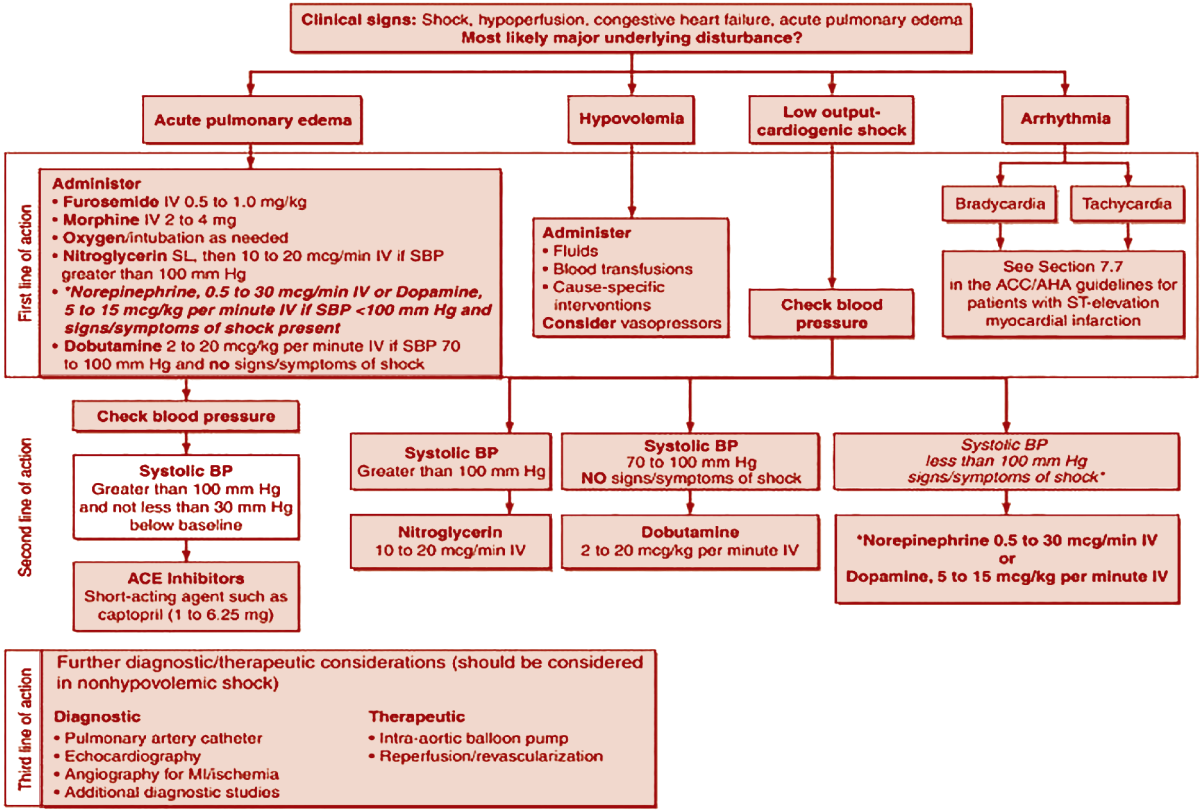
The goal in management of the patient during the hospitalization are

(i) to complete the diagnostic and acute therapeutic processes that were initiated at the time of initial presentation

(ii) to optimize the patient's hemodynamic profile and volume status and control clinical symptoms

(iii) to initiate or optimize chronic HF therapy

Monitoring of daily weights, fluid intake and output, and vital signs, daily assessment of symptoms and signs imperative. Dietary sodium restriction (to 2 g daily) and fluid restriction (to 2 L daily) may be useful to help treat congestion. Venous thromboembolism prophylaxis is indicated in all patients unless a clear contraindication is recognized. Most outpatient medications should be continued during hospitalization, although in patients with worsening renal function, ACE inhibitors and mineralocorticoid receptor antagonists are often withheld. Patients should continue ß-blocker therapy during hospitalization for AHF, unless significant hypotension or cardiogenic shock is present. In the absence of contraindications, ACE inhibitors, angiotensin receptor blockers, mineralocorticoid receptor antagonists, and isosorbidedinitrate/hydralazine should be continued during the hospitalization as well. Identification of other untreated targets (e.g., revascularization, consideration of cardiac resynchronization therapy in appropriate candidates) should be considered during the hospitalization. The management also includes providing education and behavioral therapies to patients.


Clinical signs: Shock, hypoperfusion, congestive heart failure, acute pulmonary edema
Most likely major underlying disturbance?
Acute pulmonary edema
Hypovolemia
Low output-cardiogenic shock
Arrhythmia
First line of action
Administer
• Furosemide IV 0.5 to 1.0 mg/kg
• Morphine IV 2 to 4 mg
• Oxygen/intubation as needed
• Nitroglycerin SL, then 10 to 20 mcg/min IV if SBP greater than 100 mm Hg
• *Norepinephrine, 0.5 to 30 mcg/min IV or Dopamine, 5 to 15 mcg/kg per minute IV if SBP <100 mm Hg and signs/symptoms of shock present
• Dobutamine 2 to 20 mcg/kg per minute IV if SBP 70 to 100 mm Hg and no signs/symptoms of shock
Administer
• Fluids
• Blood transfusions
• Cause-specific interventions
Consider vasopressors
Check blood pressure
Bradycardia
Tachycardia
See Section 7.7 in the ACC/AHA guidelines for patients with ST-elevation myocardial infarction
Second line of action
Check blood pressure
Systolic BP
Greater than 100 mm Hg and not less than 30 mm Hg below baseline
ACE Inhibitors
Short-acting agent such as captopril (1 to 6.25 mg)
Systolic BP
Greater than 100 mm Hg
Nitroglycerin
10 to 20 mcg/min IV
Systolic BP
70 to 100 mm Hg
NO signs/symptoms of shock
Dobutamine
2 to 20 mcg/kg per minute IV
Systolic BP
less than 100 mm Hg
signs/symptoms of shock*
*Norepinephrine 0.5 to 30 mcg/min IV
or
Dopamine, 5 to 15 mcg/kg per minute IV
Third line of action
Further diagnostic/therapeutic considerations (should be considered in nonhypovolemic shock)
Diagnostic
• Pulmonary artery catheter
• Echocardiography
• Angiography for MI/ischemia
• Additional diagnostic studies
Therapeutic
• Intra-aortic balloon pump
• Reperfusion/revascularization

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I. 5. PREGNANCY AND HEART DISEASE

Cardiovascular disease is the major cause of death during pregnancy. A study in eastern Nepal revealed 0.6% prevalence of the heart disease among 9463 pregnancies. The spectrum includes congenital (9%), acquired (89%), and arrhythmia (2%). Thus, the concern rises for reducing the threat of safe motherhood.

Diagnosis

Usually involves:

- Clinical Evaluation
- Echocardiography

Risk Stratification

Modified World Health Organization (WHO) classification is preferred to estimate the cardiovascular risk in women with cardiovascular disease contemplating pregnancy. The risk stratification involving all three spectra i.e congenital, acquired and arrythmia is shown in table below.

WHO Pregnancy Risk Classification (Risk of pregnancy by medical condition)	**Cardiovascular Conditions by WHO Risk Class**

WHO Risk Class I
No detectable increased risk of maternal mortality and no or mild increase in morbidity.
	• Uncomplicated, small or mild
	  ○ Pulmonary stenosis
	  ○ Patient ductus arteriosus
	  ○ Mitral valve prolapse
	• Successfully repaired simple lesions (atrial or ventricular septal defect, patent ductus arteriosus, anomalous pulmonary venous drainage).
	• Atrial or ventricular ectopic beats, isolated

WHO Risk Class II (If otherwise well and uncomplicated) *Small increased risk of maternal mortality or moderate increase in morbidity.*	• Unoperated atrial or ventricular septal defect • Repaired tetralogy of Fallot • Most arrhythmias

WHO Risk Class II or III (Depending on individual) *Risk as indicated in Class II (above) or Class III (below).*	• Mild left ventricular impairment • Hypertrophic cardiomyopathy • Native or tissue valvular heart disease not considered WHO I or IV • Marfan syndrome without aortic dilatation • Aorta <45 mm in aortic disease associated with bicuspid aortic valve • Repaired Coarctation
WHO Risk Class III *Significantly increased risk of maternal mortality or severe morbidity. Expert counseling required. If pregnancy is decided upon, intensive specialist cardiac and obstetric monitoring needed throughout pregnancy, childbirth and the puerperium.*	• Mechanical valve • Systemic right ventricle • Fontan circulation • Cyanotic heart disease (unrepaired) • Other complex congenital heart disease • Aortic dilatation 40-45 mm in Marfan Syndrome • Aortic dilatation 45-50 mm in aortic disease associated with bicuspid aortic valve
WHO Risk Class IV (Pregnancy contraindicated) *Extremely high risk of maternal mortality or severe morbidity; pregnancy contraindicated. If pregnancy occurs termination should be discussed. If pregnancy continues, care as for class III.*	• Pulmonary arterial hypertension of any cause • Severe systemic ventricular dysfunction (LVEF <30%, NYHA III-IV)* • Previous peripartum cardiomyopathy with any residual impairment of left ventricular function • Severe symptomatic mitral or aortic stenosis • Marfan syndrome with aorta dilated >45 mm • Aortic dilation >50 mm in aortic disease associated with bicuspid aortic valve • Native severe Coarctation

*LVEF = left ventricular ejection fraction; NYHA = New York Heart Association

Management

Pregnant women with heart disease are a heterogenous group with different maternal cardiovascular and fetal complication risks. Involvement of cardio-obstetric team is critical to prevent maternal morbidity and mortality during the length of pregnancy and 1-year post-partum.

Pre-conception counseling is important to ensure that estimated individual risk is taken into consideration.

Pre-conception Planning: All medications should be reviewed to ensure safety during pregnancy.

1. **Women with Valvular Heart disease**
   Rheumatic heart disease is more common in our population. Women with valvular heart disease should undergo pre-conception evaluation and counseling by cardio-obstetric team.

   Either repair or replacement of the valve should be performed in symptomatic patient prior to conception. Percutanoeus mitral commissurotomy can be

performed preferably after 20 weeks of gestation in symptomatic patient despite optimal medical therapy.

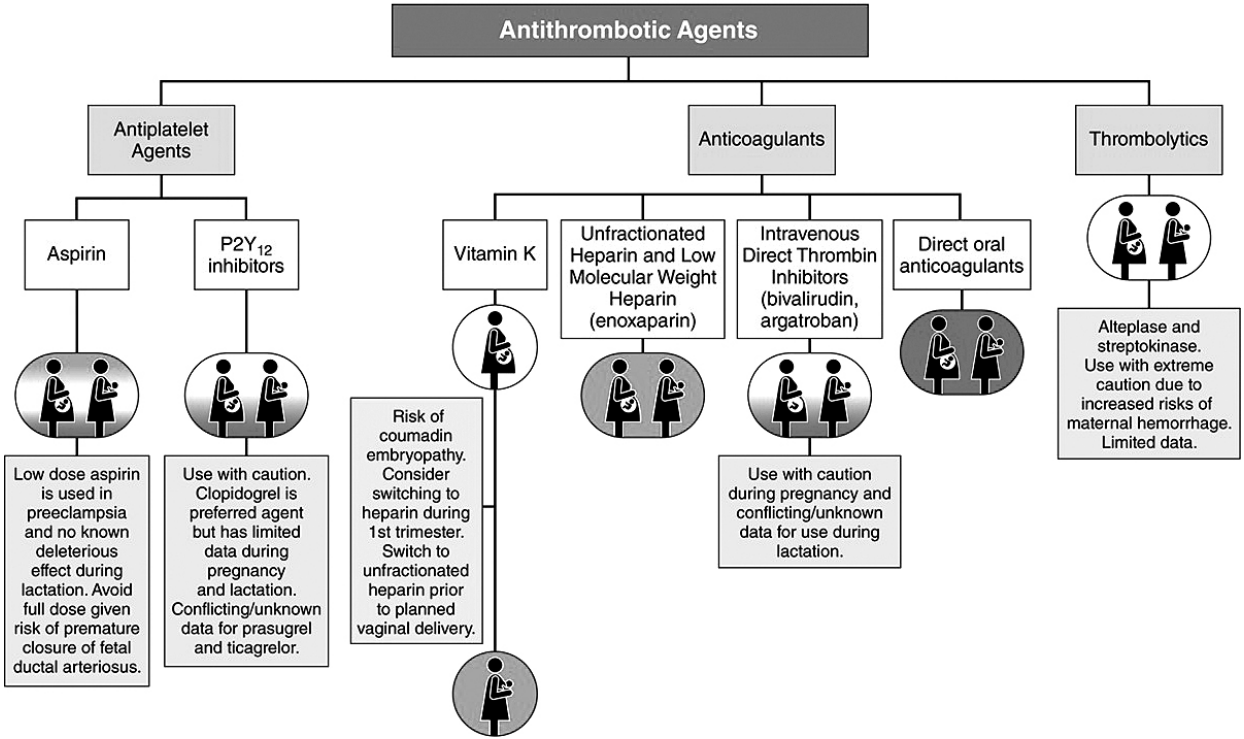
Management of isolated valvular stenotic lesions is outlined in the table below.

	Mitral Stenosis	Aortic Stenosis	Tricuspid Stenosis	Pulmonic Stenosis
Etiology	• Rheumatic disease most common followed by congenital MS	• Congenital • Rheumatic • Prosthetic valvular disease	• Rarely present in women of childbearing age	• Congenital most common
Intervention	• Balloon valvuloplasty, mitral repair/replacement • Preconception if MVA < 1.0 cm^2 • Consider if MVA < 1.5 cm^2 • DCCV if AF and symptoms	• Pre-pregnancy valve replacement • Balloon aortic valvuloplasty • TAVR		• Even severe stenosis is usually well-tolerated during pregnancy
Therapies	• Heart rate control with β1 selective blockers • Activity restriction • If symptomatic, add diuretic therapy • Anticoagulation* if AF and prior CVA	• Heart rate control with β1 selective blockers • Activity restriction • Diuretic therapy		

*Vitamin K antagonist (warfarin), low molecular weight heparin or unfractionated heparin

Regurgitant lesions are well tolerated in pregnancy.

Anticoagulation strategy peripartum : Women with mechanical prosthetic valves need to be counseled preconception about the strategy for anticoagulation. If the dose required to maintain therapeutic INR is ≤5mg/day then warfarin can be continued in first trimester. However, if the dose exceeds 5mg/day or patient wants to avoid warfarin, given the risk of teratonegenicity, then dose-adjusted LMWH or dose-adjusted UFH are the alternatives. Warfarin can be administered safely during second trimester. Patient is transitioned to dose-adjusted LMWH or UFH at 36 weeks. 36 hours before planned delivery patient should be on Intravenous UFH, which is discontinued 4 to 6 hours before delivery. Intravenous UFH can be restarted after 4 to 5 hours of delivery once the bleeding risk has subsided. Women who go on labour while still on warfarin should undergo cesarean section.


Antithrombotic Agents
Antiplatelet Agents
Anticoagulants
Thrombolytics
Aspirin
P2Y12 inhibitors
Vitamin K
Unfractionated Heparin and Low Molecular Weight Heparin (enoxaparin)
Intravenous Direct Thrombin Inhibitors (bivalirudin, argatroban)
Direct oral anticoagulants
Low dose aspirin is used in preeclampsia and no known deleterious effect during lactation. Avoid full dose given risk of premature closure of fetal ductal arteriosus.
Use with caution. Clopidogrel is preferred agent but has limited data during pregnancy and lactation. Conflicting/unknown data for prasugrel and ticagrelor.
Risk of coumadin embryopathy. Consider switching to heparin during 1st trimester. Switch to unfractionated heparin prior to planned vaginal delivery.
Use with caution during pregnancy and conflicting/unknown data for use during lactation.
Alteplase and streptokinase. Use with extreme caution due to increased risks of maternal hemorrhage. Limited data.

2. **Women with Aortic disease**
   Pregnant female with aortopathies need regular BP monitoring and serial echocardiography for evaluation of aortic diameter during pregnancy and atleast 12 weeks post-partum. For patients with mildly dilated aorta and at low risk, echocardiogram can be done at every 12 weeks. But for patients with severely dilated aorta or at high risk of dissection must have monthly echocardiogram. Patient may need prophylactic aortic root replacement prior to conceiving if at high risk for spontaneous dissection.

3. **Congenital Heart disease and pregnancy**
   Prepregnancy counseling is important for women with either repaired or unrepaired congenital heart disease. Risk stratification using various tools is helpful for joint decision involving cardio-obstetric team and the patient in planning for safe motherhood or discouraging pregnancy in high-risk cases.

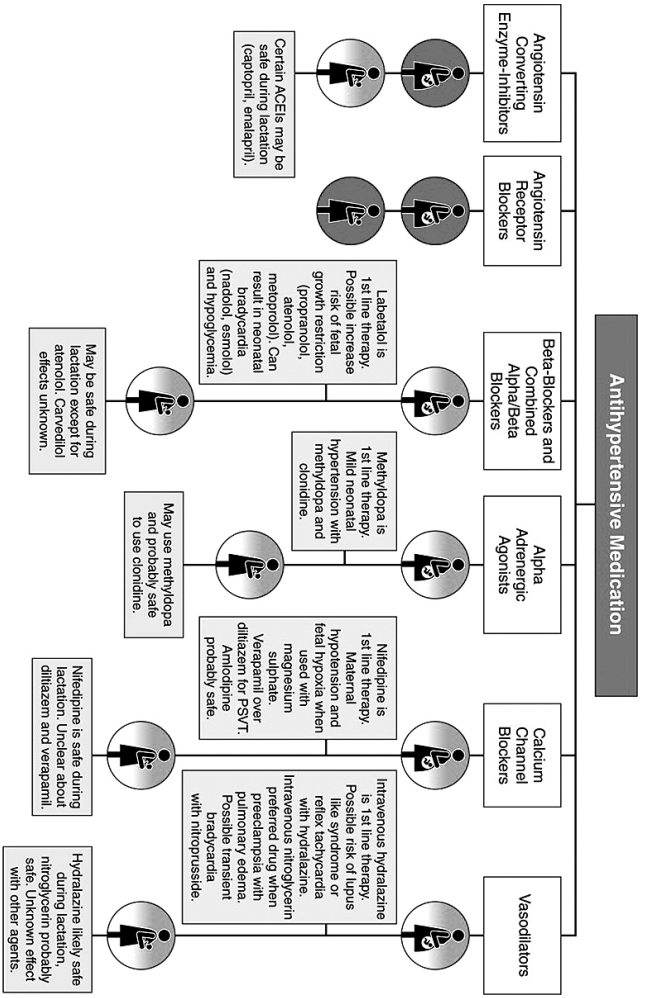
   Clinical assessment associated with regular comparative echocardiograms is wise for all patients, but follow up requires an individual approach for each patient, especially in the presence of impaired right ventricular function. Fetal heart scanning is traditionally offered at 18 weeks. Fetal growth, especially in cyanotic women, has to be carefully monitored.

4. **Cardiovascular Conditions During Pregnancy**
   A. **Hypertensive disorders in pregnancy**

      Hypertensive disorders of pregnancy (HDP) are classified into 4 groups as per ACOG:

      i. Preeclampsia/eclampsia: systolic BP ≥ 140mmHg or diastolic BP≥ 90mmHg in women after 20weeks of gestation who were previously normotensive alone with evidence of proteinuria.
      ii. Gestational hypertension
      iii. Chronic hypertension
      iv. Chronic hypertension with superimposed preeclampsia

Prompt treatment within 30 to 60 minutes of confirmed severe hypertension (BP ≥ 160/100mmHg and persistent for 15 min) should be initiated to reduce the risk of maternal heart failure, myocardial ischemia, stroke or renal disease. Drug of choice is IV labetalol or IV hydralazine. If IV line has not been established then immediate-release oral nifedipine may be given.If preeclampsia is associated with pulmonary edema IV nitroglycerin is preferred. For prevention of eclampsia and seizure IV magnesium sulphate is recommended. Low-dose Aspirin may be started in high risk group in the late first trimester.



For less than severe hypertension medications that can be used or contraindicated are shown in Figure above. Outpatient surveillance of BP during 1 to 2 weeks post-partum is advised. Antihypertensive medications should be continued postpartum if there is persistent hypertension.

B. Hypercholesterolemia in pregnancy

In normal pregnancies, neither triglycerides nor total cholesterol exceeds 250mg/dl. Statins are contraindicated during pregnancy. Patients with very high triglyceride level (>500mg/dl) are at increase risk of pancreatitis. Omega-3 fatty acids with or without fenofibrate or gemfibrozil may be prescribed during the second trimester. Bile acid sequestrants can be given to patients with familial hypercholesterolemia.

C. Ischemic heart disease

Ischemic heart disease during pregnancy is potentially a fatal condition. High-risk periods include third trimester and post-partum with causes being pregnancy related spontaneous coronary artery dissection and MI with non-obstructive coronary artery disease. Management for individual causative factors is:

i. Atherosclerotic STEMI: PCI with fetal radiation protection using lead shield and radiation reduction
ii. NSTEMI: if unstable, PCI, else conservative management
iii. Pregnancy related spontaneous coronary artery dissection: Conservative management with inpatient monitoring

D. Cardiomyopathies

Peripartum cardiomyopathies (PPCM) is defined as new-onset cardiomyopathy with systolic dysfunction (LVEF<45%) without a reversible cause presenting near the end of pregnancy or in post-partum period without known heart disease. Treatment includes:

i. Controlling volume status: diuretics
ii. Afterload reduction: nitrates, hydralazine
iii. Rhythm control: B-blockers, digoxin
iv. Bromocriptine: as an adjunctive treatment

Risk of recurrent PPCM in future pregnancies must be discussed with the patient.

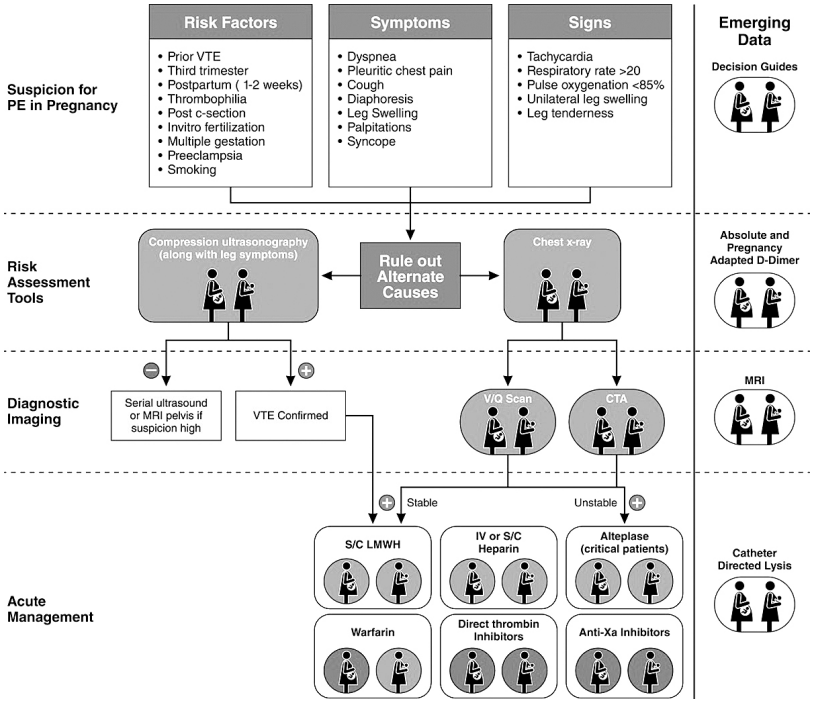
Women with hypertrophied cardiomyopathies may present in failure or arrhythmias mostly in third trimester or post-partum. Diuretics must be used cautiously.

E. Arrythmias

Pregnant women presenting with arrhythmias should be screened for structural heart disease, thyroid and electrolytes disturbances. Women with congenital long-QT syndrome should be counseled prepregnancy for the risk of malignant tachyaarythmias and may be B-blockers throughout pregnancy.

F. Deep Vein Thrombosis and Pulmonary Embolism

Patient usually complains of extremity pain and swelling. Diagnosis is made by compression ultrasonography.



Pregnancy Prevention and counseling

Assessment of the clinical status and heart function before planning pregnancy is a must in women with heart disease. Most of the patients in our setup come into recognition only after occurrence of symptoms or with complications.

Women with pulmonary hypertension, severe systemic ventricular dysfunction, left sided obstructive lesions, dilated aortopathy(>4cm) should be counseled for termination of pregnancy to avoid maternal mortality.

Women with heart disease and pregnancy should be counseled regarding maternal mortality, possible reduction in maternal life expectancy, fetal losses, switchover of anticoagulant therapy, intense feto-maternal monitoring during labor and possible recurrent admission.

Diagnostic tools

Where resources are limited clinical diagnosis should be backed up by: basic blood workup, scans for dating and fetal anomalies, electrocardiogram, echocardiogram and Chest X ray with abdominal shield can be conducted during pregnancy to support the diagnosis.

The above classifications are important in prognostication and management of the pregnancy with heart disease. Management of the moderate and high risk group requires multidisciplinary approach. Obstetrician should lead a team involving physician/cardiologist, anesthetist and pediatrician. Most women with NYHA functional class I and II can go through pregnancy without morbidities.

Recommended mode of delivery

Vaginal delivery is recommended unless there is obstetric indication for cesarean section or in certain cardiac conditions: dilated aortic root >4 cm or aortic aneurysm, congestive heart failure, history of recent myocardial infarction, severe or symptomatic aortic stenosis, warfarin administration within 2 weeks of delivery, need for emergency valve replacement following delivery.

Careful fluid balance, semi recumbent or lateral position

Continuous monitoring of vitals pulse, BP, SPO2, and input/output

Cut short 2nd stage of labour: vaccum/forcep to reduce maternal effort

Avoid Ergometrine prefer Syntocin over Ergometrine.

Close monitoring in postpartum period for at least 6 weeks period is essential.

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3. Standard Treatment Guidelines For Cardiac Diseasein pregnancy.
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5. Cardiovascular Considerations in Caring for Pregnant Patients: A Scientific Statement From the American Heart Association

I. 6. CARDIAC TRAUMA

Injuries to the heart were considered to be fatal and surgeons were discouraged from attempting to repair cardiac wounds till Dr. Ludwig Rehn successfully repaired a stab wound to the right ventricle on 9th September 1896. Much development of surgical treatment of cardiac injuries occurred during the period of World War II and during this period there was controversy regarding early surgical treatment and pericardiocentesis as the final treatment. By 1970s due to the development in surgical techniques, expertise and decreased mortality the treatment protocol for penetrating cardiac injuries was established as early thoracotomy and cardiorrhaphy.

Cardiac injury can be classified as blunt, penetrating and iatrogenic.

Blunt Cardiac Injury (BCI)

BCI is a spectrum of traumatic heart diseases with severity that can range from myocardial contusion and ECG changes to septal rupture and death. It is estimated to occur in 20% of motor vehicle collisions and in greater than 75% of thoracic blunt injuries independent of the mechanism. Overall mortality from BCI is 11.4-24.5%.

BCI becomes clinically significant when it is associated with hypotension in the absence of bleeding or neurogenic causes requiring vasopressors, cardiogenic shock requiring inotropes, ECG and structural or functional abnormality in echocardiogram.

ECG and troponin-I are used for screening BCI. Positive ECG findings include conduction abnormalities, ST segment changes, T wave inversion, and arrhythmias other than

sinus tachycardia. The combined negative predictive value of these two tests during admission and 8 hours after injury is 100%. In the setting of blunt chest injury, transthoracic echocardiography (TTE) should be done in patients with hypotension, heart failure, arrhythmia and new murmur. If adequate imaging cannot be obtained with TTE alone, then trans esophageal echocardiogram (TEE) is helpful.

Initial treatment of BCI should be guided by the clinical manifestation whether that is hypotension, cardiac shock, arrhythmia, or structural abnormality. Cardiac tamponade will require drainage, and structural cardiac abnormality may require cardiothoracic surgery. In absence of treatable manifestations, patients should be observed because the risk of developing an arrhythmia is 3-39%. Most ECG abnormalities tend to be transient and length of observation is not well defined but usually the associate injuries determine their hospital stay beyond 24 hours.

Penetrating cardiac injury

Penetrating cardiac injury mostly is the result of either gunshot injuries or stab wounds, injuries due to wild and domestic animal attack and agricultural instruments. These injuries are potentially fatal and 90% do not survive till they reach hospital.

Penetrating cardiac injury should be suspected with wounds to the chest, upper abdomen, back, and neck. The majority of the injuries are anteriorly located on the right side of the heart.

The initial care of the patients does not vary from standard Advanced Trauma Life Support (ATLS) protocols. The primary priority is ensuring the patency of the airway and establishing adequate oxygenation and ventilation, and maintaining adequate circulatory blood volume.

Stable patients allow for more complete evaluation including chest x-ray, TTE and CT scan. Unstable patients are taken directly to the operating room for exploration or are subjected to Emergency Department thoracotomy.

When the diagnosis of penetrating cardiac injury is suspected but not confirmed, a sub-xiphoid pericardial window should be performed with preparation for sternotomy. Upon opening the pericardial sac, any blood or fluid should be evacuated to allow the heart to properly fill and contract, with the universal principle of relieving tamponade, stopping the bleeding, and restoring circulating volume.

Iatrogenic injuries

Iatrogenic injuries are usually penetrating injuries caused during surgeries or intervention procedures. It causes perforation of cardiac structures leading to hemo-pericardium and cardiac tamponade. Most cases of small hemopericardium may resolve spontaneously, but sometimes emergent intervention is necessary depending on the type of injury.

References:

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UNIT - II

Preventive Cardiology

II. 1. DYSLIPIDEMIA: DIAGNOSIS AND MANAGEMENT

Introduction:

The term dyslipidemia or dys-lipoproteinemia encompasses disorders of the lipid and lipoprotein metabolism. In clinical practice, dyslipidemia can be classified into primary (inherited) and secondary (acquired). For management of patients, it is important to exclude secondary contributory causes of dyslipidemia like thyroid disorder, diabetes, kidney and liver disorder. Any of the blood lipid parameters may be elevated: total Cholesterol (TC), Low density lipoprotein-Cholesterol (LDL-C), Triglyceride (TG) or decrease high density lipoprotein (HDL). The three most common dyslipidemia patterns are as follows:

- Predominantly hypercholesterolemia: mainly of raised low-density LDL and TC, with occasionally associated with increased level of TG as well.
- Predominantly hypertriglyceridemia: mainly raised triglycerides(TGs). It is often associated with low HDL in our population
- Mixed dyslipidemias, which consist of raised TC, TGs and LDL with potentially low HDL level

Although all three lipid patterns have known primary (monogenic) causes, the vast majority of dyslipidemias are polygenic, caused by interactions between environmental and genetic factors.

Laboratory measurement of lipids:

A full lipid profile should be measured before starting treatment or for risk stratification, as most lipid screening is

performed to help in cardiovascular risk assessment. A non-fasting lipid profile lipid profile is also helpful in detection, however, fasting (12 hours fast) lipid profile is preferable, especially in conditions like familial genetic hyperlipidemia or possible hypertriglyceridemia.

The management of dyslipidemia can be basically divided into:

1. Primary prevention
2. Secondary prevention

Primary prevention:

Patient without CVD are generally at much lower risk of cardiovascular events than patients with established CVD. Primary prevention is mostly focused on addressing the overall risk reduction through management of risk factors for atherosclerotic CVD. Among all lipid components, only LDL-C analysis is recommended as primary lipid analysis and recent guidelines have focused on mainly LDL-C lowering therapy with systematic strategy to identify people that are at high risk of CVD. Recommendations for lipid lowering therapy can be divided into:

- Adults with Severe Hypercholesterolemia: High Intensity statin therapy to be initiated in adults having LDL-C levels 190 mg/dl or more to lower LDL-C by more than 50%, without considering the ASCVD risk. Ezetimibe can be used as additional drug if at maximal statin therapy the LDL-C level is not achieved. PCSK-9 inhibitor can be considered as a third addition (if available).
- For individuals at very-high risk but without Familial hypercholesterolemia (FH), an LDL-C reduction of ≥50% from baseline and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) are recommended.
- For individuals with FH at very-high risk, an LDL-C reduction of ≥50% from baseline and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) should be considered.
- In patients at high risk, an LDL-C reduction of ≥50% from baseline and an LDL-C goal of <1.8 mmol/L (<70 mg/dL) are recommended.
- In individuals at moderate risk, an LDL-C goal of <2.6 mmol/L (<100 mg/dL) should be considered.

- In individuals at low risk, an LDL-C goal <3.0 mmol/L (<116 mg/dL) may be considered.
- Statin therapy is recommended as first line drug for reducing CVD risk in high risk individual with TG>2.3mmol/L.

Secondary prevention in patients with established cardiovascular disease

Patients with established atherosclerotic CVD e.g., history of myocardial infarction, angina, coronary revascularization, PAD, TIA and ischemic stroke established; at highest risk of repeat CVD event. Twenty-seven randomized controlled trials have demonstrated significant benefit of statin therapy over placebo or comparator. The benefit was proportional to LDL-C reduction. High intensity statin is recommended by Guidelines (NICE, AHA, ESC) in patients age ≤75 years with very high-risk phenotype without contraindications to statin. Use of Ezetimibe and further of PCSK-9 inhibitor in addition to high intensity statins are recommended in such group of individuals if the goal cannot be achieved with maximal statin therapy. The CCS and ESC/EAS use treatment goals (<70mg/dL of LDL-C) to determine statin selection and dosing. Some of the recent evidences have suggested that a LDL-C goal of <55 mg/dl may further reduce the risk and is equally safe.

In secondary prevention for patients at very-high risk, an LDL-C reduction of ≥50% from baseline and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) are recomended. For patients with ASCVD who experience a second vascular event within 2 years (not necessarily of the same type as the first event) while taking maximally tolerated statin-based therapy, an LDL-C goal of <1.0 mmol/L (<40 mg/dL) may be considered.

If patients are unable to tolerate high intensity statin due to either drug interactions, side-effects or patient preference, a lower dose of atorvastatin can be used. In patients of age ≤75 years and not with very high risk phenotype, the goal is to cut down LDL-C by 50% using moderate to high intensity statins. Ezetimibe in addition has been recommended when LDL-C levels remain above 70mg/dl despite maximal tolerated statin therapy. In all patients above 75 years of age moderate to high intensity statins has been recommended.

Cardiovascular risk categories

Very-high-risk People with any of the following: Documented ASCVD, either clinical or unequivocal on imaging. Documented ASCVD includes previous ACS (MI or unstable angina), stable angina, coronary revascularization (PCI, CABG, and other arterial revascularization procedures), stroke and TIA, and peripher alarterial disease. Unequivocally documented ASCVD on imaging includes those findings that are known to be predictive of clinical events, such as significant plaque on coronary angiography or CT scan (multivessel coronary disease with two major epicardial arteries having>50% stenosis), or on carotid ultrasound. DM with target organ damage, or at least three major risk factors, or early onset of T1DM of long duration(>20 years). Severe CKD (eGFR<30 mL/min/1.73 m2). A calculated SCORE ≥10% for 10-year risk of fatal CVD.FH with ASCVD or with another major risk factor.

High-risk People with: Markedly elevated single riskfactors, in particular TC>8 mmol/L (>310 mg/dL), LDL-C >4.9 mmol/L(>190 mg/dL), or BP ≥180/110 mmHg. Patients with FH without other major risk factors. Patients with DM without target organ damage, with DM duration ≥10 years or another additional riskfactor. Moderate CKD (eGFR 3059 mL/min/1.73 m2).A calculated SCORE ≥5% and <10% for 10-year riskof fatal CVD.

Moderate-risk Young patients (T1DM <35 years; T2DM <50 years)with DM duration <10 years, withoutotherriskfactors. Calculated SCORE ≥1 % and <5% for 10-yearrisk of fatal CVD.

Low-risk Calculated SCORE <1% for 10-year risk of fatal CVD

Treatment strategies and goals for LDL-C across categories of total CV risk are further illustrated in following Table1 and figures 1 A and B.

Table 1 treatment strategies for untreated LDL level as per CV risk score

	Total CV risk (SCORE) %	Untreated LDL-C levels					
		<1.4 mmol/L (55 mg/dL)	1.4 to <1.8 mmol/L (55 to <70 mg/dL)	1.8 to <2.6 mmol/L (70 to <100 mg/dL)	2.6 to <3.0 mmol/L (100 to <116 mg/dL)	3.0 to <4.9 mmol/L (116 to <190 mg/dL)	≥4.9 mmol/L (≥190 mg/dL)
Primary prevention	<1, low-risk	Lifestyle advice	Lifestyle advice	Lifestyle advice	Lifestyle advice	Lifestyle intervention, consider adding drug if uncontrolled	Lifestyle intervention and concomitant drug intervention
	Class[a]/Level[b]	I/C	I/C	I/C	I/C	IIa/A	IIa/A
	≥1 to <5, or moderate risk	Lifestyle advice	Lifestyle advice	Lifestyle advice	Lifestyle intervention, consider adding drug if uncontrolled	Lifestyle intervention, consider adding drug if uncontrolled	Lifestyle intervention and concomitant drug intervention
	Class[a]/Level[b]	I/C	I/C	IIa/A	IIa/A	IIa/A	IIa/A
	≥5 to <10, or high-risk	Lifestyle advice	Lifestyle advice	Lifestyle intervention, consider adding drug if uncontrolled	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention
	Class[a]/Level[b]	IIa/A	IIa/A	IIa/A	I/A	I/A	I/A
	≥10, or at very-high risk due to a risk condition	Lifestyle advice	Lifestyle intervention, consider adding drug if uncontrolled	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention
	Class[a]/Level[b]	IIa/B	IIa/A	I/A	I/A	I/A	I/A
Secondary prevention	Very-high-risk	Lifestyle intervention, consider adding drug if uncontrolled	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention
	Class[a]/Level[b]	IIa/A	I/A	I/A	I/A	I/A	I/A

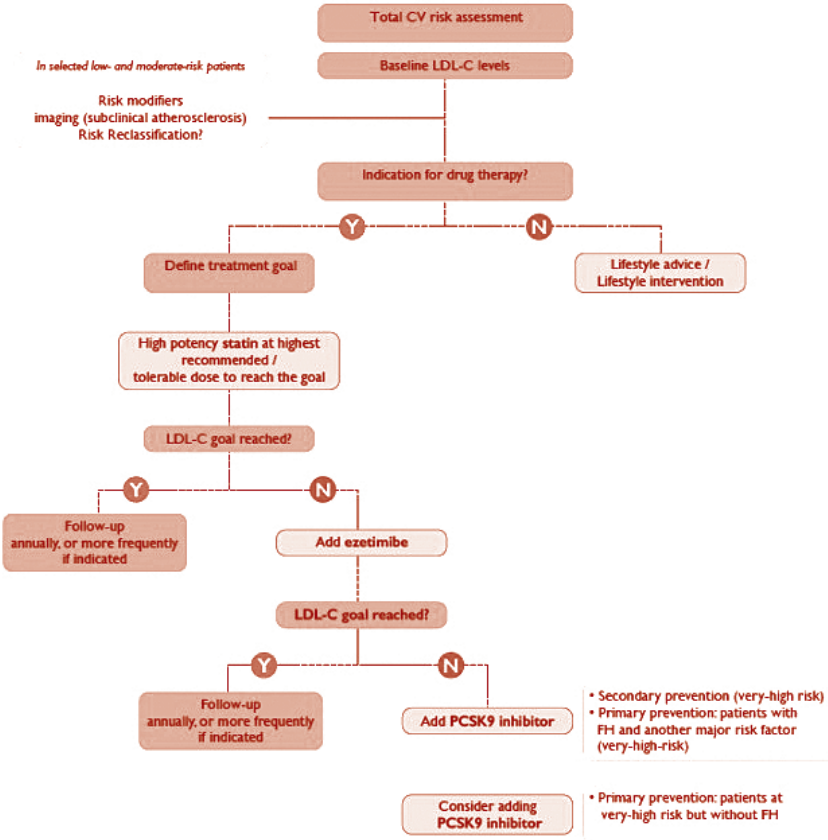

Figure 1 (A) Treatment algorithm for pharmacological low-density lipoprotein cholesterol lowering.

Figure 1 (B) Treatment goals for low-density lipoprotein cholesterol across categories of total cardiovascular disease risk.

Special population and patients with underlying high CVD risks

Type 2 Diabètes patients:

Lifestyle intervention (diet, weight loss, increased physical activity) is recommend to improve the lipid profile in all patients with diabetes, initiation of statin is based on the cardiovascular risk rather than LDL-C level.

a. Patients with T2DM at very high risk, an LDL reduction at least 50% from baseline and LDL-C goal of <1.4mmol/L is recommended.
b. Patients with T2DM at high risk an LDL reduction of at least 50%from baseline and an LDL-C goal of <1.8mmol/L is recommended.
c. Statins are recommended in patients with T1DM who are at high or very high risk.
d. Patients with clinical CVD or over age 40 years: High intensity statin therapy should be added. LDL-C goal should be <2.6mmol/L.
e. Patients without clinical CVD and under age 40 years: Statin therapy can be considered to add in those with multiple (2 or more) CVD risk factors.
f. Triglyceride levels <150 mg/dL and HDL levels >40 mg/ for men and >50 mg/dL for women are preferable.
g. Pre-menopausal women with DM: Statin therapy is not recommended in pre-menopausal patients with DM who are considering pregnancy or not using adequate contraception.

Familial hypercholesterolemia:

Patients with familial hypercholesterolemia (FH) or other familial dyslipidemic conditions are characterized by extremely elevated levels of LDL-C are at high risk of early onset atherosclerotic cardiovascular disease. In general, homozygotes manifest the disease at a much earlier age than heterozygotes and the diseases being more severe.

Familial combined hyperlipidaemia (FCH) is a highly prevalent mixed dyslipidaemia (1:100–200) characterized

by elevated levels of LDL-C, TGs, or both, and is an important cause of premature CAD, early commencement of statin treatment is advised.

FH patient at very high risk, an LDL-C reduction of ≥50% from baseline and an LDL-C goal of <1.4 mmol/L should be considered, for primary prevention.

Diagnosis of FH should be considered in patients with CHD aged,55 years for men and ,60years for women, in people with relatives with premature fatal or non fatal CVD, in people with relatives who have tendon xanthomas, in people with severely elevated LDL-C(>5mmom/L in adult and >4mmol/L in children.) and in first degree relatives of FH patients.Treatment options available for FH are high-dose statin with ezetimibe, a PCSK9 inhibitor (antibody), or both if necessary. Heterozygous FH patients often have untreated LDC-C >190mg/dL. Intensive lipid lowering therapy is recommended.

Treatment of dyslipidaemia in older patients

Treatment with statins is recommended for primary prevention, according to the level of risk, in older people aged ≤75. A statin may be considered for primary prevention in older people aged >75, if at high risk or above.

Statin treatment should be started at a low dose if there is significant renal impairment and/or if there is potential for drug interactions, and then titrated upwards to achieve LDL-C treatment goals.

Patients with ACS

Patients who present with ACS are at increased risk of experiencing recurrent CV events. For these patients, lipid management should be undertaken in the context of a comprehensive global risk reduction strategy including lifestyle adaptations, risk factor management, and the implementation of cardioprotective drug strategies.

In all ACS patients without any contraindications or definite history of intolerance, it is recommended that high intensity statin therapy is initiated or continued as early as possible.

Lipid levels should be re-evaluated 4-6 weeks after ACS to determine whether a reduction of more than 50% from baseline and goal levels of LDL-C <1.4 mmol/L have been achieved.

If the LDL-C goal is not achieved after 4-6 weeks with maximally tolerated statin dose , combination with ezetimibe is recommended. Addition of PCSK9 inhibitor recommended if the LDL-C goal is still not achieved with above mentioned drug combinations. In patients with confirmed statin intolerance or in whom statin is contraindicated, ezetimibe should be considered.

Dyslipidemia in women

Statin treatment is recommended for primary prevention of ASCVD in high-risk women. Statins are recommended for secondary prevention in women with the same indications and goals as in men.

Lipid-lowering drugs should not be given when pregnancy is planned, during pregnancy, or during the breastfeeding period. However, for severe FH patients, bile acid sequestrants (which are not absorbed) and/or LDL apheresis may be considered

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II. 2. CARDIOVASCULAR RISK FACTORS AND LIFESTYLE MODIFICATIONS

Cardiovascular disease (CVD) risk factors, both traditional and novel emerging risk factors are responsible for the prevalence of CVD. Traditional risk factors, such as systemic hypertension and hypercholesterolemia, all described more than half a century ago, account for over 75% of CVD and attribute for almost more than 90% population attributable risk (PAR).

CVD risk factors are defined as characteristics, both modifiable and non-modifiable, that increase the risk of developing CVD. Advancing age, gender, family history and ethnicity are non-modifiable risk factors, while modifiable risk factors include; tobacco use, hypertension, diabetes mellitus, dyslipidemia, physical inactivity, obesity and nutrition.

Traditional risk factors were identified in the Framingham Heart Study, which were later incorporated into prediction equations in identifying individuals at higher risk, and also included depression, psychosocial stress, alcohol use and low socioeconomic status. Nontraditional risk factors include items that were not described in the original Framingham studies; and included lipid related factors, inflammation (such as C-reactive protein) / oxidative stress, endothelial dysfunction, thrombosis/ coagulation, arrhythmic risk, etc. (Table-1).

Table-1: Traditional and emerging cardiovascular risk factors

Traditional risk factors

Non-modifiable

Advancing age	Heredity or family history
Gender	Ethnicity or race

Modifiable

Major modifiable	Other modifiable
Hypertension	Depression
Dyslipidemia	Psychosocial stress
Tobacco use	Excessive alcohol use
Physical inactivity	Low socioeconomic status
Diabetes mellitus	
Unhealthy diet	
Obesity	

Novel emerging risk factors

Lipid related factors
Inflammation (such as C-reactive protein) / oxidative stress, endothelial dysfunction
Thrombosis/ coagulation
Arrhythmic risk
Others

Impact of Lifestyle Behaviors on Cardiovascular Risk

Modest alterations of lifestyle risk factors have powerful effects on cardiovascular risk. The approach should be both individual and community based. For effective lifestyle modification, screening, identification and continuous effort on the modification of cardiovascular risk factors is crucial. Tobacco use, excessive use of alcohol, unhealthy diet, insufficient physical activity, overweight, hypertension and dyslipidemia are commonly recognized cardiovascular risk factors in Nepal. The harmful effects of smoking and tremendous benefits of smoking prevention and cessation are well established. The increasing trend of CVD burden in Nepal is anticipated. However large-scale nationwide study on the identification and detection of CVD risk factors

including novel emerging risk factors is yet to be explored (Table-2).

Table-2 Parameters recommended for healthy cardiovascular health

■ No tobacco use. No excessive alcohol uses.
■ Ideal body weight, BMI < 23 kg/m2
■ Adequate physical exercise, at least 30 minutes brisk walk every day
■ Blood pressure <140/90 mmHg, if no other cardiovascular factors. Most ideal blood pressure < 120/80 mmHg
■ Fasting plasma glucose < 100 mg/dl
■ Total cholesterol < 200 mg/dl, LDL < 100 mg/dl, TG < 150 mg/dl and HDL > 40 mg/dl
■ Healthy eating habits, less carbohydrate (rice, potato etc) and sugar, and more vegetable, fruits and adequate protein

Proper implementation of lifestyle modification for preventive management should be reinforced at various levels

Population level : Mass media messages

Community level: Use of community health workers, promote awareness

Health post level: WHO SCORE risk charts for screening, referral of high-risk cases to higher center

Primary Health Care level: Screening, treatment decisions guided by absolute CVD risk and management of CVD.

Secondary and above: Treatment and control of CVD risk factors with comorbidities and complications

Policy Level: Mass Awareness government program using social media regarding CVD risk factor modification and promotion of

- Physical activity and Exercise
- Diet modification/ heart healthy eating
- Healthy weight or weight reduction
- Quit smoking and tobacco related products
- Avoid or reduce intake of alcohol
- Stress Management

- Ban on Trans fats with replacement of polyunsaturated fats
- Reduce salt in manufactured food products and discourage discretionary use
- Discourage consumption of unhealthy foods including restrictions on marketing to children and sales in schools

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UNIT - III

Valvular Heart Disease

III. 1. ACUTE RHEUMATIC FEVER

Background

Acute Rheumatic Fever (ARF) is the result of bacterial throat infection caused by B-hemolytic group A streptococcus (GAS). It is a delayed autoimmune response to an untreated GAS infection. ARF develops about 2-3 weeks after the onset of a GAS infection. In ARF, an abnormal immune response leads to an acute inflammatory illness that most commonly affects the joints, central nervous system, heart, and/or skin. The illness usually lasts up to 3 months and resolves without treatment. With treatment the symptom resolves within 1-2 weeks. ARF can occur in children who continue to be exposed to high levels of GAS in their environment.

Diagnosis

In ARF, the patient complains of fever accompanied by pain and swelling in more than one joints (particularly the large joints). Pain may shift from one joint to another. In addition, some patients may present with involuntary movements of the limbs (Chorea), skin rashes (Erythema Marginatum) and Subcutaneous Nodules.

Diagnosis of ARF is based on Revised Jones Criteria 2015, which include major manifestations, minor manifestations, and evidence of a preceding GAS infection. As Nepal falls on moderate to high risk population category (RHD prevalence more than 1/1000 children), the diagnostic criteria are applied as follows:

Major manifestations

1. Carditis (clinical and/or subclinical diagnosed with the use of echocardiography)
2. Monoarthritis or Migratory Polyarthritis
3. Polyarthralgia (only after excluding other causes)
4. Sydenham's Chorea (Involuntary jerky movements)
5. Erythema Marginatum(non itching skin rashes)
6. Subcutaneous nodules

Minor manifestations

1. Fever (more than or equal to 38 degree C)
2. Monoarthralgia
3. Prolonged P-R interval in ECG
4. Increased acute phase reactants (raised ESR more than or equal to 30mm/h and/or raised CRP more than or equal to 3.0 mg/dl)

Evidence of preceding GAS Infection

1. GAS on throat swab (positive culture)
2. Raised Anti-Streptolysin O titer (ASOT)
3. Raised Anti-deoxyribonuclease B (Anti-DNase B)
4. Positive quick strep test

The diagnosis of ARF can be confirmed in the presence of following situations

1. Two major manifestations and any evidence of preceding GAS infection

OR

2. One major and two minor manifestations and any evidence of preceding GAS infection

OR

3. Presence of Rheumatic Chorea (Sydenham's Chorea)

Treatment of the acute illness

Treatment of ARF includes antibiotic to eradicate GAS

infection and prevent future reinfection, anti-inflammatory therapy for symptomatic relief, and management of heart failure if present and other supportive treatment.

Antibiotic

All cases of ARF should receive

- A single injection of Benzathine penicillin G (BPG) (1.2 million units for > 30kg 0.6 million units if <30 kg body weight), OR
- Oral Penicillin V (Children 250 mg QID, Adults 500 mg TDS) for 10 days OR Erythromycin if allergic to penicillin

Aspirin (Aspirin may hide symptoms of polyarthritis and fever. Paracetamol can be used until the diagnosis is confirmed). The usual dose of Aspirin is 80-100 mg/kg/day for children and 6-8 gm/day for adults in 4 divided doses (QID) for 4 weeks. Taper the dose once symptoms are resolved and the acute phase reactants (ESR, CRP) decrease. Total duration of treatment is 12 weeks or should be individualized depending upon the severity of illness.

Naproxen: If Aspirin intolerance is detected – 10-20mg/kg/day

Steroids (prednisolone):

Prednisolone is indicated in following situations:

1. Patients who do not tolerate aspirin.
2. Patients who do not improve with aspirin.
3. Patients with moderate to severe carditis

Dose of steroid is 1-2mg/kg/day for 2 weeks then taper by 5mg every 2-3 days. While tapering steroid overlap with aspirin (initial dose 60mg/kg/day)

Heart failure should be treated according to the standard guidelines with anti-failure medications (e.g. Diuretics, ACEI, B-Blocker).Limitation of physical activity and rest is recommended until symptoms get better. Fluid and salt restriction is advised.

Anti-coagulant is indicated if atrial fibrillation is present

Mild-moderate cases of Chorea do not need medication. For severe cases Haloperidol or Carbamazepine or Valproic acid can be given.

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III. 2. PRIMARY AND SECONDARY PREVENTION OF RHEUMATIC HEART DISEASE

Rheumatic Heart Disease (RHD) is a preventable disease. The first episode of ARF can be prevented by treating GAS throat infection with antibiotic. In patients who already have ARF, recurrent episodes of ARF can be prevented with long-term Penicillin prophylaxis at regular intervals. This can prevent the progression of ARF to RHD.

ARF and RHD can be prevented at population level by sustainable control strategies. For regions with high rates of disease, WHO recommended a dedicated, register based program, which focuses on identifying cases, delivering regular prophylaxis, treatment and education.

Primary Prevention of Acute Rheumatic Fever

The primary prevention of ARF is defined as the adequate antibiotic therapy of GAS throat infection to prevent an initial attack of ARF.

Effective antibiotic therapy eradicates group A streptococcus from the throat and can prevent ARF, if therapy is started within nine days after the onset of symptoms.

Tonsillopharyngitis: Bacterial or Viral?

It is very important to differentiate bacterial and viral tonsillopharyngitis before initiating treatment. Following are the differentiating signs and symptoms. (Table 1)

Table 1. Tonsillopharyngitis

Type	Signs and Symptoms
GAS	Throat pain, Difficulty swallowing, Enlarged and red tonsils, Enlarged lymph nodes of neck, Enlarged tonsils with white or yellow spots, Fever, absence of cough, Headache
Viral	Cough, Sneezing, Runny Nose, Fever

Tonsillopharyngitis management protocol in low resources settings

1. Establish Clinical Diagnosis of GAS throat infection on the basis of signs and symptoms (Table 1). Although Throat swab culture is a gold standard confirmatory test, it is not feasible in low income countries including Nepal. There is no role of ASO titre in the diagnosis of acute GAS tonsillopharyngitis as the titers increase only 7 to 14 days after the onset of infection.
2. Treat definite, borderline (doubtful) bacterial and mixed (bacterial plus viral) throat infection with antibiotic. (Table 2)
3. Viral throat infection should not be treated with antibiotic.

Table 2: Primary prevention of rheumatic fever (treatment of streptococcal tonsillopharyngitis)

Agent*	Dose	Mode	Duration
Penicillin			
Penicillin V	Children <27 kg : 250 mg three times daily Adolescents and adults: 500 mg two to three times daily	Oral	10 days
Amoxicillin	50mg/kg (maximum 1 g) once daily	Oral	10 days
Injection Benzathine Penicillin G	600,000 IU for patients <27 kg 1,200,000 IU for patients >27 kg	IM	Single dose

Cephalosporins			
Cephalexin	Adult: 500mg twice daily Child: 25-50mg/kg twice daily	Oral	10days
Cefuroxime	Adult: 250mg twice daily Child: 20mg/kg/d divided into 2 doses	Oral	10days
Cefpodoxime	>12years: 100mg twice daily <12 years: 5mg/kg twice daily	Oral	5 to 10days
Allergic to penicillin			
Clindamycin	20mg/kg/d divided into 3 doses (maximum 1.8g/d)	Oral	10 days
Azithromycin	12 mg/kg once daily (maximum 500 mg)	Oral	5 days
Clarithromycin	15 mg/kg/d divided into 2 doses (max. 250 mg bid)	Oral	10 days

Secondary Prevention of ARF

Secondary prevention of ARF is defined as the continuous administration of specific antibiotic to patients with a previous attack of ARF, or well documented RHD. (Table 3) The purpose is to prevent colonization or infection of the throat with group A ß-hemolytic streptococcus (GABHS) and the development of recurrent attack of ARF. Secondary prophylaxis is mandatory for all patients who have had ARF, whether or not they have residual RHD.

- Secondary prophylaxis with Penicillin should be continued during pregnancy.

  There is no evidence of teratogenicity associated with Benzathine Penicillin G(BPG).
- Since ARF is endemic in Nepal, Penicillin prophylaxis once in three weeks is recommended.

Table 3: Secondary Prevention of acute rheumatic fever

Antibiotic	Mode of administration	Dose
Benzathine Penicillin G	Intramuscular injection	For adults and children >27kg in weight: 1200000 units. For children <27kg in weight: 600000 IU.
Penicillin V.	Oral	<27 kg: 125 mg twice daily. >27 kg: 250mg twice daily.
Erythromycin (for individuals allergic to penicillin)	Oral	<27 kg: 125 mg twice daily. >27 kg: 250mg twice daily.
Sulfadiazine	Oral	<27kg: 500mg once daily >27 kg: 1gm once daily
Azithromycin	Oral	6mg/kg once daily

Table 4: Duration of Secondary Prevention of Rheumatic Fever

Category	Duration after Last Attack
Rheumatic fever without carditis	5 years or until 21 years of age (whichever is longer)
Rheumatic fever with carditis but no residual heart disease (no valvular disease)	10 years or until 21 years of age (whichever is longer)
Rheumatic fever with carditis and residual heart disease (persistent valvular disease)	until 40 years of age or lifelong
After valve surgery for RHD	Until 40 years of age or lifelong

Issues and Challenges in Secondary prevention delivery

1. **Penicillin allergy and penicillin skin testing (PST).**

   The incidences of allergic and anaphylactic reactions to Benzathine Penicillin G injection are reported to be 3.2% and 0.2% respectively and the fatal reactions are rare. The long-term benefits of Benzathine Penicillin G therapy in preventing RF far outweigh the risk of a serious allergic reaction. Skin test is recommended before first penicillin injection, with change in batch number and brand.

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III. 3. MITRAL VALVE DISEASE

Mitral stenosis (MS)

The obstruction to blood flow between left atrium (LA) and left ventricle (LV), is caused by narrowing of mitral valve. Mostly the cause of MS is previous rheumatic carditis. Involvement of mitral valve is present in 60 % of the RHD cases. Multiple valve involvement occurs in about of 36% of the cases. Isolated MS constitutes about 25% of the total RHD cases. Other rare cause of mitral stenosis is annular calcification, congenital mitral stenosis, and rheumatoid arthritis. The combination of commissural fusion, leaflet contracture and fusion of chordae tendineae and tethering of the leaflets results in narrowing of valve opening.

Pathophysiology: Obstruction of flow from LA to LV → pressure gradient between two chambers increases with increase in heart rate and cardiac output → symptoms increase simultaneously → LA gradually increase in size → gradually pulmonary venous pressure and PA pressure rises → RV enlarges causing systemic venous congestion.

Physical findings: Loud S1, opening snap and mid-diastolic rumbling murmur are the typical auscultatory features in MS. The murmur is best heard with bell of stethoscope applied to apical area with patient lying supine on left lateral decubitus position.

Chest x-ray: Straightening of the left heart border, double right heart border, splaying of carina, features of pulmonary venous congestion and pulmonary artery hypertension.

ECG: Classical P Mitrale where P wave is notched and broad in lead II and is biphasic, however, this finding is infrequently detected. Atrial fibrillation (Af) is common

Echocardiogram: 2D echo allows the evaluation of mitral valve anatomy and assessment of severity based on mitral valve area and gradient. Clinically significant mitral stenosis is defined by a mitral valve area (MVA) ≤1.5 cm^2.

Stages of mitral stenosis

Stage	Definition	Valve anatomy	Valve hemodynamics	Hemodynamic consequences	Symptoms
A	At risk of MS	• Mild valve doming during diastole	Normal transmitral flow velocity	None	None
B	Progressive MS	• Rheumatic valve changes with commissural fusion and diastolic doming of the mitral valve leaflets • Planimetered MVA >1.5 cm2 • (MVA ≤1 cm2 with very severe MS)	• Increased transmitral flow velocities • MVA >1.5 cm^2 • Diastolic pressure half-time <150 ms	• Mild-to-moderate LA enlargement • Normal pulmonary pressure at rest	None
C	Asymptomatic, severe MS	• Rheumatic valve changes with commissural fusion and diastolic doming of the mitral valve leaflets • Planimetered MVA ≤1.5 cm^2 • (MVA ≤1 cm^2 with very severe MS)	• MVA ≤1.5 cm^2 • (MVA ≤1 cm^2 with very severe MS) • Diastolic pressure half-time ≥150 ms • (Diastolic pressure half-time ≥220 ms with very severe MS)	• Severe LA enlargement • Elevated PASP >30 mmHg	None

D	Symptomatic severe MS	• Rheumatic valve changes with commissural fusion and diastolic doming of the mitral valve leaflets • Planimetered MVA ≤1.5 cm2	• MVA ≤1.5 cm2 • (MVA ≤1 cm2 with very severe MS) • Diastolic pressure half-time ≥150 ms • (Diastolic pressure half-time ≥220 ms with very severe MS)	• Severe LA enlargement • Elevated PASP >30 mmHg	• Decreased exercise tolerance • Exertional dyspnea

The transmitral mean pressure gradient should be obtained to further determine the hemodynamic effect of the MS and is usually >5 to 10 mmHg in severe MS; however, due to the variability of the mean pressure gradient with heart rate and forward flow, it has not been included in the criteria for severity.

LA: left atrial; LV: left ventricular; MS: mitral stenosis; MVA: mitral valve area; PASP: pulmonary artery systolic pressure.

Mitral regurgitation (MR)

Common causes of MR are rheumatic heart disease, mitral valve prolapse, ischemic heart disease with papillary muscle involvement and myxomatous mitral valve disease.

Chronic MR produces volume overload to left atrium. Left atrial and ventricular dilatation occurs slowly, whereas acute MR causes rapid rise in LA pressure and leads to pulmonary edema.

Mitral valve prolapse is associated with an increased incidence of arrhythmias.

Signs and symptoms: Symptoms of MR include exertional palpitation, dyspnea, fatigue and pedal edema. Acute

regurgitation causes pulmonary edema. Signs of MR include Af, displaced apex beat, pansystolic murmur and crepitations.

ECG usually shows AF, features of enlarged LA and LV.

Chest Xray shows enlarged LA and LV and pulmonary venous congestion

Echo shows dilated LA and LV and detectable regurgitant jet in color Doppler

Management

Diuretics relieves pulmonary congestion, peripheral edema and symptoms of dyspnea. Digitalis, beta-blocker and diltiazem is useful to control ventricular rate in patients with AF. Anticoagulation is indicated in the patient with AF and LA/LAA clot.

Mitral Stenosis

The type of treatment (PTMC or surgery), as well as its timing, should be decided based on clinical characteristics, anatomy of the valve and subvalvular apparatus, and local expertise. In general, indication for intervention should be limited to patients with clinically significant (severe) rheumatic mitral stenosis (valve area less than or equal to1.5 cm2.

Asymptomatic patient with MVA of 1cm2 or less and symptomatic patient of MVA less than 1.5 cm2 with suitable valve anatomy should be subjected to percutaneous transvenous mitral commissurotomy (PTMC) if not contraindicated. Contraindication for PTMC are severely calcified valve, LA/LAA clot and more than mild MR.

For patient with severe MS or symptomatic moderate MR and calcified valve, more than moderate MR, mitral valve replacement (MVR) is recommended.

Mitral Regurgitation

Primary severe symptomatic MR with LVEF more than 30% is the indication for mitral valve repair/replacement. Similarly asymptomatic severe MR with LVESD greater than or equal to 40mm and/or LVEF less than or equal to

60%. Mitral regurgitation of less severity can be treated medically with diuretics, vasodilators, ACE inhibitors and digoxin as indicated. When MR is due to myocardial diseases, treatment is done accordingly.

Stages of primary MR

Grade	Definition	Valve anatomy	Valve hemodynamics*	Hemodynamic consequences	Symptoms
A	At risk of MR	• Mild mitral valve prolapse with normal coaptation • Mild valve thickening and leaflet restriction	• No MR jet or small central jet area <20% LA on Doppler • Small vena contracta <0.3 cm	None	None
B	Progressive MR	• Severe mitral valve prolapse with normal coaptation • Rheumatic valve changes with leaflet restriction and loss of central coaptation • Prior IE	• Central jet MR 20 to 40% LA or late systolic eccentric jet MR • Vena contracta <0.7 cm • Regurgitant volume <60 mL • Regurgitant fraction <50% • ERO <0.40 cm2 • Angiographic grade 1-2+	• Mild LA enlargement • No LV enlargement • Normal pulmonary pressure	None

C	Asymptomatic severe MR	• Severe mitral valve prolapse with loss of coaptation or flail leaflet • Rheumatic valve changes with leaflet restriction and loss of central coaptation • Prior IE • Thickening of leaflets with radiation heart disease	• Central jet MR >40% LA or holosystolic eccentric jet MR • Vena contracta ≥0.7 cm • Regurgitant volume ≥60 mL • Regurgitant fraction ≥50% • ERO ≥0.40 cm2 • Angiographic grade 3 to 4+	• Moderate or severe LA enlargement • LV enlargement • Pulmonary hypertension may be present at rest or with exercise • C1: LVEF >60% and LVESD <40 mm • C2: LVEF ≤60% and LVESD ≥40 mm	None
D	Symptomatic severe MR	• Severe mitral valve prolapse with loss of coaptation or flail leaflet • Rheumatic valve changes with leaflet restriction and loss of central coaptation • Prior IE • Thickening of leaflets with radiation heart disease	• Central jet MR >40% LA or holosystolic eccentric jet MR • Vena contracta ≥0.7 cm • Regurgitant volume ≥60 mL • Regurgitant fraction ≥50% • ERO ≥0.40 cm2 • Angiographic grade 3 to 4+	• Moderate or severe LA enlargement • LV enlargement • Pulmonary hypertension present	• Decreased exercise tolerance • Exertional dyspnea

ERO: effective regurgitant orifice; IE: infective endocarditis; LA: left atrium/atrial; LV: left ventricular; LVEF: left ventricular ejection fraction; LVESD: left ventricular end-systolic dimension; MR: mitral regurgitation.

** Several valve hemodynamic criteria are provided for assessment of MR severity, but not all criteria for each category will be present in each patient. Categorization of MR severity as mild, moderate, or severe depends on data quality and integration of these parameters in conjunction with other clinical evidence.*

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III. 4. AORTIC VALVE DISEASES

Aortic Valve Stenosis (AS)

Calcific aortic stenosis (congenital) is secondary to heavy dystrophic calcification of congenitally abnormal valve which is slowly progressive and symptoms start around 5th-6th decade of life. Males are more prone than females. Bicuspid aortic valve(BAV) accounts to 0.5-2% of total population. Degenerative AS appears above the age of 65 years of age. Usually associated with hypertension, dyslipidemia, diabetes mellitus and smoking. Rheumatic AS may have lesser incidence worldwide, but has been the preponderance in our part of the world.

Clinical Features

Usually, patients are asymptomatic and most patients are diagnosed incidentally. Patients present with angina pectoris, syncope and dyspnea. In clinical finings, patient have small volume and slow upstroke arterial pulse with pulsus parvus et tardus. On auscultation patient presents with aortic ejection systolic murmur at right 2nd intercostal space radiating to carotids and expiratory splitting of S2.

ECG shows left ventricular hypertrophy (LVH) with or without T-wave inversion in V6. Chest X-ray shows features of LVH and sometimes aortic calcification. Graded exercise testing is not risky for asymptomatic AS but not advised for symptomatic patients. Echocardiography is done to measure AV peak gradient(PG), mean gradient(MG), area and jet velocity. Severity is categorized as following table.

Stage	Description and symptoms	Valve anatomy		Hemodynamic consequences		LVEF
		Ca++	Mobility	Key criteria	Additional measures	
A	At risk (asymptomatic)	+	Normal	Aortic Vmax <2 m/s		Normal
B	Progressive (asymptomatic)	++	↓ to ↓↓	Mild AS: Aortic Vmax 2.0 to 2.9 m/s or mean ΔP <20 mmHg Moderate AS: Aortic Vmax 3.0 to 3.9 m/s or mean ΔP 20 to 39 mmHg		Normal
C1	Asymptomatic severe AS with normal LVEF	+++	↓↓↓	Aortic Vmax ≥4 m/s or mean ΔP 40 mmHg (severe) Aortic Vmax ≥5 m/s or mean ΔP ≥60 mmHg (very severe)	AVA typically ≤1 cm^2 (or AVAi ≤0.6 cm2/m^2)	Normal
C2	Asymptomatic severe AS with low LVEF	+++	↓↓↓	Aortic Vmax ≥4 m/s or mean ΔP ≥40 mmHg (severe)	AVA typically ≤1 cm^2 (or AVAi ≤0.6 cm^2/m^2)	<50%
D1	Symptomatic severe high-gradient AS	++++	↓↓↓↓	Aortic Vmax ≥4 m/s or mean ΔP ≥40 mmHg	AVA typically ≤1 cm^2 (or AVAi ≤0.6 cm^2/m^2) but may be larger with mixed AS/AR	Normal or ↓
D2	Symptomatic severe low-gradient AS with low LVEF	++++	↓↓↓↓	Resting AVA ≤1 cm^2 with aortic Vmax<4 m/s or mean ΔP <40 mmHg	Dobutamine stress shows AVA ≤1 cm^2 with Vmax ≥4 m/s at any flow rate	<50%

D3	Symptomatic severe low-gradient AS with normal LVEF	++++	↓↓↓↓	AVA ≤1 cm2 with aortic Vmax <4 m/s or mean ΔP <40 mmHg Measured when the patient is normotensive (systolic BP <140 mmHg)	Indexed AVA ≤0.6 cm2/m2 and stroke volume index <35 mL/m2	Normal

Ca++: calcification; LVEF: left ventricular ejection fraction; +: present, with severity indicated by number of symbols; Vmax: maximum transvalvular aortic velocity; ↓: decreased, with degree indicated by number of arrows; AS: aortic stenosis; ΔP: pressure gradient; AVA: aortic valve area; AVAi: valve area indexed for body surface area; AR: aortic regurgitation; BP: blood pressure.

The average survival after angina and syncope is 3 years and 1.5 years after patient has developed heart failure.

Treatment

Indications for aortic valve replacement in patients with aortic stenosis

Arrows show the decision pathways that result in a recommendation for AVR. Periodic monitoring is indicated for all patients in whom AVR is not yet indicated, including those with asymptomatic AS (stage D or C) and those with low gradient AS (stage D2 or D3) who do not meet the criteria for intervention.

For the strength of recommendations: Class I means the procedure/treatment should be performed/administered. Class IIa means it is reasonable to perform procedure/administer treatment. Class IIb means the procedure/treatment may be considered. Class III means that procedure or treatment is not useful/effective and may be harmful.

For the level of evidence: Level A means multiple populations evaluated; data derived from multiple randomized clinical trials or meta-analyses. Level B means limited populations evaluated; data derived from a single randomized trial or nonrandomized studies. Level C means very limited populations evaluated; only consensus opinion of experts, case studies, or standard of care.

AS: aortic stenosis; AVA: aortic valve area; AVR: aortic valve replacement by either surgical or transcatheter approach; BP: blood pressure; DSE: dobutamine stress echocardiography; ETT: exercise treadmill test; LVEF: left ventricular ejection fraction; ΔPmean: mean pressure gradient; Vmax: maximum velocity.

** AVR should be considered with stage D3 AS only if valve obstruction is the most likely cause of symptoms, stroke volume index is <35 mL/m2, indexed AVA is ≤0.6 cm2/m2, and data are recorded when the patient is normotensive (systolic BP <140 mmHg).*

Asymptomatic patients should be kept on regular follow-up. Hypertensive severe AS should be treated with titred dosing of medication to control high blood pressure and statin should be considered to prevent the cardiovascular events. Surgical intervention is considered in patients with Stage C and D disease with variable conditions. In patients under the age of 50 years is advised with metallic prosthesis, whereas patients between the age of 50-65 years of age can be considered for metallic or bioprosthetic valve. Patients above the age of 65 years should be considered for bioprosthetic valve.

Aortic Valve Regurgitation (AR)

Aortic valve regurgitation is also known as aortic incompetence or aortic insufficiency.

Morphology

Acute AR is usually caused by valve pathology itself, as in valve endocarditis, or secondary to aortic pathology. It can also occur as an iatrogenic complication or due to chest trauma. Chronic AR are secondary to aortic root pathology, which can be due to Marfan's syndrome, Loeys-Dietz syndrome, Ehler-Danlos Syndrome, anulo-aortic ectasia. It is also associated with arteriosclerotic or syphilitic ascending aortic aneurysm, aortitis secondary to rheumatoid arthritis, ankylosing spondylitis or Reiter disease. Rheumatic AR, congenital aortic valve disease, floppy aortic valve and trauma are other causes of AR.

Clinical Features

Most patients are asymptomatic. Patients present with palpitation, shortness of breath and angina. On physical examination the left ventricular apical impulse is displaced and hyperdynamic with early diastolic murmur at aortic and neo aortic area. Patient with significant AR has peripheral signs of aortic regurgitation. Chest X-ray will reveal LV type cardiomegaly with features of pulmonary venous hypertension. ECG will reveal LV enlargement. Echocardiography helps in determining the severity of AR and LV function.

Stages of chronic aortic regurgitation in adults

Grade	Definition	Valve anatomy	Valve hemodynamics*	Hemodynamic consequences	Symptoms
A	At risk of AR	• Bicuspid aortic valve (or other congenital valve anomaly) • Aortic valve sclerosis • Diseases of the aortic sinuses or ascending aorta • History of rheumatic fever or known rheumatic heart disease • IE	• AR severity: None or trace	None	None

B	Progressive AR	• Mild to moderate calcification of a trileaflet valve bicuspid aortic valve (or other congenital valve anomaly) • Dilated aortic sinuses • Rheumatic valve changes • Previous IE	» Mild AR: • Jet width <25% of LVOT; • Vena contracta <0.3 cm; • RVol <30 mL/beat; • RF <30%; • ERO <0.10 cm2; • Angiography grade 1+ » Moderate AR: • Jet width 25 to 64% of LVOT; • Vena contracta 0.3 to 0.6 cm; • RVol 30 to 59 mL/beat; • RF 30 to 49%; • ERO 0.10 to 0.29 cm2; • Angiography grade 2+	• Normal LV systolic function • Normal LV volume or mild LV dilation	None
C	Asymptomatic severe AR	• Calcific aortic valve disease • Bicuspid valve (or other congenital abnormality) • Dilated aortic sinuses or ascending aorta • Rheumatic valve changes • IE with abnormal leaflet closure or perforation	**» Severe AR:** • Jet width ≥65% of LVOT; • Vena contracta >0.6 cm; • Holodiastolic flow reversal in the proximal abdominal aorta • RVol ≥60 mL/beat; • RF ≥50%; • ERO ≥0.3 cm2; • Angiography grade 3+ to 4+; • In addition, diagnosis of chronic severe AR requires evidence of LV dilation	• C1: Normal LVEF (≥50%) and LVESD ≤50 mm • C2: Abnormal LV systolic function with depressed LVEF (<50%), LVESD >50 mm, or indexed LVESD >25 mm/m2	• None; exercise testing is reasonable to confirm symptom status

D	Symptomatic severe AR	• Calcific valve disease • Bicuspid valve (or other congenital abnormality) • Dilated aortic sinuses or ascending aorta • Rheumatic valve changes • Previous IE with abnormal leaflet closure or perforation	» **Severe AR:** • Jet width ≥65% of LVOT; • Vena contracta >0.6 cm; • Holodiastolic flow reversal in the proximal abdominal aorta; • RVol ≥60 mL/beat; • RF ≥50%; • ERO ≥0.3 cm2; • Angiography grade 3+ to 4+; • In addition, diagnosis of chronic severe AR requires evidence of LV dilation	• Symptomatic severe AR may occur with normal systolic function (LVEF ≥50%), mild to moderate LV dysfunction (LVEF 40 to 50%), or severe LV dysfunction (LVEF <40%) • Moderate to severe LV dilation is present	• Exertional dyspnea or angina or more severe HF symptoms

AR: aortic regurgitation; IE: infective endocarditis; LVOT: left ventricular outflow tract; RVol: regurgitant volume; RF: regurgitant fraction; ERO: effective regurgitant orifice; LV: left ventricular; LVEF: left ventricular ejection fraction; LVESD: left ventricular end-systolic dimension; HF: heart failure.

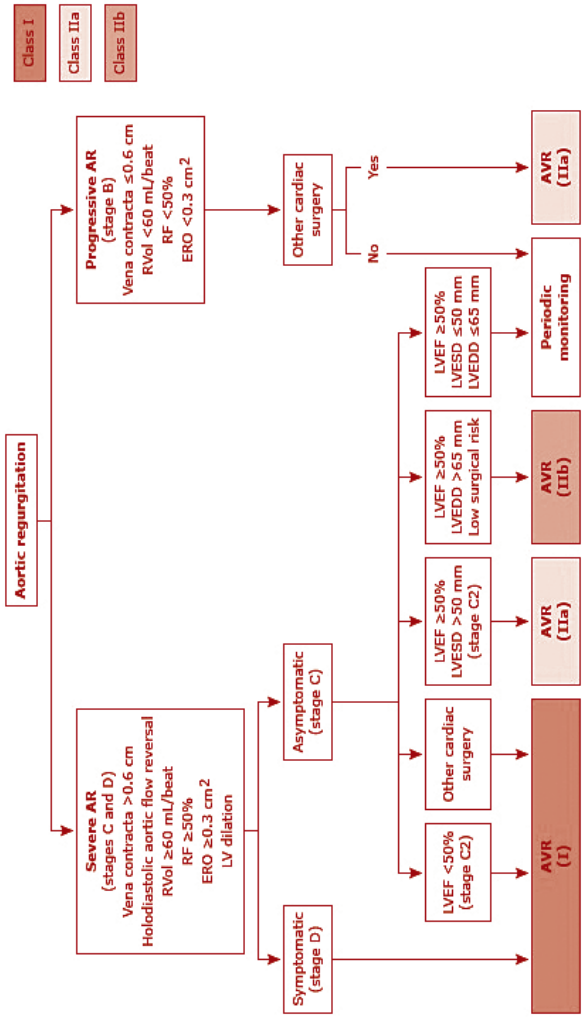
Original figure modified for this publication. Nishimura RA, Otto CM, Bonow RO, et al. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2014; e82. Table used with the permission of Elsevier Inc. All rights reserved.

Information still current as of 2021, as found in: Otto CM, Nishimura RA, Bonow RO, et al. 2020 ACC/AHA guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation 2021;143:e72.

Some studies have found 81% survival rate at 5 years without surgical treatment.

Treatment

Indications for AVR for chronic AR



For the strength of recommendations: Class I means the procedure/treatment should be performed/administered. Class IIa means it is reasonable to perform the procedure/administer treatment. Class IIb means the procedure/treatment may be considered. Class III means that procedure or treatment is not useful/effective and may be harmful.

For the level of evidence: Level A means multiple populations evaluated; data derived from multiple randomized clinical trials or meta-analyses. Level B means limited populations evaluated; data derived from a single randomized trial or nonrandomized studies. Level C means very limited populations evaluated; only consensus opinion of experts, case studies, or standard of care.

AR: aortic regurgitation; AVR: aortic valve replacement (valve repair may be appropriate in selected patients); ERO: effective regurgitant orifice; LV: left ventricular; LVEDD: left ventricular end-diastolic dimension; LVEF: left ventricular ejection fraction; LVESD: left ventricular end-systolic dimension; RF: regurgitant fraction; RVol: regurgitant volume.

Vasodilators as ACE-I's and ARB's helps to control hypertension and helps alleviate symptoms. But surgery is advised for patients in Stage C and D. Choice of prosthesis depends on the age and requirement of anticoagulation for any other cardiac problems. Age variable choice of prosthetic heart valve remains same as in aortic stenosis surgical management.

Bicuspid Aortic Valve

Morphology

It's one of the common congenital cardiac anomalies. Males have higher incidence than females at 3:1 ratio. Aortic root dilatation is almost twice higher than in tricuspid aortic valve. These patients are 9 times more prone to aortic dissection. Cusp calcification progresses to aortic stenosis by the age of 40. 12-37% patients develop moderate or greater aortic stenosis. Aortic root dilation is almost twice higher than in tricuspid aortic valve. 13-30% patients develop moderate or greater aortic regurgitation.

Treatment

Surgical treatment mainly depends on the findings of the aortic sinus and the ascending aorta. Significant aortic valve pathology without significant aortic sinus or ascending aortic dilatation will require valve repair or replacement surgery and vigilant monitoring of the aorta post-operatively. Ascending aortic replacement is done if the aortic sinus or ascending aorta is dilated more than 4.5cm.

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III. 5. TRICUSPID AND PULMONARY VALVE DISEASE

Tricuspid Valve Disease

Background. Tricuspid valve disease can be further classified into tricuspid regurgitation(TR), tricuspid stenosis(TS) and tricuspid atresia(TA).

TR is the most common abnormality of tricuspid valve. A small degree of TR is detected in approximately 70% of normal adults in echocardiography. It is considered physiological and does not produce any sign and symptoms even in the long run. TR can be further classified into primary TR and secondary TR. Abnormal degree of TR are mostly secondary due to annular dilatation in the setting of RV volume and pressure overload because of other cardiac conditions like rheumatic mitral valve disease, pulmonary hypertension, left to right shunts etc. Examples of such cases include involvement of tricuspid valve in rheumatic heart disease, carcinoid syndrome, congenital abnormality of tricuspid valve like Ebstein's anomaly etc. Irrespective of etiology, Severe TR is associated with reduced survival.

TS is relatively uncommon valvular abnormality, which occurs most commonly in association with other valvular lesions, particularly in patients with rheumatic heart disease. Pure TS is rare, concomitant TR is also present in majority of the cases. Other causes of tricuspid stenosis include congenital tricuspid valve disease, carcinoid syndrome, infective endocarditis, fibrosis of tricuspid valve apparatus associated with pacemaker leads, hypereosinophilic syndrome etc.

TA is a cyanotic congenital heart disease characterized by congenital absence of tricuspid valve resulting in no direct communication between right atrium and right ventricle.

Diagnosis

Tricuspid regurgitation. There are no specific symptoms associated with mild or moderate TR. With severe TR, there may be a sensation of pulsation in the neck and symptoms of right heart failure like peripheral edema, ascites, hepatomegaly etc. There will be a distinct regurgitation wave in jugular vein. On auscultation, TR is associated with a holosystolic murmur best heard at the right or left mid sternal border at subxiphoid area. Echocardiography is the main diagnostic modality for identification of TR and evaluation of its causes, severity and pulmonary arterial pressure. Severe TR is identified using the following criteria: central jet area >10 cm^2, vena contracta width >7 mm and dense triangular doppler CW jet contour.

Tricuspid stenosis. Patients with TS complain of fluttering in the neck and abdominal discomfort due to venous congestion. Physical findings include jugular venous distention, hepatomegaly, ascites, peripheral edema. A low frequency diastolic murmur is heard at the lower left sternal border. The diagnosis is usually confirmed by echocardiography, which shows thickened tricuspid valve leaflets with reduced mobility.

Tricuspid Atresia. Typical symptoms of tricuspid atresia are cyanosis and heart murmur. Patients present within one month of age. Other manifestations and clinical course vary depending on the presence of associated cardiac lesions .On auscultation, single heart sound is heard. Definite diagnosis is generally made by echocardiography which includes both anatomic and hemodynamic evaluation.

Management and Prognosis.

Tricuspid regurgitation. Small degree of TR with structurally normal valve leaflets does not need any further evaluation and follow up. For other conditions with significant TR, management of TR is based upon the presence and extent of symptoms and signs of heart failure, severity of TR, extent of associated abnormalities like other valve disease and pulmonary hypertension. In case of Ebstein's anomaly with severe TR, patients should be evaluated every 6-12 months if they are asymptomatic. Surgery is indicated if signs and

symptoms of right heart failure appear. Symptomatic newborns with Ebstein's who have cyanosis and heart failure should be managed medically with supportive therapy until pulmonary vascular resistance drops and becomes normal with time and surgery should be delayed as much as possible. However, symptomatic older children with cyanosis and heart failure should undergo surgical repair.

Management of TR include:

A. Medical Management:
    (a) Treatment of heart failure: Diuretic, including loop diuretic and aldosterone antagonists are used to treat volume overload. If patient also has concomitant left sided heart disease, standard therapy including beta blockers and ACE-inhibitor/ARB are also recommended.
    (b) Treatment of cause of pulmonary hypertension: This includes treatment that reduces secondary TR like PTMC in case of mitral stenosis and pulmonary thrombendarteriectomy in cases of chronic thromboembolic pulmonary hypertension.

B. Tricuspid valve surgery : For patients undergoing, left sided valve surgery, concomitant tricuspid valve repair is suggested if there is significant tricuspid annular dilatation. This is particularly important in our set up as many patients who have undergone left sided heart valve surgery, have significant morbidity or mortality due to unrepaired or sub optimally repaired tricuspid valve during surgery. The optimum timing of isolated tricuspid valve surgery in case of functional TR is not well established.

Tricuspid stenosis. For patients with isolated severe TS with low to moderate surgical risk or those having concomitant TR, tricuspid valve surgery is preferred. For patients with isolated symptomatic severe TS with high surgical risk, balloon valvotomy is reasonable approach. For patients requiring tricuspid valve surgery, tricuspid valve repair is attempted if possible but valve replacement is preferred if there is significant valvular or sub valvular disease. A bio prosthesis is usually preferred over a mechanical prosthesis

as there is higher risk of thrombosis with mechanical valve. In hospital mortality of tricuspid valve surgery is around 10%.

Tricuspid atresia. The main treatment of tricuspid atresia is surgery after initial medical management. Type of surgery may depend on associated congenital heart defects. Surgical management of tricuspid atresia consists of three staged palliative procedures performed respectively in neonatal period, three to six months of age and two to three years of age. First stage is either B-T shunt or PA banding depending on decreased or increased pulmonary blood flow. Second stage is Glenn procedure and third stage is Fontan procedure. Without surgery, mortality is about 75% in one year. Survival rate of Fontan procedure is reported to be 82% at 10 year.

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III. 6. PROSTHETIC HEART VALVES

1. Background

Replacement of diseased valves reduces the morbidity and mortality associated with native valvular disease but comes at the expense of probable associated complications related to the implanted prosthetic valves.

The outcome of patients undergoing valve replacement is affected by prosthetic valve hemodynamics, durability and thrombogenicity. Many of the prosthesis related complications can be prevented through optimal prosthesis selection in the individual patient and careful medical management and follow up after implantation.

Prosthetic valve implantation, especially in rheumatic patients, is the commonest operations being done in Nepal. Every patient, that needs valve surgery, should be evaluated by Heart Valve team to decide suitable prosthesis.

Types of Prosthetic Heart Valves:

There are basically two types of Prosthetic heart valves, mechanical and Bioprosthetic. Both types of valves have their advantages and disadvantages.

I. Mechanical Valves

Mechanical valves are made of metals, most of them consisting of Pyrolytic carbon which is one of the least thrombogenic metal. Three basic types of mechanical valve design exist:

Ball and cage valves:

MonoleaftletValves:

Bileaftlet Valves:

II. Bioposthetic Valves

A. Stented Bioprostheses:

B. StentlessBioprostheses:

C. Percutaneous Bioprostheses:

Advantages and Disadvantages of Different Prostheses

Both Mechanical and bioprosthetic valves have merits and demerits.

I. Mechanical Valves:

A. Benefits:

- Long durability, useful in young patients with longer life expectancy
- Excellent Implantability
- Good hemodynamic performance
- Cheaper than bio prostheses

B. Problems/Disadvantages:

- Need for lifelong anticoagulation, associated with its complications of thrombosis/supra therapeutic INR.
- Prosthetic valve endocarditis.
- Limitation to contact sports.
- Pregnancy and fetal abnormalities.

II. Bioprosthetic valves:

A. Benefits:

- No need of anticoagulation
- Beneficial for young women of child bearing age.

B. Problems/Disadvantages:

- Structural valve deterioration (SVD) with time.
- Early deterioration with unpredictable longevity in younger patients especially in rheumatics, more so in mitral position.
- Expensive.
- Inferior implantability to mechanical valves.

2. Complications of Prosthetic Heart Valves:

Mechanical valves have a substantial risk of thrombotic obstruction of valve and thromboembolic episodes requiring lifelong anticoagulation therapy. On the other hand they have equal chances of hemorrhagic complications. Bioprosthetic valves have a lower risk of thromboembolism but they have a limited durability.

I. Valve Thrombosis:
II. Hemorrhage
III. Systemic Emboli
IV. Structural Valve Deterioration (SVD)
V. Infective Endocarditis
VI. Paravalvular Regurgitation
VII. Hemolysis

Special considerations:

Pediatric Patients

Pediatric valve replacements in rheumatic patients are increasing every day. Almost all of them are implanted with mechanical valves. Issues of INR management, warfarin compliance, diet restrictions is a real challenge in this group of patients. Because of longer life expectancy and most of these patients needing either MVR or DVR, there is increased re-operation requirement.

Pregnancy

One of the major issues of mechanical valve implantation in young females is pregnancy. The number of young female patients requiring valve replacement is increasing. There are higher chances of fetal abnormality in patients taking warfarin. On the other hand, there is early degeneration of bio prostheses in younger patients especially in mitral position and the degeneration is worsened by pregnancy. A well accepted strategy during pregnancy is using heparin during the first trimester, followed by oral anticoagulation up to 36th week and ultimately using heparin until delivery.

3. Recommendations for selection of the optimal prosthesis in individual patient

We should try to choose the right valve for the right patient. The most important factors that should be considered selecting prosthetic valve for a patient are patient's age, life expectancy, sex, patient's preference, patient ability to manage the INR, indication/contraindication for warfarin therapy and associated comorbidities.

I. Use mechanical valve in

   i. Young patient with long life expectancy who has no contraindication for long term warfarin use and who can get regular INR checked and take anticoagulant for life.
   ii. Patient is already on anticoagulation (Atrial fibrillation, mechanical prosthesis in another position).
   iii. Patient at risk of accelerated bio prostheses SVD (young age, mitral position, renal insufficiency, hyperparathyroidism).
   iv. Use bileaflet valve with low thrombogenicity.

II. Use Bioprosthetic valve in

   i. Patients where regular INR monitoring is not feasible, like in patients from very remote places.
   ii. Contraindication to warfarin, like history of intracranial bleeding.
   iii. Poor compliance of drugs.
   iv. Patient's preference
   v. Young women of child bearing age.
   vi. Patient ≥ 60 years of age and/or has limited life expectancy.
   vii. Patient who wish to participate in competitive sports.

4. Conclusion

Heart valve disease, especially rheumatic valve disease in Nepal, is a major public health problem with huge surgical and socio-economic burden. Every valve replacement candidate should be individualized in all aspects to give the best surgical outcome by using the best available prosthetic valve giving longevity as well as good quality of life to patients.

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III. 7. INFECTIVE ENDOCARDITIS: BACKGROUND, DIAGNOSIS AND MANAGEMENT

Background

Infective endocarditis(IE) is defined as infection of endothelium of heart, or iatrogenic foreign bodies like prosthetic valves and other intracardiac devices. IE usually involves heart valves, but also can involve septal defects, arterial venous shunts, arterio-arterial shunts and coarctation of aorta. IE can be classified according to temporal evolution of disease (acute and subacute), site of infection, type of acquisition (community acquired, nosocomial or IV drug user), or the predisposing risk factor. Acute endocarditis is severe disease, rapidly progresses, damages heart valves, has extracardiac embolization, and leads to death within weeks if left untreated. Subacute IE gradually progresses over weeks, causes structural damage of heart slowly and rarely metastasizes.

Etiology

More than 80-85% of IE is caused by Staphylococcus, streptococcus and enterococcus.

Diagnosis

Clinical features:

Any patient with predisposing heart conditions and fever, IE should be suspected. IE can occur with IV drug users in native valve.

Predisposing conditions:

Rheumatic Heart disease, Degenerative valvular heart disease, Congenital heart disease, Intracardiac devices like Prosthetic heart valves, Implantable devices; IV drug abusers.

Symptoms:
Fever, chills, weakness, malaise, sweats, anorexia, headache, cough, shortness of breath, myalgia, arthralgia, chest pain, abdominal pain, nausea/vomiting, edema.

Physical findings:
Fever, Heart murmur, changing murmur, new murmur, central neurological abnormality, petechiae/conjunctival hemorrhage, splinter hemorrhage, Janeway lesion, Osler node, Roth spots, splenomegaly, clubbing, pallor.

Investigations

- Complete blood count
- ESR/CRP
- Blood culture
    - In subacute IE, 3 sets of blood samples should be collected for C/S from three different venipuncture over 24 hours.
    - In acute IE, 3 sets of blood samples should be collected for C/S from three different venipuncture over 1 hour. Appropriate antibiotics should be started once the blood sample is collected.
- ECHOCARDIOGRAM
    - Transthoracic
        - Can identify vegetation size>2 mm
        - Sensitivity and specificity in diagnosis IE 80-90%
    - Transesophageal
        - Should be done if transthoracic echo is inconclusive
        - Sensitivity and specificity >90%

Diagnostic criteria

Duke criteria helps to establish the diagnosis of definite or possible IE, and also to reject the diagnosis of IE. It has sensitivity of 80% and specificity of 90% in diagnosing IE.

Pathological Criteria

- Microorganisms demonstrated by culture or histological examination
- Active endocarditis (vegetation, intracardiac abscess) demonstrated by histological examination

Major criteria

Positive blood cultures

Typical microorganisms consistent with endocarditis from two separate blood cultures

Microorganisms consistent with endocarditis from persistently positive blood cultures

Evidence of endocardial involvement–echocardiography

Oscillating intracardiac structures, Abscess formation

New partial dehiscence of prosthetic valve, new valvular regurgitation

Minor criteria

Predisposing heart disease

Fever › 38°C

Vascular phenomena (major arterial emboli, mycotic aneurysm, conjunctival hemorrhage, Janeway lesions

Immunological phenomena (Osler node, Roth spots, rheumatic factor, glomerulonephritis)

Microbiological evidence (not meeting major criterion)

Suspect echocardiography (not meeting major criterion)

Categories

Definite IE

Pathological criteria

or 2 major criteria positive

or 1 major and 2 minor criteria positive

or 5 minor criteria positive

Possible IE

1 major and 1 minor criterion

Or 3 minor criterion

Rejected IE

Firm alternating diagnosis

Resolution of the infection with antibiotic treatment for < 4 days

No histological evidence of surgery or autopsy after 4 days of antibiotic therapy or less

Does not meet the criteria for possible IE

Treatment

Antimicrobial therapy is the cornerstone in treating IE. Empirical therapy with combination of antibiotics based on clinical and epidemiological clues to the etiology can be started till the culture sensitivity reports come. As >80% of IE are caused by staphylococcus, streptococcus and enterococcus, initial antimicrobial therapy should cover all these organisms. These can be covered with combination of ceftriaxone, gentamycin and/or vancomycin. Once the culture sensitivity report comes, appropriate antibiotics can be initiated.

Therapeutic Principles

- Bactericidal antibiotics are the choice.
- High concentrations of appropriate antibiotics in serum are necessary.
- Long-term therapy is required

  To achieve these principles, antibiotics are given intravenously for prolonged period of time.

Organism specific treatment:

ORGANISMS	DRUGS(DOSE AND DURATION)
1. Penicillin sensitive streptococcus, s. gallalyticus **2. Moderately penicillin resistant streptococcus**	i. Penicillin G (12-18 million U IV q4h for 4 weeks) **OR** Ceftriaxone (2gm/day IV single dose for 4 weeks) **OR** Vancomycin (30 mg/Kg IV q12h for 4 weeks) (For patients allergic to beta lactams) ii. Penicillin G (24 million U IV q4h or ceftriaxone (2 gm IV OD) for 4 weeks **OR** Vancomycin (15 mg/Kg IV q12h for 4 weeks) (For patients allergic to beta lactams) **plus** Gentamycin (3mg/kg qd IV or IM as a single dose for 2 weeks)
Enterococci	i. Amoxicillin (200mg/Kg/day IV in 4-6 doses) for 2-4 weeks **plus** Gentamycin (3 mg/kg IV OD) both for 2-6 weeks **OR** ii. Vancomycin (30 mg/Kg IV q12h) for 6 weeks **plus** Gentamycin (3 mg/kg IV OD) both for 6 weeks **OR** iii. Ampicillin (200mg/Kg/day in 4-6 doses IV for 6 weeks) **plus** Ceftriaxone (4gm/day IV in 2 doses) for 6 weeks

Staphylococcus	
1. Methicillin sensitive native valve	i. Flucloxacillin (12gm/day IV in 4-6 doses for 4-6 weeks) **OR** ii. Vancomycin (30-60 mg/Kg IV in 2-3 doses for 4-6 weeks)
2. MRSA native valve	i. Vancomycin (30-60 mg/Kg IV in 2-3 doses for 4-6 weeks) **OR** ii. Daptomycin (10mg/kg/day OD for 4-6 weeks)
3. Methicillin sensitive prosthetic valve	i. Flllucloxacillin 12gm/day IV in 4-6 doses for 6-8 weeks **plus** Gentamycin (3 mg/kg IV or IM in 1-2 doses for 2 weeks) **plus** Rifampin (900 -1200mg PO in 2-3 doses for 6-8 weeks)
4. Methicillin Resistant Prosthetic valve	i. Vancomycin (30-60 mg/Kg IV in 2-3 doses for 6-8 weeks) **plus** Gentamycin (3 mg/kg IV or IM in 1-2 doses for 2 weeks) **plus** Rifampin (900-1200 mg PO in 2-3 doses for 6-8 weeks)
HACEK organisms	i. Ceftriaxone (2gm/day IV single dose) both for 4 weeks **OR** ii. Ampicillin/ sulbactam 2 gm IV q6hfor 4 weeks) **OR** iii. Ciprofloxacin 1gm orally once daily **OR** 800mg IV every 12h for 4 weeks

Indications for surgery in IE

Emergency Surgery:

Aortic or mitral native valve endocarditis with severe aortic regurgitation, obstruction or fistula causing refractory pulmonary edema or cardiogenic shock.

Urgent Surgery:

1. Heart failure
    a. Moderate to severe CHF
2. Uncontrolled Infection
    a. Left sided IE caused by Staphylococcus aureus, fungal or other highly resistant organisms
    b. Uncontrolled infection despite optimum antimicrobial therapy
    c. Locally uncontrolled infection (Abscess, false aneurysm, fistula, and enlarging vegetation).
3. Prevention of embolism
    a. Persistent vegetation greater than 10mm after one or more embolic episode despite appropriate antibiotic therapy.
4. In right sided I.E, refractory right sided heart failure and/or vegetation size greater than 20mm with recurrent pulmonary embolism.

IE Prophylaxis

IE prophylaxis is required when there is manipulation of gingival tissue or the periapical region of teeth or perforation of oral mucosa, including surgery of the respiratory tract, in following group of patients:

1. Prosthetic heart valves
2. Prior endocarditis
3. Unrepaired cyanotic congenital heart disease
4. Completely repaired congenital heart defects during the 6 months after repair
5. Incompletely repaired congenital heart disease with residual defects
6. Valvulopathy developed after cardiac transplantation

Antibiotic regimen for IE prophylaxis

1. Standard oral regimen
    a. Amoxicillin 2 gm PO 1h before procedure
2. Inability to take oral medication
    a. Ampicillin 2gm IV or IM within 1 hour before procedure
3. Penicillin allergy
    a. Azithromycin 500mg PO 1 h before procedure
    b. Clindamycin 600 mg PO 1 h before procedure
4. Penicillin allergy, inability to take oral medication
    a. Ceftriaxone 1 gm IV or IM 30 min before procedure
    b. Clindamycin 600 mg IV or IM 1 h before procedure

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UNIT - IV

Disease of the pulmonary vascular bed and disease of the Aorta, Carotid arteries and Peripheral Artery

IV. 1. PULMONARY EMBOLISM

Introduction

Pulmonary embolism (PE) is a common, potentially life-threatening cardiopulmonary illness. PE and deep vein thrombosis (DVT) are two manifestations of the same disease. Severity of PE ranges from completely asymptomatic incidental finding to cases of sudden death. Diagnosis is sometimes difficult and it is not unusual to find patients with symptoms lasting several days. Suspicion of the disease is the key for diagnosis as symptoms are non-specific.

Risk factors for PE

Previous venous thromboembolism, surgery or trauma within three months, cancer, immobilization, acute medical disease (stroke, heart failure, respiratory failure, sepsis), oral contraceptives, hormone replacement therapy and air travel are some of the risk factors for PE.

Clinical presentation

Common symptoms are dyspnea either at rest or exertion which may be sudden or progressive, chest pain, cough, palpitation and syncope. Hemoptysis and pleuritic chest pain suggest pulmonary infarction. Sudden cardiac arrest can be the presentation. Symptoms of DVT may be present. Arterial hypotension and shock are rare but important clinical presentations, since they indicate central PE and/or a severely reduced haemodynamic reserve.

As the clinical sign and symptom are non-specific suspicion of pulmonary embolism based upon the clinical presentation is important for the diagnosis of pulmonary embolism.

Assessment of clinical probability

Despite the limited sensitivity and specificity of individual symptoms, signs and common tests, the combination of findings evaluated by clinical judgment or by the use of prediction rules allows to classify patients with suspected PE into distinct categories of clinical or pre-test probability that correspond to an increasing actual prevalence of confirmed PE. Wells and the revised Geneva rule, both the original and the simplified version, are frequently used to access the probability of PE.

Items	Clinical decision rule points	
Wells rule	**Original version[35]**	**Simplified version[107]**
Previous PE or DVT	1.5	1
Heart rate ≥100 b.p.m.	1.5	1
Surgery or immobilization within the past four weeks	1.5	1
Haemoptysis	1	1
Active cancer	1	1
Clinical signs of DVT	3	1
Alternative diagnosis less likely than PE	3	1
Clinical probability		
Three-level score		
Low	0–1	N/A
Intermediate	2–6	N/A
High	≥7	N/A
Two-level score		
PE unlikely	0–4	0–1
PE likely	≥5	≥2

European Heart Journal (2014) 35, 3033–3080

Clinical prediction rules for PE

Revised Geneva score	Original version[93]	Simplified version[186]
Previous PE or DVT	3	1
Heart rate		
75–94 b.p.m.	3	1
≥95 b.p.m.	5	2
Surgery or fracture within the past month	2	1
Haemoptysis	2	1
Active cancer	2	1
Unilateral lower limb pain	3	1
Pain on lower limb deep venous palpation and unilateral oedema	4	1
Age >65 years	1	1
Clinical probability		
Three-level score		
Low	0–3	0–1
Intermediate	4–10	2–4
High	≥11	≥5
Two-level score		
PE unlikely	0–5	0–2
PE likely	≥6	≥3

Investigation

ECG: ECG may reveal sinus tachycardia, atrial fibrillation, RV strain, incomplete or complete RBBB, T wave inversion in the anterior precordial leads, and S wave in Lead I and Q wave and T wave inversion in lead III (the S1Q3T3 patterns) or may mimic an old inferior MI. The most specific finding on an ECG is the classic S1Q3T3 pattern.

Arterial blood gas: PE can result in significant hypoxia, however, a normal Pao2 cannot rule out PE. But hypoxia in the absence of cardiopulmonary diseases should raise suspicion for PE. In patients with cardiopulmonary collapse, a normal Pao2 suggests that PE is unlikely.

Chest X-ray: Chest X-ray findings in PE include pleural effusion, atelectasis, and consolidation. The classic signs,

including Westermark sign (regional oligemia), Hampton's hump (Pleural-based, wedge-shaped shadow),and Palla's sign (enlarged right inferior pulmonary artery) are very rarely seen in PE patients.

Echocardiography: Patients with hemodynamic collapse will generally have severe right ventricular dysfunction and echo can provide rapid bedside assessment in these critically ill patients and those unable to perform CT Pulmonary Angiogram (CTPA). Echo findings include RV dilation, RV hypokinesia, Tricuspid regurgitation, septal flattening, paradoxical septal motion, diastolic LV impairment secondary to septal displacement, pulmonary artery hypertension, lack of inspiratory collapse of IVC, and rarely direct visualization of the thrombus. In patients with large PE, there is a moderate to severe right ventricular free wall hypokinesia with relative sparing of the RV apex called as McConnell's sign. Hemodynamically stable patients with PE may not have evidence of right ventricular dysfunction.

Troponin: Elevated Cardiac troponins levels correlate with ECG and echo findings of RV pressure overload. Overall mortality and in-hospital complications are higher in patients with PE and elevated cardiac troponin than in patients without elevated troponin.

D-dimer: can be used to exclude PE in patients with a low suspicion of PE and has high negative predictive value. This test is of limited value in high probability of PE. In high pre-test probability cases, D-dimer has limited role in the diagnosis of the PE. False positive D-dimer results may occur in elderly people, in cancer patients, in pregnant women, in patients with shock etc.

CT pulmonary angiogram: As it directly visualizes thrombus, CT pulmonary angiogram has become the standard imaging technique for the diagnosis of acute PE. It not only directly visualizes the thrombus but it also can exclude other disease like aortic dissection, pneumonia and malignancy.

Ventilation-perfusion (V/Q) scanning: V/Q scan is now considered as second line imaging method for the diagnosis of PE and is rarely performed.

Conventional Pulmonary Angiogram: remains the gold standard diagnosis test for PE but it is now used infrequently due to the advent of CT pulmonary angiogram.

Prognostic assessment

Various prediction rules based on clinical parameters have been shown to be helpful in the prognostic assessment of patients with acute PE. Of those, the pulmonary embolism severity index (PESI) is the most extensively validated score to date.

Original and simplified PESI score

Parameter	Original version[214]	Simplified version[215]
Age	Age in years	1 point (if age >80 years)
Male sex	+10 points	–
Cancer	+30 points	1 point
Chronic heart failure	+10 points	1 point
Chronic pulmonary disease	+10 points	
Pulse rate ≥110 b.p.m.	+20 points	1 point
Systolic blood pressure <100 mm Hg	+30 points	1 point
Respiratory rate >30 breaths per minute	+20 points	–
Temperature <36 °C	+20 points	–
Altered mental status	+60 points	–
Arterial oxyhaemoglobin saturation <90%	+20 points	1 point
	Risk strata[A]	
	Class I:≤65 points very low 30-day mortality risk (0–1.6%) **Class II: 66–85 points** low mortality risk (1.7–3.5%) **Class III: 86–105 points** moderate mortality risk (3.2–7.1%) **Class IV: 106–125 points** high mortality risk (4.0–11.4%) **Class V: >125 points** very high mortality risk (10.0–24.5%)	**0 points**= 30-day mortality risk 1.0% (95% CI 0.0%–2.1%) **≥1 point(s)**= 30-day mortality risk 10.9% (95% CI 8.5%–13.2%)

European Heart Journal (2014) 35, 3033–3080

Classification of patients with acute PE based on early mortality risk

Early mortality risk		Risk parameters and scores			
		Shock or hypotension	PESI class III–V or sPESI ≥1[a]	Signs of RV dysfunction on an imaging test[b]	Cardiac laboratory biomarkers[c]
High		+	(+)[d]	+	(+)[d]
Intermediate	Intermediate–high	–	+	Both positive	
	Intermediate–low	–	+	Either one (or none) positive[e]	
Low		–	–	Assessment optional; if assessed, both negative[e]	

European Heart Journal (2014) 35, 3033–3080

High risk (>15% mortality at one month) Patients with persistent hypotension or shock

Non-high risk (<15% mortality at one month) further stratify into:

Intermediate risk (3-15% one month mortality) if RV dysfunction is present or myocardial injury markers are elevated;

low risk (<1% one month mortality) if all cited prognostic factors are absent.

Management

Acute treatment

Anticoagulation with low-molecular-weight heparin (LMWH), or intravenous unfractioned heparin (UFH), or fondaparinux followed by the addition of a VKA and supportive treatment has remained the standard of care in the management of acute PE. LMWH or fondaparinux are preferred over UFH for initial anticoagulation in PE, as they carry a lower risk of inducing major bleeding and heparin-induced thrombocytopenia (HIT).UFH is recommended for patients in whom primary reperfusion is considered, as well as for those with serious renal impairment (creatinine clearance, <30 mL/min), or severe obesity.

If clinical suspicion is high, initiate anticoagulation treatment while awaiting the results of diagnostic tests.

Thrombolysis for the treatment of Acute PE is highly individualized, it offers 50% reduction in mortality and is indicated in patients with haemodynamic instability. Thrombolysis should be reserved for hemodynamically unstable patients and a low risk bleeding. Streptokinase, Urokinase and recombinant tissue plasminogen activator(rTPA) are the current agents. Two-hour infusion of rTPA appeared to be superior to a 12-hour streptokinase infusion (at 100000IU/h) but no difference was observed when the same streptokinase dose was given over 2 hours which is also known as accelerated regimen. After the thrombolysis parental and oral anticoagulant should be started as the management of non-high risk PE.

Approved thrombolytic regimens for PE are:

Thrombolytic therapy	Doses	Accelerated regimen
Streptokinase	2,50,000IU as a loading doses over 30 minutes, followed by 1,00000IU every hour for 12-24 hour	1.5million IU over 2 hours
Urokinase	4400IU/kg as a loading dose over 10min, followed by 4400IU/kg per hour over 12-24 hour	3million IU over 2 hours
Recombinant TPA	100mg over 2 hours; or 0.6mg/kg over 15 min (maximum dose 50mg)	

Percutaneous mechanical thrombectomy (Thrombus fragmentation and aspiration) and surgical embolectomy are offered to high-risk PE patients with contraindication to thrombolytic therapy and those in whom thrombolytic treatment has not improved hemodynamic status.

In non-high risk PE, acute treatment is short term subcutaneous low-molecular-weight heparin (LMWH), or intravenous unfractioned heparin (UFH), or fondaparinux, followed by vitamin K antagonists(VKAs) monitoring INR

levels, with a therapeutic range 2.0-3.0. LMWH, UFH or fondaparinux should be continued for at least 5 days and until INR is >2 for two consecutive days.

Monitoring aPTT is essential in UFH- treated patients. Warfarin can be started at a dose of 10 mg in younger (e.g., 60 years of age), otherwise healthy outpatients and in older patients and in those who are hospitalized at a dose of 5 mg. The daily dose is adjusted according to the INR over the next 5–7 days, aiming for an INR level of 2.0–3.0. Adequate oxygen support is essential if hypoxia is present.

Parenteral anticoagulation available in Nepal

Drug	Doses
LMWH	Enoxaparin -1mg/kg/dose in two divided dose; 1.5mg/kg/day Dalteparin- 100 U/kg/dose in two divided dose
UFH	80 units/kg IV bolus,then continuous infusion or 5000 units IV bolus, then continuous infusion to maintain aPTT of 60-90 sec 8000-10,000 units IV initially, then 50-70 units/kg (5000-10,000 units) q4-6hr
Fondaparinux	5mg (body weight <50kg) once daily 7.5mg (body weight 50-100kg) once daily 10mg (body weight >100kg once daily

Long-term management

In patient with a provoked PE, three months of anticoagulant is recommended.

In patients with unprovoked PE three months of anticoagulant is recommended followed by thrombophilia screening, screening for malignancy in elderly.

In patients with second unprovoked PE, anticoagulant is for indefinite duration.

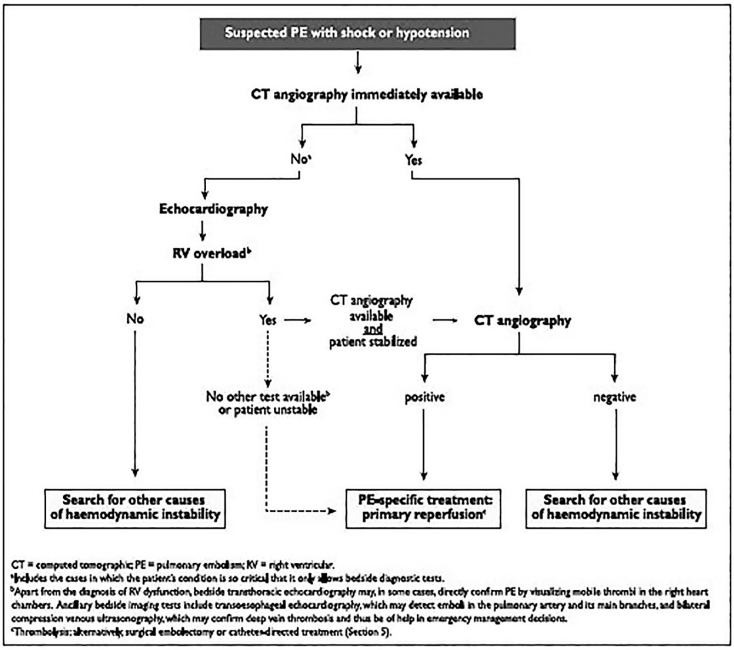
In patients with idiopathic PE, provoked PE with permanent risk factors or with previous venous thromboembolic event, long term secondary prevention should be considered, periodically assessing benefits and risks of continuing anticoagulant.

Among anticoagulants, VKA or NOACs [dabigatran 150 mg twice daily, 110mg twice daily for patients age >80years, rivaroxaban (15 mg twice daily for 3 weeks followed by 20 mg once daily) or apixaban (10 mg twice daily for a week followed by 5 mg twice daily)] can be used except in patients with renal dysfunction. Dose reduction is recommended for rivaroxaban and apixaban for extended anticoagulation longer than 6 months.

In patients with cancer, LMWH is preferred over VKAs in the first 6 months. Endoxaban and Rivaroxaban can be considered as an alternative to LMWH in patient without GI cancer.

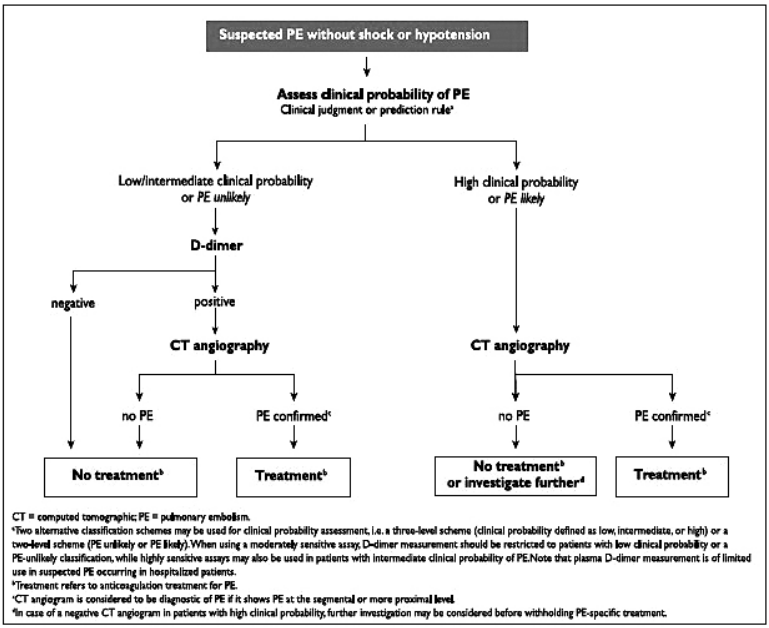
Routine use of IVC filter is contraindicated in patients with PE, but it can be used in patients with Acute PE with absolute contraindication of anticoagulant therapy or in patients with recurrent PE despite therapeutic level of anticoagulant.

Proposed diagnostic algorithm for patients with suspected high-risk PE, i.e. presenting with shock or hypotension.



European Heart Journal (2014) 35, 3033–3080

Proposed diagnostic algorithm for patients with suspected not high-risk PE



CT = computed tomographic; PE = pulmonary embolism.
[a]Two alternative classification schemes may be used for clinical probability assessment, i.e. a three-level scheme (clinical probability defined as low, intermediate, or high) or a two-level scheme (PE unlikely or PE likely). When using a moderately sensitive assay, D-dimer measurement should be restricted to patients with low clinical probability or a PE-unlikely classification, while highly sensitive assays may also be used in patients with intermediate clinical probability of PE. Note that plasma D-dimer measurement is of limited use in suspected PE occurring in hospitalized patients.
[b]Treatment refers to anticoagulation treatment for PE.
[c]CT angiogram is considered to be diagnostic of PE if it shows PE at the segmental or more proximal level.
[d]In case of a negative CT angiogram in patients with high clinical probability, further investigation may be considered before withholding PE-specific treatment.

European Heart Journal (2014) 35, 3033–3080

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IV. 2. PULMONARY HYPERTENSION

1. Introduction:

Pulmonary hypertension (PH) is classified into five groups based upon etiology. Patients in the first group are considered to have pulmonary arterial hypertension (PAH), whereas patients in the remaining four groups are considered to have PH (table 1). In this topic we discuss PAH-specific therapy for treating PAH, while the pathogenesis, diagnosis, classification, and prognosis of PAH are beyond scope of this topic.

Table 1: Clinical classification of pulmonary hypertension (6th World Symposium on Pulmonary Hypertension)

1 PAH
1.1 Idiopathic PAH
1.2 Heritable PAH
1.3 Drug- and toxin-induced PAH
1.4 PAH 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 long-term responders to calcium channel blockers
1.6 PAH with overt features of venous/capillaries (PVOD/PCH) involvement
1.7 Persistent PH of the newborn syndrome

2 PH due to left heart disease
2.1 PH due to heart failure with preserved LVEF
2.2 PH due to heart failure with reduced LVEF
2.3 Valvular heart disease
2.4 Congenital/acquired cardiovascular conditions leading to post-capillary PH
3 PH due to lung disease and/or hypoxia
3.1 Obstructive lung disease
3.2 Restrictive lung disease
3.3 Other lung disease with mixed restrictive/obstructive pattern
3.4 Hypoxia without lung disease
3.5 Developmental lung disorders
4 PH due to pulmonary artery obstructions (refer to the UpToDate table on PH due to PA obstruction)
4.1 Chronic thromboembolic PH
4.2 Other pulmonary artery obstructions
5 PH with unclear and/or multifactorial mechanisms (refer to the UpToDate table on PH due to unclear or multifactorial mechanisms)
5.1 Hematologic disorders
5.2 Systemic and metabolic disorders
5.3 Others
5.4 Complex congenital heart disease

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2. General Approach:

PAH-specific therapy (also known as PAH-targeted or PAH-directed therapy) is directed at the PAH itself rather than the underlying cause of the PAH. PAH-specific agents include prostacyclin pathway agonists, endothelin receptor antagonists, nitric oxide (NO)-cGMP enhancers, or rarely, select calcium channel blockers (table 2).

Table2: Characteristics of medications used in the treatment of pulmonary hypertension

Generic (Brand[s])	Use	Dosage and Route	Common Adverse Effects
Calcium Channel Blockers			
Amlodipine (Norvasc)	Idiopathic PAH patients responsive to vasodilator testing[a]	2.5-20 mg/day po	Flushing, palpitations, angina, headache, dizziness, angioedema, peripheral edema
Diltiazem (Cardizem CD, Cardizem LA)	Idiopathic PAH patients responsive to vasodilator testing[a]	60-240 mg qd to tid po	Bradyarrhythmia, peripheral edema, heart block, dizziness, headache, congestive heart failure
Nifedipine ER (Procardia XL, Nifedical XL)	Idiopathic PAH patients responsive to vasodilator testing[a]	30-240 mg bid po	Hypotension, palpitations, peripheral edema, flushing, ventricular arrhythmia, dizziness, headache
Prostacyclin Analogues			
Epoprostenol (Flolan)	NYHA III-IV	2-40 ng/kg/min IV	Flushing, NV, hypotension, bradycardia, angina, anxiety/nervousness, dyspnea
Iloprost (Ventavis)	NYHA III-IV	2.5-5 mcg/dose using AAD system, 6-9 times/day; max 45 mcg/day	Flushing, trismus, insomnia, NV, hypotension, increased liver enzymes, palpitations, syncope, muscle cramps, hemoptysis, pneumonia
Treprostinil (Remodulin)	NYHA II-IV	SC/IV infusion: 1.25-40 ng/kg/min using ambulatory infusion pump; titrate slowly over several wk	Infusion-site pain/reaction, headache, rash, diarrhea, nausea, jaw pain, vasodilation, dizziness, edema, pruritus, hypotension
Treprostinil (Tyvaso)	NYHA III	3-9 breaths/session qid po using Tyvaso Inhalation System	Cough, headache, throat irritation, nausea, flushing, syncope
Endothelin Receptor Antagonists			
Ambrisentan (Letairis)	NYHA II-III	5-10 mg qd po	Hepatotoxicity, peripheral edema, nasal congestion, sinusitis, flushing
Bosentan (Tracleer)	NYHA II-IV	62.5-125 mg bid po	Hepatotoxicity, fluid retention, headache, angina, syncope, flushing, hypotension, palpitations
Phosphodiesterase Inhibitors			
Sildenafil (Revatio)	NYHA II-III	10 mg tid IV bolus; 20 mg tid po taken 4-6 h	Hypotension, vision loss, hearing loss, priapism, vaso-occlusive crisis
Tadalafil (Adcirca)	NYHA II-III	40 mg qd po	Hypotension, vision loss, hearing loss, priapism

[a] Non–FDA-approved indication.
AAD: adaptive aerosol delivery; CD: controlled-release; ER: extended-release; LA: long-acting; max: maximum; min: minute; NV: nausea and vomiting; NYHA: New York Heart Association; PAH: pulmonary arterial hypertension; SC: subcutaneous; XL: extended-release.
Source: References 13, 15-18, 24, 25, 30, 31.

Pre-Treatment Evaluation (Agent Selection)

Patients with pulmonary arterial hypertension (PAH) should be referred to a specialized center for evaluation and management, since the administration of PAH-specific therapy can be harmful. Before PAH-specific therapy is administered:

- The diagnosis of PAH, and any potential associated etiology, should be confirmed, since PAH-specific therapy has not been found to be beneficial in most other forms of PH and may in fact be harmful
- When indicated, vasoreactivity testing should be performed.

- The baseline risk of disease progression and death should be assessed.

Vasoreactivity testing (select patients) – Select patients with PAH (ie, group 1 PH) should undergo acute vasoreactivity testing (AVT) to identify the small subset of PAH patients (10 to 20 percent) who may respond to calcium channel blocker (CCB) therapy. This includes patients with idiopathic PAH (IPAH), heritable PAH, and drug/toxin-induced PAH (ie, patients who are most likely to be vasoreactive).

Patients with associated forms of PAH are rarely vasoreactive and, as such, vasoreactivity testing is not indicated. This includes patients with PAH due to connective tissue disease, congenital heart disease, human immune deficiency virus, portal hypertension, and schistosomiasis, and patients with suspected pulmonary veno-occlusive disease/pulmonary capillary hemangiomatosis.

Contraindications to AVT include low systemic blood pressure (eg, systolic BP <90 mmHg), low cardiac index (cardiac index <2 L/min/m2), or the presence of severe (functional class IV) symptoms, since hypotension and occasionally cardiovascular collapse can occur with the administration of the vasodilator. Caution should also be exercised if it is suspected that patients have a component of group 2 PH (ie, cardiovascular causes of PH).

Patients with a positive vasoreactivity test are candidates for a trial of CCB therapy (see 'Calcium channel blockers (trial)' below). In contrast CCB therapy should be avoided in patients with a negative test since CCBs can have serious adverse effects, including systemic hypotension and death, in this population.

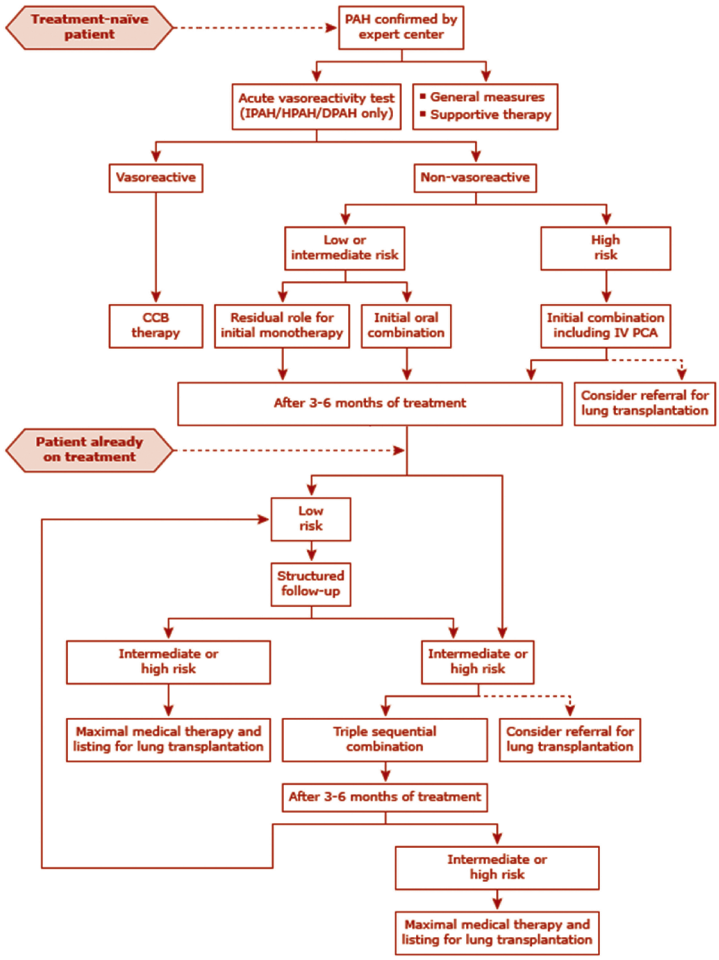
AVT involves the administration of a short-acting vasodilator followed by measurement of the hemodynamic response using a right heart catheter (RHC). Agents commonly used for vasoreactivity testing include inhaled nitric oxide, epoprostenol, adenosine, and inhaled iloprost:

The test is considered positive if mean pulmonary artery pressure decreases at least 10 mmHg and to a value less than or equal to 40 mmHg, with an increased or unchanged cardiac output, and a minimally reduced or unchanged systemic blood pressure. "Borderline" results are considered as nonreactive.

Baseline risk assessment

In patients with PAH, the baseline risk of disease progression and death should be assessed prior to the initiation of PAH-specific therapy. Risk stratification determines the initial regimen chosen and is also used to determine disease progression and response to therapy (algorithm 1).

Algorithm 1 : Sixth World Symposium on Pulmonary Hypertension (WSPH): Risk stratification



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The one optimal approach is to choose an agent primarily based upon AVT and World Health Organization (WHO) functional class (table 5). This approach is a practical one since WHO functional class is a major determinant of outcome; consequently, regulatory approvals have been traditionally based upon WHO functional class

3. SPECIFIC TREATMENT

Vasoreactive Patients

Calcium channel blockers (trial) – For patients with PAH who are vasoreactive, an initial trial of calcium channel blocker (CCB) therapy (eg, one to three months) can be administered. This only applies to patients with World Health Organization (WHO) class I to III since patients with WHO functional class IV do not typically undergo acute vasoreactivity testing nor are they generally candidates for oral therapy.

- Among patients who are vasoreactive, about one-half clinically respond to CCB therapy.
- Among those who clinically improve, the response is generally short-lived, eventually requiring the addition of another agent of a different class.
- Long-term response is defined as an improvement in WHO functional class that is sustained for at least one year while on CCB therapy only

Non-Vasoreactive Patients

WHO functional class I (monotherapy) – Patients rarely present with functional class I (because they are typically asymptomatic)

- may be monitored closely for disease progression to a functional level that warrants therapy (eg, class II),
- or start PAH-specific monotherapy, particularly when patients have "high risk" features

WHO functional class II and III OR low or intermediate –

- Single agent therapy –may be appropriate only for patients with very early class I/II disease who have a low risk profile and for patients who have been stable on

monotherapy for a prolonged period (eg, 5 to 10 years).

- In general, it is recommended to administer dual combination therapy with an endothelin receptor antagonist (ERA) and an agent that targets the nitric oxide-cyclic guanosine monophosphate (cGMP) pathway, typically a phosphodiesterase 5 inhibitor (PDE5I). For instance, available combination in Nepal would be

Tadalafil plus bosentan

Sildenafil plus bosentan

WHO functional class IV or high risk

- Should be treated with a parenteral prostanoid-containing combination regimen. Most of these patients are already receiving single or combination oral therapy from treatment administered for class III symptoms and the parenteral prostanoid is added to that regimen. Most clinicians consider intravenous (IV) epoprostenol as the preferred agent

Follow-Up

Initiation of PH-specific therapy (including calcium channel blocker therapy) requires close follow-up. Frequent reassessment is necessary because of the complex nature of the disease and its treatments, and the tendency of PAH to progress.

Outpatients visits – Patients should be seen as an outpatient in a PH center but patient logistics may dictate alternative forms of follow-up, such as frequent telephone contact and co-management with local physicians.

The initial visit usually occurs within the first six weeks. Thereafter, patients should ideally be seen every three months. However, for patients receiving parenteral or combination therapy and patients who have advanced symptoms, right heart failure, or advanced hemodynamic abnormalities, more frequent visits are typical.

Follow-up visits should ideally include a thorough history and examination to assess symptoms of right heart failure, exercise tolerance, and resting and ambulatory oximetry.

The frequency of follow-up testing with brain natriuretic peptide (BNP or N-terminal pro-BNP [NTproBNP]), six minute walk test (6MWT), echocardiogram, and right heart catheterization (RHC) should be determined on a case-by-case basis and varies among centers.

Refractory Patients

PAH is a progressive disease and in some cases, patients progress to a point where they are refractory to PAH-specific therapy. Such patients have a high mortality.

- Lung transplantation is a definitive form of therapy for such cases
- while the creation of a right to left shunt is a temporizing measure only.(atrial septostomy ,transcatheter Potts shunt)

IV. 3. DISEASE OF THE GREAT VESSELS– AORTIC ANEURYSM AND AORTIC DISSECTION

Background

Aortic Disease contribute to a wide spectrum of arterial diseases which encompasses a broad range of degenerative, structural, acquired, genetic based and traumatic diseases. It comprises of aortic aneurysms, acute aortic syndromes (which includes aortic dissection, intramural hematoma, penetrating aortic ulcers), traumatic injury, pseudo aneurysm, aortic rupture, atherosclerotic and inflammatory aortic disease. It includes genetic disease such as Marfan's syndrome, Loey's Dietz that may present as aortic aneurysm, and congenital abnormalities which include disease such as coarctation of the aorta.

Diagnosis

Most ascending aortic aneurysm are asymptomatic and diagnosed incidentally on chest X ray or trans thoracic echocardiography(TTE) or until an acute and often catastrophic event occurs. However some do present with symptoms of chest pain. The pain may be acute in onset signifying impending rupture, or a chronic pain from compression of overlying sternum. Patients may present with compression symptoms such as - superior vena cava obstruction, hoarseness of voice or airway obstruction.

Severe unrelenting chest pain is present in acute dissection, which often causes anxiety, located in mid sternum for ascending aortic aneurysm and in inter-scapular region for descending aneurysm. Patients may present with symptoms of mal-perfusion of the brain, limbs and various visceral organ.

Diagnositic Studies

Electrocardiogram – if aortic valve regurgitation is present can present with left ventricular hypertrophy or strain is evident. ECG findings of myocardial ischemia can be seen in dissection involving coronary arteries.

Chest Radiography – mediastinal widening can be present.

Transthoracic and Transesophageal Echocardiography– are easily available diagnostic tools for detection of aneurysm, dissection flap or intramural hematoma.

Computed Tomography Aortogram– It is the most widely used noninvasive technique for imaging the thoracic and abdominal aorta. It delineates the aortic anatomy and is useful for detection of abnormalities.

Magnetic Resonance Imaging – can provide axial and three-dimensional reconstruction of ascending aorta.

Management

Medical

Stringent control of hypertension is recommended along with lipid profile optimization.

Smoking cessation and risk reduction for atherosclerosis should be instituted.

Anti HTN therapy should be administered to achieve goal of less than 140/90 in patients without Diabetes and 130/80 for diabetes and renal disease.

Beta-adrenergic blocking drugs should be administered with Marfan's syndrome with aortic aneurysm followed be Angiotensin converting enzyme receptor blockers or angiotensin receptor blockers. Angiotensin receptor blocker is reasonable for patients with Marfan syndrome to reduce risk of aortic dilatation.

Role of Doxycyline in aortic aneurysm is still uncertain and its usage will depend on result of the larger trials that are being conducted.

Acute Aortic Syndrome medical management includes therapeutic agents to reduce cardiac contractility with IV

Labetolol, Propanolol or Esmolol with target Heart rate of less than 60bpm and then initiation of therapy to reduce systemic arterial pressure with target systolic blood pressure of <120mmHg using drugs like nitroprusside, i.v. labetalol etc.

Indications for Surgical intervention

1. All new onset acute ascending aortic dissection or rupture warrants emergent surgery. With regards to intra mural hematoma (IMH), it is reasonable to treat as dissection based on the corresponding segment of aortic involvement.
2. Acute aortic dissections involving the descending aorta should be managed medically unless life-threatening complications such as malperfusion syndrome, progression of dissection, enlarging aneurysm, inability to control blood pressure. There has been an expanding role of endovascular procedures in acute type B dissection, which should be taken in to considereation
3. It is reasonable to consider repair of the aorta in adult patients with Loeys-Dietz syndrome at an aortic diameter of 4.2 cm or greater by TEE or 4.4-4.6 by CT and MRI.
4. For women with Marfan's syndrome contemplating pregnancy, is reasonable to replace aorta at 4 cm diameter.
5. Asymptomatic patients with degenerative aneurysm, chronic dissection, IMH, psuedo-aneurysm and penetrating ulcers should undergo surgical repair if ascending aorta or root diameter is greater than 5.5 cm.
6. Patients with Marfan syndrome, Ehler Danlos syndrome, Turner syndrome, bicuspid aortic valve or familial thoracic aortic aneurysm or other genetically mediated disorders should undergo elective operation at diameters of 4 – 5 cm to avoid dissection or rupture unless there is family history of AoD at < 5 cm, a rapidly expanding aneurysm or presence of AR
7. If maximum cross sectional area in square cm of the ascending aorta or root divided by patient's height in meters exceeds a ratio of 10, surgical repair is reasonable.

8. Patients with a growth rate of more than 0.5 cm / year of the aorta should undergo surgical replacement.
9. Patients undergoing other cardiac surgical procedures (example. aortic valve repair or replacement) and who have an ascending aorta or aortic root of greater than 4.5 cm should be considered for repair of root or replacement of ascending aorta
10. Patients with involvement of arch aneurysm should be considered for partial replacement with ascending aorta.
11. Replacement of the entire arch is reasonable for acute dissection when the arch is aneurysmal, or has extensive destruction and leakage.
12. Replacement of the arch should be considered in asymptomatic patients when diameter of the arch exceeds 5.5 cm.
13. Patients without significant comorbid disease and descending aortic diameter exceeding 5.5 cm even due to chronic dissection should be considered for open repair
14. For patients with thoraco-abdominal aneurysms, elective surgery is recommended it the aortic diameter exceeds 6 cm.
15. For Acute type B dissection, medical management is to be done but however considered for intervention if persistent or recurrent pain, uncontrolled hypertension despite full medication, early aortic expansion, malperfusion or has signs of rupture.
16. Patients with symptoms suggestive of expansion of thoracic aneurysm suggestive by pain in a patient with aneurysm should be evaluated for prompt surgical intervention unless severely limited by comorbid conditions.

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IV. 4. CAROTID ARTERY DISEASE

Carotid artery atherosclerosis is a major cause of neurological morbidity and mortality and is responsible for 20% of strokes and 1 -2% per year in the adult population. Medical, surgical and endovascular therapies aim to reduce the risk of stroke by relieving stenosis and preventing thromboembolism.

Diagnosis:

Major symptoms of carotid artery disease include alteration in vision, headache, and features of transient ischemic attack to variable degree of stroke. Clinical evaluation suggestive of carotid artery disease include a high-pitched bruit at the ipsilateral neck auscultation and occasionally changes in the retinal examination.

The degree of stenosis of the carotid artery is determined by non-invasive tests such as duplex ultrasonography, or computed tomographic angiography (CTA) or magnetic resonance angiography (MRA). Duplex ultrasound imaging is safe, quick, and considered reliable method for initial screening for carotid artery disease. Conventional carotid angiography remains an option.

Treatment :

1.Medical therapy

Mainstays of medical therapy include antiplatelet, anti-hypertensive and lipid lowering agents, control of diabetes if present and correcting the modifiable risk factors like smoking and lifestyle changes. Treatment with a statin medication is recommended for all patients with extracranial carotid or vertebral atherosclerosis to reduce low-density lipoprotein (LDL) cholesterol to target level.

Lifestyle modification including diet modification, reduction of alcohol intake, exercise prescription, and smoking cessation is advised.

2. Surgical Therapy

The operation involves clamping of the carotid arteries, incision and plaque extraction to remove stenosis, occasionally patch enlargement of various forms of bypass may be required. The importance of such surgery is cerebral protection strategies by monitoring cerebral flow with transcranial Doppler, EEG, assessment of post occlusion pressure and the use of carotid shunts when required remain the mainstay of such procedures.

The various ECST, NASCET and VA309 (Veterans Affairs 309) trials have demonstrated significant benefit of surgical intervention over medical treatment for secondary stroke prevention in patients with ipsilateral 50%–99% symptomatic carotid artery stenosis, with maximal efficacy in patients with 70%–99% carotid stenosis. In asymptomatic carotid stenosis, ACAS (Asymptomatic Carotid Atherosclerosis Study) and ACST-1 (Asymptomatic Carotid Surgery Trial) established the benefit of carotid artery endarterectomy (CEA) over medical therapy alone in patients with 60%–99% carotid stenosis.

3. Endovascular therapy :

Endovascular carotid artery angioplasty and stenting (CAS) for the prevention of stroke is still evolving as a treatment modality. Stenting and angioplasty involve the intra-arterial introduction of a catheter via guidewire and the deployment of a balloon, with or without stent, to expand the lumen of the carotid artery. Advantages of endovascular therapy include it being a quicker and less invasive than open procedure. Carotid artery stenting maybe preferred over surgery when: the lesion is not suitable for surgical access, radiation induced stenosis, restenosis after endarterectomy or clinically significant cardiopulmonary disease which increases the risk of anesthesia or surgery.

The primary limitation for performing CAS is an unfavorable anatomy of the arch or tortuosity of the arteries and certain specific arterial lesions can reduce success with this approach.

Cerebral Hyper Perfusion Syndrome:

This is one of the complications following correction of carotid artery stenosis. It is defined as sudden increase in cerebral blood flow of more than 100 % from the baseline with associated neurological sequel. A sudden increase in ipsilateral blood flow may occur to the affected cerebral hemisphere after carotid artery stenting or endarterectomy. Patients with severe (› 90 %) stenosis and limited collateral supply are at the greatest risk for hyper perfusion. Clinically may present from headache to extreme cases of cerebral edema.

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IV. 5. PERIPHERAL ARTERIAL DISEASES

Introduction

The term Peripheral Arterial Diseases (PAD) encompasses all arterial diseases other than coronary arteries and aortic pathology. Atherosclerosis remains the post prevalent etiology of this disease although inflammation of the arteries or thrombosis may cause the disease. The lower extremity vessels are affected more commonly than the upper extremity vessels. The major territories affected includes carotid and vertebral artery diseases, upper limb artery diseases, mesenteric artery diseases, renal artery diseases and lower limb artery disease.

Risk Factors

The risk of PAD increases with age and with exposure to major cardiovascular risk factors such as smoking, hypertension, dyslipidemia and diabetes. The following risk factors for peripheral arterial disease should be looked for:

- Age: The prevalence of PAD increases progressively with age, beginning after age of 40 years.
- Sex: PAD is cited historically as more prevalent in males compared with females.
- Family history of cardiovascular disease - coronary artery disease, cerebrovascular disease, aortic aneurysm, lower limb arterial disease and premature cardiovascular disease - fatal or non-fatal cardiovascular disease event or/and established diagnosis of cardiovascular disease in first degree male relatives before 55 years or female relatives before 65 years.
- History of Hypertension, diabetes, dyslipidemia, smoking, chronic kidney disease, sedentary life, dietary habits, Radiation therapy.

Clinical Presentation

The presentation may be silent or present with a variety of symptoms and signs indicative of ischemia. The clinical manifestations of PAD depend upon the location and severity of arterial stenosis or occlusion, and range from mild extremity pain with activity (i.e. claudication) to excruciating pain which may result in loss of limb or organ. Patients with PAD tend to have a higher risk of cardiovascular events as well.

Carotid and vertebral artery diseases present with transient ischemic attack (TIA), variable degree of stroke.

Upper limb artery diseases may present with subclavian steal syndrome - limb pain on exertion, limb ischemia or vertebra-basillar insufficiency.

Mesenteric artery diseases causing ischemia typical present as abdominal pain, particularly following meals and may be associated with weight loss

Renal artery diseases cause secondary hypertension or renal failure.

Lower limb artery disease generally present with typical claudication on walking, discoloration of lower limbs, ulcers in feet and poor healing of wounds of the extremities.

Bedside ABI – The resting ankle-brachial systolic pressure index (ABI) is a simple test that can be performed at the bedside and should be measured in patients with one or more findings consistent with PAD. The ABI is the ratio of the ankle systolic blood pressure divided by the brachial systolic pressure detected with a Doppler probe.

ABI readings- 1. Abnormal ≤ 0.9

2. Borderline 0.91-0.99

3. Normal 1.00- 1.40

4. Non compressible ≥1.40

Neurologic assessment – Lower extremity neurologic examination is important and should include motor and sensory testing. In the patient with acute limb ischemia, sensory loss and progressive lower extremity motor loss are ominous signs indicating the need for prompt intervention.

Investigations

A. Routine investigations
    a. Fasting blood glucose
    b. Fasting Lipid profile
    c. Serum creatinine and creatinine clearance
    d. Urine analysis- urinary protein, microalbuminuria
    e. Blood count
    f. Uric acid

B. Specific investigations
    a. HBA1c or impaired glucose tolerance test if fasting blood glucose is > 5.6mmol/l
    b. Lipoprotein (a) if family history of premature cardiovascular disease
    c. Quantitative proteinuria if positive urinary protein
    d. Ankle brachial index
    e. Exercise ABI performed in patients with exertional pain, and have non joint related leg symptoms and normal or borderline resting ABI
    f. In patient suspected of having critical limb ischemia an anatomic study such as duplex ultrasound, computed tomography angiogram, magnetic resonance angiogram or invasive angiogram should be performed.

Management of Peripheral arterial disease

A. Risk factor modification and medical management
    a. Smoking cessation
    b. Healthy diet
    c. Weight loss
    d. Regular physical exercise

e. Lipid Lowering agents to reduce LDL- C < 1.8 mmol/l or decrease by ≥50% if baseline values are 1.8- 3.5 mmol/l

f. Cilostazol to improve symptoms and increase walking distance in patient with claudication

g. Strict glycemic control in diabetic patients

h. Antiplatelet therapy in symptomatic patient

i. Control BP <140/90mmHg

j. ACEIs or ARBs should be considered in patient with PADs with hypertension

B. Antithrombotic therapy in patient with peripheral artery disease

a. Lower limb arterial disease

i. Symptomatic patients- long term Aspirin or Clopidogrel

ii. Revascularized patients- long term Aspirin or Clopidogrel

iii. Infra inguinal bypass- Aspirin or Clopidogrel or Vitamin K antagonist

iv. Infra inguinal stenting- Aspirin and Clopidogrel for at least one month

v. Below knee bypass with prosthetic graft- Aspirin and Clopidogrel

b. Oral anticoagulation

i. Patient with atrial fibrillation

ii. Patients with a mechanical prosthetic valve – Vitamin K anticoagulant advised

iii. After endovascular revascularization with low risk of bleeding and high risk of stent/ graft occlusion-OAC is combined with either Aspirin or Clopidogrel

iv. After endovascular revascularization with high risk of bleeding and high risk of stent/ graft occlusion, individualized decision should be done.

v. High risk patient- OAC is combined with either Aspirin or Clopidogrel

C. Endovascular or surgical revascularization is a reasonable treatment option for patient with lifestyle limiting claudication and inadequate response to medical management and exercise.

References:

1. Gerhard Herman et al. 2016 AHA/ACC guideline on management of patients with lower extremity peripheral artery disease. Circulation 2016;000:000-000
2. Victor Aboyans et al. 2017 ESC guidelines on diagnosis and treatment of peripheral artery diseases. Eur Heart J 2017, 39: 9, 763-816.
3. R Morcos, B Louka, A Tseng, S Misra, R McBane, H Esser, F Shamoun. The Evolving Treatment of Peripheral Arterial Disease Through Guideline Directed Recommendations. J Clin Med 2018,7,9.
4. 2012 NICE clinical guidelines on peripheral arterial disease: diagnosis and management

UNIT - V

Pericardial Disease

V. 1. ACUTE PERICARDITIS

Introduction

Acute pericarditis is a clinical syndrome caused by inflammation of pericardium and is associated with chest pain, a pericardial rub, and characteristic electrocardiographic changes. Etiology includes

1. Infectious causes: (Viral, Bacterial, Fungal, Parasitic),
2. Non-Infectious causes: Autoimmune, Neoplastic, Metabolic, Traumatic and iatrogenic, Drug related and
3. Other: Amyloidosis, aortic dissection, pulmonary arterial hypertension and chronic heart failure.

Table 1: Definitions and diagnostic criteria for pericarditis.

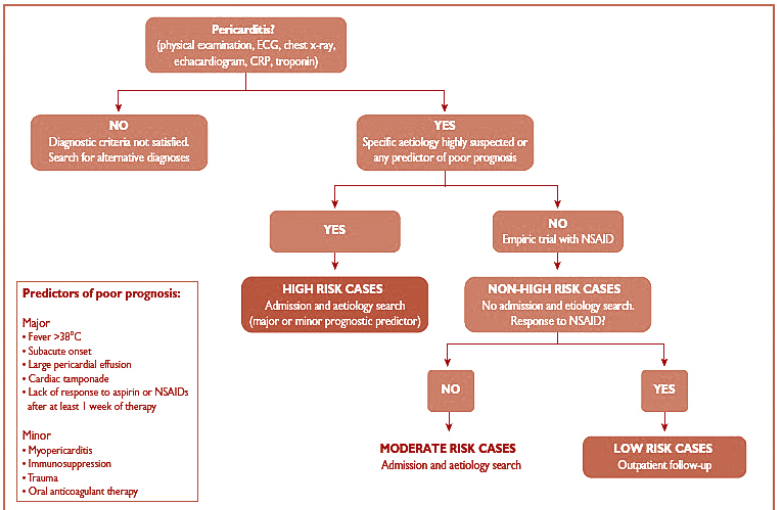
Acute	Inflammatory pericardial syndrome to be diagnosed with at least 2 of the 4 following criteria: 1. pericarditic chest pain (›85–90% of cases) 2. pericardial rubs (≤33% of cases) 3. new widespread ST-elevation or PR depression on ECG (up to 60% of cases) 4. pericardial effusion (new or worsening) (up to 60% of cases, generally mild). – Additional supporting finding: – Elevation of markers of inflammation i.e.CRP, ESR, and white blood cell count); – Evidence of pericardial inflammation by an imaging technique (CT, CMR).

Incessant	Pericarditis lasting for >4–6 weeks but <3 months without remission
Recurrent	Recurrence of pericarditis after a documented first episode of acute pericarditis and a symptom-free interval of 4–6 weeks or longer.
Chronic	Pericarditis lasting for >3 months.

The chest pain is typically sharp and pleuritic, improved by sitting up and leaning forward. The pericardial friction rub is a superficial scratchy or squeaking sound best heard with the diaphragm of the stethoscope over the left sternal border.

A chest X-ray is generally normal in patients with acute pericarditis since an increased cardiothoracic ratio only occurs with pericardial effusions exceeding 300 ml.

Although patients with purely fibrinous acute pericarditis may have a normal echocardiogram, the presence of a pericardial effusion is consistent with acute pericarditis and is one of the criteria for its diagnosis.



CRP = C-reactive protein; ECG = electrocardiogram.
Proposed triage of acute pericarditis according to epidemiological background and predictors of poor prognosis at presentation (modified from refs 5, 6, 8, and 12). At least one predictor of poor prognosis is sufficient to identify a high risk case. Major criteria have been validated by multivariate analysis,(9) minor criteria are based on expert opinion and literature review. Cases with moderate risk are defined as cases without negative prognostic predictors but incomplete or lacking response to non-steroidal anti-inflammatory drug (NSAID) therapy. Low risk cases include those without negative prognostic predictors and good response to anti-inflammatory therapy. Specific aetiology is intended as non-idiopathic aetiology

Treatment

Most cases of acute pericarditis are uncomplicated and self-limited and such patients can be managed in the outpatient setting. Any clinical presentation that may suggest an underlying etiology (e.g. a systemic inflammatory disease) or with at least one predictor of poor prognosis (major or minor risk factors) warrants hospital admission and an etiology search.

The first nonpharmacological recommendation is to restrict physical activity beyond ordinary sedentary life until resolution of symptoms and normalization of CRP for patients. Aspirin or NSAIDs are mainstays of therapy for acute pericarditis.

Table 2: Commonly prescribed anti-inflammatory therapy for acute pericarditis

Drug	Usual dosing[a]	Tx duration[b]	Tapering[a]
Aspirin	750–1000 mg every 8h	1–2 weeks	Decrease doses by 250–500 mg every 1–2 weeks
Ibuprofen	600 mg every 8h	1–2 weeks	Decrease doses by 200–400 mg every 1–2 weeks
Colchicine	0.5 mg once (<70 kg) or 0.5 mg b.i.d. (≥70 kg)	3 months	Not mandatory, alternatively 0.5 mg every other day (< 70 kg) or 0.5 mg once (≥70 kg) in the last weeks

Corticosteroids should be considered as a second option in patients with contraindications and failure of aspirin or NSAIDs because of the risk of favoring the chronic evolution of the disease and promoting drug dependence; in this case they are used with colchicine. If used, low to moderate doses (i.e. prednisone 0.2–0.5 mg/kg/day or equivalent) should be recommended. The initial dose should be maintained until resolution of symptoms and normalization of CRP, then tapering should be considered.

Table 3: Commonly prescribed anti-inflammatory therapies for recurrent pericarditis (for further details see Web Tables 1A and 1B)

Drug	Usual initial dose[a]	Tx duration[b]	Tapering[a]
Aspirin	500–1000 mg every 6–8 hours (range 1,5–4 g/day)	weeks-months	Decrease doses by 250–500 mg every 1–2 weeks[b]
Ibuprofen	600 mg every 8 hours (range 1200–2400 mg)	weeks-months	Decrease doses by 200–400 mg every 1–2 weeks[b]
Indomethacin	25–50 mg every 8 hours: start at lower end of dosing range and titrate upward to avoid headache and dizziness.	weeks-months	Decrease doses by 25 mg every 1–2 weeks[b]
Colchicine	0.5 mg twice or 0.5 mg daily for patients <70 kg or intolerant to higher doses.	At least 6 months	Not necessary, alternatively 0.5 mg every other day (<70 kg) or 0.5 mg once (≥70 kg) in the last weeks

Prognosis

Most patients with acute pericarditis (generally those with presumed viral or idiopathic pericarditis) have a good long-term prognosis. Cardiac tamponade rarely occurs in patients with acute idiopathic pericarditis, and is more common in patients with a specific underlying etiology such as malignancy, TB or purulent pericarditis. Constrictive pericarditis may occur in <1% of patients with acute idiopathic pericarditis, and is also more common in patients with a specific etiology. Approximately 15–30% of patients with idiopathic acute pericarditis who are not treated with colchicine will develop either recurrent or incessant disease, while colchicine may halve the recurrence rate.

References:

1. ESC 2015 Guidelines for the diagnosis and management of pericardial diseases. Eur Heart J. 2015; 36 :2921–64

V. 2. CONSTRICTIVE PERICARDITIS

Background

Constrictive pericarditis (CP) is a chronic inflammatory process, often characterized by chronic scarring, fibrosis, loss of elasticity of the pericardial sac and calcification of the pericardium associated with diastolic dysfunction, eventually leading to low cardiac output and heart failure. Constrictive pericarditis can occur after virtually any pericardial disease process, but only rarely follows recurrent pericarditis. The risk of progression is especially related to the etiology: low (<1%) in viral and idiopathic pericarditis, intermediate (2–5%) in immune-mediated pericarditis and neoplastic pericardial diseases and high (20–30%) in bacterial pericarditis, especially purulent pericarditis. However, Tuberculous and purulent bacterial pericarditis are major causes in developing countries like Nepal.

Clinical presentation

Constrictive pericarditis is characterized by impaired diastolic filling of the ventricles due to pericardial disease. The classic clinical picture is characterized by signs and symptoms of right heart failure with preserved right and left ventricular function in the absence of previous or concomitant myocardial disease or advanced forms. Patients complain about fatigue, peripheral oedema, breathlessness and abdominal swelling. Venous congestion, hepatomegaly, pleural effusions and ascites may occur. Although classic and advanced cases show prominent pericardial thickening and calcifications in chronic forms, constriction may also be present with normal pericardial thickness in up to 20% of the cases.

Diagnosis

A diagnosis of constrictive pericarditis is based on the association of signs and symptoms of right heart failure and impaired diastolic filling due to pericardial constriction by one or more imaging methods, including echocardiography, CT, CMR, and cardiac catheterization. The main differential diagnosis is with restrictive cardiomyopathy.

Diagnostic evaluation	Constrictive pericarditis	Restrictive cardiomyopathy
Physical findings	Kussmaul sign, pericardial knock	Regurgitant murmur, Kussmaul sign may be present, S3 (advanced).
ECG	Low voltages, non-specific ST/T changes, atrial fibrillation.	Low voltages, pseudoinfarction, possible widening of QRS, left-axis deviation, atrial fibrillation.
Chest X-ray	Pericardial calcifications (1/3 of cases).	No pericardial calcifications.
Echocardiography	• Septal bounce. • Pericardial thickening and calcifications. • Respiratory variation of the mitral peak E velocity of >25% and variation in the pulmonary venous peak D flow velocity of >20% • Colour M-mode flow propagation velocity (Vp) >45 cm/sec. • Tissue Doppler: peak e' >8.0 cm/s.	• Small left ventricle with large atria, possible increased wall thickness. • E/A ratio >2, short DT. • Significant respiratory variations of mitral inflow are absent. • Colour M-mode flow propagation velocity (Vp) <45 cm/sec. • Tissue Doppler: peak e' <8.0 cm/s.
Cardiac Catheterization	'Dip and plateau' or 'square root' sign, right ventricular diastolic, and left ventricular diastolic pressures usually equal, ventricular interdependence (i.e. assessed by the systolic area index >1.1).[a]	Marked right ventricular systolic hypertension (>50 mmHg) and left ventricular diastolic pressure exceeds right ventricular diastolic pressure (LVEDP >RVEDP) at rest or during exercise by 5 mmHg or more (RVEDP <1/3 RVSP).
CT/CMR	Pericardial thickness >3–4 mm, pericardial calcifications (CT), ventricular interdependence (real-time cine CMR).	Normal pericardial thickness (<3.0 mm), myocardial involvement by morphology and functional study (CMR).

Management

Although the mainstay of treatment of chronic permanent cases is surgery, medical therapy may have a role in 1) therapy of specific etiologies (i.e. tuberculous pericarditis) e.g. antituberculosis antibiotics may significantly reduce the risk of constriction from >80% to <10%, 2) may solve the transient constriction occurring in 10–20% of cases within a few months, generally as a temporary phenomenon during the resolution of pericarditis, 3) is supportive and aimed at controlling symptoms of congestion in advanced cases and when surgery is contraindicated or at high risk.

Table 1 Definitions and therapy of main constrictive pericardial syndromes (adapted from Imazio *et al.*[51])

Syndrome	Definition	Therapy
Transient constriction (d.d. permanent constrictive pericarditis, restrictive CMP).	Reversible pattern of constriction following spontaneous recovery or medical therapy.	A 2–3-month course of empiric anti-inflammatory medical therapy.
Effusive-constrictive pericarditis (d.d. cardiac tamponade, constrictive pericarditis).	Failure of the right atrial pressure to fall by 50% or to a level below 10 mmHg after pericardiocentesis. May be diagnosed also by non-invasive imaging.	Pericardiocentesis followed by medical therapy. Surgery for persistent cases.
Chronic constriction (d.d. transient constriction, restrictive CMP).	Persistent constriction after 3–6 months.	Pericardiectomy, medical therapy for advanced cases or high risk of surgery or mixed forms with myocardial involvement.

References:

1. ESC 2015 Guidelines for the diagnosis and management of pericardial diseases. Eur Heart J. 2015; 36 :2921–64

V. 3. PERICARDIAL EFFUSION AND CARDIAC TAMPONADE

Pericardial effusion:

Collection of fluid in the pericardium is called pericardial effusion. Any pathological process usually causes an inflammation with the possibility of increased production of pericardial fluid (exudate). An alternative mechanism of accumulation of pericardial fluid may be decreased reabsorption due to a general increase in systemic venous pressure as a result of congestive heart failure or pulmonary hypertension (transudate).

Table 1: 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

Causes include idiopathic, infectious, autoimmune, acute Myocardial infarction, aortic dissection, metabolic disorders, neoplastic, trauma, drugs and radiation. TB is the dominant cause in developing countries (.60%), where TB is endemic.

Clinical picture

The clinical presentation of pericardial effusion varies according to the speed of pericardial fluid accumulation. Classic symptoms include dyspnea on exertion, orthopnea, chest pain and/or fullness. Other symptoms due to local compression may include nausea (diaphragm), dysphagia (oesophagus), hoarseness (recurrent laryngeal nerve) and hiccups (phrenic nerve). Non-specific symptoms include cough, weakness, fatigue, anorexia and palpitations.

Physical examination may be absolutely normal in patients without haemodynamic compromise. When tamponade develops, classic signs include neck vein distension with elevated jugular venous pressure at bedside examination, pulsus paradoxus and diminished heart sounds on cardiac auscultation in cases of moderate to large effusions. Pericardial friction rubs are rarely heard; they can usually be detected in patients with concomitant pericarditis.

Diagnosis

ECG reveals sinus tachycardia, low voltage ECG, electrical alternans. The diagnosis of pericardial effusion is generally performed by echocardiography, which also enables semiquantitative assessment of the pericardial effusion size and its haemodynamic effects. Although echocardiography remains the primary diagnostic tool for the study of pericardial diseases CT and CMR provide a larger field of view, allowing the detection of loculated pericardial effusion and pericardial thickening and masses, as well as associated chest abnormalities or systemic diseases.

Treatment

First step is to assess its size, hemodynamic importance (especially the presence of cardiac tamponade) and possible associated diseases (either cardiovascular or systemic diseases). Therapy of pericardial effusion should be targeted at the etiology. In about 60% of cases, the effusion is associated with a known disease and the essential treatment is that of the underlying disease. When pericardial effusion is associated with pericarditis, management should follow that of pericarditis. When pericardial effusion becomes symptomatic without evidence

of inflammation or when empiric anti-inflammatory drugs are not successful, drainage of the effusion should be considered. Pericardiocentesis alone may be necessary for the resolution of large effusions, but recurrences are also common, and pericardiectomy or less invasive options (i.e. pericardial window) should be considered whenever fluid reaccumulates, becomes loculated or biopsy material is required.

The prognosis of pericardial effusion is essentially related to the etiology.

Triage and management recommended by ESC is mentioned below.

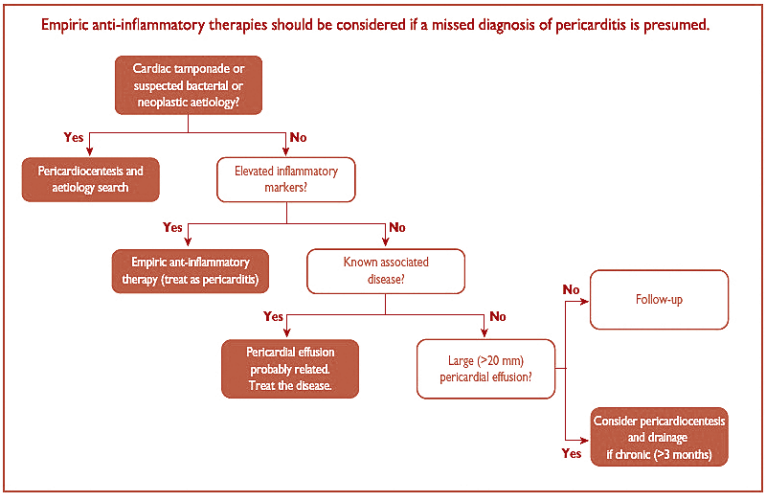


Figure 1: A simplified algorithm for pericardial effusion triage and management.

Cardiac tamponade

Cardiac tamponade is a life-threatening, slow or rapid pericardial accumulation of fluid, pus, blood, clots or gas compressing the heart as a result of inflammation, trauma, rupture of the heart or aortic dissection. The development of tamponade is based on size of effusion and rate of fluid accumulation.

Clinical signs in a patient with cardiac tamponade include tachycardia, hypotension, pulsus paradoxus, raised jugular venous pressure, muffled heart sounds, decreased electrocardiographic voltage with electrical alternans and an enlarged cardiac silhouette on chest X-ray with slow-accumulating effusions. A key diagnostic finding is pulsus paradoxus (inspiratory drop in systolic blood pressure >10mmHg).

Signs of tamponade can be identified by echocardiography: swinging of the heart, early diastolic collapse of the right ventricle, late diastolic collapse of the right atrium, abnormal ventricular septal motion, exaggerated respiratory variability (>25%) in mitral inflow velocity, inspiratory decrease and expiratory increase in pulmonary vein diastolic forward flow, respiratory variation in ventricular chamber size, aortic outflow velocity (echocardiographic pulsus paradoxus) and inferior vena cava plethora.

Treatment:

The treatment of cardiac tamponade involves drainage of the pericardial fluid, preferably by needle pericardiocentesis, with the use of echocardiographic or fluoroscopic guidance, and should be performed without delay in unstable patients. Alternatively, drainage is performed by a surgical approach, especially in some situations such as purulent pericarditis or in urgent situations with bleeding into the pericardium.

References:

1. ESC 2015 Guidelines for the diagnosis and management of pericardial diseases. Eur Heart J. 2015; 36 : 2921–64

UNIT - VI

Myocarditis, Cardiomyopathy, Heart Failure

VI. 1. HEART FAILURE WITH PRESERVED EJECTION FRACTION (HFpEF)

Heart failure with preserved ejection fraction (HFpEF), also referred to as diastolic heart failure, is characterized by signs and symptoms of heart failure and a left ventricular ejection fraction (LVEF) greater than 50%.

Epidemiology

HFpEF accounts almost one-half of patients of heart failure. Risk factors include older age, female sex, obesity, hypertension, tobacco use, diabetes mellitus, coronary artery disease (CAD), valvular heart disease, and atrial fibrillation.

Signs and Symptoms of HFpEF

Common symptoms of HFpEF include fatigue, weakness, dyspnea, orthopnea, paroxysmal nocturnal dyspnea, and edema.

Diagnosis

The diagnosis should include the following:

(1) Symptoms and signs of HF.

(2) An LVEF ≥50%.

(3) Objective evidence of cardiac structural and/or functional abnormalities consistent with the presence of LV diastolic dysfunction/raised LV filling pressures, including raised Natriuretic Peptides (NPs)

Table: Objective evidence of cardiac structural, functional and serological abnormalities consistent with the presence of left ventricular diastolic dysfunction/raised left ventricular filling pressures

Parameter[a]	Threshold	Comments
LV mass index **Relative wall thickness**	≥**95** g/m^2 (Female), ≥**115** g/m^2 (Male) >**0.42**	Although the presence of concentric LV remodelling or hypertrophy is supportive, the absence of LV hypertrophy does not exclude the diagnosis of HFpEF
LA volume index[a]	>**34** mL/m^2 (SR)	In the absence of AF or valve disease, LA enlargement reflects chronically elevated LV filling pressure (in the presence of AF, the threshold is >40 mL/m^2)
E/e' ratio at rest[a]	>**9**	Sensitivity 78%, specificity 59% for the presence of HFpEF by invasive exercise testing, although reported accuracy has varied. A higher cut-off of 13 had lower sensitivity (46%) but higher specificity (86%).[71,259,274]
NT-proBNP **BNP**	>**125** (SR) or >**365** (AF) pg/mL >**35** (SR) or >**105** (AF) pg/mL	Up to 20% of patients with invasively proven HFpEF have NPs below diagnostic thresholds, particularly in the presence of obesity
PA systolic pressure **TR velocity at rest**[a]	>**35** mmHg >**2.8** m/s	Sensitivity 54%, specificity 85% for the presence of HFpEF by invasive exercise testing[259,261]

AF = atrial fibrillation; BNP = B-type natriuretic peptide; E/e'ratio = early filling velocity on transmitral Doppler/early relaxation velocity on tissue Doppler; HFpEF = heart failure with preserved ejection fraction; LA = left atrial; LV = left ventricular; NP = natriuretic peptide; NT-proBNP = N-terminal pro-B-type natriuretic peptide; PA = pulmonary artery; SR = sinus rhythm; TR = tricuspid regurgitation.
Note: The greater the number of abnormalities present, the higher the likelihood of HFpEF.
[a]Only commonly used indices are listed in the table; for less commonly used indices refer to the consensus document of the ESC/HFA.[259]

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Management:

To date, no treatment has been shown to convincingly reduce mortality and morbidity in patients with HFpEF.

Patients with HFpEF and symptoms of volume overload should be treated with diuretics.Hypertension should be treated according to appropriate guidelines. Although RCTs of several medications showed fewer heart failure hospitalizations, this benefit was offset by increases in hospitalizations for other reasons. Thus, in the absence of hypertension, the evidence does not support treating patients with HFpEF with any medication except diuretics. Reducing body weight in obese patients and increasing exercise may further improve symptoms and exercise capacity and should therefore be considered in appropriate patients. Comorbid like atrial fibrillation and CAD should be treated.

References:

1. Shaha KB, Tamrakar R, KC MB et al.Heart failure with preserved ejection; the other half of the heart failure, how it stands in 2013. Nepalese Heart Journal 2013;10(1):46-56.
2. Owan TE, Hodge DO, Herges RM, et al.Trends in prevalence and outcome of heartfailure with preserved ejection fraction. NEngl J Med. 2006;355:251-9.
3. Curtis JP, Sokol SI, Wang Y, et al. The association of left ventricular ejection fraction, mortality, and cause of death in stable outpatients with heart failure. J Am Coll Cardiol. 2003; 42:736.
4. Henkel DM, Redfield MM, Weston SA, et al. Death in heart failure: a community perspective. Circ Heart Fail. 2008;1:91.
5. Fukuta H, Goto T, Wakami K, Ohte N. Effects of drug and exercise intervention on functional capacity and quality of life in heart failure with preserved ejection fraction: a meta-analysis of randomized controlled trials. Eur J Prev Cardiol 2016;23:78–85
6. ESC guideline in the management of Heart failure 2021.

VI. 2. HEART FAILURE WITH REDUCED EJECTION FRACTION

Heart Failure with reduced Ejection Fraction (HFrEF) is defined as the clinical diagnosis of heart failure and Left ventricle ejection fraction(LVEF) ≤ 40%. Also referred to as systolic HF. The diagnosis of HFrEF requires the presence of symptoms and/or signs of HF and a reduced ejection fraction (LVEF≤ 40%). This is most usually obtained by echocardiography. It accounts for approximately 50% of all cases of heart failure.

Etiology of HFrEF

Coronary artery disease, hypertension are the most common cause of HFrEF. Dilated cardiomyopathy (DCM) is the most common type of cardiomyopathy to result in HFrEF.

Clinical manifestations

Symptoms

Dyspnea, Orthopnea, Paroxysmal nocturnal dyspnea. exercise intolerance, fatique

Physical examination

Sinus tachycardia, atrial fibrillation, raised jugular venous pulse, third heart sound, basal pulmonary rales, peripheral oedema with ankle swelling and hepatomegaly.

Investigations

Hematocrit, leukocyte, blood urea nitrogen and creatinine, glucose, serum electrolytes, liver function tests, lipid profile and thyroid function test should be done routinely. Natriuretic peptides and its precursor N terminal pro-BNP are sensitive and specific indices for discriminating between

causes of dyspnea. A normal BNP level in an untreated patient virtually excludes cardiac diseases.

ECG

Left ventricular hypertrophy, atrial enlargement, previous myocardial infarction, active ischaemia, conduction abnormalities, and arrhythmias may be present. An entirely normal ECG makes the diagnosis of HFrEF unlikely (<10%).

Chest X-ray

Pulmonary congestion (Kerley B lines and interstitial oedema with upper lobe blood diversion). Pleural effusions may be present in patients with biventricular failure.

Echocardiopraphy

The most useful test is the two-dimensional (2-D) echocardiogram /Doppler. Semiquantitavie assessment of LV size and function as well as presence and absence of valvular disease, global or regional wall motion.The most useful index of LV function is the EF.

MRI

MRI provides the most accurate estimation of ventricular structure and function. The use of gadolinium contrast allows detection of inflammation and scarring.

Coronary Angiogram

It is indicated when patients has angina or coronary artery disease.

Myocardial Ischaemia and viability studies

Ischemic patients in whom intervention is planned. Imaging modalities with comparable diagnostic accuracy are dobutamine echocardiography, nuclear imaging by SPECT and/or by PET, MRI with dobutamine and/or with contrast agent , CT with contrast agents.

Cardaic biopsy

Cardiac biopsy on a routine basis is not recommended in HFrEF.It is only indicated when specific cause is considered.

Prognosis

It remains incurable with poor prognosis and high mortality. Community based studies indicate that 30-40% of patients

die within 1 year of diagnosis and 60-70% die within 5 years, mainly from worsening HF or as a sudden cardiac arrest probably because of ventricular arrhythmia.

Management of HFrEF

Goal is to reduce morbidity (ie, reducing symptoms, improving health-related quality of life and functional status, decreasing the rate of hospitalization), retard progression of HF and to reduce mortality.

General measures

Regular aerobic exercise, weight loss, salt restriction, fluid restriction (1.5-2L/day in patients with severe symptoms and hyponatraemia), smoking cessation, avoidance of high altitude (>1500m) and vaccination against influenza and pneumococcus are recommended.

Drug therapy

b-blocker, CEI/ARB, Aldosterone antagonist and SGLT2 inhibitors are 4 pillars of HF therapy and reduce mortality. Diuretics and digoxin are helpful in improvement symptoms.

Diuretics

They are the first-line drugs in the treatment of patients with HF with reduced ejection fraction. They reduces the symptoms and oedema. Loop diuretic are the preferred diuretic. In loop diuretic resistant patients, other options include thiazide diuretic such metolazone or hydrochlorthiazide.

Drug	Starting dose	Target dose	Maximum dose
Furosemide	20mg once daily	As required	240mg twice daily
Torsemide	10mg once daily	As required	200mg once daily
Metolazone	2.5mg once daily	As required	10mg once daily
Hydrochlorothiazide	25mg once daily	As required	50mg once daily

Dose of available diuretic in HFrEF in Nepal

Angiotensin-converting enzyme inhibitors (ACEI)/ Angiotensin receptor blockers (ARB)

Meta analysis suggest a 23% reduction in mortality and a 35% reduction in the combination endpoint of mortality and hospitalization for HF in patients treated with ACEIs. ACEI improves symptoms, quality of life and exercise tolerance in patients with HFrEF. It also increases survival in patients with HFrEF. Benefit was seen across various subgroups but greatest in patients with the lowest LVEF.

Drug	Starting dose	Target dose
Enalapril	2.5mg twice daily	10mg twice daily
Ramipril	1.25mg once daily	10mg once daily

Dose of available ACEI in HFrEF in Nepal

ARB are equivalent but not superior to ACEI so ARBs are recommended to reduce morbidity and mortality in patients with prior or current symptoms of chronic HFrEF who are intolerant to ACE inhibitors because of cough or angioedema.

Drug	Recommended starting dose	Recommended target dose
Valsartan	40mg twice daily	160mg twice daily
Losartan	25mg daily	150mg daily
Irbesartan	150 once daily	300mg once daily
Telmisartan	40mg once daily	80mg once daily

Dose of available ARB in HFrEF in Nepal

Contraindication to the use of ACEI and ARB are bilateral renal stenosis, serum potassium of >5mmol/L and serum creatinine >2.25mg/dL.A history of angioedema edema or development of severe cough are contraindication of ACEI therapy. Half the ACEI/ARB dose if creatinine increases more than 50% compared to baseline. Stop ACEI/ARB if the increase is more than 100%.There is an evidence that use of low-dose(15-25% of maximal dose) ACEI or ARB in patients with advance renal disease (creatinine upto 5mg/dL) may be beneficial.

ß-blocker

ß-blockers reduce all cause of mortality, cardiovascular mortality, sudden death and death from worsening HF in HFrEF. Beneficial effects of ß-blocker are limited to specific drugs. Carvedilol, sustained release metoprolol and bisoprolol are the approved b-blocker in HFrEF. HFrEF patients should be treated with ACEI or ARB and be in relatively stable condition without the need of intravenous inotropes therapy and without signs of fluid retention before b-blocker therapy. ß-blockers should be started in a low dose, such as carvedilol 3.125mg twice daily, extended-release or control release metoprolol 12.5mg/d if there is NYHA III or IV HF, or 25mg/d if there is NYHA II HF, Bisoprolol 1.25mg once daily.The dose of ß-blocker should be doubled at 2 to 3 week interval with the maintenance dose of ß-blockers reached over 3 months. Contraindication to the use of ß-blocker are asthma (but not COPD),second or third degree AV block, sick sinus syndrome (bradycardia<50bpm) without permanent pacemaker.

Drug	Starting dose	Target dose
Carvedilol	3.125 twice daily	25 mg twice daily*
Metoprolol succinate	25mg once daily	200mg once daily
Bisoprolol	1.25mg once daily	10mg once daily

**In patients more than 84kg 50mg twice should be used.*

Dose of availableb-blockers in HFrEF in Nepal

Aldosterone Antagonist

Blockade of aldosterone receptor in addition to standard therapy substantially reduces the risk of both morbidity and death.ACC/AHA guideline recommend an aldoaterone antagonist in selected patients with class NYHA II to IV HFrEF patients who can be monitored carefully for renal function and potassium concentration. Patients should have a serum creatinine of 2.5mg/dl or lower in men and 2.0mg/dL or lower in women and the serum potassium should be <5.0mEq/L. It is believed that aldosterone inhibitors work via a class effect. Spironolactone is the treatment of choice due to its low cost and to use eplerenone if patient develop gynaecomastia.

Drug	Starting dose	Target dose
Spironolactone	12.5 to 25mg once daily	25mg once daily
Eplerenone	25mg once daily	50mg once daily

Dose of available Aldosterone antagonist in HFrEF in Nepal

Angiotensin receptor-neprilysin inhibitor (ARNI)

ARNI is a recent major advances in the management of HF.LCZ696 is a novel, orally active, first-in-class ARNI that combined valsartan (an ARB) and sacubitril. It acts by augmenting the natriuretic peptide system(NPS) and inhibiting the RAAS. Sacubitril/valsartan should be started from 50 mg twice daily and the targeted dose 200 mg twice daily.

Sodium-glucose co-transporter 2 inhibitors (SGLT2 inhibitors)

SGLT2 inhibitors (dapagliflozin or empagliflozin) are recommended, in addition to optimal medical therapy with an ACE-I/ARNI, a beta-blocker and an MRA, for patients with HFrEF regardless of diabetes status. The diuretic/natriuretic properties of SGLT2 inhibitors may offer additional benefits in reducing congestion and may allow a reduction in loop diuretic requirement.

Drug	Starting dose	Target dose
Dapagliflozin	10mg once daily	10mg once daily
Empagliflozin	10mg once daily	10mg once daily

Dose of SGLT2 inhibitors

Digoxin

DIG trail showed that it can reduces rate of hospitalization but does not improves survival in HF. In a recent meta-analysis digoxin use is associated with increased all-cause mortality in patients with AF regardless of concomitant HF. It should be used only in patients who have refractory HF despite optimal medical management, in patients with atrial fibrillation to control ventricular rate. A typical starting dose of 0.125mg of digoxin daily is appropriate in patients with normal renal function.

Ivabradine

Ivabradine reduced the combined endpoint of mortality or hospitalization for HF in patients with symptomatic HFrEF or LVEF ≤35%, in sinus rhythm and with a heart rate ≥70 beats per minute (bpm) who had been hospitalized for HF within the previous 12 months, receiving treatment with an evidence-based dose of b-blocker (or maximum tolerated dose), an ACEI (or ARB) and an aldosterone antagonist. Ivabradine should be started from 5mg twice daily and the target dose should reach 7.5mg twice daily.

Use of implantable devices-Implantable cardioverter defibrillator(ICD) and Cardiac Resynchronising therapy (CRT) and surgical intervention are specific specialist options in the management of HFrEF.

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VI. 3. HYPERTROPHIC CARDIOMYOPATHY

Background

Hypertrophic cardiomyopathy (HCM) is a genetic disorder transmitted by autosomal dominant pattern characterized by left ventricular hypertrophy in absence of another cardiac, systemic or metabolic diseases. It is the most common genetic heart disease with prevalence in the range of 0.02-0.23% in adults and the prevalence is similar in all racial groups. It is also the most frequent cause of sudden cardiac death in young individuals

HCM is frequently confused with athlete's heart in younger patients and hypertensive heart disease in older patients. It manifests as diastolic dysfunction and dysrhythmias.

Diagnosis

History and physical examination

Dyspnoea, angina, giddiness, palpitations or syncope are the common clinical manifestation, although the disease may be clinically silent and detected incidentally.

Cardiovascular examination is often normal except in patients with LVOT obstruction, where ejection systolic murmur at the left sternal edge and apex may be appreciated. The intensity of the murmur is increased by manoeuvres that reduce ventricular preload or afterload, such as standing up from the squatting position and during Valsalva manoeuvre.

Family history of sudden cardiac death, unexplained heart failure, cardiac transplantation, pacemaker of defibrillator implants may carry prognostic implications.

Resting and ambulatory electrocardiography

A standard 12-lead ECG may be normal (less than 6% of patients) but generally shows a variable combination of LVH, ST- and T-wave abnormalities and pathological Q-waves Asymptomatic non-sustained ventricular tachycardia (NSVT) occurs in 25% of adults and paroxysmal supraventricular arrhythmia occur in 38% of patients.

Ambulatory ECG monitoring is recommended at the initial clinical assessment to assess the risk of sudden cardiac death and stroke.

Echocardiography and other imaging modalities

Echocardiography is central to the diagnosis and monitoring of HCM.

In most patients, hypertrophy preferentially involves the basal interventricular septum, however an increase in ventricular wall thickness may be found in any location. Approximately one-third of patients have resting SAM of the mitral valve leaflets that results in obstruction of the LVOT, while another third have latent obstruction only during manoeuvres that change the loading conditions and LV contractility.

Other imaging modalities like cardiac magnetic resonance imaging or high resolution computed tomography provide superior images and are useful especially when acoustic window is poor. Detection of Late Gadolinium Enhancement (LGE) in MRI is indicative of fibrosis and is of prognostic significance.

Diagnostic criteria

In an adult, HCM is defined by a wall thickness ≥ 15mm in one or more LV myocardial segments-as measured by any imaging technique (echocardiography, cardiac magnetic resonance imaging (CMR) or computed tomography (CT)-that is not explained solely by loading conditions. However, in first-degree relatives of patients with unequivocal disease (LVH≥15mm), the clinical diagnosis is based on presence of otherwise unexplained increased LV wall thickness ≥ 13mm in one or more LV myocardial segments.

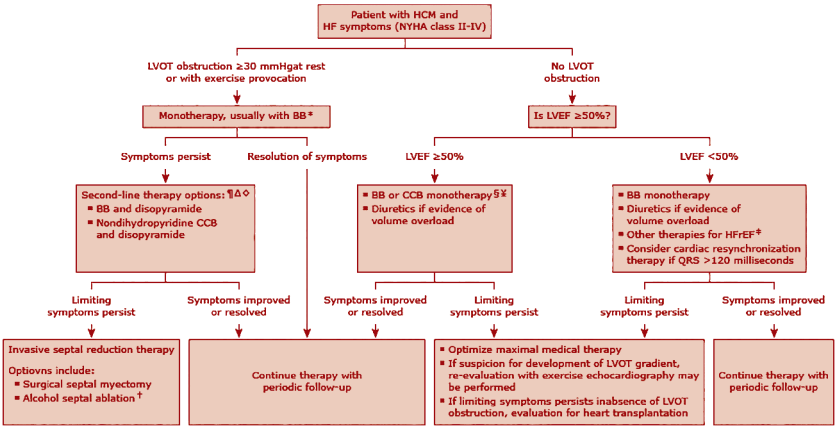
In children, the diagnosis of HCM requires LV wall thickness more than two standard deviations greater than the predicted mean (z-score›2), where a z-score is defined as the number of standard deviations from the population mean.

Management

Objectives of management of HCM are

- Alleviation of symptoms
- Improvement of functional capacity
- Prevention of complications and sudden cardiac death.

Algorithm for medical therapy in hypertrophic cardiomyopathy



Management of HCM with Left ventricular tract obstruction

All patients with LVOT obstruction should avoid dehydration and excess alcohol consumption, and weight loss should be encouraged.

Diuretics, arterial or venous dilators, including nitrates and phosphodiesterase type 5 inhibitors should be avoided.

Atrial fibrillation should be managed by prompt restoration of sinus rhythm or ventricular rate control. Digoxin should be avoided in patients with LVOT obstruction because of its positive inotropic effects.

By consensus, it is recommended to introduce all patients with symptomatic LVOT obstruction initially with maximum tolerated doses of non-vasodilating beta-blockers. Patients who are intolerant to beta-blockers or are symptomatic despite beta blockers are treated with rate limiting calcium channel blockers like verapamil or diltiazem. However, routine combination of both may not confer benefit and in fact may increase risk of hypotension and bradycardia.

These drugs improve functional capacity by reducing the force of ventricular contraction which in turn leads to reduced LVOT obstruction and improved cardiac output.

Disopyramide if available can be considered as addition for treating obstructive HCM which is beneficial because of its negative inotropic effect.

Surgery

It is typically reserved for those patients with symptoms despite optimal medical therapy.

Transaortic ventricular septal myectomy (Morrow procedure), in which a rectangular trough that extends distally to beyond the point of the mitral leaflet-septal contact is created in the basal septum below the aortic valve, is the most commonly performed surgery. It abolishes or substantially reduces LVOT gradients in over 90% of cases, reduces SAM related mitral regurgitation, and improves exercise capacity and symptoms. Long term symptomatic benefit is achieved in 70-80% of patients with a long term survival comparable to that of the general population

Septal alcohol ablation

In experienced centres, selective injection of alcohol into a septal perforator artery to create a localized septal scar has outcomes similar to surgery in terms of gradient reduction and symptomatic relief. The main non-fatal complication is AV block in 7-20% of the patients and the procedural mortality is similar to isolated myectomy.

Dual chamber pacing

Dual chamber pacing with short AV interval to reduce the LVOT gradient or to facilitate medical therapy with beta-

blockers and/or Verapamil, may be considered in selected patients with resting or provocable LVOTO ≥50mm Hg, sinus rhythm and drug refractory symptoms, who have contraindications for septal myectomy or are not suitable candidate for septal alcohol ablation.

Management of HCM without Left ventricular outflow tract obstruction

In patients with HCM without LVOT obstruction, the aim of therapy is to reduce LV diastolic pressures and improve LV filling by slowing the heart rate with beta-blockers, verapamil or diltiazem and cautious use of loop diuretics.

Standard principles of chronic heart failure management are followed in patients HCM without LVOT obstruction, with beta-blockers, angiotensin converting enzyme inhibitors, angiotensin receptor blockers, and mineralo-corticoid receptor antagonists

Prevention of Sudden Cardiac Death in HCM Patients

One of the most dreaded complications of HCM with or without obstruction is sudden cardiac death (SCD) from ventricular arrhythmia. All patients with HCM should be advised against participation in competitive sports and discouraged from intense physical activity, especially when they have risk factors for SCD and/or LVOT obstruction.

Implantable cardioverter defibrillator (ICD) must be considered to prevent SCD only in carefully selected individuals as a large number of ICD recipients experience inappropriate shocks and implant complications.

Primary prophylaxis

It is recommended that patients undergo a standardized clinical evaluation that records a pre-defined set of prognostic variable including age, family history of sudden cardiac death, unexplained syncope, LVOT gradient, maximum LV wall thickness, left atrial diameter and NSVT, to estimate 5-year risk of SCD using a web based calculator, HCM Risk-SCD model.

ICD are not recommended when the estimated 5-year risk of SCD is low (<4%). ICD may be considered when the risk

of SCD is Intermediate (4%-6%) and should be considered when the risk is high (≥6%).

Secondary prophylaxis

Patients with HCM who survive VF or sustained ventricular tachycardia are at very high risk of subsequent lethal cardiac arrhythmias and should receive and ICD. Beta-blockers and/ or amiodarone are recommended in patients with an ICD, who have symptomatic ventricular arrhythmias or recurrent shocks despite optimal treatment and device reprogramming.

Endocarditis Prophylaxis

Infective endocarditis in HCM is virtually confined to patients with LVOT obstruction and often the anterior mitral leaflet gets involved. Good oral hygiene should be encouraged but routine antibiotic prophylaxis is not recommended in patients with LVOT gradients.

Recommendation For Routine Follow-Up

Patients with HCM require lifelong follow-up to detect changes in symptoms, risk of adverse events, LVOT obstruction, LV function and cardiac rhythm. The frequency of monitoring is determined by the severity of disease, age and symptoms. Annual clinical examination, 12 lead electrocardiography, trans-thoracic echocardiography and ambulatory electrocardiography is recommended.

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VI. 5. MYOCARDITIS

Background

Myocarditis is defined as an inflammatory disease of the heart muscle and is an important cause of acute heart failure, sudden death, and dilated cardiomyopathy. Myocarditis is caused by a variety of bacterial and viral infections. Enteroviruses, especially coxsackievirus B, are often associated with acute myocarditis. However, with the advent of genetic analysis, adenovirus and parvovirus B19 have also been found to be frequent causes of myocarditis. Exposure to drug treatment, physical stimuli such as radiation and heat, metabolic disorders, immune disorders, and pregnancy are also causes of myocarditis. In the case of idiopathic myocarditis, the etiology is yet to be determined.

Myocarditis is a challenging diagnosis due to the heterogeneity of clinical presentations. The actual incidence of myocarditis is difficult to determine as endomyocardial biopsy, the gold standard is used infrequently. Autopsy studies in sudden cardiac death in young people is variable with prevalence ranging from 2 to 42,and in 46% children with Dilated Cardiomyopathy. The annual mortality rate per 100,000 people from cardiomyopathy and myocarditis in Nepal is reported as 2.9% and has increased by 25.8% since 1990, an average of 1.1% a year.

Clinical presentation

Myocarditis is preceded by flu-like symptoms (chills, fever, headache, skin rashes, muscle aches, joint pains, and general malaise) or gastrointestinal symptoms such as decreased appetite, nausea, vomiting, and diarrhea. Cardiac manifestations of myocarditis appear a few

hours to a few days after the initial signs and symptoms. Cardiac symptoms consist of those of heart failure, chest pain due to pericardial irritation, and symptoms associated with variable degrees of heart block or arrhythmia (tachy / bradyarrythmia). The possibility of myocarditis must be considered if a patient with such symptoms is febrile.

The clinical signs of myocarditis include fever, cardiac rhythm disturbance (tachycardia, bradycardia, and arrhythmia), hypotension, gallop rhythm, basal rales, jugular venous dilatation, and occasionally pericardial effusion and cardiac tamponade.

Diagnosis

Elevation in acute phase reactants like transient elevation of C-reactive protein (CRP), leukocytosis, aspartate aminotransferase (AST), lactate dehydrogenase (LDH), the MB form creatine kinase (CK-MB), and cardiac troponin T or I in blood. Troponin T is especially usefulfor immediate diagnosis however other potential causes of myocardial necrosis such as acute coronary syndromes need to be excluded.

Electrocardiography (ECG) is a sensitive and convenient means of diagnosis of myocarditis. It must be timely repeated, since minor abnormalities in the ECG detected initially may become clearer over time. Abnormal ST-T waves, ST segment elevation mimicking acute myocardial infarction or conduction block are frequently observed in myocarditis. A gradual increase in the width of the QRS complex (>120ms) is a sign of exacerbation of myocarditis. Continuous ECG monitoring is crucial to detect potentially fatal arrhythmias.

Echocardiography remains the key method for analyzing ventricular function in suspected myocarditis and helps to rule out other entities such as valve disease. Thus, all patients with suspected myocarditis should undergo echocardiographic studies at presentation and during follow-up. However, findings are nonspecific, and include global ventricular dysfunction, regional wall motion abnormalities, or diastolic dysfunction. Both in acute

and fulminant myocarditis, wall thickness may be mildly increased, but left ventricular (LV) diastolic dimensions are typically larger in acute myocarditis. As for systolic function, better recovery is normally seen in patients that survive after the acute phase of fulminant myocarditis when compared with acute myocarditis.

A chest X-ray is useful for visualizing cardiac enlargement due to pericardial effusion and also for evidence on pulmonary edema due to heart failure and any evidence of pneumonia or pleural effusion.

Cardiac magnetic resonance (CMR) can help confirm the diagnosis of myocarditis, especially in the acute phase of the disease.

Cardiac catheterization (if the patient's condition allows and after excluding coronary lesion) and endomyocardial biopsy is performed and is the gold standard technique for the diagnosis of myocarditis and inflammatory cardiomyopathy. The toxic, infectious-inflammatory, infiltrative or autoimmune processes that cause myocarditis occur at a cellular level, and no other diagnostic techniques can establish the nature of the etiological agent. However this is usually not always possible in our context.

Treatment

The inflammatory phase lasts one to two weeks, and is followed by a recovery phase. Myocarditis causes myocardial necrosis and inflammation, which result in cardiac dysfunction and failure.

As many cases of myocarditis are not clinically obvious, a high degree of suspicion is required to identify acute myocarditis. Fortunately, most patients have mild symptoms consistent with viral syndromes, and they recover with simple supportive care on an outpatient basis, including with slow rehabilitation and the implementation of evidence-based medical therapy. Repeat assessment with echocardiography may be helpful to determine the persistence of cardiac dysfunction.

Patients with asymptomatic or mildly symptomatic myocarditis with cardiac signs and symptoms should be admitted to the hospital, kept at bed rest, and monitored carefully. Treatment of myocarditis includes supportive therapy for symptoms of acute heart failure with salt restriction, use of diuretics, nitroglycerin/nitroprusside, and angiotensin-converting enzyme (ACE) inhibitors or Angiotensin Receptor Blockers (ARBs). Inotropic drugs (eg, dobutamine, milrinone) may be necessary for severe decompensation, although they are highly arrhythmogenic. Long-term treatment follows the same medical regimen of heart failure, including ACE inhibitors, beta blockers, and aldosterone receptor antagonists.

Treatment of underlying infectious or systemic inflammatory etiology if established is necessary. Nonsteroidal anti-inflammatory agents should be avoided in the acute phase, as their use may impede myocardial healing and actually exacerbate the inflammatory process and increase the risk of mortality.

Anticoagulation may be advisable as a preventive measure, as in other causes of heart failure, although no definitive evidence is available.

Antiarrhythmics can be used cautiously, although most antiarrhythmic drugs have negative inotropic effects that may aggravate heart failure.

Patients are usually very sensitive to digoxin and should use it with caution and in low doses or be avoided.

Patients who present with Mobitz II or complete heart block require temporary pacemaker placement. Very few patients require permanent pacemaker or automatic implantable cardioverter-defibrillator (AICD) placement.

Steroid is usually helpful in Giant Cell Myocarditis, Eosinophilic Myocarditis and Sarcoidosis. However, endomyocardial biopsy for confirmation of these diagnosis is not routinely performed. So, refractory myocarditis with persistent inflammation without signs of hemodynamic improvement, short-term treatment with high doses

of corticosteroids may be attempted. Treatment with immunoglobulin (IVIG) may also be considered. Mechanical circulatory support(Ventricular assist device or ECMO support) can be considered for those with refractory heart failure or cardiogenic shock not responding to medical management if available.

Follow up

Myocarditis patients can have partial or full clinical recovery; some may relapse many years after the first episode. Relapses should be managed similarly to the index episode. In patients who do not resolve, disease may continue subclinically and lead to Dilated Cardiomyopathy.

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UNIT - VII

Arrythmia

VII. 1. ARRHYTHMIAS - TACHYARRHYTHMIAS

Background:

Tachyarrhythmias, defined as abnormal heart rhythms with a ventricular rate of 100 or more beats per minute, are frequently symptomatic and often result in patients seeking care at their provider's office or the emergency department. . The symptoms of tachyarrhythmias can range from no symptoms or simple palpitations to sudden cardiac death. The awareness of regular or irregular cardiac rhythm varies greatly among the population. People with apparently structurally normal heart can develop cardiac arrhythmias.

Diagnosis:

1. Clinical: History (Palpitations, syncope, unusual symptoms like chest pain, shortness of breath and choking sensations) and Physical examination (Pulse, auscultation of heart sounds). Documentation of rapid heart rate by a health personal during the previous episode(s).
2. Investigations:

   In anyone who presents with a symptomatic tachyarrhythmia, a 12-lead electrocardiogram (ECG) should be obtained while a brief initial assessment of the patient's overall clinical assessment is performed.

Other investigation to record tachyarrhythmia's are

   a. Cardiac Monitor (Bed side monitor)
   b. Holter ECG Monitoring (24 hours)
   c. Event Recorders (up to a week) and Loop Recorder (up to 2 years) if available

Management:

Modality of management depends on the available facilities and the level of expertise.

The most important in initial management of tachyarrhythmia is assessment of clinical symptoms, identifying the haemodynamic stability of the patients and to determine whether the rhythm is sinus tachycardia. If the rhythm is not sinus tachycardia, or if there is any doubt that the rhythm, urgent cardioversion with DC shock to sinus rhythm is recommended in haemodynamically unstable patients.

Steps of Management in Acute Treatment:

1. Lay the patient on bed. Reassure the patient and make him/her feel comfortable.
2. Check vitals, oxygen saturation.
3. 12 lead ECG
4. Make diagnosis: Wide Complex Tachycardia (WCT) or Narrow Complex Tachycardia .
5. IV access:Open a peripheral vein.
6. Send blood for CBC, Renal Function test, Na+, K+, S. Creatinine, Cardiac enzymes (Only if necessary as per symptoms).
7. Sedate if necessary. (IV Midazolam 1 – 2 mg slowly: watch for apnea)
8. Attach monitor (if available)
9. Echocardiogram (if available)

Approach to 12 lead ECG for making diagnosis of narrow complex and wide complex tachyarrhythmia's are shown in Figure 1 and 2.

A narrow QRS complex is ‹120 milliseconds in duration, whereas a wide QRS complex is ≥120 milliseconds in duration.

ECG: electrocardiogram; AVNRT: atrioventricular nodal reentrant tachycardia; AVRT: atrioventricular reciprocating (bypass-tract mediated) tachycardia; AT: atrial tachycardia; SANRT: sinoatrial nodal reentrant tachycardia; AF: atrial fibrillation; AV: atrioventricular; VT: ventricular tachycardia; SVT: supraventricular tachycardia; WPW: Wolff-Parkinson-White.

∆ Monomorphic VT accounts for 80% of wide QRS complex tachycardias;

Figure 1. Algorithm for the initial ECG review and differential diagnosis of tachycardia

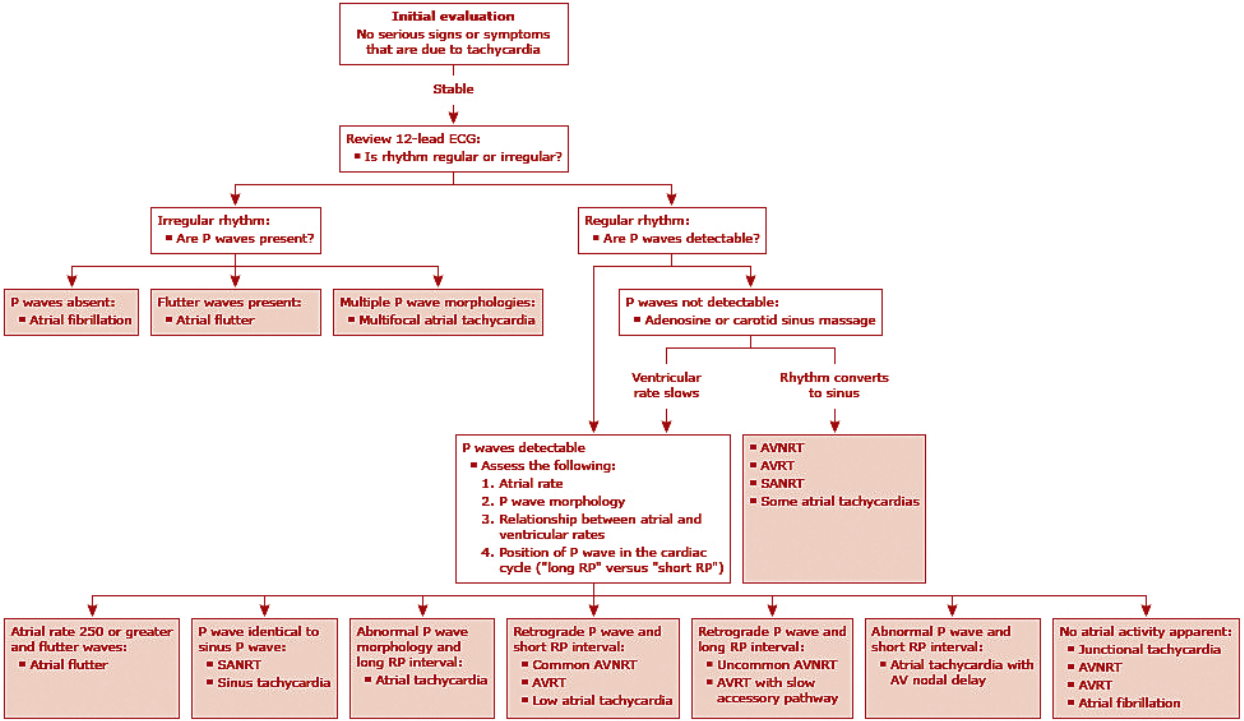

Figure 2. Algorithm for the evaluation of narrow QRS complex tachycardias in stable patients.

Management according to diagnosis:

A. If narrow complex (QRS width less than 120 msec) and haemodynamically stable (Paroxysmal Supraventricular Tachycardia (PSVT) or Atrial Tachycardia):

Steps:

1. Try Valsalva maneuver:
   Ask the patient to forcefully exhale against closed glottis and nasal passage. (Breath held against expiration). The patient should maintain the strain for 10 to 15 seconds and then release it and resume normal breathing. A modified Valsalva maneuver, which involves the standard strain (40 mmHg pressure for 15 seconds in the semirecumbent position) followed by supine repositioning with 15 seconds of passive leg raise at a 45 degree angle.
2. If not successful, try Carotid massage: Apply firm pressure with thumb over the carotid artery (with caution in elderly, check for carotid bruit first)

   Patient is placed in the supine position with the neck extended (ie, raising the chin away from the chest) to maximize access to the carotid artery. The carotid sinus is usually located inferior to the angle of the mandible at the level of the thyroid cartilage near the arterial impulse. Pressure is applied to one carotid sinus for 5 to 10 seconds. Although pulsatile pressure via vigorous circular motion may be more effective, steady pressure is recommended because it may be more reproducible
3. If not successful give 6 mg of adenosine rapid push with immediate flush, attach one 5 to 10 cc syringe in the medicine port of the IV cannula. (Don't mix blood with adenosine as it will cause deamination). Repeat with 12 mg of adenosine if not reverted. Inform the patient that he/she may devlop chest pain.

   Note : Adenosine can also precipitate bronchial asthma and sometimes atrial fibrillation.
4. If not controlled the Inj. Verapamil 2 to 2.5 mg slow push over 2 minutes. 5 to 10 mg may be repeated after 15 – 30 minutes.

5. Injection Metoprolol 5 mg IV over 1 – 2 minutes, can be repeated after 5 minutes (max dose 15 mg).
6. Other alternatives if available
    - Injection Esmolol 0.5 mg/kg over 1 minute then 0.05 mg/kg/min IV for 4 minutes (may increase by 0.05mg/kg up to 0.2 mg/kg/min)
    - Injection Diltiazem 0.25 mg/kg (average adult dose, 20 mg) IV over 2 minutes and after 15 minutes 0.35 mg/kg over 2 minutes.

Atrioventricular nodal reentrant tachycardia (AVNRT) and Orthodromic Atrioventricular reentrant tachycardia (AVRT)

- Hemodynamically unstable related to their arrhythmia, we recommend immediate DC cardioversion
- For haemodynamically stable patients Vagal Maneuvers, adenosine, ß- blockers or nondihydropyridine calcilum channel blcocker recommended.

Note Orthodromic AVRT: anterograde conducation via AV node and Retrograde Conduction Via Accessary pathway.

Focal Atrial tachycardia : hemodynamically unstable related to their arrhythmia immediate DC cardioversion recommended.

For Hemodynamically stable patient with beta blocker or non-dihydropyridine calcium channel blocker (ie, diltiazem or verapamil) and amiodarone is an acceptable alternative that may be preferred in a patient with borderline hypotension as amiodarone may slow the rate or convert the rhythm back to normal sinus.

Multifocal atrial tachycardia : Should be aimed at the treating underlying disease, correction of hypokalemia or hypomagnesemia . Rate control with non-dihydropyridine calcium channel blockers and beta blockers.

B. For Atrial Fibrillation with fast ventricular response:

Intravenous administration of a beta blocker or nondihydropyridine calciumchannel blocker is recommended to slow the ventricular heart rate in the acutesetting in patients without pre-excitation.

1. Injection Metoprolol 5 mg IV over 1 – 2 minutes, can be repeated after 5 minutes (max dose 15 mg).
2. If not reverted give Injection Amiodarone 150 mg bolus over 10 minutes, followed by maintenance of 1 mg/min over 8 hours and 0.5 mg/min over next 16 hours.
3. Injection Digoxin 0.5 mg IV slowly over 10 minutes in cases where b-blocker and nondihydropyridine calcium channel blocker are contraindicated.(Lower dose if already on Digoxin).
4. If haemodynamic unstable patient: Electrical cardioversion (synchronized) i.e. 120 - 200 Joules (Biphasic) or 360 Joules (if mono phasic).
5. Note: The need of anticoagulation is described in the separate chapter ie "Atrial Fibrillation".

If narrow complex and irregular (Atrial Fibrillation) and Haemodynamically stable:

Management of AF and the need of anticoagulation is described in the separate chapter ie "Atrial Fibrillation".

C. If narrow complex with "Flutter Waves in between QRS complexes" i.e. Saw Tooth Pattern (Atrial Flutter)

1. Injection Digoxin 0.5 mg IV slowly over 10 minutes
2. Amiodarone should be used only with other AV nodal blocking agents.
3. If Haemodynamically unstable: Synchronized defibrillation with 50 Joules (Bi Phasic) or 100 Joules (if Uni phasic) shock.

D. If Wide Complex Tachycardia (Can be SVT with aberrancy, Pre-excited tachycardia or VT) :

First is to differentiate between the various causes of Regular wide complex tachycardia and Irregular Wide complex tachycardia.

Regular Wide Complex Tachycardia:

- Monomorphic ventricular tachycardia
- Supraventricular tachycardia with aberrant conduction,
- Antidromic AVRT (Anterograde conduction Accesary pathway and retrograde Conduction through AVnode)

Irregular Wide Complex Tachycardia

- Polymorphic VT, including torsades de pointes
- Irregular narrow complex tachycardias with aberrant conduction, antegrade conduction over an accessory pathway (eg, preexcited AF), or underlying conduction delay (eg, AF with right bundle branch block)
- Ventricular fibrillation

Note : The most concerning potential cause of a wide QRS complex tachycardia is VT, and, in the majority of patients, the arrhythmia should be assumed to be VT until proven otherwise.

1. Trial of injection adenosine 6 mg IV fast push can be given (has a short half life of 9 seconds) if SVT with aberrancy .
2. If not reverted give Injection Amiodarone 150 mg bolus over 10 minutes, followed by maintenance of 1 mg/min over 8 hours and 0.5 mg/min over next 16 hours.(Watch for QT prolongation).
3. If Amiodarone is not successful we can give Injection Lignocaine 0.5 to o.75 mg/kg bolus every 5 to 10 minutes (maximum cumulative dose: 3 mg/kg), followed with continuous infusion (1 – 4 mg/min). Injection Procainamide also can be tried (but not available in Nepal).
4. If haemodynamically unstable:Treat as VT. Electrical D.C. Cardioversion (synchronized) 120 - 200 Joules (Biphasic), 360 Joules (if monophasic).

For Pre Excited Atrial Fibrillation (Atrial Fibrillation with WPW and anterograde conduction):

1. Procainamide injection is drug of choice (not available currently in Nepal).
2. Avoid IV Amiodarone, if recommended drug is unavailable, consider DC cardioversion
3. Other Drugs to be avoided: Digoxin, Beta Blockers, Verapamil, Diltiazem (As these medications blocks the AV node instead of the accessory pathway, thereby favoring conduction across AP which may result in Ventricular Fibrillation).

4. Haemodynamic Unstable : Electrical cardioversion maximum energy: 120 - 200 Joules (Biphasic), 360 Joules if monophasic. Note: No synchronization required.

E. If Ventricular Fibrillation or Pulseless VT,give D.C. Cardioversion (unsynchronized) 120 - 200 Joules (Biphasic), does not revert, can go the maximum energy available in the defibrillator. that can be given.

Note: The newer defibrillator machines are Bi Phasic.

Important point : Failure to record BP is not to be taken as haemodynamic collapse. If the patient is alert and comprehending your command then it might be possible that due to fast heart rate one is unable to record BP by a sphygmomanometer.

Clues to differentiate VT versus SVT in case of WCT:
Points favoring VT:

Clinical: Prior history of MI or PTCA, CABG. Dilated Cardiomyopathy (but may have supraventricular tachycardia as well). Q waves in old ECGs. Haemodynamic collapse

ECG:

1. Wide QRS (> 120 msec)
2. Atypical Bundle Branch block
3. RBBB with left axis deviation in the absence of preexisting RBBB+LAHB
4. LBBB with right axis deviation.
5. QS pattern in leads V5, V6.
6. Initiation with Premature Ventricular Contraction (PVC)
7. Tachycardia identical to the PVC during sinus rhythm
8. QRS onset to its peak (+ve or –ve) ≥ 50 msec
9. In aVR: r > 40 msec or notched 'Q'
10. VA dissociation, Fusion beats or capture beats
11. Concordance of "R" wave in pre cordial leads
12. Left Axis Deviation (esp. – 90 to 1800)
13. Absence of an "rS" complex in any of the precordial leads

14. Contralateral BBB pattern from the resting rhythm. (e.g. if tachycardia is in LBBB morphology and resting ECG shows RBBB pattern).
15. "Q" waves, ST elevations in old / past ECGs
16. Positive QRS in aVR

Clues for Pre excited AF (WPW):

1. Presence of delta waves in previous ECGs
2. Irregular wide complex rhythm(with varying QRS width but same axis and no significant change in morphology).

Clues for polymorphic VT: Irregular wide QRS rhythm with significant change in QRS width, morphology and axis.

Drugs use for Chronic Management in Various Arrhythmias:

1. Beta blockers to maximum tolerable dose (in absence of contraindications) i.e. Atenolol 25 to 100 mg OD, Metoprolol Succinate 25 to 200 mg OD (comes as extended release tablets), or Metoprolol Tartrate 12.5 to 100 mg BD.
2. Calcium channel blockers (Non dihydropyridines): i.e. Verapamil 40 tid (max 360 mg OD) or Diltiazem 30 tid (max 360 mg OD)
3. Amiodarone 100 – 200 mg OD (Need to check Thyroid Function Tests, Liver Function Tests and Chest X – ray every 6 months).

Radiofrequency Catheter Ablation

1. PSVTs
2. Typical Atrial Flutter (Isthmus dependent flutter)
3. Atypical atrial flutter
4. Atrial Tachycardias
5. Atrial fibrillation
6. VT in structural heart disease(Ischemic cardiomyopathy, non-ischemic cardiomyopathy
7. VTs in structurally normal heart
    a. Fascicular VT
    b. Out flow tract Premature Ventricular Contractions (PVCs)
    c. Out flow tract VT

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VII. 2. BRADY ARRHYTHMIAS

Background:

Bradyarrhythmias are caused by failure of impulse formation (sinus node dysfunction) or by failure of impulse conduction over the atrioventricular (AV) node to His Purkinje system. Symptoms of slow heart rate ranges from dizziness to syncope. The causes can be diseases that alter the structure and function of the conduction system or by extrinsic factors like (autonomic disturbances, drugs and electrolyte imbalance) can cause bradyarrhythmias.

Diagnosis:

Brady Arrhythmia is arbitrarily defined as a heart rate below 60 beats per minute. It can be physiologic, as in trained athletes who may have with low resting heart rates. Sinus bradycardia during sleep in elderly is common.

1. Clinical: History, (Dizziness, light headedness and syncope) and Physical examination (Pulse, auscultation of heart sounds). Documentation of slow heart rate by a health personal during previous episode(s).
2. Investigations:
   a. Bedside Electrocardiogram (ECG)
   b. Cardiac Monitor (Bed side monitor)
   c. Holter Monitoring (24 hours)

   Othere recorders.
   - Event recorders (up to one week)
   - - Loop Recorder (up to 2 years)

Causes of Bradyarrhythmias:

1. Sinus Bradycardia: Heart rate less than 60 (by pulse or ECG)
2. Sick Sinus Syndrome:
    a. Persistent spontaneous bradycardia not caused by drugs and inappropriate for physiological circumstances.
    b. Sinus arrest or Sinus exit block (P to P interval, exact multiple of baseline P to P Interval).
    c. Paroxysmal atrial tachycardia or atrial fibrillation.
3. Atrioventricular Block (AV Block):
    a. First degree (Delay in conduction): PR > 0.2 seconds
    b. Second degree (Intermittent Delay in conduction)
        i. Mobitz Type I (Gradual prolongation of PR till a P is not followed by QRS)
        ii. Mobitz Type II (Sudden blockage of P ie P is not followed by QRS)
    c. Third degree (Permanent blockage of conduction): No impulse from atria passes through the AV node. No relation of P to QRS and PP interval constant and RR interval also constant
    d. 2:1 AV block: Every 2nd P wave are blocked (ie not conducted to the ventricles)
    e. High degree AV block: Every 3rd or more 'P's are blocked (ie not conducted to the ventricles).

Management:

1. Sinus bradycardia: Treatment Per se not necessary, unless cardiac output is inadequate of results in or arrhythmias appear due to slow heart rate. Atropine (0.6 mg IV as an initial dose, repeated if necessary). Need to rule out reversible causes; such as drugs (beta blockers, non dihydropyridines, Amiodarone etc) and if trained athletes.

Indications of Permanent Pacemaker Implantation:

1. Sick Sinus Syndrome:
    a. To treat brady episodes in combination with antiarrhythmic medications to treat tachyarrhythmias.
    b. Symptomatic sinus bradycardia including sinus pauses.
    c. Patient becoming symptomatic with exercise or exertion.
    d. Symptomatic patient with documented bradycardia but there is no correlation between symptomsand brady episodes.
2. Acquired AV block(Without reversible causes):
    a. Symptomatic or asymptomatic Third degree or high degree AV block. Symptoms includes heart failure and ventricular arrhythmias presumed to be due to AV block.
    b. Third degree or high degree AV block asystole of more than 3 seconds or escape rate less than 40 beats per minute.
    c. Third degree or high degree AV block in patients with atrial fibrillation and pauses of more than 5 seconds.
    d. Second degree AV block (Mobitz type one or two) with symptomatic bradycardia.
    e. Second or third degree AV block with exercise (in absence of myocardial ischaemia).
    f. Asymptomatic type II AV block.
    g. Bifascicular block with
        - Intermittent third degree or high degree AV block.
        - Mobitz type II AV Block
        - Alternating Bundle Branch Block (LBBB at one instance and RBBB at other, RBBB with LAHB at one instance and LPHB at other).
        - Syncope when VT is excluded.
        - In patients with unexplained syncope and bifascicular block, in the presence of either

a baseline HV of ›_70 ms, second- or third-degree intra- or infra-Hisian block during incremental atrial pacing, or an abnormal response to pharmacological challenge

In patients with Normal sinus rhythm / Atrial arryhtmia:

Pacing is indicated In Sinus rhythm with permanent or paroxysmal third- or second-degree type 2, infranodal 2:1, or high-degree AVB, irrespective of symptoms

In patients with atrial arrhythmia (mainly AF) and permanent or paroxysmal third- or high-degree AVB irrespective of symptoms

3. After Myocardial Infarction:
   a. Persistent and symptomatic second or third degree AV block (AVB does not resolve within a waiting period of at least 5 days after MI)
   b. Bundle branch block with transient third degree or high degree AV block
4. Reflex Syncope: Indicated to reduce recurrent syncope in patients aged ›40 years, with severe, unpredictable, recurrent syncope who have:
   - Spontaneous documented symptomatic asystolic pause(s) ›3 s or asymptomatic pause(s) ›6 s due to sinus arrest or AVB; or
   - Cardioinhibitory carotid sinus syndrome; or
   - Asystolic syncope during tilt testing

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VII. 3. SUDDEN CARDIAC DEATH

Definition of Sudden Cardiac Death and allied terms:

- Sudden Cardiac Death(SCD) is natural death from cardiac causes due to abrupt loss of consciousness within one hour of the onset of an acute change in cardiovascular status. SCD is mostly due to VT/VF and less commonly due to pulseless electrical activity or asystole.
- Sudden cardiac arrest(SCA): sudden circulatory arrest within one hour of the symptoms. If resuscitation unsuccessful, it is then called Sudden Cardiac death; if successful, it is called aborted sudden cardiac arrest.
- Primary prevention of SCD: Prevention in a patient who has not yet experienced an aborted cardiac arrest or life-threatening arrhythmias.
- Secondary prevention of SCD: Prevention in a patient who has already experienced an aborted cardiac arrest or life threatening arrhythmias.

Impact of SCA:

- The chance of survival is reduced to 7-10 % each minute after the cardiac arrest. Therefore early CPR and defibrillation is the paramount.
- However, most of the SCA occurs out of hospital, 80% SCA occurs at home, 40% occurs during sleep or not witnessed and less than 1/3rd receive bystander CPR. That's why, even in the country with best EMS/ defibrillation programs, the survival is merely 8%.

Causes of SCD:

The causes and the incidence of SCD are different in different age groups:

- Below 30 years of age, the incidence of SCD is the lowest, 1 per 100,000person per year and the usual causes are cardiomyopathies and channelopathies.
- At the transition age of 30 to 45 years, the incidence of SCD is higher 1 per 1000person per year and the usual causes are concealed Coronary Artery Disease (CAD) and Dilated Cardiomyopathy (DCM).
- General population of age more than 35 years, the incidence is 1 in 500 to 1000 person per year and the usual causes are CAD and DCM.
- In advanced heart disease, the incidence of SCD is highest, 1 in 4to 10person per year.

Prevention of SCD:

- The biggest challenge for the prevention of SCD is to identify people who are at the risk of SCD
- Approximately 50% of cardiac arrests occur in individuals without a known heart disease or their first clinical presentation is SCD.There are no reliable markers to predict SCD.
- Although various markers have been studied to identify people who are at risk of SCD, Left Ventricular Ejection Fraction (LVEF) remains the only reliable parameters in heart failure patient to identify the patients who are at the risk of SCD.

Approach for SCD prevention:

Recommendations:

1. Screening first degree relative of SCD victims .
2. Screening athletes prior to participation in competitive sports.
3. As most common cause of SCD is CAD,measures to control controlling CAD risk factors is important..
4. Correction of myocardial ischemia with revascularization.
5. Medications like aspirin/clopidogrel, statins, ACEI/ARB, beta-blocker and aldosterone antagonist has shown to reduce mortality and SCD.

6. None of the antiarrhythmic medicine has shown survival benefit or to reduce SCD.
7. Implantable cardioverter Defibrillators (ICD) has shown to reduce SCD in high-risk patients.
8. If ICD is implanted for primary prevention in heart failure patients, the absolute risk reduction is 7% during 2 to 5 years follow up; number needed to treat being 14.
9. If ICD is inserted for secondary prevention in heart failure patients, the absolute risk reduction in 3 years follow up period is 11.3%; number needed to treat being nine.
10. Other than heart failure, ICD is recommended in cardiomyopathy like Hypertrophic Cardiomyopathy (HCM) Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC), Channelopathies like Long QT syndrome, Brugada syndrome and Catacholaminergic Polymorphic Ventricular Tachycardia (CPVT), if they have high-risk features.

Indications of ICD implantation:

1. ICD should be implanted in the following conditions:
    a. Survivors of cardiac arrest due to VF or haemodynamically unstable VT without any reversible cause(s).
    b. Structural heart disease with VT.
    c. Syncope of unknown origin with VF or haemodynamically significant VT induced in an electrophysiological study.
    d. In Myocardial Infarction (MI):
        i. 40 days post MI with LVEF ≤ 35% and NYHA Class II or III
        ii. 40 days post MI with LVEF ≤ 30% and NYHA Class I
        iii. Old MI with non sustained VT and inducible VF or sustained VT in an electrophysiological study and LVEF < 40%
    e. Dilated Cardiomyopathy (Non Ischaemic): LVEF ≤ 35%, NYHA Class II or III after 3 months of Optimal Medical therapy.

2. ICD may be considered in the following conditions:
    a. Dilated Cardiomyopathy (non ischaemic) with unexplained syncope and significant LV dysfunction.
    b. Sustained VT in normal or near normal ventricular function.
    c. In inheritable diseases and channelopathies
        i. Hypertrophic Cardiomyopathy (HCM) with one or more than one risk factors for SCD
        ii. Arrhythmogenic Right Ventricular Dysplasia / Cardiomyopathy (ARVD) with one of more than one risk factors for SCD
        iii. Long QT Syndrome (LQTS) with syncope and / or VT while on betablockers
        iv. Brugada Syndrome with syncope and / or VT
        v. Catacholaminergic Polymorphic VT (CPVT) with syncope and / or VT while on beta blockers
3. ICD is not indicated in:
    a. Expected survival with accepted functional class for less than 1 year
    b. Incessant VT (VT continuous and sustained VT during several hours which recurs promptly despite repeated interventions for termination) or VF
    c. Syncope of undetermined cause without inducible ventricular arrhythmias during EP study and structurally normal heart.
    d. VT/VF due to reversible conditions like electrolyte imbalance, drugs and trauma.
    e. If VT can be treated by catheter based ablation e.g VTs in structurally normal heart, Fascicular VT, Right Ventricular Outflow Tract VT and Idiopathic VT or Pre excited tachycardia due to WPW syndrome)
    f. Drug refractory severe heart failure, NYHA Class IV
    g. Severe psychiatric illness which might be aggravated following ICD implantation or preclude follow up

Special issue for ICD implantation in Nepal:

The most important reason is the device is pretty much costly. The patient need to know that he should be in constant and systematic follow up with periodic ICD interrogation with the programmer. The ICD generator needs to be changed approximatelyin 5 to 7 years' time and it depends on the number of shocks it delivers. The sensation of shock can range from small thump to being hit by a large stick. The patient also need to know that ICD does not improve the left ventricular function ie the heart failure symptoms doesn't get improved .A number of patients may receive an inappropriate shocks. In elderly people the benefit of ICD not much as compared to young. Likewise benefit of ICD is less evident in Non Ischaemic Dilated Cardiomyopathy in comparison to ischaemic. Post ICD there are still no guideline(s) in Nepal regarding driving private and or public vehicles, for sportsman, athletes and for high risk occupations.

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VII. 4. ATRIAL FIBRILLATION

Background

Atrial fibrillation(AF) is one of the major causes of stroke, heart failure, sudden death, and cardiovascular morbidity in the world. AF is independently associated with a two-fold increased risk of all-cause mortality in women and a 1.5-fold increase in men. Twenty to thirty percentage of patients with ischemic stroke is diagnosed to have AF. A single centre study in Nepal, the prevelance of AF in ischemic stroke is 12%.Non valvularAF is associated with a 5-fold increased risk of stroke, whereas AF in the setting of mitral stenosis is associated with 20 –fold increased risk of stroke. AF-related stroke is likely to be more severe than non–AF-related stroke.

Risk factors of AF:

Many cardiovascular diseases and the concomitant conditions increase the risk of developing AF.

1. Older age with HR 4.98-9.33
2. Hypertension with HR 1.32
3. Heart failure with HR 1.43
4. Valvular Heart Disease with HR 2.42
5. Myocardial infarction with HR 1.42
6. Obesity with HR 1.13-1.37
7. Diabetes with HR 1.25
8. COPD with HR 1.28 to 2.53
9. Sleep apnea with HR 2.18
10. Smoking with HR 1.32-2.05
11. Genetic with HR 0.4-3.2

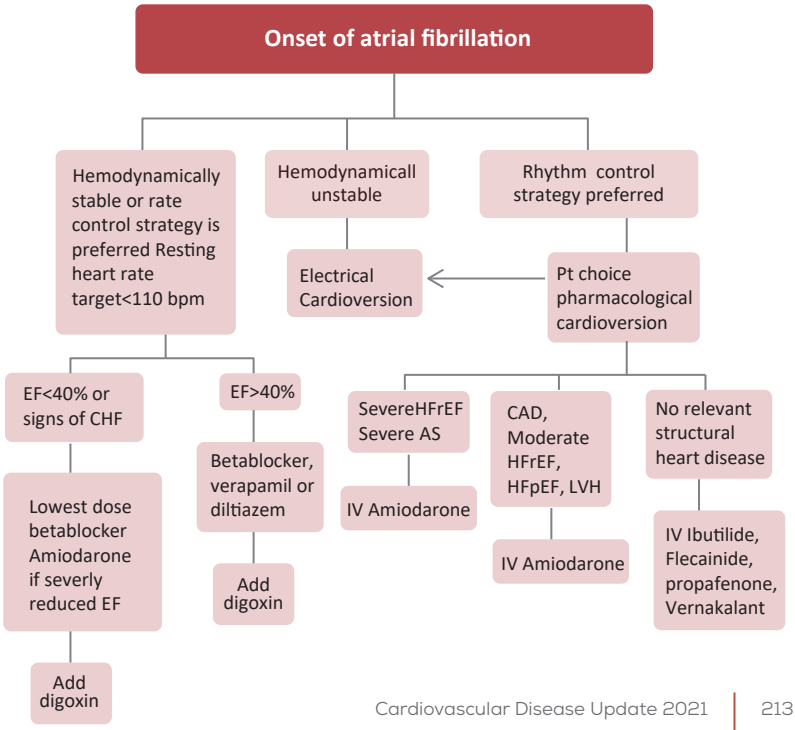
Classification of AF

1. First diagnosed AF- AF that has not been diagnosed before.
2. Paroxysmal AF- Episodes of AF shorter than 7 days, either self terminated or cardioverted. Most paroxysmal AF usually self terminates within 48 hrs
3. Persistent AF- Episodes of AF longer than 7 days, either self terminated or cardioverted
4. Long standing persistent AF- AF lasting more than 1 year and rhythm control strategy is being adopted
5. Permanent AF- Continuous AF where no more rhythm control strategy is adopted, in other words, AF is being accepted by physician and the patient.
6. Non-valvular AF: AF in the absence of rheumatic moderate to severe mitral stenosis, a mechanical or bioprosthetic heart valve, or mitral valve repair

Acute management of AF

Anticoagulation during cardioversion:

1. Immediate initiation of anticoagulation for all patients



scheduled for cardioversion

2. For AF>48 hours, anticoagulation 3 weeks prior to cardioversion and 4 weeks post cardioversion is required, thereafter requirement of long term anticoagulation depend on CHA_2DS_2-Vasc score.
3. If early cardioversion is desired, TOE can be done to exclude LA thrombus allowing immediate cardioversion

Long term management of AF

1. Management of precipitating factors:
   Lifestyle changes, medication and control of risk factors and treatment of underlying cardiovascular conditions

Table 1: Rate Controlling drugs their doses available in Nepal

	Intravenous administration	Oral maintenance dose	Contraindicated
Beta blockers			In case of asthma use beta-1- blockers Contraindicated in acute HF and history of severe bronchospasm Note : No data on atenolol and should not be used in HFrEF
Metoprolol tartrate	2.5 - 5 mg i.v. bolus; up to 4 doses	25 - 100 mg b.i.d	
Metoprolol XL (succinate)	N/A	50 - 400 mg o.d.	
Esmolol	500 mg/kg i.v. bolus over 1 min; followed by 50 - 300 mg/kg/min	N/A	
Nebivolol	N/A	2.5 - 10 mg o.d.	
Carvedilol	N/A	3.125 - 50 mg b.i.d.	
Atenolol	N/A	25 - 100 mg o.d	
Non-dihydropyridine calcium channel antagonists			
Verapamil	2.5 - 10 mg i.v. bolus over 5 min	40 mg b.i.d. to 480 mg (extended release) o.d.	Contraindicated in HFrEF Adapt doses in hepatic and renal impairment
Diltiazem	N/A	60 mg t.i.d. to 360 mg (extended release) o.d.	
Others			

Digoxin	0.5 mg i.v. bolus (0.75 - 1.5 mg over 24 hours in divided doses)	0.0625 - 0.25 mg o.d.	High plasma levels associated with increased mortality Check renal function before starting and adapt dose in CKD patients
Amiodarone	300 mg i.v. diluted in 250 mL 5% dextrose over 30 - 60 min followed by 900 - 1200 mg i.v. over 24 hours diluted in 500 - 1000 mL	200 mg o.d. (after loading 3 *200 mg daily over 4 weeks, then 200 mg daily)	In case of thyroid disease, only if no other options

2. Assess stroke risk and anticoagulation:
   a. In non-valvular AF, oral VKAs (warfarin) or Newer Oral Anticoagulant (NOAC) is indicated CHA_2DS_2-VASc score ≥2 in men and ≥3 in women and should be considered if CHA_2DS_2-VASc score > 1 in men and 2 in women.
   b. In Valvular AF, VKAs (Warfarin) should be considered. The role of NOAC in prosthetic valve is inferior to warfarin, andits role in Rheumatic MS is not known ; the ongoing INVICTUS trial might answer this question.
   c. When oral VKA(Warfarin) is used, target INR should be 2-3, or higher for high risk group. INR should be monitored periodically.
   d. Recommended NOAC are Dabigatran (RELY trial), Rivoraxiban (ROCKET-AF trial), Apixaban (ARISTOTLE trial), Edoxaban (ENGAGE AF-TIMI 48 trial)

Table 2: Doses of NOACS

	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
Standard dose	150 mg b.i.d.	20 mg o.d.	5 mg b.i.d.	60 mg o.d.
Lower dose	110 mg b.i.d.			
Reduced dose		15 mg o.d.	2.5 mg b.i.d.	30 mg o.d.
Dose-reduction criteria	Dabigatran 110 mg b.i.d. in patients with: • Age ≥80 years • Concomitant use of verapamil, or • Increased bleeding risk	CrCl 15 - 49 mL/min	At least 2 of 3 criteria: • Age ≥80 years, • Body weight ≤60 kg, or • Serum creatinine ≥1.5 mg/dL (133 µmol/L)	If any of the following: • CrCl 15 - 50 mL/min, • Body weight ≤60 kg, • Concomitant use of dronedarone, ciclosporine, erythromycin, or ketoconazole

Currently Only Rivaroxaban and Dabigatran are available in Nepal

Note :

Rivaroban should not be used in in hepatic insufficiency with Child-Turcotte-Pugh score B and C . Dabigatran Should note be used in Child-Turcotte-Pugh score C and use with caution with score of B

Rivaroxban and Dabigatran should not to be used with eGFR less than 15ml/min .

e. For bleeding risk assessment, a formal structured risk-score-based bleeding such as HASBLED risk assessment is recommended to help identify nonmodifiable and address modifiable bleeding risk factors in all AF patients, and to identify patients potentially at high risk of bleeding who should be scheduled for early and more frequent clinical review and follow-up.

f. Antiplatelet monotherapy is not recommended for stroke prevention in AF

g. LAA occlusion may be considered for stroke prevention if contraindication to oral anticoagulation

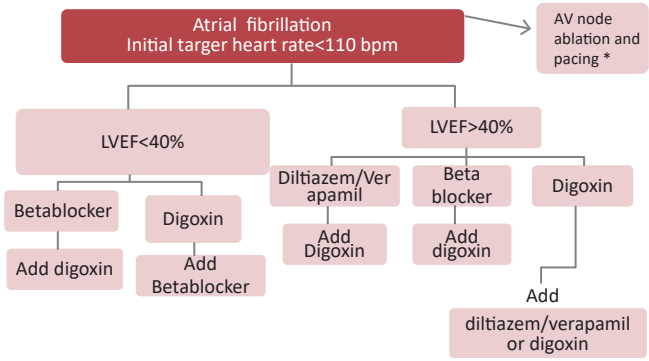
CHA_2DS_2-Vasc	Score	CHA_2Ds_2-VAsc	Adjusted stroke rate (% per year
		0	0
Congestive Heart failure	1	1	1.3
Hypertension	1	2	2.2
Age>75 years	2	3	3.2
Diabetes Mellitus	1	4	4.0
Stroke/TIA/TE	2	5	6.7
Vascular disease	1	6	9.8
Age:65-74	1	7	9.6
Female sex	1	8	6.7
Maximum score	9	9	15.20

Assessment of stroke risk in atrial fibrillation: CHA_2DS_2-VASc

Risk factors and definitions		Points awarded
H	Uncontrolled hypertension SBP ›160 mmHg	1
A	Abnormal renal and/or hepatic function Dialysis, transplant, serum creatinine ›200 mmol/L, cirrhosis, bilirubin › 2 upper limit of normal, AST/ALT/ALP ›3 upper limit of normal	1 point for each
S	Stroke Previous ischaemic or haemorrhagica stroke	1
B	Bleeding history or predisposition Previous major haemorrhage or anaemia or severe thrombocytopenia	1
L	Labile INRb TTR	1
E	Elderly Aged ›65 years or extreme frailty	1
D	Drugs or excessive alcohol drinking Concomitant use of antiplatelet or NSAID; and/or excessivec alcohol per week	1 point for each
Maximum Score		9

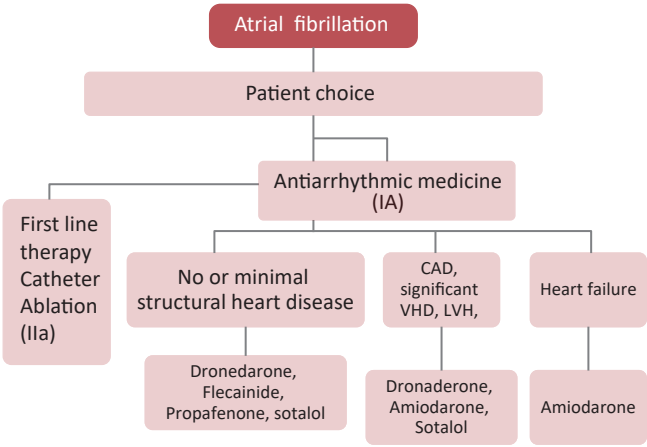
Clinical risk factors in the HAS-BLED score for bleeding risk assessment.

3. Long term rate control strategy



** If no adequate heart rate control with rate/rhythm control strategy*

4. Long term rhythm control strategy



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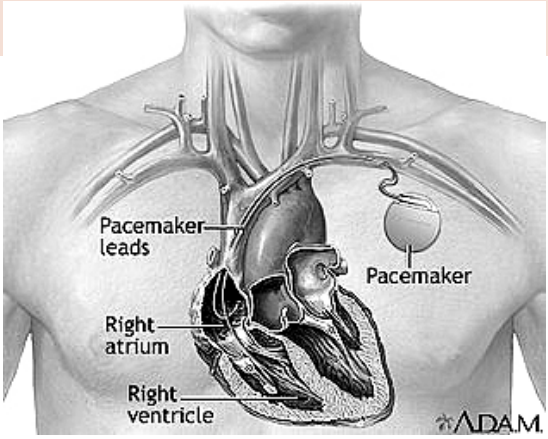
VII. 5. CARDIAC PACEMAKERS



1. Background

A cardiac pacemaker is a device that produces electrical stimuli that in turn causes cardiac contraction when intrinsic cardiac electrical activity is inappropriately slow or absent.

A pacemaker has basically two components: Pulse generator and pacing leads. The pulse generator houses the power supply(battery) and circuits that produce the pacing stimulus and provide other therapeutic and diagnostic functions. The leads are connected to the pulse generator with standard ports and transmit current to the endocardium.Pacemaker leads are unipolar or bipolar. Endocardial fixation of leads can be either passive or active. Epicardial leads are used most commonly in pediatric pacing and pacing during and after cardiac surgery. With recent advances, leadless pacemakers are also available.

Pacemakers may be classified based on the cardiac chambers in which the pacing system is able to operate. Single chamber pacemaker has single lead placed in right

atrium or right ventricle. Dual chamber pacemakers have two leads placed in right atrium and right ventricle and Triple chamber pacemaker or Biventricular pacemakers have 3 leads placed in right atrium, right and left ventricles. While the conventional single and dual chamber pacemakers are used to address the fundamental problems of bradycardia, biventricular pacemakers (CRT- cardiac resynchronization therapy) improve left ventricular pump function in patients with systolic heart failure.

Pacemaker Code

The code has been developed to make uniformity throughout the world. It has 5 letters or position and called NBG code which has combined version of NASPE (North American Society of Pacing and Electrophysiology) and BPEG (British Pacing and Electrophysiology Group).

TABLE 1 **Revised NASPE/BPEG Generic (NBG) Code for Antibradycardia, Adaptive Rate, and Multisite Pacing**

Position	I	II	III	IV	V
Category	Chamber(s) paced	Chamber(s) sensed	Response to sensing	Programmability, rate modulation	Multisite pacing
Letters	O = none	O = none	O = none	O = none	O = none
	A = atrium	A = atrium	T = triggered	R = rate modulation	A= atrium
	V = ventricle	V = ventricle	I = inhibited		V = ventricle
	D = dual (A + V)	D = dual (A + V)	D = dual (T + I)		D = dual (A + V)
Manufacturers' designation only	> S = single (A or V)	S = single (A or V)			

BPEG, British Pacing and Electrophysiology Group; NASPE, North American Society of Pacing and Electrophysiology. *Pacing Clin Electrophysiol*. 2002;25:260–264.

The general indications for pacemaker implantations are mention in section of Bradyarrhytmia.

Pacemaker implantation is done in cardiac catheterization labs by well-trained professionals.

A. Basic pacing modes used
    - AAI
        - atrial demand pacing
        - only used for sinus node dysfunction with intact AV conduction
    - VVI
        - ventricular demand pacing
        - mainly used in temporary pacing and AV block with chronic atrial fibrillation.
    - DDD
        - the most physiological pacing mode
        - most commonly indicated pacing mode except for atrial fibrillation.
        - Automatic mode switching is a programmable response of a dual chamber pacemaker during atrial tachyarrhythmia in which mode switches to VVI to avoid rapid ventricular pacing.

B. Common pacemaker problems
    - Acute complication of pacemaker implantation
        - Pneumothorax/Hemothorax
        - Pocket Hematoma
        - Cardiac or central vein perforation
        - Lead dislodgement
    - Chronic complication of pacemaker implantation
        - Infection
        - Pocket erosion
        - Intravascular thrombosis or obstruction
        - Twiddler's syndrome
    - Pacemaker Malfunction
        - Failure to pace
            - Pulse generator failure
            - Lead failure
            - Over-sensing

- Failure to capture
  - Increased capture threshold
  - Lead malfunction(fracture/ dislodgement)
- Failure to sense
  - Lead dislodgement
  - Insulation failure
- Extracardiac stimulation(Diaphragmatic/ local muscle stimulation)
- Pacemaker syndrome
- Pacemaker mediated tachycardia

C. Pacemaker Follow-up

Pacemaker device follow-up is done 4-6 weeks after implantation and subsequently at least yearly. 'PBL STOP' – acronym for a standardized follow-up.

- P – Presenting rhythm, rate and percentage pacing
- B – battery status (voltage, longevity)
- L – Lead status (Impedance)
- S – Sensing
- T – Threshold
- O – Observation (data and events likes arrhythmias)
- P – Programming and Print

Temporary pacing

Temporary pacing can be used in patients with symptomatic bradycardia, either transiently if the cause is reversible (acute MI, dyselectrolytemia, drug or toxin-induced bradyarrhythmias, during and after cardiac surgery, etc) or as a bridge to permanent pacing. It is done via femoral or internal jugular route. Other options include transcutaneous pacing (uncomfortable to patient) and epicardial pacing (in post-cardiac surgery patients).

Common issues in patients with pacemaker

- Perioperative patients
  - Use of magnet over the pacemaker or switching the pacemaker to asynchronous mode(VOO) before surgery
  - Post-operatively the pacemaker needs to be re-evaluated for proper function and reseting the normal mode.
- Electromagnetic interference

  Pacemaker response to EMI
  - Pacing inhibition
  - Rapid pacing
  - Reversion to asynchronous pacing

In hospital

- MRI – recent pacemaker devices are MRI compatible but non-compatible devices should not undergo MRI.
- Electrocautery – results in temporary inhibition of pacemaker output due to oversensing of electromagnetic interference, so it should be used sparingly and should be placed at a distance from pacemaker site.
- Cardioversion/defibrillation – can damage the pulse generator, so patch electrodes should be positioned as far as possible from the pulse generator. Pacemaker evaluation should be done post-procedure.

In environment

- Cellphone – Use the hand opposite to the implanted device while talking and avoid carrying it in the shirt pocket over the pacemaker
- Electronic article surveillance/ Metal detectors – relatively safe but avoiding close proximity to the pacemaker is advised.
- High-voltage electricity lines – should be avoided.

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VII. 6. CARDIAC RESYNCHRONIZATION THERAPY (CRT)

Background:

Cardiac resynchronization therapy (CRT) also known as biventricular pacing is the most recent interventional modality in the treatment of heart failure. QRS delay >120 ms is associated with increased mortality and morbidity in heart failure. QRS delay, especially left bundle branch block, impairs cardiac function by causing intraventricular dysynchrony. Conduction delay also worsens AV dysynchrony and interventricular dysynchrony which all lead to worsening LV function. CRT abbreviates the dysynchronus heart failure by partially or totally correcting AV dysynchrony, interventricular dysynchrony and most importantly left ventricular dysynchrony.

Major CRT trials:

Trial	No	Design	NYHA#	LVEF	QRS (ms)	Main finding
Miracle[3]	453	CRT vs OMT*	III-IV	≤35%	≥130	CRT improves functional class and LVEF
Companion[4]	1520	OMT vs CRT-P vs CRT-D	III-IV	≤35%	≥120	CRT-P and CRT-D reduced all cause mortality and hospitalization
Care-HF[5]	813	OMT vs CRT-P**	III-IV	≤35%	≥120	CRT-P improves all cause mortality, functional class and hospitalization
REVERSE[6]	610	CRT off vs CRT on	I-II	≤40%	≥120	Improves LV remodeling but no mortality benefit

MADIT-CRT[7]	1820	CRT-D*** vs ICD	I-II	≤30%	≥130	CRT-D reduced combined end point of all cause mortality, hospitalization and LVESV but not all cause mortality alone
RAFT[8]	1798	CRT-D vs ICD	II-III	≤30%	≥120	CRT-D reduced combined end point of all cause mortality and hospitalization, In NYHA III, reduced all cause mortality
BLOCK-HF[9]	692	RV pacing vs CRT	I-II-III	≤50%		CRT reduced composite end point of all cause mortality, heart failure needing urgent care or LVESV but no mortality benefit

N0: number of patients, NYHA: New York Heart Association, CRT P: CRT pacing only, CRT D: CRT Pacing and Defibrillation , OMT : Optimal Medical Therapy.

Indications of CRT

Indication of CRT can be categorized in 3 types based on the rhythm.

A. Sinus Rhythm

1. CRT is recommended in chronic heart failure and LVEF≤35% who remains in NYHA functional class II, III and ambulatory IV despite adequate medical management and has **LBBB with QRS duration of >120 ms and in sinus rhythm**
2. CRT should be considered in chronic heart failure and LVEF≤35% who remains in NYHA functional class II, III and ambulatory IV despite adequate medical management and has non-**LBBB with QRS duration of >150 ms and in sinus rhythm**

B. Atrial Fibrillation

1. CRT should be considered in chronic heart failure and LVEF ≤35% who remains in NYHA functional class III and ambulatory class IV despite adequate medical management and has **QRS ≥120 ms**

in atrial fibrillation provided that Biventricular Pacing could be achieved as close to 100% either pharmacologically or by AV node ablation

C. Ventricular Paced Rhythm

1. CRT upgrade is recommended in HF patients with LVEF ‹35% and **high percentage of ventricular pacing** who remain in NYHA class III and ambulatory class IV despite adequate medical management
2. CRT should be considered in HF patients, reduced EF and **expected high percentage of ventricular pacing** in order to decrease the risk of worsening HF.

Note: CRT implantation should be performed only when the LVEF meets guideline criteria for patients with nonischemic cardiomyopathy who have received three months of GDMT(Guideline Directed Medical Treatment), or for patients with ischemic cardiomyopathy 40 days after myocardial infarction receiving GDMT when there was no intervening revascularization, or 3 months if revascularization was performed.

Important points:

1. **Patient selection:** QRS duration remains the only prospectively validated parameter for selecting patients who would benefit from CRT. Current echocardiographic criteria are unable to identify patients with mechanical but no electrical dysynchrony who would benefit from CRT.
2. **Magnitude of benefit:** Meta-analyses of initial clinical experiences and larger subsequent trials of CRT confirmed an approximately 30% decrease in hospitalizations and a mortality rate benefit of24% to 36%.
3. **CRT responder:**
   a. Not all patients will benefit from CRT. The data indicate that depending on the endpoint measure, up to 30% of patients may not receive at least one of the potential benefits of CRT.
   b. Wider QRS, left bundle branch block, females and non-ischemic cardiomyopathy are the highest responder group

c. CRT should be avoided in narrow QRS and non-LBBB with QRS duration <150 ms.

4. **Technical aspects:**
   a. LV lead should be avoided in the apical position
   b. Should try to have close to 100% Bi V pacing for good response
   c. If there is indication for ICD as well, CRT should be combined with ICD
5. Very sick patient with acute heart failure should be stabilized first and CRT should be planned only after discharge.

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UNIT - VIII

Ischemic Heart Disease

VIII. 1.STABLE CORONARY ARTERY DISEASE

Introduction

- Coronary artery disease (CAD) is one of the important causes of cardiovascular morbidity and mortality globally, giving rise to more than 7 million deaths annually.
- Stable coronary artery disease (SCAD) is a non-acute condition due to coronary artery atherosclerosis of epicardial coronary arteries and/or microcirculation.
- SCAD is characterized by episodes of transient central chest pain (angina pectoris), often triggered by exercise, emotion or other forms of stress, generally triggered by a reversible mismatch between myocardial oxygen demand and supply resulting in myocardial ischemia or hypoxia.
- A stabilized, frequently asymptomatic phase following an acute coronary syndrome (ACS) is also classified as SCAD. This definition of SCAD also encompasses vasospastic and microvascular angina under the common umbrella.

The common clinical presentation of SCAD is chronic stable angina. The underlying mechanisms may include atherogenesis and plaque formation in epicardial arteries, spasm of normal or plaque containing arteries, micro-vascular, or left ventricular dysfunction due to prior acute myocardial necrosis or ischaemic cardiomyopathy.

- In addition to chest discomfort, dyspnoea, palpitations, syncope or fatigue may also be present and sometimes may be the only symptom.

- Classical angina and micro-vascular angina are difficult to differentiate owing to the fact that both are exercise induced. Vasospastic angina, on the other hand, occurs at rest and has preserved effort tolerance. As opposed to ACS, SCAD lesions are more fibrotic, have a small necrotic core and little or no overlying thrombus.
- Besides, they do not display erosion or rupture of endothelial lining. Vasospasm is mostly due to various vasoconstrictor stimuli acting on hyper-reactive vascular smooth muscle cells, like cellular rho-kinase activity, abnormalities in adenosine triphosphate (ATP) sensitive potassium channels and/or membrane Na+-H+ counter-current transport. The diffuse distal spastic reaction usually underlies micro-vascular angina, while focal spasm is classically observed in variant angina.

Diagnosis:

- The initial and important step in the management of stable angina is the ascertainment of diagnosis and disease severity.
- A detailed clinical history of angina includes assessing magnitude, location, severity, duration and precipitating factors of angina.
- Presence of typical nature of the discomfort, precipitating factors and relieving factors should be suggestive of angina.
- Taking the medical history of a patient is the foremost and most vital process. In most of the cases, a clear diagnosis can be made based on the history alone of a patient. Physical examination is required to corroborate and strengthen the diagnosis. Besides history and physical examination, diagnosis of stable angina needs the supporting evidence from non-invasive investigations to confirm it, which sometimes provide additional prognostic information.
- Other important investigations usually done in such cases are ECG, chest X-ray, Echocardiography, blood counts, kidney function test, lipid profile, blood glucose, thyroid panel etc. Exercise ECG testing, if possible,

should be preferred in patients with a pre-test probability (based on character of symptom, age and sex) of 15–65% as it is more relevant to their activities than pharmacological testing. In patients who cannot exercise to an adequate workload, pharmacological testing with dobutamine echocardiography should be considered.

- An invasive coronary angiogram is indicated in patients with frequent, significant symptoms, patients with high risk features on non-invasive testing. Certain specific types of angina (microvascular, vasospastic and silent angina) should be diagnosed by a combination of available diagnostic techniques and should be individualised.

Management:

The treatment of stable angina includes anti anginal medication, medication to modify atherosclerosis and aggressive treatment of causative risk factors. All patients with SCAD require life-long supervised treatment. Overall, management strategy includes lifestyle changes, pharmacological management and prevention of cardiovascular events, various revascularization techniques and management considerations for special groups such as women, elderly, renal dysfunction and diabetic patients.

A. Recommendations on lifestyle management and risk factor modifications:

1. It is recommended to stop all forms of tobacco (smoking and smokeless) for the prevention and control of cardiovascular risk.
2. Patients with previous acute MI, coronary artery bypass graft (CABG), percutaneous coronary interventions (PCI), stable angina pectoris, or stable chronic heart failure should be enrolled in exercise programs. Exercise should be gradually instituted and exercise prescription should be individualized with a goal of at least moderate intensity aerobic exercise training, >3 times a week and 30 min per session. Sedentary patients

should be strongly encouraged to start light intensity exercise programme after adequate exercise-related risk stratification.

3. Weight reduction in overweight and obese people is recommended to have favourable effects on blood pressure and dyslipidemia, which may lead to less CVD. More precisely, it is recommended to attain BMI <22.9 kg/m2 and Waist Circumference (WC) (men: 90 cm; women: 80 cm) to minimize the cardiovascular risk.
4. All the SCAD patients should be treated with statins to achieve optimal LDL-C goal <70 mg/dl.
5. All the SCAD patients with hypertension should be recommended to attain SBP/DBP goal of 130/80 mmHg with medical management.
6. HbA1C of <7.0% should be the objective while treating SCAD patients with diabetes.
7. Patients should be counseled regarding proper diet with the aim to reduce dietary saturated fat and cholestrerol, sugar, other refined carbohydrate and increase fruits, vegetable and dietary fiber intake.

B. Pharmacological Management

a. Relief of angina symptoms

1. Short-acting nitrates are indicated for the immediate relief of anginal symptoms.
2. Beta-blockers and/or CCBs are the initial agents for long-term symptoms management and heart rate control based on co-morbidities, contraindications and patient preference.
3. The combination of non-DHP CCB with beta-blocker should be avoided in patients with anticipated risk of atrioventricular block or severe bradycardia.
4. The addition of long-acting nitrates, trimetazidine, ivabradine, ranolazine or nicorandil is proposed in case of intolerance or contraindications or failure in achieving control by beta-blockers and/

or CCBs. The choice of the drug should be made on the basis of blood pressure, heart rate and tolerance.

5. Ivabradine may be considered in symptomatic patients who do not tolerate beta-blockers or in whom the resting heart rate remains above 70 bpm, despite administration of the full tolerable dose of beta-blockers.
6. When two haemodynamically acting drugs fail to achieve the desired results in reducing angina, preference may be given to cardio-metabolic agents like trimetazidine or ranolazine as they have a different mode of action and may offer better efficacy in combination with a haemodynamic agent.

b. Recommendations on event prevention:

1. Indefinite daily low-dose aspirin is recommended in all SCAD patients if not contraindicated.
2. Clopidogrel is recommended in patients with aspirin intolerance.
3. In view of absence of any trial showing the benefit of prasugrel or ticagrelor in stable angina patients and also considering their cost in this sub-set of patients, they may be avoided pending results of the trials addressing this issue.
4. High intensity statin should be prescribed in all patients with SCAD irrespective of lipid levels.
5. All stable angina patients with diabetes, hypertension, heart failure or chronic kidney disease should be recommended to receive ACEIs if not contraindicated.
6. Rest of the patients with SCAD also be recommended to receive Angiotensin converting enzyme inhibitors (ACEIs)
7. A combination of ACEI and amlodipine may be considered in hypertensive CAD patients for improving cardiovascular outcomes.

8. Angiotensin receptor blockers (ARB) treatment may be used as an alternative therapy for patients who are intolerant to ACEIs.
9. Pnuemocooccal vaccine and Annual influenza vaccination should be recommended to all patients with SCAD.

c. Treatment of certain forms of stable CAD

1. Silent Angina

i. Silent myocardial ischaemia should be managed like asymptomatic CAD and may need administration of anti-ischaemic therapy and revascularization as required.

ii. Use of optimal medical therapies such as lipid-lowering agents, beta-blockers and metabolic modulators such as trimetazidine or ranolazine can be prescribed after careful examination of the patient on individual case by case basis.

2. Microvascular angina

i. Patients with micro-vascular angina patients can be initially treated with beta-blockers in addition to secondary preventive agents including aspirin and statins.

ii. Calcium channel blockers can be prescribed if beta-blockers are inadequate or intolerable.

iii. Novel agents like trimetazidine, ranolazine and ivabradine may be considered..

3. Vasospastic angina

i. The treatment of vasospastic angina should be individualized according to the diagnosis of each case.

ii. Calcium channel blockers can be used for effective prevention of vasospastic angina.

iii. In patients who continue to be symptomatic, agents like trimetazidine, nicorandil, ranolazine and ivabradine may be effective.

C. Revascularization

1. The decision of considering revascularization in patient with SCAD should be individualized. Revascularization can be opted early when patients symptoms are uncontrolled by medical therapy alone and/or have high-risk features.
2. While selecting whether PCI or CABG for revascularization, the decision should be purely individualized based on consensus and available evidence.

D. Treatment of special groups of population

a. Patients with diabetes

1. An objective for HbA1C of <7.0% and blood pressure <130/ 80 mmHg is recommended for the prevention of micro-vascular disease.
2. All SCAD patients should be recommended to receive an aspirin, high intensity statin and ACE inhibitor if not contra-indicated.
3. For symptomatic treatment of SCAD patients with diabetes, classical anti-anginal agents are 1st line agents but long-acting nitrates, trimetazidine, ivabradine, ranolazine or nicorandil may be considered as an alternate especially when b-blockers are contraindicated.
4. Trimetazidine may be beneficial in diabetic multi-vessel coronary artery disease patients who may also have diffuse disease and LV dysfunction
5. SCAD patients with diabetes should be treated with Oral Anti-diabetics (OADs) which have shown cardiovascular safety/ benefits such as metformin,gliptins and SGLT2 inhibitors.
6. Revascularization is recommended in diabetic patients, with persistent symptoms despite optimal medical therapy or those having high risk features on non-invasive testing.

7. Coronary artery bypass grafting can be recommended in diabetic patients with multi-vessel disease, left main coronary artery disease or in the presence of LV dysfunction.
8. PCI may be considered in single vessel disease and select cases of multi-vessel disease in consultation with heart team.

b. Patients with Chronic Kidney Disease

1. All stable angina patients with chronic kidney disease should receive optimal medical therapy. ACE inhibitors can be used if not contraindicated with careful monitoring of serum creatinine and potassium levels

c. Elderly SCAD patients

1. The management of SCAD in elderly patients should be individualized based on all the prognostic factors.

d. Refractory angina

Refractory angina is a clinical condition where angina cannot be controlled by medical therapy, angioplasty or revascularization. To address refractory angina a number of new pharmacological and non-pharmacological modalities has been developed. Enhanced external counter pulsation (EECP) therapy and neurostimulatory techniques [trans-cutaneous electrical nerve stimulation (TENS)], spinal cord stimuation (SCS) have shown that they can ameliorate symptoms and improve the quality of life. With regard to EECP, a meta-analysis demonstrated that approximately 86% of chronic stable angina patients who underwent EECP treatment improved by at least one CCS (Canadian Cardiovascular Society) class at the end of therapy. Further, it is suggested that EECP therapy should be considered for patients with stable angina who are refractory to or not suitable for invasive therapy and/or medical management.

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VIII. 2.ACUTE ST ELEVATION MYOCARDIAL INFARCTION

- ST elevation myocardial infarction (STEMI) is a clinical syndrome defined by characteristic symptoms of myocardial ischemia in association with persistent electrocardiographic (ECG) ST elevation and subsequent release of biomarkers of myocardial necrosis.
- STEMI comprises approximately 25% to 40% of MI presentations.
- In the present era, the in-hospital and 1 year mortality rates from STEMI have decreased significantly (4-12% and ~10 %) in association with a substantial increase in the frequency of care that includes guideline directed medical therapy and intervention.

Diagnosis

Signs & Symptoms:

- Acute onset, precordial retrosternal discomfort, commonly described as a pressure, crushing, aching, or burning sensation.
- Pain is prolonged and lasts for more than 30 minutes duration and may radiate to neck , back and arms which is associated with nausea and vomiting, sweating, breathlessness, extreme distress and a fear of impending death.
- approximately 20% of AMI patients are asymptomatic or have atypical symptoms specially in elderly women and diabetics.

Physical Examination:

- Patients are often anxious and in considerable distress.
- Heart rate vary from normal to marked bradycardia, rapid regular or irregular tachycardia, depending on the underlying rhythm and degree of LV failure.
- Blood pressure is usually normal, but hypertensive response may be a consequence of adrenergic discharge secondary to pain, anxiety, and agitation.
- Left ventricular (LV) dysfunction at presentation may have tachypnea, tachycardia, pulmonary rales , and a third heart sound (S3)
- In patients with right ventricular (RV) infarction, increased jugular venous pressure, Kussmaul sign (rise in jugular venous pressure with inspiration), and an RV third sound may be present

Cardiac biomarkers:

- High-sensitive cardiac troponin T (hs-cTnT) is currently the preferred biomarkers for myocardial damage because of their high sensitivity and specificity.
- Cardiac troponin (cTnT and cTnI) is the best alternative and CK-MB if cardiac troponin assays are not available.
- CK-MB, because of its more rapid appearance and disappearance from the blood, can be used in patients presenting early after symptom onset, to time the onset of injury if the troponin is increased and to detect re-infarction later in the hospital course. CK-MB appears in serum within approximately 3 hours after the onset of infarction, reaches peak levels at 12 to 24 hours, and has a mean duration of activity of 1 to 3 days.
- The preferred biomarker to detect myocardial injury is cardiac troponin. The level start to rise 3 to 12 hours after the onset of ischemia, peak at 12 to 24 hours, and may remain elevated in cTnI for 7 to 10 days and cTnT for up to 10 to 14 days. The prolonged time course of the elevation in cTnT and cTnI is advantageous for the late diagnosis of MI.

Causes of Elevated CK-MB	Causes of elevated Troponin
• Post cardioversion • Cardiac surgery • Myopericarditis • Percutaneous coronary intervention • After rapid tachycardia • Hypothyroidism • Skeletal muscle trauma • Rhabdomyolysis. • Muscular dystrophy • Some neuro-muscular dystrophy	• Tachyarrhythmia. • Heart failure • Critical illness (eg. Shock/ sepsis/burns) • Myocarditis. • Takotsubo cardiomyopathy. • Structural heart disease (e g. aortic stenosis) • Aortic dissection. • Pulmonary embolism/Pulmonary hypertension. • Renal dysfunction and associated heart disease • Coronary spasm • Acute neurological event(e g stroke, subarachnoid hemorrhage) • Cardiac contusion or procedure (eg. PCI,CABG, ablation) • Hypo or Hyperthyroidism. • Myocardial drug toxicity or poisoning • Rhabdomyolysis.

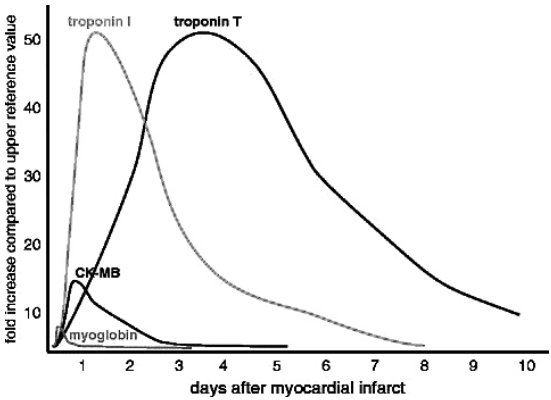

Figure rise and fall of "myocardial biomarkers " after myocardial infarction.

Electrocardiogram(ECG):

- New ST elevation at the J point in two contiguous leads of >0.1mV in all leads other than leads V2-V3
- For leads V2-V3 the following cut points apply:

  ≥0.2 mV in men≥40 years,

  ≥0.25 mV in men <40 years, or

  ≥0.15 mV in women

*STEMI with LBBB or paced rhythm:

A Sgarbossa criterion is well validated for STEMI.

- Concordant ST-Elevation of 1mm = 5 points
- Concordant ST-depression of in V1-V3 = 3 points
- Discordant ST-elevation of 5 mm = 2 points

  ***Score of 3 or more has 90% specificity for myocardial infarction.**

Modified Sgarbossa Criteria: "Discordant ST-elevation of > than 5mm" replaced with "ST elevation > 25% of the S-wave amplitude"

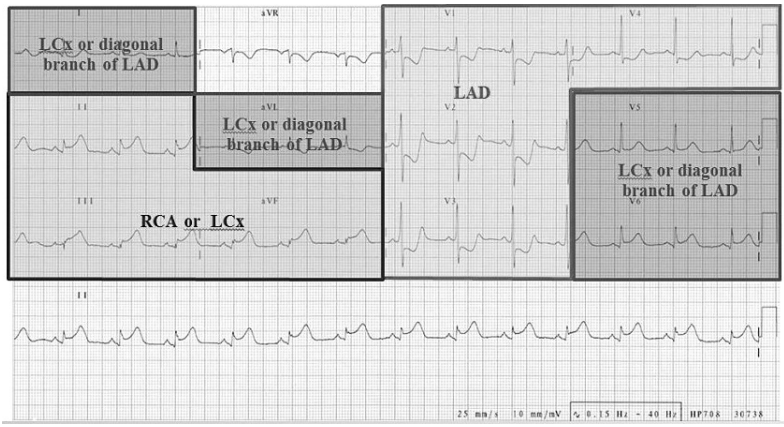

Figure: ECG localization of coronary artery territories

Emergency Room assessment and Management:

***Risk stratification:**

- Five baseline parameters which include Age, SBP, Killip classification, heart rate and location of MI are capable of providing prognostic information for 30 day mortality.
- The most common risk model used to estimate short term risk in STEMI is TIMI risk score

Management:

- The cornerstone of STEMI therapy is a rapid and accurate evaluation at first medical contact. Focused history and physical examination assessing the symptoms and signs should be quickly performed.

ECG:

- ECG should be obtained within the first 10 minutes of arrival at the emergency department.

If STEMI is diagnosed, following measures should be administered:

- Absolute bed rest.
- Continuous hemodynamic monitoring and ready access to defibrillation should be available.
- Intravenous (IV) access is mandatory.
- Oxygen supplement if clinically significant hypoxemia (SPO2 < 90 %.) or if there is evidence of heart failure. Oxygen is not routinely indicated in Acute STEMI.
- Pain management: For STEMI Patients with ongoing ischemic discomfort Morphine sulphate (2 to 4 mg IV) is the analgesic of choice. It could be repeated at 5 to 15 minutes intervals with increment of 2 to 8 mg IV. IV Pethidine with prochlorperazine can be considered.
- Sublingual nitroglycerin 0.5 mg (can repeat every 5 minutes for a total of 3 doses, after that intravenous nitroglycerin should be considered.
- ST elevation in right sided lead (RV3/RV4) in inferior MI indicates RV infarction. It should be treated initially with 1-2 liters of normal saline and/or inotropes, nitrate should be avoided.
- Emergency Echocardiography: In the acute phase when the diagnosis is in doubt emergency echocardiography

may be useful , to rule out complications of MI and to see ejection fraction .

- Aspirin ~ chewable tablet 300 mg.
- Clopidogrel ~ 300 mg orally if thrombolytic therapy (600 mg, if Primary PCI) is planned. Newer platelet P2Y12 receptor blocker prasugrel (loading dose 60 mg) and Ticagrelor (loading dose 180mg) can be also considered if patient is being considered for primary PCI.
- Prasugrel is not recommended in patients with previous history of stroke, more than 75 yrs of age and body weight less than 60 kg.

Reperfusion Therapy:

- The primary goal in the management of acute STEMI is to institute reperfusion therapy as soon as possible if patients present less than 12 to24 hrs. of symptom onset. It may be either- **Primary PCI** or thrombolytic therapy or **pharmaco-invasive** strategy depending on the local set up.
- Primary PCI is also indicated beyond 12 hrs. in conditions like hemodynamic instability, cardiogenic shock, ongoing chest pain refractory to medical therapy, acute heart failure, life threatening arrhythmia and cardiac arrest.

Primary PCI is recommended if patient can be transferred to Primary PCI capable hospital within 120 minutes of first medical contact. If time duration is › 120 minutes or no such facility is available then fibrinolytic therapy should be initiated within 10 minutes of STEMI diagnosis.

In the context of our country "**HUB and SPIKE**" model may be implemented on national level for better outcomes. Centers with 24X7 cath lab facilities for Primary PCI should act as a hub and should be in contact with different centers within the geographical area as spikes.

- If feasible, the current recommendation is to transfer patient for coronary angiogram to PCI capable hospital 2-24 hrs. Even after successful thrombolysis or for rescue PCI in case of failed thrombolysis.
- If Primary PCI could not be done within the recommended time frame, then thrombolysis becomes the treatment of choice.

Indications of thrombolytic therapy:

1. ST elevation as described above. (STEMI)
2. Symptom onset less than 12 hrs. prior to presentation.
3. No contraindications.

Contraindications to Fibrinolytic therapy

Absolute contraindications:

- Previous Intra-Cranial Hemorrhage (ICH)
- Stroke of unknown origin at any time
- Ischemic stroke in the past 6 months
- Central Nervous System damage
- Malignant intracranial neoplasm
- Other intracranial lesions (aneurysm or AV malformation)
- History of closed head or facial trauma within 3 months
- Major trauma/surgery within preceding 3 weeks Suspected aortic dissection
- Active bleeding or known bleeding diathesis (excluding menses)
- Gastrointestinal bleeding within the past month Non-compressible punctures in the past 24 hours (Eg: liver biopsy, lumber puncture)

Relative contraindications:

- Previous ischemic stroke beyond 12 months
- Transient ischemic attack in the preceding 6 months
- Oral anticoagulation therapy
- Pregnancy or within 1 week postpartum
- Recent (2-4 weeks) internal bleeding
- Prolonged or traumatic CPR
- Active peptic ulcer (only if the ulcer is actively bleeding; if only stool occult blood positivity, may be considered for thrombolysis)
- Severe uncontrolled hypertension (SBP >180mm Hg and/or DBP 110 mm Hg)
- Patients presenting with hypertension should be administered beta blockers, nitroglycerin and analgesics promptly to lower blood pressure and reduce risk of ICH following thrombolysis
- Patients on warfarin therapy have higher rates of hemorrhage: higher the INR, higher the risk Advanced liver disease
- Infective endocarditis

** Hemorrhagic diabetic retinopathy is not a contraindication for thrombolysis.*

**Change in the neurological status especially 24 hours following reperfusion should be considered to be due to ICH until proven otherwise.*

Thrombolytic agents:

- Tenecteplase is fibrin specific, more potent,can be repeated, single dose hence is preferred.
- Streptokinase is cheaper (fibrin nonspecific) . Other agents are Alteplase, Reteplase.

The benefit of thrombolytic therapy appears to be greatest when agents are administered as early as possible, with the most dramatic results occurring when the drug is given less than 1 to 2hours after symptom onset

Doses of thrombolytic agents:

Streptokinase (STK) - 1.5 million units over 30 to 60 minutes IV - Specific contraindications: Prior SK or anistreplase

Tenecteplase (TNK) - Single IV bolus

- 30 mg if < 60 kg
- 35 mg if 60-70 kg
- 40 mg if 70-80 kg
- 45 mg if 80-90 kg
- 50 mg if ≥ 90 kg
- Half dose should be given if patient is > 75 years.

Alteplase: 15 mg. IV bolus, 0.75 mg/kg IV over 30 minutes (up to 50 mg)then 0.5 mg /kg iv over 60 mins. (Up to 35 mg)

Reteplase: 10 units +10 units IV bolus given 30 minutes apart.

Criteria for Successful thrombolysis: Resolution of ST segment elevation at least 50 % in 60-90 minutes, relief of ischemic symptom, reperfusion arrhythmia and early peaking of cardiac enzymes.

Routine Medical Therapies:

Antiplatelet therapy:

- **Aspirin:** Aspirin is recommended indefinitely in all patients with STEMI. (75–100mg).
- **P2Y12 Inhibitors:** Thienopyridines (Clopidogrel and Prasugrel) and now direct P2Y12inhibitors such as Ticagrelor are oral antiplatelet agents that inhibit

platelet activation through the adenosine diphosphate (ADP)-mediated pathway. Unless contraindicated, these antiplatelet agents should be initiated upon presentation of STEMI.

- One of the following P2Y12 inhibitors should be used along with aspirin, ideally at least for 12 months.
    - Clopidogrel: Loading dose 300 -600 mg. orally, followed by 75 mg. daily
    - Ticagrelor: Loading dose 180 mg. orally, followed by 90 mg twice daily.
    - Prasugrel: 60 mg. daily Loading dose followed by 10 mg. daily
- **Abciximab:** Bolus of 0.25 mg/kg IV and 0.125 µg/kg/min infusion (maximum 10 µg/min) for 12 hours.
- **Eptifabatide:** Double bolus of 180 µg/kg IV (given at a 10 minutes interval) followed by an infusion of 2.0 µg/kg/min for 18 hours.
- **Tirofiban:** 25 µg/kg over 3 minutes IV o Followed by a maintenance infusion of 0.15 µg/kg/min for 18 hours

Antithrombin therapy:

Unfractionated heparin:

- 60 U/kg IV bolus with maximum of 4000 U followed by an IV infusion of 12 U/ Kg with a maximum of 1000 U/ hours for 24 to 48 hours .
- Target aPTT: 50 to 70s or 1.5 to 2.0 times that of control to be monitored at 3,6,12 and 24 hours.

Enoxaparin:

- In patients <75 years of age:
    - 30 mg IV bolus followed 15 minutes later by 1 mg/kg SC every 12 hours until hospital discharge or maximum of 8 days.
    - The first two doses should not exceed 100 mg
- In patients >75 years of age:
    - No IV bolus.
    - Start with first SC dose of 0.75 mg kg with a maximum of 75 mg for the first two SC doses

- In patients with creatinine clearance of <30 mL/min regardless of age the SC doses are given once every 24 hours.

Fondaparinux:

- 2.5 mg IV bolus ; followed by a SC dose of 2.5 mg once daily up to 8 days or hospital discharge

Special attention must be given to proper dosing of antithrombotic in elderly and renal failure patients.

Beta Blocker:

- Oral beta blockers should be initiated in the first 24 hours in patients with STEMI who do not have signs of HF, evidence of a low output state, increased risk for cardiogenic shock, or other contraindications to use of oral beta blockers (PR interval more than 0.24 seconds, second- or third-degree heart block, active asthma, or reactive airway disease).

Renin-Angiotensin-Aldosterone System Inhibitors:

- Administered within the first 24 hours to all patients with STEMI with anterior location, HF, or ejection fraction (EF) less than or equal to 40%, unless contraindicated. ACE inhibitors are also reasonable for all patients with STEMI and no contraindications to their use

Angiotensin receptor blocker (ARB):

- It should be given to patients with STEMI who have indications for but are intolerant of ACE inhibitors. It should also be used for all STEMI with LV systolic dysfunction with EF 35 %.

Lipid Management:

- High-intensity statin therapy should be initiated or continued in all patients with STEMI and no contraindications to its use Atorvastatin 40-80 mg, Rosuvastatin 20-40 mg daily. Fasting lipid profile in patients with STEMI, preferably within 24 hour should be obtained.

Nitrates:

- It should not be given to patients with hypotension, marked bradycardia or tachycardia, RV infarction, or 5'phosphodiesterase inhibitor use within the previous 24 to 48 hours. There is no role for the routine use of oral nitrates in the convalescent phase of STEMI.

Calcium Channel Blockers:

- Calcium channel blockers may be useful, however, to relieve ischemia, lower BP, or control the ventricular response rate to atrial fibrillation (AF) in patients who are intolerant of beta blockers. Caution is advised in patients with LV systolic dysfunction.

Coronary Artery Bypass Graft (CABG) Indications for CABG:

Patients with STEMI and coronary anatomy not suitable for PCI who have:

1. Ongoing or recurrent ischemia
2. Cardiogenic shock
3. Severe heart failure
4. Other high risk factors

Should undergo urgent CABG:

1. Patients with STEMI at time of operative repair of mechanical defects
2. Aspirin should not be withheld before urgent CABG
3. Clopidogrel or Ticagrelor should be discontinued at least 24 hours before urgent on-pump CABG if possible.
4. Eptifabatide and Tirofiban should be discontinued at least 2 to 4 hours before urgent CABG
5. Abciximab should be discontinued at least 12 hours before urgent CABG

Risk Assessment after STEMI

Noninvasive testing for ischemia should be performed before discharge to assess the presence and extent of inducible ischemia in patients with STEMI who have not had coronary angiography and do not have high-risk clinical features for which coronary angiography would be warranted.

LVEF should be measured in all patients with STEMI by Echocardiography.

Life style modification and Long term therapy

- Smoking cessation
- Diet: Mediterranean diet, which includes low fat, low salt, food rich in fiber, plenty of fruits and vegetables.
- Weight loss for obese.
- Exercise-based cardiac rehabilitation
- Management of co morbidity : blood sugar control, tight blood pressure control
- Duration of dual antiplatelet therapy:
- DAPT, combining aspirin and a P2Y12 inhibitor (i.e. Prasugrel, Ticagrelor, or Clopidogrel), is recommended in patients with STEMI who are undergoing primary PCI or thrombolysis (for up to 12months).
- Aspirin is recommended indefinitely in all patients with STEMI (75–100mg)
- Adherence to treatment prescribed by cardiologist/ physician

Cardiac Rehabilitation

The objectives of contemporary exercise-based cardiac rehabilitation are to increase functional capacity, decrease or alleviate anginal symptoms, reduce disability, improve quality of life, modify coronary risk factors, and reduce morbidity and mortality rate.

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VIII. 3.ACUTE CORONARY SYNDROME (NSTEMI/UNSTABLE ANGINA)

- ACS is broad ranging from those for ST-segment elevation myocardial infarction (STEMI) to presentations found in non–ST-segment elevation myocardial infarction (NSTEMI) or in unstable angina (UA).
- UA can be defined as new onset or worsening angina within the previous 60 days or post infarction angina after the first 24 hours from the onset of infarction. It is an acute coronary syndrome distinguished from non STEMI only by the absence of elevated serological markers. The usual underlying pathological mechanism in both the conditions involves rupture or erosion of an atherosclerotic plaque with thrombus formation that severely obstructs the coronary artery lumen.
- Acute worsening of a coronary stenosis causes primary UA by limiting coronary blood flow. Secondary UA arises as a result of increased oxygen demand for example as a result of tachyarrhythmia, fever, anemia, severe hypertension, thyrotoxicosis etc.

Variant or prinzmetal angina is caused by coronary spasm which is more common among female and can usually be controlled by calcium channel blockers.

Evaluation of patient of ACS:

Symptoms:

- The pain of myocardial ischemia usually located in the retrosternal area but it may be felt in epigastrium, upper back, arms or jaw; the description may be expressed as burning squeezing heaviness .

- Patients can present with prolonged (>20 min) chest discomfort at rest. , New-onset (de novo) less than 3 months), angina (class II or III) , Recent destabilization of previously stable angina with at CCS Class III angina characteristics (crescendo angina) , Post-myocardial infarction (MI) angina.

Typical chest discomfort is characterized by a retrosternal sensation of pain, pressure, or heaviness ('angina') radiating to the left arm, both arms, the right arm, the neck, or the jaw, which may be intermittent (usually lasting several minutes) or persistent. Additional symptoms such as sweating, nausea, epigastric pain, dyspnoea, and syncope may be present.

*Atypical complaints (include isolated epigastric pain, indigestion-like symptoms, and isolated dyspnea or fatigue) are more often observed in the older patient, in women, and in patients with diabetes, chronic renal disease, or dementia. The exacerbation of symptoms by physical exertion, and their relief at rest, increase the probability of myocardial ischaemia. The relief of symptoms after nitrate administration increases the likelihood of NSTE-ACS, but this is not diagnostic as it is also reported in other causes of acute chest pain.

Note: **Older age, male sex, family history of coronary artery disease (CAD), diabetes, hyperlipidaemia, smoking, hypertension, renal dysfunction, previous manifestation of CAD, and peripheral or carotid artery disease increase the likelihood of NSTE-ACS.**

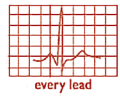
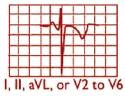
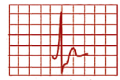
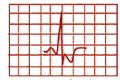
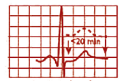
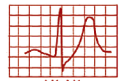
Conditions that may exacerbate or precipitate NSTE-ACS include anaemia, infection, inflammation, fever, hypertensive peak, anger, emotional stress, and metabolic or endocrine (particularly thyroid) disorders has to be evaluated

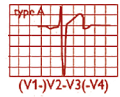
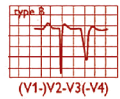
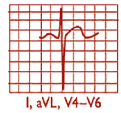
** Physical examination is frequently unremarkable in patients with suspected NSTE-ACS. Physical examinations are done to look for signs of heart failure or hemodynamic or electrical instability.

Electrocardiogram :

- The resting 12-lead ECG is recommended to be performed it within 10 mins of the patient's arrival in the emergency room and to obtain an additional 12-lead ECG in case of recurrent symptoms or diagnostic uncertainty.
- The ECG in the setting of NSTE-ACS may be normal in more than 30% of patients, characteristic abnormalities include ST-segment depression, transient ST-segment elevation, and T-wave changes. If the standard leads are inconclusive and the patient has signs or symptoms suggestive of ongoing myocardial ischaemia, additional leads should be recorded; V7 to V9 or V3R and V4R. In patients with right bundle brunch block (RBBB), ST-segment depression in lead I, aVL, and V56 is indicative of ACS. In patients with paced ventricular beats, the ECG is often of no help for the diagnosis of ACS.

The various ECG changes are shown below:

	ECG pattern	Criteria	Signifying	Figure
a	Normal ECG		No clue	 every lead
b	Isolated T-wave inversion	T-wave inversion >1 mm in ≥5 leads considering I, II, aVL, and V2–V6	Only mildly impaired prognosis	 I, II, aVL, or V2 to V6
c	ST-segment depression	J point depressed by ≥0.05 mm in leads V2 and V3 or ≥1 mm in all other leads followed by a horizontal or downsloping ST-segment for ≥0.08 s in ≥1 leads (except aVR)	More severe ischaemia	 every lead  every lead
d	Transient ST-segment elevation	ST-segment elevation in ≥2 continuous leads of ≥0.25 mV in men <40 years, ≥2 mm in men ≥40 years, or ≥0.15 mV in women in leads V2 through V3 and/or ≥0.1 mV in other leads lasting <20 min	Only mildly impaired prognosis	 <20 min every lead
e	De Winter ST-T	1–3 mm upsloping ST-segment depression at the J point in leads V1–V6 that continue into tall, positive, and symmetrical T waves	Proximal LAD occlusion/severe stenosis	 V1–V6

f g	Wellens sign	isoelectric or minimally elevated J point (<1 mm) + biphasic T wave in leads V2 and V3 (type A) or symmetric and deeply inverted T waves in leads V2 and V3, occasionally in leads V1, V4, V5, and V6 (type B)	Proximal LAD occlusion/severe stenosis	 
h	Resting U wave inversion	discrete negative deflection in the T-P segment (negative in comparison to the following P-R segment) no initial positive U wave deflection not obscured by fusion with terminal T wave or following P wave in I, aVL, and V4 through V6	Occlusion or severe stenosis of the left main artery or LAD	
i	Low QRS voltage	peak to peak QRS complex voltage <0.5 mV in all limb leads and <1.0 mV in all precordial leads	High risk for in-hospital mortality	

Cardiac biomarker - to be sent at presentation and 6 hours of chest pain

- To send preferably High-sensitivity cardiac troponin and CKMB at presentation and after 6 hrs.
- To send complete blood count, RBS, RFT.

Echocardiography to evaluate regional and global LV function and to rule in or rule out other differential diagnosis. Echocardiography should be performed immediately following a 12-lead ECG in hemodynamically unstable patients.

Diagnosis :

1. Chest pain (typical angina,atypical angina) ECG changes and cardiac marker elevated : **NSTEMI**
2. Chest pain (Rest Angina, crescendo angina, New onset angina) / ECG changes and cardiac enzyme normal = **Unstable angina**
3. In patients with no recurrence of chest pain, normal ECG findings, and normal levels of cardiac troponin (preferably high sensitivity), but still with a suspected ACS, a non-invasive stress test (TMT) for inducible

ischaemia or Cardiac CT angiography (CCTA) to be done .

Low risk and intermediate risk patients (categorized according to absence of, severe angina, positive cardiac markers, ECG changes and multiple CAD risk factors) whose symptoms stabilize with medical therapy may undergo stress testing for advanced risk stratification. Those with high risk findings such as ST segment depression at low exercise levels can undergo coronary arteriography.

** CCTA to be done as an alternative to invasive angiography to exclude ACS when there is a low-to-intermediate likelihood of CAD and when cardiac troponin and/or ECG are normal or in conclusive .

Once the diagnosis of ACS is made then TIMI and GRACE RISK SCORE should be calculated at ER before admission and all patients diagnosed with ACS has be risk stratified.

Very high-risk criteria:

- Haemodynamic instability or Cardiogenic shock.
- Recurrent or refractory chest pain despite medical treatment.
- Life-threatening arrhythmias.
- Mechanical complications of MI.
- Heart failure clearly related to NSTE-ACS.
- Presence of ST-segment depression >1 mm in ≥6 leads additional to ST-segment elevation in aVR and/or V1

High-risk criteria:

Diagnosis of NSTEMI.

- Dynamic or presumably new contiguous ST/T-segment changes suggesting ongoing ischaemia.
- Transient ST-segment elevation.
- GRACE risk score >140.

Admission: After Risk Stratification In CCU : High Risk and Very high Risk, In Ward : Low Risk with frequent monitoring.

Medical Therapy :

1. Aspirin Loading Dose (LD) of 300 mg orally or, followed by oral Maintenance Dose (MD) of 75 or 100 mg o.d.
2. Clopidogrel LD of 600 mg orally, followed by a MD of 75 mg OD, no specific dose adjustment in CKD patients.
   OR
   Prasugrel LD of 60 mg orally, followed by a MD of 10 mg o.d. In patients with body weight <60 kg, a MD of 5 mg o.d. is recommended. In patients aged ≥75 years, prasugrel should be used with caution, but a dose of 5 mg o.d. should be used if treatment is deemed necessary. No specific dose adjustment in CKD patients. Prior stroke is a contraindication for prasugrel.
   OR
   Ticagrelor LD of 180 mg orally, followed by a MD of 90 mg b.i.d., no specific dose adjustment in CKD patients.

   Note : It is not recommended to administer routine pre-treatment with a P2Y12 receptor inhibitor (prasugrel and ticagrelor) in patients in whom coronary anatomy is not known and an early invasive management is planned
3. High dose statin therapy (Atorvastatin 80 mg or Rosuvastatin 20 to 40 mg)
4. Sublingual or i.v. nitrates and early initiation of beta-blocker treatment to be started in patients with ongoing ischaemic symptoms and without contraindications .IV nitrates are recommended in patients with uncontrolled hypertension or signs of heart failure.
5. In Low molecular weight heparin : LMWX 1mg/kg BD if Creatinine clearance <30ml/min : 1mg/kg od

   Heparin is recommended for the acute treatment of all UA patients except those with low risk features
6. ACE inhibitors (or ARBs in cases of intolerance to ACE inhibitors) in patients with heart failure with reduced LVEF (<40%), diabetes, or CKD unless contraindicated (e.g. severe renal impairment, hyperkalaemia, etc
7. Beta-blockers in patients with systolic LV dysfunction or heart failure with reduced LVEF (<40%).
8. MRAS in patients with heart failure with reduced LVEF (<40%).

Coronary revascularization:

- An immediate and early invasive management strategy (2 to 24 hrs) in patients with very high-risk criteria or high-risk criteria.
    - The aggressive approach involves early coronary angiography with revascularization by either coronary angioplasty or bypass surgery depending upon the coronary anatomy. Usually patients with one or two severe narrowing are treated with angioplasty and those with more extensive disease undergo bypass surgery.
    - Immediate invasive approach is taken within 2 hours if the patient has refractory angina, signs of heart failure, hemodynamic instability and recurrent angina at rest or with low level activities, despite of medical therapy, or sustained VT/ VF. Early invasive approach is followed within 24 hours if above features are not present but cardiac biomarkers are raised and ST depression/ dynamic ECG changes ,ongoing chest pain is present.
    - Delayed invasive approach can be followed in patients with post infarction angina, PCI within 6 months, prior CABG. Ischemia guided strategy is followed in patients with low risk and intervention is proceeded only when patients has angina despite GDMT.
- Patients with one or two vessel disease with significant stenosis amenable to revascularization and unacceptable angina despite guideline directed medical therapy can undergo PCI or CABG according to patient preference.
- In a patient with unprotected left main or complex coronary artery disease heart team approach is recommended.
- In patient with three vessel disease CABG is usually preferred unless syntax score is less than 22 and patient is high risk for surgery because of comorbidities. In patients with complex three vessel CAD (syntax score

›22) with or without proximal LAD CABG is preferred over PCI .

- In previous CABG with more than one significant stenosis and unacceptable angina despite GDMT PCI is reasonable option.
- PCI may be offered for patients with multi- vessel disease and stable angina with proximal LAD who have anatomy suitable for catheter based therapy and has normal LV function and no treated diabetes and whose syntax score is less than 22.
- CABG should be done for patient with stable with left main coronary artery disease or multi vessel disease with significant left anterior descending CAD with compromised LV function.

New Key Recommendations in ESC 2021 guidelines:

a. Diagnosis – Use of new 0 hr / 2 hour blood sampling with high sensitive Troponin assay

b. Risk Stratification – Use of NT proBNP for prognostic information

c. Antithrombotics- Choice of prasugrel over ticagrelor in proceed PCI in NSTE ACS –
   - In patients with AF (CHA2DVAS 2›1 men, ›2 women) – after one week of triple antithrombotic therpary should be switched to dual antithrombotic with a NOAC (preferably clopidogrel) after which single monotherapy after one year .

d. Invasive treatment – Early invasive strategy is to be used within 24 hour in case of high risk criteria is present , with transient ST elevation, GRACE score ›140 , dynamic or new ST – T changes .
   - Complete revascularization should be recommended in NSTEACS without cardiogenic shock.

VIII. 4.COMPLICATIONS OF ACUTE MYOCARDIAL INFARCTION

Left Ventricular failure:

- A series of change occurs in shape, size and thickness in infarcted and non-infarcted segments leading to ventricular remodeling which causes left ventricular dysfunction.
- important predictor of mortality following STEMI.
- The left ventricle begin to dilate due to expansion of infarct, with greater dilatation following infarction of anterior wall and apex of left ventricle.

Management:

- Oxygenation is required to correct hypoxemia.
- Diuretics should be given to decrease pulmonary capillary pressure and lower LV wall tension by decreasing left ventricular diastolic volume. It improves oxygenation by reducing pulmonary vascular congestion.
- Intravenous nitroglycerine (10mcg/min starting dose, increased every 5 minutes) reduces left ventricular filling pressure
- Dopamine and dobutamine can be used (started at 3mg/kg/min to 20mg/kg/min). Noradrenaline is also useful in cardiogenic shock.
- Milrinone, a phosphodiesterase inhibitor is useful in patients unresponsive to diuretics and not hypotensive (loading dose 0.5mg/kg/min over 10min with maintenance dose of 0.375-0.75mg/kg/min.

Cardiogenic shock:

- It is the most severe clinical expression of left ventricular failure.
- Risk factors for cardiogenic shock are - **older age, diabetes mellitus, previous MI, congestive heart failure.**
- Anterior wall infarction have more propensity for cardiogenic shock.
- More than two thirds of patients with cardiogenic shock have multivessel coronary disease. Other causes mechanical defects such as ventricular septum rupture , papillary muscle rupture or free wall rupture with tamponade or RV and needs immediate hemodynamic, angiographic and echocardiographic evaluations are required.

Management:

- Inotropic and vasopressor agents should be used at lowest possible doses.
- If patient has end organ hypoperfusion despite pharmacologic support, mechanical circulatory support is reasonable such as Intra-Aortic Balloon Counterpulsation (IABP) or Percutaneous left ventricular assist devices (such as Impella device). IABP decreases preload, increases coronary blood flow and improves cardiac performance.
- SHOCK trial showed long term survival benefit in patients with cardiogenic shock who underwent early revascularization.

Mechanical complications:

- Trans mural infarction can lead to rupture of free wall of ventricle or ventricular septum or papillary muscle. These are life threatening complications in the setting of AMI with worse prognosis.
- Each of these complications can result in cardiogenic shock and are thus associated with reduced short-term and long-term survival.
- Use of **NSAIDs and steroids** are said to increase the incidence of mechanical complications of AMI and are best avoided.

- Any new murmur in the setting of AMI should raise the suspicion of mechanical complication of AMI and needs immediate referral to a specialized center as surgical therapy is mandatory in order to decrease the high mortality in this group of patients.

Free wall rupture:

- Its incidence is 0.8 -6.2% of all cases of STEMI.
- Shows a bimodal appearance, within 24 hrs and 3-5 days' average (1-14 days range).
- Clinically present as chest pain, syncope, hypotension or sudden death due to cardiac tamponade.
- It occurs when there is a large infarct with subsequent expansion near the junction of infarct and normal muscle.
- Left ventricular wall (anterior or lateral) is more common than right ventricular wall rupture.
- **Common associations are fibrinolytic agent use, older age, female, hypertension, absence of collaterals and a first MI.**
- Inotropic agent and IABP and prompt surgical repair are warranted. Mortality of free wall rupture in AMI without treatment approaches 100% and even with operation is very high.

Ventricular Septal Rupture:

- Transmural infarction underlies rupture of ventricular septum.
- Incidence is 1-3% without reperfusion therapy and 0.2-0.34% with fibrinolytic therapy.
- may occur within 24 hrs or 3-5 days (1-14 days range)
- It ranges from one to several centimeters. The anterior infarction leads to rupture in apical location of septum whereas inferior infarction leads to basal septum perforation, the latter has worse prognosis.
- It is characterized by new harsh, loud holo systolic murmur heard best at the lower left sternal border usually accompanied by a thrill. Biventricular failure ensues.

- Associated with high 30-day mortality. The diagnosis is confirmed by echocardiography. Prompt surgical repair of ventricular septal defect is necessary. Trans catheter device closure of VSD is an alternative option in selected patients.

Papillary muscle rupture:

- Posteromedial papillary muscle rupture is more frequent than anterolateral papillary muscle
- Inferior wall infarction can lead to rupture of posteromedial papillary muscle due to its singular blood supply either from right coronary artery or left circumflex artery.
- results in acute severe mitral regurgitation with evidence of new pansystolic murmur can be heard loudest at the cardiac apex and radiating to the axillae.
- Management includes inotropes to support adequate cardiac output, IABP if medical therapy not tolerated.
- Immediate surgical repair or replacement of mitral valve is indicated usually accompanied by coronary revascularization.

Arrhythmias:

Ventricular arrhythmias:

- Primary ventricular fibrillation occurs without antecedent warning arrhythmias such as multiform VPCs, early coupling (the R on T phenomenon).
- Electrolyte imbalance should be checked especially potassium and magnesium .
- VPCs accompanying sinus tachycardia could be due to sympathoadrenal stimulation for which beta-blockers can help after ruling out the contraindications of beta blockers.

Accelerated Idioventricular rhythm:

- It also termed "slow VT" with heart rate between 40 to 110bpm.
- Occurs in upto 20% of AMI patient and is often observed after successful reperfusion.
- It doesn't affect the prognosis. So, treatment is not necessary.

Ventricular Tachycardia / Ventricular Fibrillation:

- Primary VF occurs suddenly and unexpectedly in patients with no signs or symptoms of LV failure.
- Secondary VF is often the final event of a progressive downhill course with LV Failure and cardiogenic shock.
- Late VF develops more than 48 hours after AMI and mostly occurs in patients with large infarcts and LV dysfunction.
- VF in association with marked LV failure or cardiogenic shock entails a poor prognosis, with an in-hospital mortality rate of 40-60%.
- VF is treated with electrical cardioversion and prevention of refractory recurrence can be facilitated by amiodarone .
- Correction of underlying abnormalities like hypoxia, hypotension, acid-base or electrolyte disturbances is needed. Revascularization should be done urgently.

Brady arrhythmias:

Sinus bradycardia: It occurs particularly in inferior and posterior infarctions. If it is not associated with hypotension, it can be left untreated.

Atrioventricular and intraventricular block:

First degree AV block: It doesn't generally require treatment unless higher degree block is seen.

Second degree AV block: First and Mobitz Type I second degree AV block are most commonly associated with RCA artery occlusion due to ischemia of AV node. Unless the patient is symptomatic or develop bundle branch block or HR <50 beats/min treatment generally isn't required.

Mobitz Type II second degree AV block (2:1 AV block) occurring due to inferior/posterior STEMI is usually temporary but however is more common in anterior/lateral STEMI where it occurs due to lesion in conduction system below bundle of His and is potent to progress to complete heart block. So temporary pacemaker is needed as well as permanent pacemaker may be needed.

High degree AV block:

- It is the AV block with P: QRS ratio of 3:1 or higher, producing an extremely slow ventricular rate. Unlike 3rd degree heart block there is still some relationship between the P waves and the QRS complexes.
- However, it is the premonitory feature before occurrence of complete heart block. As with Type II second degree AV block, it is more common with anteroseptal wall MI. It occurs with lesion in distal conduction system beyond His bundle. With inferoposterior wall MI, it is usually transient and will almost never require permanent pacemaker. But with anteroseptal wall MI, it may be transient but some may persist requiring temporary as well as permanent pacemaker.

Complete (third degree) heart block:

- It can occur in either inferior or anterior infarction. In case of inferior wall infarction, it is often transient so may not require pacing generally.
- In patients with anterior infarction, third degree AV block can occur suddenly but however may be preceded by intraventricular block in the form of right bundle branch block and type II second degree AV block.
- It develops due to extensive septal necrosis involving the bundle branches resulting in severe LV failure and shock, thus leading to high mortality.

Supraventricular Tachyarrhythmia:
Sinus tachycardia:

- Can occur because of anxiety, pain, left ventricular failure, fever, pericarditis, hypovolemia, pulmonary embolism or certain drugs like atropine, epinephrine or dopamine.
- common in patients with anterior wall infarction
- increases myocardial oxygen demand and decrease the time for coronary perfusion, thus aggravating myocardial ischemia.

Atrial Flutter and Fibrillation:

- usually transient and occur because of augmented sympathetic stimulation of atria, left ventricular failure, pulmonary embolism or atrial infarction.
- Often may lead to decrease in cardiac output, hence increasing mortality and stroke
- Atrial fibrillation (AF) is a marker of poor prognosis. If AF is causing hemodynamic compromise, cardioversion should be considered. However, if the patient is hemodynamically stable, beta blockers should suffice.
- Amiodarone can also be considered. Recurrent AF should be treated with oral anticoagulants to prevent risk of stroke.

Recurrent ischemia and Reinfarction:

- It is important to differentiate re-infarction from other causes like pericarditis, pulmonary embolism or non cardiac causes of chest pain.
- may be due to acute re-occlusion of previously re-canalized or stented vessel or new non-infarct related coronary artery.
- Diagnosis is done by ECG and response to sublingual nitroglycerine. Re-infarction after PCI often reveal post PCI coronary dissection or stent thrombosis on angiography.
- If dynamic ST segment elevation occurs patient should be taken for coronary angiography. High risk patient who underwent fibrinolysis due to unavailability of primary PCI facilities may benefit from facilitated PCI.

Pericardial Effusion:

- more commonly with anterior STEMI, with larger infarcts and congestive heart failure.
- If tamponade occurs, that is usually attributable to ventricular rupture or hemorrhagic pericarditis.

Pericarditis:

- can occur as early as first day and as late as 8 weeks after STEMI
- characterized by chest pain that radiates to either trapezius ridge, become worse during deep inspiration and diminishes while leaning forward.
- Transmural MI causes local pericardial inflammation causing acute pericarditis producing pericardial rub.
- Pericarditis with detection of pericardial effusion on echocardiography indicates discontinuation of anticoagulation.
- Treatment includes aspirin 650mg orally every 4 hours. NSAIDs and steroids are avoided. Colchicine maybe beneficial in patients with recurrent pericarditis.

Dressler syndrome:

- usually occurs 1 to 8 weeks after infarction
- the syndrome includes pyrexia, pericardial effusion, chest discomfort, leukocytosis, raised ESR.
- Immune mediated with presence of antibodies to cardiac tissue has been detected.
- Treatment is similar as pericarditis. NSAIDs and steroids are avoided as they interfere with infarct healing and may cause ventricular rupture.

Left Ventricular Aneurysm:

- a discrete, dyskinetic area of LV wall with a broad neck (true aneurysm).
- The true LV aneurysm wall is composed of fibrous tissue and necrotic mulscle occasionally mixed with some viable myocardium
- usually occurs due to stretching of non contracting heart muscle when intraventricular tension increases producing expansion of the infarct that bulges with each cardiac contraction leading to ineffective stroke volume
- more common with anterior infarction towards the apex and anterior wall of LV. Rupture is uncommon but leads to thrombus formation, ventricular tachyarrhythmia and heart failure.

- ECG shows persistent ST-segment elevation and confirmed by echocardiography, MRI or left ventriculography.
- Surgical aneurysmectomy may prevent worsening of heart failure, but significant improvement would be if non aneurismal portion of LV is functioning well

Ventricular pseudo aneurysm:

- Incomplete rupture of heart occurs when organizing thrombus and hematoma along with pericardium seal a rupture of left ventricle preventing development of hemopericardium, thus forming pseudoaneurysm that communicates with LV cavity.
- It doesn't contain myocardial elements in its wall unlike true aneurysm where both can lead to systemic thromboembolism
- diagnosis is by echocardiography.

Management:

- Surgical resection of the necrotic and ruptured myocardium with primary reconstruction is needed.

Left ventricular thrombus and arterial embolism:

- usually develop within 48 to 72 hours of infarction.
- Anticoagulation reduces development of LV thrombus by 50%.
- Fibrinolysis reduces rate of thrombus formation but when formed may lead to embolization. After primary PCI if mural thrombi is seen, along with dual antiplatelets anticoagulation with warfarin for 3 to 6 months is reasonable.

RV infarction:

- One third of inferior wall myocardial infarction develop extension to right ventricular wall leading to variable degree of RV dysfunction
- Patients have shock but clear lung fields and raised JVP and Kussmual's sign.
- ECG shows ST segment elevation (0.1mV or more) in lead V4R, V5R and V6R but typically V4R
- echocardiography shows abnormal wall motion, dilation and reduced ejection fraction of right ventricle.

Management:

- Due to its ability to reduce preload, nitrates and diuretics which are routinely prescribed for LV infarction may produce profound hypotension in RV infarction so they should be avoided.
- Should be managed with plasma volume expansion to increase RV preload and cardiac output and when LV failure is also present, arterial vasodilators should be used.
- Inotropic therapy may be necessary. If required pulmonary artery catheter should be placed for hemodynamic monitoring. If pacing is required, atrial or AV sequential pacing should be done.
- Reperfusion of right coronary artery increases RV function and decreases in-hospital mortality.

Venous thrombosis and pulmonary embolism (PE):

- Bed rest and heart failure precipitates lower limbs venous thrombosis and thus pulmonary embolism.

VIII. 5. ADVANCED CARDIAC LIFE SUPPORT

Definition:

Advanced Cardiac Life Support (ACLS) is a modality of life-saving treatment and is the continuation of the basic life support (BLS) in the patient who suffers sudden cardiac arrest or cardiopulmonary arrest. The basic life support may be provided both by health care professionals or non-healthcare personnel without the use of equipment or drugs. ACLS is performed only by health care professionals with the help of necessary equipment, drugs and monitoring. It also incorporates the post-resuscitation care of the victim after the return of the spontaneous circulation (ROSC) following cardiac arrest. It is performed mostly in hospitals or well-equipped ambulances and with proper human resources.

Cardiac arrest in the adult population is mostly (about 85%) due to cardiac causes. The causes might be pulseless ventricular tachycardia (pVT) or ventricular fibrillation (VF). Other causes include asystole or pulseless electrical activities (PEA). In children, however, the cause of cardiac arrest is mostly respiratory problems leading to hypoxia.

During the cardiopulmonary arrest, the blood in the body ceases to circulate. If resuscitation is not performed within 5-10 minutes there will be a permanent injury to the brain. Since shockable rhythms are the common cause of cardiac arrest in adults, during CPR, defibrillation increases the rate of survival. Every minute delay of defibrillation reduces successful resuscitation by 10%.

Diagnosis:

The aim should be early detection and diagnosis of cardiac arrest, early and effective initiation of chest compressions and ventilation and early defibrillation when the rhythm is shockable. When one witness a collapsed victim, we have to assure that the scene is safe. The victim then should be placed on a firm surface in the supine position. If there is a chance the person has a spinal injury, two people should move the person to prevent the head and neck from twisting. Give a shout near the patient's ear and gently shake the victim, if unresponsive, call for help and ask for a defibrillator or Automatic External Defibrillator (AED). Healthcare professionals can check for the presence or absence of a pulse in the carotids and simultaneously look for respiratory movement.

Treatment:

If the victim has no pulse and is not breathing or is gasping, start chest compressions and ventilation at a 30:2 ratio. When a defibrillator or AED is available, give shock immediately if the rhythm is amenable to defibrillation i.e, if the rhythm is pulseless VT or VF. In the meantime obtain intravenous access. After 2 min of the defibrillation and chest compression/ventilation reassess the rhythm. If the rhythm is still shockable, defibrillate and inject 1 mg of the adrenaline intravenously followed by 10 ml flush with normal saline, repeat the 1 mg adrenaline every 3 – 5 minutes till spontaneous circulation is achieved. If the pulseless VT or VF is refractory to defibrillation, inject 300 mg of Amiodarone intravenously, 150 mg can be repeated if necessary. Look for the underlying causes (5H & 5T given in the chart below).

If the rhythm is PEA or Asystole, start chest compression/ ventilation, insert an IV cannula and immediately give 1 mg adrenaline intravenously followed by a flush. If the rhythm converts to pulseless VT or VF then follow the instructions according to the above paragraph. If not continue the CPR, repeat adrenaline every 3-5 min & search for the underlying causes (follow the Adult ACLS flow chart).

If ROSC is achieved, follow the post-resuscitation care protocol (see flow chart). Optimize the oxygenation (SpO2 >94%), respiration and blood pressure (MAP > 65 mmHg). If the victim remains unconscious, then the trachea should be intubated, mechanical ventilation should be initiated and body temperature should be targeted to 32-36 degree centigrades for the next 24 hours. The main aim is to prevent hyperthermia.

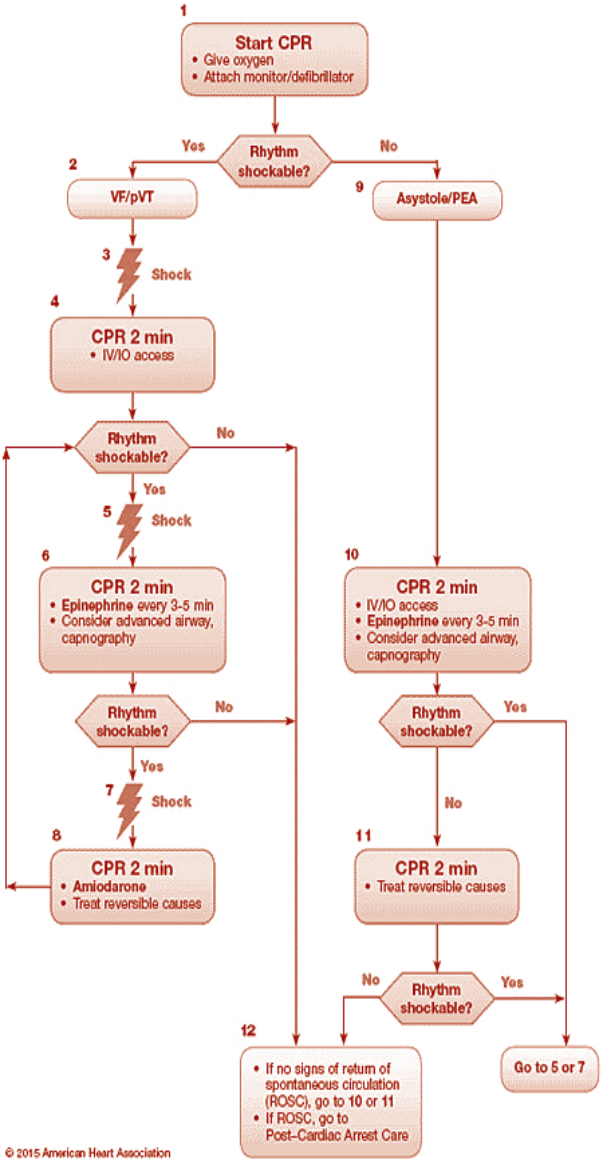
For the unresponsive/refractory VT, VF, Asystole or PEA search for the underlying precipitating causes and try to address them (see the flowchart).

Monitor quality of the resuscitation: End-tidal carbon dioxide (EtCO2) or capnography if available and it should be more than 10-12 for effective resuscitation and which increases after ROSC. If already inserted invasive arterial pressure, the arterial diastolic pressure should be more than 20 mmHg.

Shock energy: For the adult defibrillation select the maximum joules whether it is a monophasic or biphasic defibrillator. In the pediatric age group 4 – 10 joules per kg body weight.

Drugs: Adrenaline (epinephrine) is the drug of choice. Adrenaline is given 1 mg bolus IV every 3-5 minutes till the ROSC. It can be given via endotracheal tube if no IV access but the dose is 2-3 times the IV dose. If IV access is difficult, an intraosseous (IO) route can be tried, which is commonly employed in small children and infants. In refractory VF amiodarone, 300 mg bolus is given IV/IO and can be repeated 150 mg once in adults. In infants and children, the dose is 5mg/kg first bolus and half of the initial bolus can be repeated once. If suspected of opioid overdose then 0.4 mg naloxone for the adults is recommended.

Adult Cardiac Arrest Algorithm—2015 Update



CPR Quality

- Push hard (at least 2 inches [5 cm]) and fast (100-120/min) and allow complete chest recoil.
- Minimize interruptions in compressions.
- Avoid excessive ventilation.
- Rotate compressor every 2 minutes, or sooner if fatigued.
- If no advanced airway, 30:2 compression-ventilation ratio.
- Quantitative waveform capnography
  - If P_{ETCO_2} <10 mm Hg, attempt to improve CPR quality.
- Intra-arterial pressure
  - If relaxation phase (diastolic) pressure <20 mm Hg, attempt to improve CPR quality.

Shock Energy for Defibrillation

- Biphasic: Manufacturer recommendation (eg, initial dose of 120-200 J); if unknown, use maximum available. Second and subsequent doses should be equivalent, and higher doses may be considered.
- Monophasic: 360 J

Drug Therapy

- Epinephrine IV/IO dose: 1 mg every 3-5 minutes
- Amiodarone IV/IO dose: First dose: 300 mg bolus. Second dose: 150 mg.

Advanced Airway

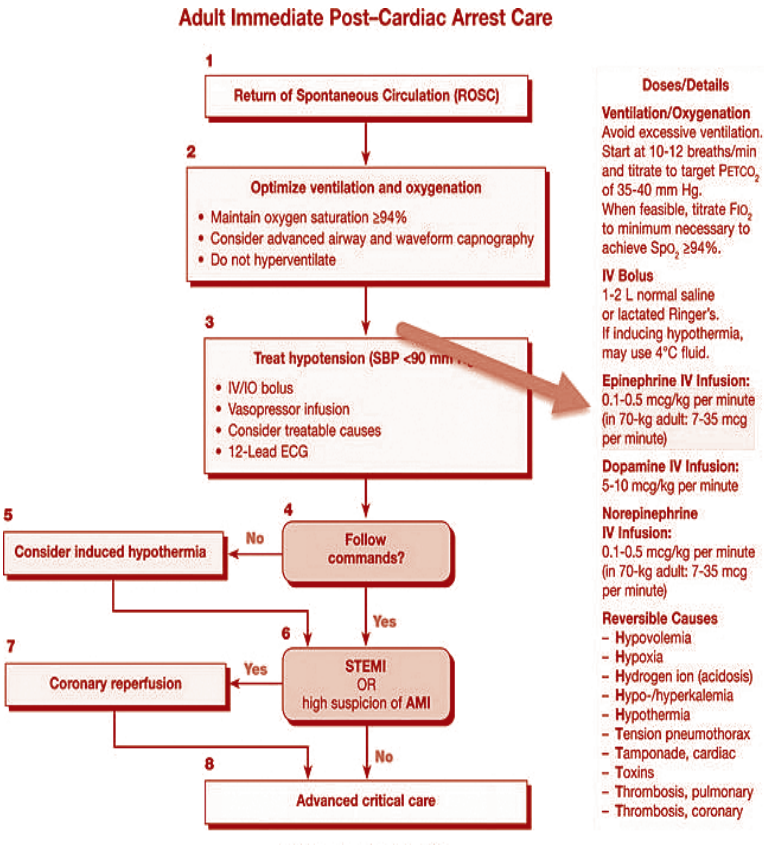
- Endotracheal intubation or supraglottic advanced airway
- Waveform capnography or capnometry to confirm and monitor ET tube placement
- Once advanced airway in place, give 1 breath every 6 seconds (10 breaths/min) with continuous chest compressions

Return of Spontaneous Circulation (ROSC)

- Pulse and blood pressure
- Abrupt sustained increase in P_{ETCO_2} (typically ≥40 mm Hg)
- Spontaneous arterial pressure waves with intra-arterial monitoring

Reversible Causes

- Hypovolemia
- Hypoxia
- Hydrogen ion (acidosis)
- Hypo-/hyperkalemia
- Hypothermia
- Tension pneumothorax
- Tamponade, cardiac
- Toxins
- Thrombosis, pulmonary
- Thrombosis, coronary



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VIII. 6.PRIMARY PERCUTANEOUS INTERVENTION IN ACUTE MYOCARDIAL INFARCTION

- Primary PCI (PPCI) is an emergent ,nonsurgical , percutaneous catheter intervention in the setting of acute ST elevation myocardial infarction(STEMI)for treating obstructive coronary artery disease.
- The goal of PPCI is to open occluded artery urgently to restore myocardial blood flow, salvage myocardium, prevent re-occlusion and thus improve short term and long term outcome including reduction in mortality.
- Reperfusion therapy with PPCI and fibrinolytic therapy both improve outcomes in patients with acute STEMI or an MI with a new or presumably new left bundle branch block or a true posterior MI.
- If performed in a timely fashion, PPCI of the infarct related artery(IRA) is the reperfusion therapy of choice compared to fibrinolysis.
- It achieves a higher rate of TIMI 3 flow (more than 90 percent with PPCI Vs 55-60% in thrombolysis) in shorter duration.
- In comparison to Fibrinolysis , PCI is associated with less risk of intracranial haemorrhage, has less re-occlusion of the culprit lesion, less residual ischemia and is associated with improved outcomes including in-hospital mortality and has been well demonstrated in different trials and meta- analysis.

Indications for primary PCI :

1. STEMI/ new LBBB with chest discomfort/ true posterior MI presenting within 12 hrs of symptoms onset
2. Patients presenting beyond 12 hrs with hemodynamic

or electrical instability, severe heart failure or ongoing ischemic symptoms

3. Routine PPCI should not be performed in stable patients presenting beyond 48 hours of symptom onset.

ER assessment and management

*Please refer to STEMI chapter for ER assessment and management.

- "Time is Muscle" –
- ECG should be done and interpreted within 10 minutes of first medical contact (FMC).
- Primary PCI should be the preferred reperfusion strategy if it can be performed within 120 minutes of STEMI diagnosis.
- If it cannot be done within 120 minutes then fibrinolysis should be the method of reperfusion. If patient presented in primary PCI capable set up, it should be ideally performed within 60 minutes of the diagnosis.

Technical issues/ Practical tips:

1. Radial vs femoral approach: Radial approach is preferred over femoral approach if operators are experienced as bleeding events, which are associated with poor prognosis, are less common in radial approach.
2. Angiography in PPCI

   The views should be taken to identify infarct related artery (IRA) and it characteristics like the thrombus burden, type of lesion, which helps to plan further steps in PCI. A quick conclusion on the nature of the non IRA should also be made. In a sick patient, time and contrast load is an important issue and should be taken into account

3. **Identifying the IRA:** (Useful tips)

   a. Good angiography and good views are important

      - ECG localization of the site of occlusion , definite thrombus in the affected vessel , absence of collateral .

b. Look at the normal course of the vessel and try to identify any area of flush occlusion

c. Abnormal origin of RCA may be a difficult situation and if not able to hook/ identify, better not to use a lot of contrast and cause harm.

d. In 5% of cases of AMI the coronaries are normal.

e. Urgent second opinion may be important if IRA could not be identified.

4. Operator should be continuously aware of blood pressure, heart rate, oxygen saturation of the patient while doing procedure. This will enable the operator to get an overall picture of how the PCI is going to be and risk involved in the patient and the preparations to be made (Need for an anaesthetist, IABP, ionotropes etc)
5. Minimal contrast load, swift wiring, adequate bed preparation, and proper stenting should be done without wasting much time.
6. **Slow flow** is not uncommon in PPCI and should be tackled using any of the following drugs : Intracoronary nitroglycerine, nitroprusside, adenosine, adrenaline, diltiazem, nikorandil.
7. **Direct stenting** (i.e. without predilation) of the culprit lesion is preferred technique.
8. **Drug eluting stents** are preferred over bare metal stents(BMS) as they have better outcomes in terms of safety as well as efficacy.
9. Guidelines have recommended Non-culprit PCI during index procedure in patients presenting with cardiogenic shock. However, recent evidences have indicated that such approach may be associated with increased adverse events and mortality.
10. Patients undergoing PPCI usually receive intravenous unfractionated heparin during the procedure to prevent acute vessel closure due to thrombosis. ACT(activated clotting time) is used for monitoring the efficacy of UFH(target of ACT 250-350 sec)
11. **Glycoprotein IIIb/IIa inhibitors** (abciximab, tirofiban and eptifibatide) are not routinely used in PPCI but should

be reserved to cases with slow flow, no reflow or huge thrombus load.

12. Routine use of **IABP** is not recommended in most cases of STEMI undergoing PPCI, even in cardiogenic shock but may be considered only in selected cases with mechanical complications.
13. Routine thrombus aspiration is not indicated in PPCI.
14. Conditions where PPCI should be abandoned in AMI include
    - Small distal artery,
    - Large thrombus with TIMI III flow- where anticoagulation should be given and maybe the patient can be brought to catheterization lab a few days later,
    - Inability to clearly identify the IRA.
    - If the operator feels that the safety of the patient is being compromised.

Periprocedural complications:

- Death in about 5% of the cases and 40-50% in case of cardiogenic shock
- Abrupt vessel Closure: <1%
- Coronary perforation 0.1 to 2%.
    - Management includes prolonged balloon inflation , reversal of anticoagulation by protamine sulphate and deployment of covered stent.
- Vascular access site complications in upto 5% , include bleeding requiring transfusion(3%),arteriovenous fistula(<2%), pseudoaneurysm (upto 5%).
    - Radial access, shorter anticoagulation regimens, vigilant monitoring of ACT, smaller sheath can result in reduction of complications.
- Contrast induced nephropathy (CIN) in 3 to 7%.
    - Adequate hydration may help to prevent CIN.
- Anaphylactoid reaction 1 to 2 %, may be severe in 0.1%
- Stent thrombosis in 0.5 to 1% per year. It can be procedure related, related to patient profile and compliance on medication, types and duration of DAPT.

In Hospital management And Discharge :

- Patients who have undergone primary PCI should be transferred to CCU and monitored for 24 hours. If stable, early mobilisation and transfer to ward can be done after 24 hours.
- Other adjunctive and supportive therapy are discussed in the chapter of STEMI. Stable patients can be discharged after 72 hours.
- They should be followed up in one to two weeks time in OPD and also need to be referred to cardiac rehabilitation program.

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VIII. 7.SECONDARY PREVENTION IN ISCHEMIC HEART DISEASE

Therapy to reduce recurrent cardiovascular events and decrease cardiovascular mortality in patients with established atherosclerotic vascular disease is known as secondary prevention. Aggressive comprehensive risk factor management improves survival, reduces recurrent events and the need for interventional procedures, and improves the quality of life. The secondary prevention patient population includes those with established coronary and other atherosclerotic vascular disease, including peripheral arterial disease, atherosclerotic aortic disease and carotid artery disease.

Components of Secondary Prevention

1. **Cigarette Smoking Recommendations**

   Goal: Complete Cessation and No Exposure to Environmental Tobacco Smoke

- Ask about tobacco use status at every visit. Advise every tobacco user to quit.Assess the tobacco user's willingness to quit. Assist by counseling and developing a plan for quitting. referral to special programs, or pharmacotherapy (including nicotine replacement and bupropion). Arrange follow-up. Urge avoidance of exposure to environmental tobacco smoke at work and home.

2. **Blood Pressure Control Recommendations**

   Goal: <140/90 mm Hg

   Blood pressure 120/80 mm Hg or greater:

- Initiate or maintain **lifestyle modification:** weight control, increased physical activity, alcohol moderation, sodium reduction, and increased consumption of fresh fruits vegetables and low fat dairy products
- **Blood pressure ≥140/90 mm Hg should be treated, as** tolerated, add blood pressure medication, treating initially with **beta blockers** and/or **ACE inhibitors** with addition of other drugs as needed to achieve goal blood pressure

3. **Lipid Management Goal**

   LDL-C should be less than 100 mg/dL

   If TG >200 mg/dL, non-HDL-C should be < 130 mg/dL*

   For very high risk patients: further reduction to LDL-C to < 70 mg/dL is reasonable, whereas non-HDL-C should be < 100 mg/dL*

   *Non-HDL-C = total cholesterol minus HDL-C

   ****Very high risk includes a history of multiple major ASCVD events or 1 major ASCVD event and multiple high-risk conditions**

   Major ASCVD Events: 1.Recent ACS (within the past 12 months), 2. History of MI (other than recent ACS), 3. History of ischemic stroke, 4. Symptomatic peripheral arterial disease (history of claudication with ABI<0.85, or previous revascularization or amputation)

   High-Risk Conditions: 1.Age ≥65years, 2. Heterozygous familial hypercholesterolemia, 3. History of prior coronary artery bypass surgery or percutaneous coronary intervention outside of the major ASCVD event(s), 4. Persistently elevated LDL-C (LDL-C ≥100mg/dl [≥2.6mmol/L]) despite maximally tolerated statin therapy and Ezetimibe, 5. Hypertension, 6. CKD (eGFR 15-59ml/min/1.73m2), 7. Current smoking, 8. Diabetes mellitus, 9. History of congestive HF

   1. A **lipid profile** in all patients should be established, and for hospitalized patients, lipid-lowering therapy should be initiated before discharge.

2. Lifestyle modifications including **daily physical activity** and **weight management** are strongly recommended for all patients.
3. Dietary therapy for all patients should include reduced intake of **saturated fats (<7%** of total calories), **trans fatty acids (<1%** of total calories), and **cholesterol (<200 mg/d).**
4. In addition to therapeutic lifestyle changes, **statin therapy** should be prescribed **in the absence of contraindications or documented adverse effects.**
5. An adequate dose of statin should be used that reduces **LDL-C <100 mg/dL** AND achieves **at least a 30% lowering of LDL-C.**
6. Patients who **have triglycerides ≥200 mg/dL** should be treated with statins to **lower non–HDL-C <130mg/dL.**
7. Patients who have **triglycerides >500 mg/dL** should be started on **fibrate therapy** in addition to statin therapy to prevent acute pancreatitis.

High Intensity statin Therapy	Moderate Intensity statin Therapy	
High intensity lowers LDL by ≥50%	Moderate intensity lowers LDL by 30-49%.	
Rosuvastatin 20 or 40mg Daily	Rosuvastatin 5 or 10mg	Pravastatin 40 or 80mg
Atorvastatin 40 or 80mg Daily	Atorvastatin 10 or 20mg	Lovastatin 40mg
	Simvastatin 20 or 40mg	Fluvastatin 40mg BID

4. **Physical Activity Recommendations**

   Goal: 30 minutes 7 days/week, minimum 5 days/week

   Assess risk with a physical activity history and/or an exercise test, to guide prescription Encourage **30 to 60 minutes** of **moderate intensity aerobic activity** such as **brisk walking**, on most, preferably all days of the week, supplemented by an increase in daily lifestyle activities (e.g., Walkingbreaks at work, gardening, household

work) to improve cardiorespiratory fitness.

Counsel patients to report and be evaluated for symptoms related to exercise.

Recommend complementary resistance training at least 2 days per week (IIA)

5. **Weight Management Recommendations**

   Goal: BMI 18.5 to 24.9 kg/m2

   Waist Circumference: Men: < 40 inches (<102cm) Women: < 35 inches (<89cm)

   Assess BMI and/or waist circumference on each visit and consistently encourage weight maintenance/ reduction through an appropriate balance of physical activity, caloric intake, and formal behavioral programs when indicated.

   If waist circumference (measured at the iliac crest) **≥35 inches in women** and **≥40 inches in men**,initiate lifestyle changes and consider treatment strategies for metabolic syndrome as indicated.

   The i**nitial goal** of weight loss therapy should be to reduce body weight by **approximately 10 percent from baseline.** With success, further weight loss can be attempted if indicated.

   *BMI is calculated as the weight in kilograms divided by the body surface area in meters^2.

   Overweight state is defined by BMI=25-30 kg/m2. Obesity is defined by a BMI >30 kg/m^2.

6. **Diabetes Mellitus Recommendations**

   Goal: Hb A1c ≤ 7%

   1. Care for diabetes should be **coordinated** with the patient's primary care physician and/or endocrinologist.
   2. **Lifestyle modifications** including daily physical activity, weight management, blood pressure control, and lipid management are recommended for all patients with diabetes.
   3. Initiation of pharmacotherapy interventions to achieve target HbA1c may be reasonable. (Class IIb)

4. **Less stringent HbA1c** goals may be considered for patients with a history of **severe hypoglycemia, limited life expectancy, advanced microvascular or macrovascular complications,** or extensive comorbidities, or those in whom the goal is difficult to attain despite intensive therapeutic interventions. (Class IIb)

7. **Antiplatelet Agents / Anticoagulation Recommendations**
    1. **Aspirin 75–162 mg daily** is recommended in all patients with coronary artery disease unless contraindicated.
        - **Clopidogrel 75 mg** daily is recommended as an alternative for patients who are intolerant of or allergic to aspirin.
    2. A P2Y12 receptor antagonist in **combination** with aspirin is indicated in patients after **ACS or PCI with stent placement.**
        - For patients receiving a bare-metal stent or drug-eluting stent during PCI for ACS, **clopidogrel 75 mg** daily, **prasugrel 10 mg** daily, or **ticagrelor 90 mg** *twice daily* should be given for **at least 12 months.**
    3. For patients undergoing coronary artery bypass grafting, aspirin should be started **within 6 hours after surgery** to reduce saphenous vein graft closure. Dosing regimens ranging from **100 to 325 mg daily for 1 year** appear to be efficacious.
    4. In patients with extracranial carotid or vertebral atherosclerosis who have had ischemic stroke or TIA, treatment with **aspirin alone (75–325 mg** daily), **clopidogrel alone (75 mg** daily), or the **combination of aspirin plus extended-release dipyridamole (25 mg and 200 mg twice daily,** respectively) should be started and continued.
    5. For patients with **symptomatic atherosclerotic peripheral artery disease of the lower extremity,** antiplatelet therapy with **aspirin (75–325 mg daily) or clopidogrel (75 mg daily)** should be started and continued.

6. **Antiplatelet therapy** is recommended **in preference** to **anticoagulant therapy** with warfarin or other vitamin K antagonists to treat patients with atherosclerosis.
    - If there is a compelling indication for anticoagulant therapy, such as **atrial fibrillation, prosthetic heart valve, left ventricular thrombus,** or concomitant **venous thromboembolic disease,** be administered in addition to the low-dose aspirin (75–81 mg daily).
    - For patients requiring warfarin, therapy should be administered to achieve the recommended INR for the specific condition.
    - Use of warfarin in conjunction with aspirin and/or clopidogrel is associated with **increased risk of bleeding** and should be **monitored** closely.

1. If the **risk of morbidity from bleeding** outweighs the anticipated benefit afforded by thienopyridine therapy after stent implantation, **earlier discontinuation** (eg. <12 months) is reasonable. (Class IIa)
2. After PCI, it is reasonable to use **81 mg of aspirin per day** in preference to higher maintenance doses.(Class IIa)
3. For patients undergoing coronary artery bypass grafting, **clopidogrel (75 mg daily)** is a **reasonable alternative** in patients who are intolerant of or allergic to aspirin. (Class IIa)

8. Renin angiotensin aldosterone system blockers

<u>ACE Inhibitor Recommendations</u>

ACE inhibitors should be started and **continued indefinitely** in all patients with **left ventricular ejection fraction ≤40%** and in those with **hypertension,** diabetes, or **chronic kidney disease,** unless contraindicated.

It is reasonable to use ACE inhibitors in **all other patients.** (Class IIa)

Angiotensin Receptor Blocker Recommendations

The use of ARBs is recommended in patients who have heart failure or who have had a myocardial infarction with left ventricular ejection fraction <40% and who are **ACE-inhibitor intolerant.**

It is reasonable to use ARBs in other patients who are ACE-inhibitor intolerant.(Class IIa)

Aldosterone Antagonist Recommendations

Use in post MI patients, without significant renal dysfunction or hyperkalemia, who are already receiving therapeutic doses of an ACE inhibitor and beta blocker, have an LVEF < 40% and either diabetes or heart failure

*Contraindications include abnormal renal function (creatinine >2.5 mg/dL in men or >2.0 mg/dL in women) and hyperkalemia (K+ >5.0 meq/L)

9. Beta-blocker Recommendations

1. ß-Blocker therapy should be used in all patients with left ventricular systolic dysfunction (ejection fraction ≤40%) with heart failure or prior myocardial infarction, unless contraindicated. (Use should be limited to carvedilol, metoprolol succinate, or bisoprolol, which have been shown to reduce mortality.)
2. ß-Blocker therapy should be started and continued for 3 years in all patients with normal left ventricular function who have had myocardial infarction or ACS.
3. It is reasonable to continue ß-blockers beyond 3 years as chronic therapy in all patients with normal left ventricular function who have had myocardial infarction or ACS.(Class IIa)
4. It is reasonable to give ß-blocker therapy in patients with left ventricular systolic dysfunction (ejection fraction ≤40%) without heart failure or prior myocardial infarction. (Class IIa)

10. **Influenza Vaccination**

    Patients with cardiovascular disease should have an annual influenza vaccination

11. **Depression**

    For patients with recent coronary artery bypass graft surgery or myocardial infarction, it is reasonable to **screen for depression** if patients have access to case management, **in collaboration** with their **primary care physician** and a **mental health specialist.** (Class IIa)

12. **Cardiac Rehabilitation**

    1. All eligible patients with ACS or whose status is immediately post coronary artery bypass surgery or post-PCI should be referred to a **comprehensive outpatient cardiovascular rehabilitation program** either **prior to hospital discharge or during the first follow-up office visit.**
    2. All eligible outpatients with the diagnosis of ACS, coronary artery bypass surgery or PCI, chronic angina, and/or peripheral artery disease **within the past year** should be referred to a comprehensive outpatient cardiovascular rehabilitation program.
    3. A **home-based** cardiac rehabilitation program can be **substituted** for a **supervised, center-based program** for **low-risk patients.**
        1. A c**omprehensive exercise-based outpatient** cardiac rehabilitation program can be **safe and beneficial** for **clinicallystable outpatients with a history of heart failure.** (Class IIa)

Secondary Prevention Conclusions

- Evidence confirms that aggressive comprehensive risk factor management improves survival, reduces recurrent events and the need for interventional procedures, and improves the quality of life for these patients.

- Every effort should be made to ensure that patients are treated with **evidence-based, guideline recommended, life-prolonging therapies** in the **absence of contraindications or intolerance.**

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UNIT - IX

Hypertension

IX. 1. ESSENTIAL HYPERTENSION

Introduction

'Essential hypertension' is high blood pressure (BP) for which there is no clearly defined etiology.[1] High BP increases the risk of cardiovascular disease (CVD) for millions of people worldwide.[2] Overall the prevalence is higher in individuals who are 60 years and older as compared with younger adults.[3,4] The prevalence of HTN in eastern Nepal was around 34% in 2011.[5,6]. Studies done in Nepal have reported a prevalence of HTN ranging from 18.8% to 41.8%. The prevalence of HTN from the latest studies from South Asian Association for Regional Coorporation(SAARC) was: Bangladesh: 17.9%; Bhutan: 23.9%; India: 31.4%; Maldives: 31.5%; Nepal: 33.8%; Pakistan: 25%; and Sri Lanka: 20.9%.[6] A cross sectional study done in Kathmandu showed that prevalence of HTN increased to three-fold over 25 year.[7] Increasing prevalence of HTN in Nepal is due to lifestyle changes with physical inactivity, increased mental stress, and alcohol intake.[3,4]. There is a trend of paradigm shift of HTN from older person to younger adult.[3,4]

Cardiovascular risk factors common in patients with hypertension are: [3,4]

- have had a prior heart attack or stroke
- have diabetes
- have chronic kidney disease (CKD)
- are obese
- use tobacco
- have a family history of heart attack or stroke

Risk factors for primary (essential) hypertension:[3,4]

- Age –advancing age
- Obesity
- Family history- twice as common in person who have one or two hypertensive parents
- Race-more common in blacks
- High sodium diet- excess sodium intake (>3 g/day) increases the risk
- Excessive alcohol consumption
- Physical inactivity

Diagnosis:

Measuring blood pressure is the only way to diagnose hypertension, as most people with raised blood pressure have no symptoms. HTN is defined SBP of 140 mmHg or above and/or DBP of 90 mmHg or more. The diagnosis of hypertension should be confirmed at an additional patient visit, usually 1 to 4 weeks after the first measurement. In general, hypertension is diagnosed if, on two visits on different days: systolic blood pressure on both days is ≥140 mmHg and/or diastolic blood pressure on both days is ≥90 mmHg.

JNC 7 has given the guidelines and the criteria for diagnosis of HTN and pre-HTN. Recently in 2017 ACC/AHA has brought new changes in definition which is more aggressive. The diagnostic criteria of HTN are bit different in guidelines by JNC 7 and 2017 ACC/AHA guidelines , both strongly recommended to lower the BP to 120/80mmHg for otherwise healthy adults.[7,8]

Blood pressure measurement optimal method:

1) Patient preparation:
    - Patient should be relaxed sitting in a chair (feet on floor, back supported) for >5min.
    - The patient should avoid caffeine, exercise, and smoking for at least 30 min before measurement.
    - Patient should have emptied his/her bladder.
    - Neither the patient nor the observer should talk

during the rest period or during the measurement.

- Thick clothing covering the location of cuff placement should be removed

Six step method of blood pressure measurement

- Relax. Before taking your reading, try to relax. ...
- Sit Right. Sit in a chair with your back straight and supported and your feet flat on the ground. ...
- Position Your Arm. ...
- Choose the Right Instrument. ...
- Get the Right Fit. ...
- Don't Stress Your Body.

2) Technique:

- Patient's arm should be supported (e.g. resting on a desk).
- Middle of the cuff is to be positioned on the patient's upper arm
- Correct cuff size should be used such that the bladder encircles 80% of the arm
- For auscultatory determinations, a palpated estimate of radial pulse obliteration pressure should be used to estimate SBP and cuff inflated 20–30 mm Hg above this level for an auscultatory determination of the BP level.
- For auscultatory readings, cuff pressure should be deflated at the 2 mm Hg per second, listening for Korotkoff sounds.
- SBP and DBP should be recorded as onset of the first Korotkoff sound and disappearance of all Korotkoff sounds.
- BP should be recorded in both arms. If the difference between two arms is more than 15 mmHg, measurement should be repeated. If the difference persists, blood pressure of the arm with high recording is considered.
- If the blood pressure in the clinic is 140/90 mm Hg or higher, take a second measurement. If two are

substantially different, third measurement should be taken. The lower of last 2 measurements is recorded as clinic blood pressure.

Out of office and self monitoring of BP

Ambulatory blood pressure measurement: Twenty four hour recording of blood pressure can be done using properly validated and calibrated ABP machine. A small digital blood pressure monitor is attached to a belt around the waist and connected to a cuff around the upper arm. Hypertension is considered when day time BP is ≥ 135/85, night BP ≥ 120/80 and the mean BP ≥130/80. [9]

Home blood pressure measurement: Measuring of blood pressure with calibrated semiautomatic digital machine twice (in one or two min interval) in the morning and evening of at least three consecutive days can provide home blood pressure which is considered high when threshold is ≥135/85.[7,8]

White coat hypertension: BP that is consistently elevated by office readings but does not meet diagnostic criteria for HTN based upon out-of-office readings. The prevalence of white coat HTN is higher with increasing age, female versus male sex, nonsmoking versus current smoking status, and routine office measurement of BP by clinician observers versus unattended BP measurements. There is an identified minimal increase in risk of CVD complications or all-cause mortality in patients who have white coat HTN.

Masked hypertension: Patient has normal clinic blood pressure (less than 140/90 mm Hg) but higher outside clinic especially using average ambulatory or home blood pressure measurement).

Evaluation of hypertensive patient

History taking includes history of hypertension, dyslipidemia, cardiovascular disease, stroke or renal disease, smoking, dietary habit and salt intake, alcohol consumption, level of physical activity, sleep history including snoring habit, erectile dysfunction, recreational drug uses and in female the oral contraceptive uses and the hypertension in previous pregnancy and other relevant

family history. History pertaining to vision, headache, stroke, shortness of breath, chest pain, leg swelling, palpitation, sweating, weight gain or loss, thirst, hematuria, polyuria, cold extremities, intermittent claudication or rest pain are important. Current and past antihypertensive medications including effectiveness and intolerance and adherence to therapy are to be taken.

Clinical examination includes measurements of waist circumference, height and weight, fundus examination for retina, palpation and auscultation of heart and carotid arteries, palpation of peripheral arteries , examination for neurologic and cognitive status and systemic examination for secondary hypertension.

There are mainly 3 objectives of investigation in a case of hypertension.

1. Detection of target organ damage (cause specific)
    - Basic Tests to all -Fasting blood glucose, Complete blood count, Lipid profile, Serum Uric acid, Kidney function test, Serum electrolytes, Urinalysis, urinary albumin to creatinine ratio, Thyroid-stimulating hormone, Electrocardiogram, Chest X-ray, USG abdomen, ambulatory blood pressure monitoring (if available) can be done.
    - Suspected Renal Involvement –RFT, creatinine clearance with eGFR, Serum sodium, potassium, calcium, Urine for Micro albumin, 24-hour urinary protein, and kidneys parenchymal involvement
    - Ophthalmology evaluation for retinopathy
    - Echocardiography- for concentric LV hypertrophy
    - Others as per requirement
2. Detection of coexisting cardiovascular risk factors
    - Diabetes Mellitus- FBS, PPBS, HbA1c
    - Dyslipidemias- Fasting Lipid profile
    - Metabolic syndrome- combination of above investigations

3. Detection of secondary causes of HTN
    - Renal artery stenosis-USG Doppler for renal blood flow
    - Pheochromocytoma- CT scan abdomen and pelvis, 24hour Urinary metanephrines
    - Other Endocrine disorder – hormonal assay other than TFT according to need
    - Autoimmune diseases and Vasculitis – ANA, RA, DsDNA and other according to need
    - Coarctation of Aorta- CXR, Echocardiography, CT aortogram
    - Others according to suspected causes

Management of Hypertension:

- Non-pharmacological
- Pharmacological

1. **Non-pharmacological/Life style modification for all patients**
    - Stop all tobacco use, smoking cessation, avoid secondhand tobacco smoke and stop tobacco consumption.
    - Abstinence of alcohol
    - Increase physical activity to equivalent of brisk walk 150 minutes per week.
    - If overweight, lose weight. Target Body mass index in range 18.5-24.9 kg/sq.m and waist circumference <90 cm for men and <80 cm for women.
    - Eat heart-healthy diet: DASH (dietary approaches to stop hypertension)
        - Eat a low-salt diet.
        - Eat ≥5 servings of vegetables/fruits per day.
        - Use healthy oils (e.g. olive, sunflower).
        - Eat nuts, legumes, whole grains and foods rich in potassium.
        - Limit red meat to once or twice a week at most.

- Eat fish or other food rich in omega 3 fatty acids (e.g., flax seeds) at least twice a week. Avoid added sugar from cakes, cookies, sweets, œfizzy drinks and juice.

2. Pharmacological therapy:

Pharmacological therapy should be started if BP>140/90 mmHg despite 3-6 months of therapeutic lifestyle changes. However, medical treatment may also be given in special cases targeting to <130/80 in high cardiovascular conditions, left ventricular dysfunction, proteinuria and diabetes mellitus.[10,11,12]

Monotherapy: First line single agent includes thiazide diuretics, CCB and ACE inhibitors or ARB. Use monotherapy for low-risk patients with stage 1 hypertension whose SBP is <150 mmHg, very high-risk patients with high–normal BP, or frail older patients. CCB or thiazide diuretics preferred for age > 65 years.

Combination therapy: Initiation with 2 first line agents of different classes either as separate agents or in fixed dose combinations is recommended with stage 2 hypertension and an average BP more than 20/10 mmHg above their target. Drug combinations can be selected depending upon additional comorbidity (Table 2). Combination can be done as enlisted below.

Step 1. Single pill dual low dose combination .A+C

Step 2. Single pill dual full dose combination. A+C

Step 3.Triple combination . A+C+D

Step 4. Add Spironolactone or other antihypertensive groups for resistant hypertension

(A:ACE inhibitors/ARBlocker;C: Calcium Channel Blocker; D: Diuretics).

Resistant Hypertension

Resistant hypertension defined as either as Office SBP/DBP ≥130/80 mm Hg with ≥ 3 antihypertensive medications at optimal doses, including diuretics or Office SBP/DBP <130/80 mmHg with ≥4 antihypertensive medications. Exclude pseudo resistance like ensuring accuracy of office

BP measurements and compliance of medications. Identify and reverse contributing life style factors. Discontinue or minimize interfering substances like NSAID, oral contraceptives and licorice. Screen for other secondary cause of hypertension. Management by increasing diuretics, adding mineralocorticoids or other agents with different mechanism of action.[10,11]

Hyperension Urgency and Emergency

Systolic BP more than 180 and/or DBP>120 is severe hypertension. Severe hypertension without acute target organ damage is hypertensive urgency. Pressure can be lowered orally over a period of days to weeks on outpatient basis. If acute target organ damage manifests in form of encephalopathy, stroke, aortic dissection, pulmonary oedema, myocardial infarction, renal failure, retinal hemorrhages and eclampsia, it is called hypertensive emergency. Systolic BP should be reduced by no more than 25% within the first hour and then if stable to 160/100 within 2 to 6 hours and then cautiously to normal during the following fir 24 to 48 hours. Common medications uses are nitroglycerine (5 ugm/min increased to 20/ugm/min), labetalol (0.1-0.3mg/kg max 20mg iv over 10 minutes), esmolol (loading dose of 500-1000 ugm/kg/min over 1 minute followed by a 50 ugm/kg/min infusion) or enaliprilat (initial 1.25mg over 5 minutes increase upto 5mg every 6 hours).[10]

Table 1. Commonly Used Anti-hypertensive medications and its common adverse effects

Class of drugs	Medications	Doses	Common Adverse effects	Definite Indications	Contraindications
CCB	Amlodipine Nifedipine Cilnidipine	2.5-10mg:OD 5-20mg: OD 5-20 mg: OD	Pedal edema	Elderly, angina, systolic HTN, MS, DM	
ARB	Losartan Telmisartan Olmesartan Irbesartan	25-100mg: OD/BD 20-80mg:OD 20-40mg: OD 150-300mg: OD	Hyperkalemia	MS, DM, proteinuria, LV dysfunction, ACEI induced cough	Bilateral renal artery stenosis, pregnancy

ACEI	Enalapril Ramipril Lisinopril	5-40mg: BD 2.5-10mg: BD 10-40mg: OD	Hyperka-lemia, dry cough	MS, DM, protein-uria, HF, LV dys-function, Post MI	Bilateral renal artery stenosis, pregnancy
BB	Atenolol Metoprolol Bisoprolol Nebivolol	25-100mg 50-200mg 2.5-10mg 5-30mg	Fatigue, depression	Angina, Post MI, tachyar-rhythmia, HF	Asthma, chronic obstructive pulmonary disease (COPD), peripheral vascular diseases, and diabetes mellitus
Diuretics	Chlorthali-done* Hydrochlo-rothiazide* Furose-mide # Torsemide# Spironolac-tone ^	12.5-25mg 25-50mg 20-80mg: BD 2.5-5mg: OD 25-100mg:OD	Increase urination, low sodium, gout	HF, Elderly patients, systolic HTN	Gout, Dyslip-idemia
AB	Prazosin sustained release	2.5-20mg	Orthostatic hypotension		
AA	Clonidine Methyldopa	0.1-0.8mg:BD 500-2000mg:BD	Rebound HTN if miss the dose, dry mouth, drowsiness	CKD Preg-nancy	

Table 2. Antihypertensive use with comorbid conditions.

Left Ventricular hypertrophy	RAAS blocker + CCB
Albuminuria	RAAS blockers + other drugs
Renal dysfunction	RAAS blockers + other drugs
Heart Failure	RAAS blockers+ Diuretics ± CCB ± mineralocorticoids
Diabetes/Metabolic syndrome	RAAS blockers + CCB ±diuretics
Peripheral arterial disease	CCB or diuretics or both
Coronary artery disease	Beta blockers+ RAAS blockers ± CCB

Cerebrovascular disease	CCB + other drugs
Pregnancy	Methylodpa, Labetalol, Nifedipine
Atrial fibrillation	ARB, Betablocker
Aortic Disease	Betablockers

*CCB: calcium channel blockers, ARB: angiotensin receptor blockers, ACEI: angiotensin converting enzyme inhibitors, BB: beta blockers, AB: alpha blockers, AA: alpha agonists, DM: diabetes mellitus, HTN: hypertension, HF: heart failure, MS: metabolic syndrome, OD: once daily dose, BD: twice daily dose, ARB: Aldosterone Receptor Blocker; CCB: Calcium Channel Blocker; RAAS: Renin Angiotensin Aldosterone System*Thiazide diuretics, #Loop diuretics, ^Aldosterone antagonist diuretics.*

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IX. 2. SECONDARY HYPERTENSION

Introduction

Hypertension is common clinical entity worldwide causing significant morbidity and mortality globally.1 It has been classified into primary and secondary forms of hypertension. Secondary hypertension is hypertension due to an identifiable cause, which may be treatable with an intervention specific to the cause. A high index of suspicion and early detection of secondary causes of hypertension are important because interventions may be curative, especially in younger patients [e.g. corrective surgery for aortic coarctation, renal angioplasty in younger patients with renal artery fibromuscular dysplasia, reversal of an endocrine cause of hypertension (e.g. by removal of an adrenal adenoma), or drug treatment of a monogenic disorder affecting a specific drug-sensitive ion channel (e.g. selective use of Amiloride in Liddle's syndrome)]. Interventions that treat the cause of secondary hypertension later in life are less likely to be curative (i.e. remove the need for antihypertensive medication) because longstanding hypertension results in vascular and other organ damage that sustains the elevated BP, but intervention is still important because it will often result in much better BP control with less medication.

The prevalence of secondary hypertension is reported to be 5–15% of people with hypertension. Screening all hypertensive patients for secondary hypertension is not feasible or cost-effective; however, there are some general patient characteristics that suggest those more likely to have secondary hypertension and in whom screening should be considered after confirming that BP is elevated with Ambulatory blood pressure monitoring or office recording.

When to look for secondary cause of hypertension?

1. Onset of hypertension in young adults <30 years
2. Onset of hypertension after age 55 years
3. Disproportionate target organ damage(TOD) for degree of hypertension
4. Abrupt onset of hypertension
5. Exacerbation of previously controlled hypertension
6. Accelerated /malignant hypertension
7. Drug induced/resistant hypertension
8. Unprovoked or excessive hypokalemia

Clinical evaluation of Secondary hypertension

We should evaluate clinically to look towards specific diagnosis of secondary hypertension. Probe into history to find out possible symptoms of secondary cause. Examination should have some essential checklist for physical findings with clue towards specific diagnosis.

History

- Diabetes
- Palpitaion, headache, flushing
- Tremor
- Fatigue, generalised weakness
- Irregular menses, amenorrhoea
- Nocturia, hematuria
- Snoring, daytime somnolence
- Abdominal and limb swelling
- Specific drug use

Physical examination

- Radiofemoral delay
- Difference of blood pressure >=20/10 mmHg upper limbs
- Obesity
- Edema
- Cafe au lait spots
- Striae, bruising

- Acromegaly
- Hirsutism
- Coarse skin
- Delayed ankle jerk
- Adominal lump
- Precordial thrill
- Carotid bruit
- Renal bruit
- Precordial murmur
- Claudication
- Thyromegaly
- Abnormal genital development

Specific clinical conditions and relevant investigations

1. Obstructive sleep apnea

   Epworth sleepiness score and Ambulatory polysomnography

2. Renal parenchymal disease

   Plasma creatinine and electrolytes, eGFR; Urine dipstick for blood and protein, Urinary albumin:creatinine ratio; Renal ultrasound

3. Atherosclerotic renovascular disease

   Duplex renal artery Doppler or CT angiography or MR angiography or Renal angiography

4. Fibromuscular dysplasia

   Duplex renal artery Doppler or CT angiography or MR angiography

5. Primary Aldosteronism

   Plasma aldosterone and renin, and aldosterone:renin ratio; Serum potassium

6. Phaeochromocytoma

   Plasma or 24 h urinary fractionated metanephrines, catecholamines, CT scan or MRI abdomen

7. Cushing's syndrome

   24 hour urinary-free cortisol

8. Thyroid disease (hyper- or hypothyroidism)

   Thyroid function test

9. Hyperparathyroidism

   Serum parathyroid hormone

10. Coarctation of the aorta

    Rib notching on chest X-ray, Echocardiogram, Thoracic and abdominal CT angiography

Rare genetic forms of secondary hypertension

1. Liddle syndrome
    - Hypokalemia, metabolic alkalosis, low PRA or PRC, low PAC
    - Responds to treatment with Amiloride
2. Apparent mineralocorticoid excess

   Hypokalemia, metabolic alkalosis, low PRA or PRC, low PAC;Decreased 11b-dehydrogenase isoenzyme 2
3. Gordon syndrome

   Hyperkalemia, metabolic acidosis, low PRA or PRC, low PAC;Overactivity of sodium chloride cotransporter
4. Geller syndrome

   Pregnancy-exacerbated hypertension, low PRA or PRC, low PAC ; Agonist effect of progesterone on the mineralocorticoid receptor
5. Glucocorticoid remediable hypertension
    - Hypokalemia, metabolic alkalosis, low PRC or PRA, and increased PAC ; Chimeric CYP11b1 to CYP11b2 gene
    - Response to treatment with glucocorticoids

Medications and other substances that may increase blood pressure

1. Alcohol
2. Amphetamines
3. Antidepressants (e.g., MAOIs, SNRIs, TCA
4. Atypical antipsychotics (e.g., clozapine, olanzapine
5. Caffeine

6. Decongestants (e.g., phenylephrine, pseudoephedrine
7. Herbal supplements (e.g., Ma Huang [ephedra], St. John's wort [with MAO inhibitors, yohimbine]
8. Immunosuppressants (e.g., cyclosporine)
9. Oral contraceptives
10. NSAIDs
11. Recreational drugs (e.g., "bath salts" [MDPV], cocaine, methamphetamine, etc
12. Systemic corticosteroids (e.g., dexamethasone, fludrocortisone, methylprednisolone, prednisone, prednisolone)
13. Angiogenesis inhibitor (e.g., bevacizumab) and tyrosine kinase inhibitors (e.g., sunitinib, sorafenib)

Summary

Secondary forms of hypertension include less frequent but significant proportion of hypertensive patents. Specific focus towards secondary cause with relevant history, examination and investigations will make us able to diagnose the secondary causes. Treatment of specific cause leads to reduction in medication, optimal control and cure of hypertension in many cases. Since specific management of the various secondary causes need different specialties, specific referral for treatment is the optimal strategy.

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IX. 3. HYPERTENSIVE CRISIS— EMERGENCIES AND URGENCIES

Hypertensive emergencies:

It is defined as severe elevations in Blood pressure >180/120 mm Hg associated with evidence of ongoing target organ damage. The 1 year death rate associated with hypertensive emergencies is >79%, and the median survival is 10.4 months if the emergency is left untreated.1 Examples of target organ damage:

- Hypertensive encephalopathy
- Intracranial hemorrhage
- Acute Ischemic Stroke
- Acute myocardial infarction
- Acute left ventricular failure with pulmonary edema
- Unstable angina pectoris
- Dissecting aortic aneurysm
- Papilledema
- Acute renal failure
- Eclampsia and severe preeclampsia/Hemolysis, elevated liver enzymes and low platlets (HELLP).

Treatment of hypertensive emergencies:

- Hypertensive emergencies can be life-threatening hence requires immediate treatment usually with parenteral medications in a monitored setting.[2]

Hypertensive Emergencies Requiring Immediate BP Lowering

Clinical Presentation	Timeline and Target BP
Malignant hypertension with or without acute renal failure	Several hours, MAP −20% to −25
Hypertensive encephalopathy	Immediate, MAP −20% to −25%
Acute ischaemic stroke and SBP ›220 mm Hg or DBP ›120 mm Hg	1 h, MAP −15%
Acute ischaemic stroke with indication for thrombolytic therapy and SBP ›185 mm Hg or DBP ›110 mm Hg	1 h, MAP −15%
Acute hemorrhagic stroke and SBP ›180 mm Hg	Immediate, 130‹SBP ‹180 mm Hg
Acute coronary event	Immediate, SBP ‹140 mm Hg
Acute cardiogenic pulmonary edema	Immediate, SBP ‹140 mm Hg
Acute aortic disease	Immediate, SBP ‹120 mm Hg and heart rate ‹60 bpm
Eclampsia and severe preeclampsia/HELLP	Immediate, SBP ‹160 mm Hg and DBP ‹105 mm Hg

Hypertensive Emergencies and Recommended treatment for BP Lowering

Clinical Presentation	First Line Treatment	Alternative
Malignant hypertension with or without acute renal failure	Labetalol	Nitroprusside
Hypertensive encephalopathy	Labetalol	Nitroprusside
Acute ischaemic stroke and SBP ›220 mm Hg or DBP ›120 mm Hg	Labetalol	Nitroprusside
Acute ischaemic stroke with indication for thrombolytic therapy and SBP ›185 mm Hg or DBP ›110 mm Hg	Labetalol	Nitroprusside
Acute hemorrhagic stroke and SBP ›180 mm Hg	Labetalol	
Acute coronary event	Nitroglycerine Labetalol	

Acute cardiogenic pulmonary edema	Nitroprusside or nitroglycerine (with loop diuretic)	loop diuretic
Acute aortic disease	Esmolol and nitroprusside or nitroglycerine	Labetalol, metoprolol
Eclampsia and severe preeclampsia/HELLP	Labetalol and magnesium sulphate	

Hypertensive Urgencies:

Hypertensive urgencies are situations associated with severe BP elevation in otherwise stable patients without acute or impending change in target organ damage or dysfunction. Many of these patients have withdrawn from or are nonadherent to antihypertensive therapy and do not have clinical or laboratory evidence of acute target organ damage. Severe hypertension can also develop in medication-adherent patients following a diet or lifestyle changes. These patients should not be considered as having a hypertensive emergency and instead should be treated by reinstitution or intensification of antihypertensive drug therapy, counseling and motivating for adherence to life style modification and treatment of anxiety if applicable.

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UNIT - X

Congenital Heart Disease

X. 1. PRENATAL DIAGNOSIS OF CONGENITAL HEART DISEASE

Congenital heart disease is the most common congenital disease of the newborn with an incidence of 8-10/1000 live births and even more in fetal life. One third of such patients require early intervention and are a major contributor of infant mortality rate. Diagnosis of heart disease prenatally significantly improves the survival rate of these patients and have an added benefit of fewer complication, lower medical costs and better functional outcome.

Benefits of fetal echocardiography

- Appropriate counselling to the expected parents to make them better prepared regarding the prognosis of the lesion, anticipation of procedures that may be required, long term morbidity and quality of life.
- Other prenatal investigations such as karyotyping or detailed ultrasound for non-cardiac abnormalities can be done when a cardiac anomaly is suspected.
- Delivery may be conducted at a higher centre with the facility for neonatal cardiac care decreasing the complication related to transfer of a sick neonate.
- Early treatment (especially in duct dependent lesions) decreases episodes of hypoxia and acidosis thus improving the long term neurological outcome.
- Management of fetal arrhythmia in utero can be lifesaving with early delivery if features of hydrops is seen and drug therapy is not effective.
- In utero treatment of certain cardiac lesions can be started in future as has already been established in certain parts of the world.

Indications of fetal echocardiography

- Maternal Indication
  - Presence of autoimmune antibodies (Anti Ro, Anti La)
  - Presence of Metabolic disorders (Diabetes mellitus, phenylketonuria)
  - Presence of Cardiac teratogen (retinoids, lithium, ethanol, phenytoin)
  - Presence of Intrauterine infection (eg. TORCH)
- Fetal indication
  - Extracardiac Anomalies (increased nuchal thickness, suspected chromosomal anomalies, abnormalities of other system such as renal, GI or CNS)
  - Non immune fetal hydrops
  - Monochorionic twins
- Familial indication
  - Congenital heart disease in parents or previous siblings
  - Mendalian syndrome (Williams, DiGeorge's)
  - Consanguineous marriage
- Indication of conversion of routine obstetric scan into fetal echo
  - Abnormal situs or chamber asymmetry
  - Altered cardiac axis, position and size of fetal heart
  - Abnormalities of fetal rate/rhythm

Timing of fetal echocardiography

- Optimal timing is at 18-22 weeks of gestation which may be repeated at 30 wks if abnormalities of atrioventricular and semilunar valves and aortic arch are suspected.
- Early trimester fetal echo (late 1st trim and early 2nd trim) can be done at 11-12 weeks in fetus with increased nuchal translucency.

- Beyond 22 wks fetal echocardiography can be done whenever an abnormality is detected in USG or fetal arrhythmia develops.

Technical factors

- Ultrasound transducer: The ultrasound probes should have the facility to choose between multiple frequencies. At 18-20 weeks, a high frequency probe (5-7 MHz) is used while the frequency is decreased 2.5-5 MHz with advancing gestational age, maternal obesity or oligohydramnios. Similarly harmonics is used to improve the quality of image.
- Imaging parameters: High frame rate of at least 20-40/sec, increase contrast, low persistence, single acoustic focal zone and narrow image field may be needed for good visualization.
- Acquisition of still image and video: The image should fill at least 1/3 to ½ of screen and moving video clips should be recorded. Frame by frame evaluation of the cardiac function and AV valves is done by freezing the moving images.

Cardiac examination

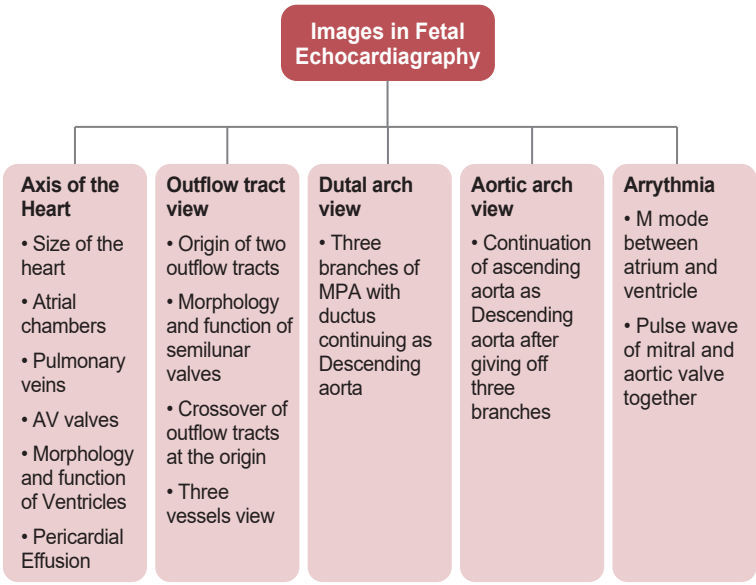
Multiple images in different standard views is necessary to maximize the detection rate of heart anomalies.

- Identification of the situs and position of heart: Confirmation of the position of the fetus is done before identifying the position and situs of the heart.
- Four chamber view: This view helps is diagnosing 40% of cardiac anomalies by fetal echocardiogram. Careful evaluation of segments to be evaluated in four chamber view are
    - Axis of heart: The angle between a line along the ventricular septum directed towards the cardiac apex and midline sagittal plane of thorax. The normal cardiac axis is 45± 15°.
    - Size of the heart: normal size is 1/3rd of total thoracic area
    - Pericardial effusion.

- Identification of atrial situs: LA identified by flap of foramen ovale. The atrium nearest the fetal anterior thoracic wall is the right. There should be presence of lower end of atrial septum(septum primum)
- Identification of ventricular situs, size and function: The intraventricular septum need to be evaluated carefully from the cardiac crux to apex for any defects. LV is identified by a smooth apical wall and RV by presence of moderator band.
- Morphology and function of AV valves: evaluation is to be done in both systole and diastole. The tricuspid valve can be identified as a more apically inserted valve with opening near the AV septal wall.
- Drainage of pulmonary veins to LA: at least two if not all veins need to evaluated.

- Outflow tract view: Addition of outflow tract views in the routine scan of fetal heart has increased the sensitivity of fetal echocardiography to almost 80%. The findings to be noted in outflow tract view are
    - Two great vessels coming off their respective ventricles need to be seen. The two vessels are usually equal in size with pulmonary artery lightly bigger than aorta.
    - Crossover of the great vessels at right angles from their origin as they exit from their respective ventricles need to be ascertained.
    - The position and function of the arterial valves need to be observed and there should be no obstruction in the flow across the valves.
    - Other cross sectional views to detect the relationship of great vessels and surrounding structures such as three vessel and three vessel trachea view require certain expertise and can be done by experts. However it greatly increases the detection rate.

- Views of the ductal and aortic arches and bicaval view: these views can be obtained by longitudinal or sagittal section of fetus.
    - The aortic arch originates from the left ventricle and has a convex appearance (candy cane) as it progresses towards descending aorta after giving three branches supplying the head.
    - The ductal arch originates from the right ventricle and continues forward from the main pulmonary artery as ductus arteriosus into the descending aorta (hockey stick appearance). The three branches of main pulmonary trunk (right and left branch PA and the ductus) need to be visualized.
    - The confirmation of drainage of IVC into the RA need to be made.



Fetal arrhythmia

The diagnosis of fetal arrhythmia can be done by simultaneous assessment of atrial and ventricular movement with the use of M mode or Doppler echocardiography. The use of pulse wave Doppler at the

mitral inflow-aortic outflow or M mode sonography of the atrium and ventricle helps to determine the number of contractions for each ventricle and atrium and analysis of corresponding P and QRS waves.

- Fetal bradycardia is defined when the heart rate of the fetus is persistently <100bpm. Maternal autoimmune disease needs to be investigated and use of beta agonist or steroids to the mother are reported to be effective in some cases.
- Fetal tachycardia is defined as fetal heart rate of >200 bpm. Supraventricular tachycardia due to Wolff-Parkinson-White syndrome is the most frequent form of fetal tachycardia. Digoxin is the first line drug given to mother while use of other drugs such as flecainide, sotalol, amiodarone, procainamide or propranolol can be considered if digoxin is ineffective and early delivery cannot be conducted.

Post diagnosis care

After the diagnosis of congenital heart disease is made in the fetal life, the expected parents should have a detailed discussion about the diagnosis and the severity along with the availability of treatment choices, necessity of treatments postnatally and the anticipated results and the quality of life after intervention. The counselling should be done by a team of doctors including the pediatric cardiologist, neonatologist and cardiovascular surgeon. The decision about the fate of the pregnancy should rest with the parents and clinicians should not direct the parents as to continuation or discontinuation of pregnancy. Treatment decisions to be made after the discovery of fetal abnormality are

- Fate of the pregnancy which is decided by the parents
- Location of delivery which is ideally done at a centre with facility for neonatal care and is near to the cardiac centre
- Timing of delivery: unless fetal insufficiency is suspected, almost all pregnancies can be continued up to term decreasing the complication of preterm delivery.

- Method of delivery: Cesarian section does not have any added benefits in fetus with congenital heart disease.

Pitfalls of fetal echocardiography

Fetal echocardiography like any investigation is extremely user and machine dependent and its sensitivity depends upon the ability of the clinician to acquire good image quality and be able to correctly interpret the findings. Some of the pitfalls of fetal echocardiography even in experienced hands are as following

- Some lesions such as minor VSDs may be missed.
- Progressive defects, such as a bicuspid aortic valve and coarctation of aorta, may not be diagnosed at 18–20 weeks of gestation.
- Outflow tract anomalies may be missed.
- Visualization of details may not be possible before 18 weeks or in cases of abnormal maternal habitus and fetal lie.
- Prediction regarding definite closure of foramen ovale and ductus arteriosus after birth cannot be made during fetal echocardiography

Conclusion and recommendations

Prenatal diagnosis of congenital heart disease significantly reduces the mortality, morbidity and improves the overall neurological outcome of the child. Fetal echocardiography is an important prenatal diagnostic tool for this commonest congenital disorder. Pregnant women with high risk for congenital heart disorder of the fetus should be referred to a facility with ability to perform fetal echo. The appropriate course of action after detection of a cardiac defect should be planned jointly by the pediatric cardiologist, neonatologist and pediatric cardiac surgeon and the decision should be left to parents.

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X. 2. APPROACH TO PATIENTS WITH CONGENITAL HEART DISEASE

Congenital heart defect (CHD), also known as a congenital heart anomaly or congenital heart disease, is a problem in the structure of the heart that is present at birth, is "a gross structural abnormality of the heart or intrathoracic great vessels that is actually or potentially of functional significance." Heart defects are the most common defect and the leading cause of birth defect related deaths. The incidence of CHD in general population is 8 to 12 per 1,000 live births. The defect can involve the septum within the heart, outflow tracts, valves & great vessels in isolation or in combination sometimes resulting in severe form of complex defect.

Causes of CHD

In most of the cases (~90%), may be either genetic or environmental, but is usually a combination of both. However suspicion of CHD should be made if there is evidence of any of the following:

- Viral infections during first trimester of pregnancy (e.g., Rubella, Cytomegalo Virus, Herpes Virus, Coxsackie Virus B etc.)
- Use of certain medications or drugs (such as Amphetamines, Lithium, Thalidomide, Hydantoin, Progesterone, Estrogen etc.)
- alcohol or tobacco consumption or exposure to radiation during pregnancy
- Maternal illness (like Diabetes, Hypertension, phenylketonuria, Systemic Lupus Erythematosus etc.),
- Consanguious parents

- poor nutritional status or obesity in mother
- Parents or siblings with a CHD
- Genetic and chromosomal anomaly of baby such as Down Syndrome, Turner Syndrome, Noonan Syndrome, Marfan Syndrome, Holt-Oram Syndrome, Hurler Syndrome, DiGeorge Syndrome. Conditions like VACTERL also increase the risk of CHD.

CHD are classified into 2 main groups: Acyanotic and Cyanotic heart defects

Acyanotic Heart defects include shunt lesions and obstructive lesions

- Shunt lesions: Ventricular Septal Defect (VSD), Atrial Septal Defect (ASD), Patent Ductus arteriosus (PDA), Atrio-Ventricular Septal Defect(AVSD), Partial Anomalous Pulmonary Venous Connection (PAPVC), Aortopulmonary Window (AP Window).
- Obstructive lesions include Pulmonary Stenosis (PS), Aortic Stenosis (AS), Coarctation of aorta (COA), Interrupted Aortic Arch and Cortriatriatum.

Cyanotic Heart Defects are usually associated with increased pulmonary flow or reduced pulmonary flow.

- Lesions with increased pulmonary flow are Tansposition of Great arteries (D-TGA), Total Anomalous Pulmonary Venous Connection (TAPVC), Tricuspid Atresia (without PS/PA), Double Outlet Right Ventricle (DORV), Truncus Arteriosus.
- Lesions with reduced pulmonary flow include Tetralogy of Fallot (TOF), Tricuspid Atresia (with PS/PA), Pulmonary Atresia, Hypoplastic right or left ventricle, Other complex defects include Ebstein's Anomaly, Congenitally Corrected TGA (CCTGA), Common Atrium and univentricular heart.

Presentation:

Signs and symptoms depend on the specific types of the defects and can vary from being asymptomatic to being life threatening

Neonate presenting as sudden shock should always be suspected of Duct dependent lesion unless proved otherwise.

Common symptoms include:

- Feeding difficulty, intermittent feeding
- Unable to wean off ventilator/oxygen
- Poor weight gain
- Central cyanosis at rest or on crying
- Excessive sweating during feeding/ at rest
- Shortness of breath
- Effort intolerance
- Recurrent lower respiratory tract infections

Examination

- Facial dysmorphism
- Failure to thrive
- Central cyanosis with clubbing
- Pallor or plethoric eyes
- Tachycardia with gallop rhythm
- Tachypnea
- Raised JVP
- Wide pulse pressure
- Crepitations in the lungs
- Hyperactive apical impulse
- Murmur on auscultation of the heart with abnormal heart sound
- Palpable liver and speen.

Diagnosis

- All mothers with increased risk factor (mentioned above) for CHD shoud undergo fetal echocardiography for early identification.
- Chest X-ray, Electrocardiography (ECG) and Echocardiography (ECHO) are the main investigations.

- ECHO is the most important imaging modality for the diagnosis of most CHDs.
- Cardiac Catheterization, CT Angiogram and cardiac MRI may be needed in selected cases.

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X. 3. ATRIAL SEPTAL DEFECT (ASD), VENTRICULAR SEPTAL DEFECT (VSD) AND PATENT DUCTUS ARTERIOSUS (PDA)

Atrial Septal Defect

Atrial Septal Defect (ASD) is one of the most common congenital heart defects (CHD). Secundum ASD is the most common ASD which is located in the central part of the atrial septum in the region of fossa ovalis and other ASDs being Primum ASD, Sinus Venosus ASD and coronary Sinus ASD.

Clinical Presentation

History

- Usually asymptomatic unless associated with pulmonary hypertension.
- Mild fatigue and dyspnea on exertion, worsening with age
- Atrial Arrhythmias (the most frequent presenting symptom).
- Cyanosis and syncope on exertion in late stages due to Eisenmenger syndrome.

Physical Examination

- Cardiovascular examination:
    - Precordial bulge with prominent right ventricular (RV) impulse.
    - Wide and fixed splitting of second heart sound (S2)
    - Ejection systolic murmur in pulmonary area with grade 2/6 ~ 3/6
    - Mid-diastolic murmur at tricuspid area due to high flow across tricuspid valve

- Loud P2 with or without early diastolic murmur of pulmonary regurgitation (PR) if pulmonary hypertension is present

Diagnostic Evaluation

Electrocardiography (ECG)

- Normal ECG
- Right axis deviation, increased amplitude of P waves with rSR' pattern (incomplete right bundle branch block) in right precordial leads
- Left or superior axis deviation in primum ASD.
- Rhythm abnormalities including junctional rhythm, atrial fibrillation or flutter.
- Q waves and tall monophasic R waves with deeply inverted T waves in pulmonary hypertension

Chest X-ray

- Normal chest x-ray.
- Cardiomegaly due to RA and RV enlargement
- Increased pulmonary vascular markings extending in significant shunt.
- Peripheral pruning in pulmonary hypertension.

Echocardiography

Transthoracic echocardiogram

Subcostal view in children and young individuals while 4C and parasternal in obese individuals can be done.

Things to look for:
Size and location of ASD along with the direction of flow: largest size in whichever plane in taken

Chamber dilatation: right atrium and ventricle larger than its left component.

Tricuspid regurgitation: to assess the severity of pulmonary hypertension.

Assessment of rims of ASD for possibility of device closure: all the four rims viz AV rim, aortic rim, posterior rim and inferior rims need to be assessed and measured.

Other associated lesions: particular attention to pulmonary and mitral valve.

Drainage of pulmonary veins: specially in sinus venosus type of ASD

Transesophageal echocardiography:
Done in patients with poor echo window to confirm the presence of ASD and to identify the rims to confirm the suitability of device closure.

Cardiac Catheterization

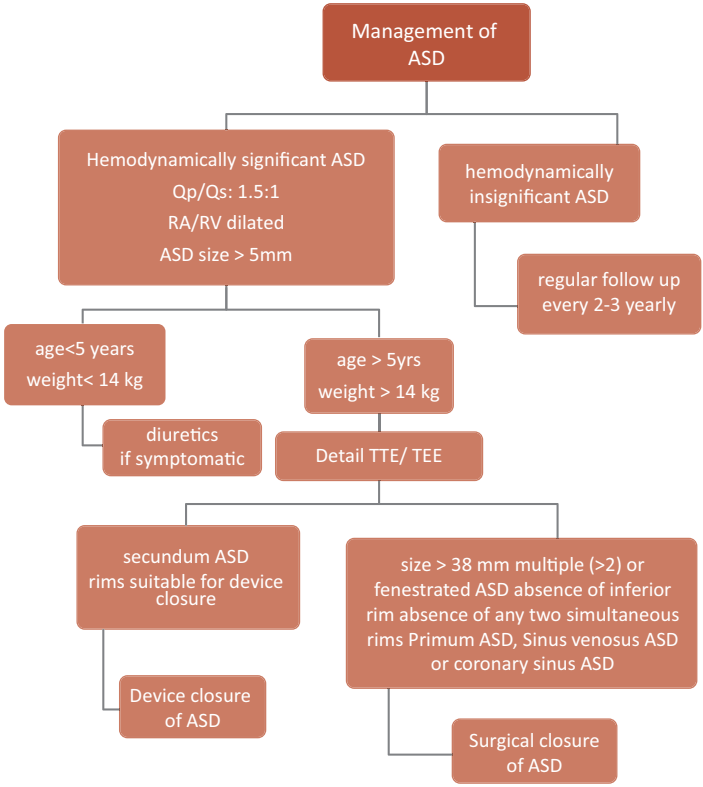
Cardiac catheterization is done in cases of severe pulmonary hypertension calculate the pulmonary vascular resistance to confirm whether the closure of ASD is contraindicated.

Management

Medical Management

Diuretics is given in small children with large shunts causing significant chamber dilatation until closure of the defect.

Management of pulmonary hypertension in older patients when pulmonary vascular resistance is high or there is reversal of shunt across ASD.



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VENTRICULAR SEPTAL DEFECT

Introduction

A ventricular septal defect (VSD) is a communication between the left and right ventricles or the left ventricle and right atrium. VSDs encompass a wide anatomic and physiologic spectrum of disease, and can occur as an isolated defect or in association with other congenital heart lesions. Isolated VSD is discussed here.

Clinical Presentation

- Asymptomatic
- Intermittent feeding
- Failure to thrive
- Frequent LRTI/ hospitalization
- Easy fatigability/ poor effort tolerance
- Shortness of breath
- Features of Eisenmengers: cyanosis on exertion, chest pain, syncope

Examination findings

- Decreased weight and height for age
- Tachypnea/tachycardia (gallop rhythm)
- Pallor
- Displaced and hyperdynamic LV apex
- Crepitation on both lungs (indicate CCF)
- Auscultation: Pansystolic murmur heard in left sternal border grade 2/6 – 4/6, variable and split S2, Mid-diastolic murmur of relative mitral stenosis (due to increase flow)

- Eisenmenger syndrome: Cyanosis/Clubbing (+/-), loud P2, Pansystolic murmur of TR and early diastolic murmur of PR
- Palpable liver

Chest Radiograph

- In small defects, the chest x-ray radiograph is usually normal.
- In moderate to large defects with increased left-to-right shunts, cardiomegaly with dilated LV, prominent pulmonary artery segment and increased bronchovascular markings
- In Eisenmenger physiology, normal heart size or dilated RV, peripheral pruning of pulmonary vasculature

Electrocardiography (ECG)

- The electrocardiogram for a patient with a VSD depends on the size of the defect and the age of the patient.
- ECG will be normal in small VSD.
- With a moderate VSD, LV hypertrophy and occasional left atrial (LA) enlargement may be seen.
- With a large VSD, the ECG shows biventricular hypertrophy with or without LA enlargement (Fig 1).
- In VSD with pulmonary vascular obstructive disease, ECG may show RV hypertrophy only.

Echocardiography

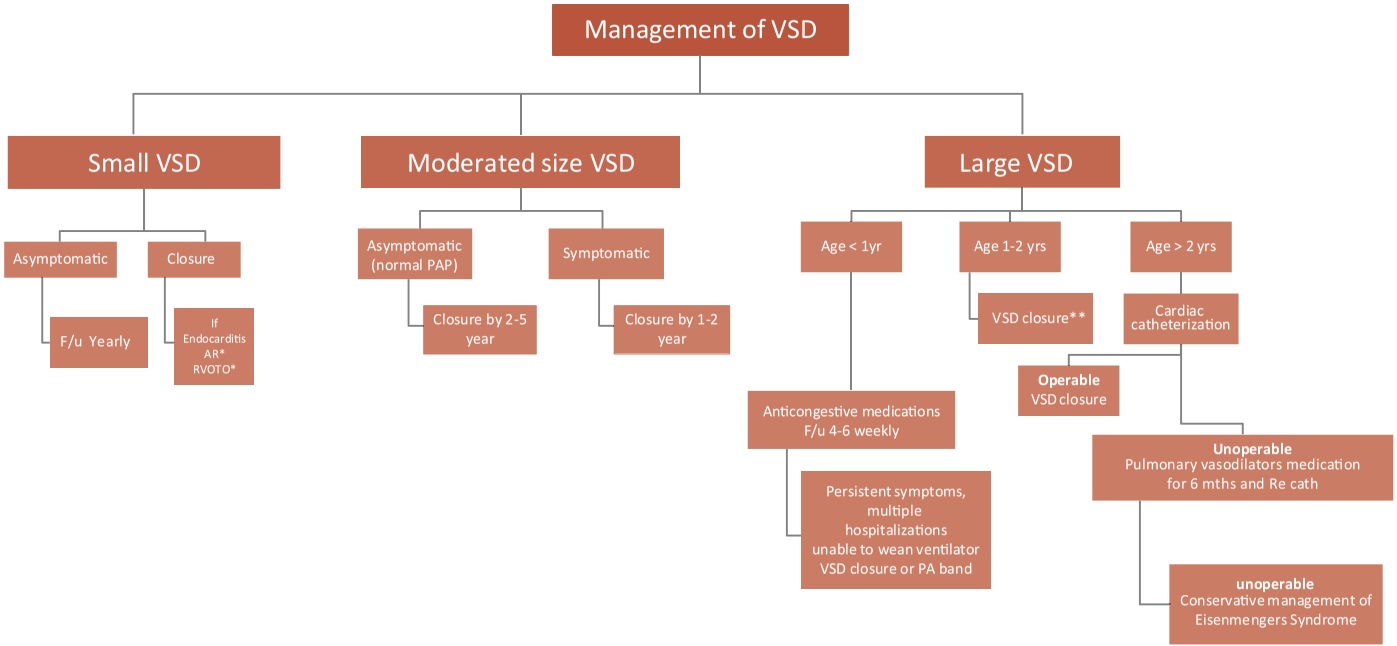
Done for confirmation of diagnosis and to facilitate the plan of management. Features to look for in echocardiography:

- Position of VSD: mostly identified in apical 4 and 5 C view and parasternal short axis view. Whole of the IVS need to be evaluated, both by 2 D and color Doppler.
- Gradient across VSD: to assess the pulmonary artery (PA) pressure as the gradient decreases with the increase in PA pressure
- Size of VSD:

    - Small- <1/3 rd of aortic annulus, normal pulmonary artery pressure
    - Moderate- 1/3 – 1/2 of aortic annulus, normal to 2/3rd systemic pulmonary artery pressure
    - Large- >1/2 of aortic annulus, systemic to near systemic pulmonary artery pressure
- Tricuspid and Aortic valve morphology and severity of regurgitation if present
- Dilatation of chambers
- Presence of multiple VSDs
- Other associated lesions (particularly coarctation of aorta)

Cardiac catheterization

Cardiac catheterization is done for calculation of Qp/Qs and PVR in patients with increased pulmonary artery pressure identified by echocardiography to look for the possibility of closure. The calculation is to be done both in room air and selective pulmonary vasodilators (e.g. inhaled nitric oxide, Iloprost etc.) to look for reversibility of pulmonary resistance. 100% oxygen can be used if selective pulmonary vasodilators are unavailable.


Management of VSD
Small VSD
Asymptomatic
F/u Yearly
Closure
If Endocarditis AR* RVOTO*
Moderated size VSD
Asymptomatic (normal PAP)
Closure by 2-5 year
Symptomatic
Closure by 1-2 year
Large VSD
Age < 1yr
Anticongestive medications F/u 4-6 weekly
Persistent symptoms, multiple hospitalizations unable to wean ventilator VSD closure or PA band
Age 1-2 yrs
VSD closure**
Age > 2 yrs
Cardiac catheterization
Operable VSD closure
Unoperable Pulmonary vasodilators medication for 6 mths and Re cath
unoperable Conservative management of Eisenmengers Syndrome

Management

- Antifailure medications include diuretics, ACE inhibitors and digoxin
- Anemia if present should be corrected
- Prolapse of aortic valve with aortic regurgitation is an indication of surgical closure of VSD irrespective of symptoms, Qp/Qs or chamber dilatation
- Cardiac catheterization can/ should be done at any age if pulmonary vasooclusive disease is suspected.
- Trans catheter closure is done in muscular VSD, residual VSD after surgical closure or in selected cases of perimembranous VSD (if it is far from aortic or tricuspid valve)

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PATENT DUCTUS ARTERIOSUS

Introduction

The ductus arteriosus (DA) is a normal fetal structure that allows communication between aorta and pulmonary arteries (PAs) and diverts blood away from the pulmonary bed. A patent ductus arteriosus (PDA) occurs when the DA fails to completely close postnatally.

Clinical Features

- A preterm neonate with patent ductus may have difficulty to wean off ventilator
- Signs and symptoms of congestive cardiac failure depending on the size of PDA may be present.

Examination

- Decreased weight and height for age
- Tachypnea/tachycardia (gallop rhythm)
- Wide pulse pressure
- Cyanosis/ clubbing (in increased PVR more pronounced on lower extremeties)
- Pallor
- Crepitation on both lungs
- Displaced and hyperdynamic LV apex
- Auscultation: continuous/machinery murmur of varying intensity in left midclavicular line of 2nd intercostal space, Pan systolic murmur if PA pressure is raised, ejection systolic murmur of tricuspid regurgitation or diastolic murmur of pulmonary regurgitation. Small PDA may have no murmur (silent PDA)

- Eisenmenger syndrome: Loud P2, Pansystolic murmur of TR and early diastolic murmur of PR
- Palpable liver

Diagnosis

Chest x-ray:

May be normal in small PDA

In larger PDA, cardiomegaly, LV dilatation, increased MPA and bronchovascular markings may be seen.

Absence of cardiomegaly and peripheral pruning in Esenmengers syndrome.

Electrocardiographic (ECG):

A hemodynamically insignificant PDA will have normal ECG.

Larger PDAs have widened P waves and changes suggestive of left ventricular hypertrophy

Echocardiography

Transthoracic echocardiography is done to establish the diagnosis, grading of severity, evaluating the need for intervention, and to estimated the type and size of device needed for the closure.

The ductus is imaged in the parasternal short-axis, high-left parasternal short-axis (also called ductal view) and suprasternal notch views.

Management

- In preterm babies if the RV pressure is below systemic pressure, pharmacological closure of PDA need to be attempted. IV paracetamol or oral or IV Ibuprofen can be used effectively. However in cases of suprasystemic PA pressure, bidirectional or right to left flow across PDA and features of RV dysfunction, closure of PDA is delayed until decrease in RV pressure possibly after resolution of hyaline membrane disease of the lungs
- Diurectics and antifailure medications for symptomatic patients improves pre and post procedural complication.
- Transcatheter closure of PDA is a preferred method approach.

- There is no indication for closure of silent PDA.
- Surgical closure of PDA is done in babies of less than 3.5 kg weight and is unable to wean of oxygen/ventilator.
- PDA with established Esenmengers syndrome (after cardiac catheterization) is managed conservatively.

X. 4. TETRALOGY OF FALLOT

Background :

Tetralogy of Fallot (TOF) is the commonest cyanotic congenital heart disease with the prevalence of 0.4/1000 live births, constituting about 5 % of all congenital heart defects.1 The classic components of the "tetrad" that comprise this defect are a ventricular septal defect (VSD), right ventricular outflow tract obstruction, aortic override and RV hypertrophy.

Clinical Presentation:

The important clinical sign of TOF is cyanosis. Most commonly, cyanosis is mild at birth and gradually progresses due to increasing hypertrophy of the right ventricular infundibulum. The severity of the cyanosis and its variability depends on the specific morphology of the RV outflow tract. Intermittent Hypercyanotic spells are one of the defining features of TOF. These spells are characterized by a marked decrease in pulmonary blood flow and an increase in the right to left shunt across the VSD, directing desaturated blood into the aorta. Presence of clubbing is typical in older children and adults with TOF. There is a moderate intensity systolic murmur maximal in the second and third left intercostal spaces. Typically the murmur disappears in the presence of a spell. Patients with untreated TOF have an estimated 1 year, 3 year, and 10 year survival of 66%, 49% and 24 % respectively.

Diagnostic Workup: Includes clinical assessment, pulse oximetry, ECG, X-ray chest and echocardiography. CT angiography (CTA) or cardiac catheterization and

angiography should be performed in older children and adults to confirm echocardiographic findings especially to delineate pulmonary artery, coronary artery anatomy and aortopulmonary collaterals.

Chest radiography

Chest radiography usually showed typical "boot shaped" heart with an absent pulmonary artery segment. The aortic arch is right sided in 25% of the cases.

Electrocardiography (ECG)

ECG in TOF shows RV hypertrophy with right axis deviation.

Echocardiography

The diagnosis of TOF is usually easily established by echocardiography. The typical finding is presence of a malalignment VSD with variable aortic override, right ventricular outflow tract obstruction and right ventricular hypertrophy. Echocardiography can also detect presence of branch pulmonary artery stenosis, if any, and determine the size of the pulmonary arteries.

Cardiac catheterization

Cardiac catheterization is indicated in complex forms of TOF, when pulmonary artery anatomy is poorly seen and in cases where the coronary artery abnormalities, presence of major aortopulmonary collateral arteries (MAPCA) are suspected.

Computed tomography angiography (CTA)

CTA can define the branch and peripheral pulmonary arteries accurately. CTA is used selectively in TOF, both in neonates and infants, as a preoperative diagnostic test and in patients after palliative surgery or reparative surgery.

Magnetic Resonance imaging (MRI)

MRI can accurately define the anatomy of the RV outflow tract and branch pulmonary arteries. The major indication for MRI is in postoperative TOF patients with chronic pulmonary regurgitation is to look for RV volume and function, pulmonary valve regurgitant fraction, coexisting pulmonary stenosis and tricuspid valve regurgitant fraction.

Management

Indications and timing of surgery:

1. All Patients need surgical repair.
2. Stable, minimally cyanosed: Total repair at 6-12 months of age or earlier according to institutional policy (class I). Those presenting later in life should undergo surgical repair whenever diagnosed.
3. Symptomatic children of <6 months of age with significant cyanosis or history of spells despite therapy: Palliation (by systemic to pulmonary artery shunt or stenting of the ductus arteriosus / right ventricular outflow tract, or pulmonary valve balloon valvuloplasty) or total repair depending upon the anatomy and center's experience (class I).
4. Lower threshold for earlier surgery if no requirement of transannular patch is anticipated.
5. Patient having TOF with absent pulmonary valve who are stable: Medical management till 1 year of age followed by total correction with repair of pulmonary artery branch dilation/ aneurysm (Class I).
6. Patients with anomalous left anterior descending artery from right coronary artery crossing the right ventricular outflow tract, who are likely to need right ventricular to pulmonary artery conduit (Class I) :
   a. <10 kgs weight with significant cyanosis: Aorto pulmonary shunt.
   b. > 10 kgs weight: Total repair using conduit, or double barrel approach after two years of age

Important determinants of long term prognosis:

1. Pulmonary regurgitation (almost invariably present after repair)
2. Residual lesions (VSD, Right ventricular outflow tract obstruction, pulmonary artery branch stenosis)
3. Right ventricular outflow tract aneursyms
4. Aortic root dilatation
5. Venticular dysfunction
6. Conduction abnormalities and arrhythmias.

Recommendations for Follow up:

1. All patients operated for TOF require life long follow-up in view of the above listed postoperative issues.
2. Asymptomatic patients with no residual lesion but with free Pulmonary regurgitation, not requiring intervention should be followed up 1-2 yearly.
3. Clinical assessment, ECG and Echocardiogram is to be done at each visit. Holter monitoring is indicated if there is suspected arrhythmias.
4. cardiac MRI is an important investigation for follow up of these patients. In asymptomatic patients, baseline study should be performed 10 years after the surgery with periodic follow-up, with frequency of repeat imaging determined by anatomic and physiological findings. Right ventricular volumes and function assessment by CMR are useful to determine the timing of pulmonary valve replacement.
5. Infective endocarditis prophylaxis is indicated in uncorrected patients, patients with percutaneous or surgical pulmonary valve replacement and after surgical repair for 6 months. However, all patients with TOF are advised to maintain good oro dental hygiene even after 6 months of surgical repair.

Indications for Pulmonary Valve Replacement

1. Symptomatic patients with symptoms attributed to severe right ventricular volume overload with moderate or severe pulmonary regurgitation (class I).
2. Asymptomatic patients with two or more of the following (class IIa):
    a. Mild or moderate right ventricular or left ventricular dysfunction.
    b. Severe right ventricular dilation: right ventricular end-diastolic volume >160 ml/m2, right ventricular end-systolic volume >80 ml/m2, or right ventricular end-diastolic volume ≥ twice the left ventricular end-diastolic volume.
    c. Right ventricular systolic pressure ≥two-thirds of systemic pressure due to right ventricular outflow tract obstruction

d. Progressive reduction in objective exercise tolerance.

3. Sustained tachyarrhythmias (class IIb)
4. Residual lesions requiring surgical intervention(class IIb).

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X. 5. TRANSPOSITION OF GREAT ARTERIES (TGA)

Transposition of Great Arteries (TGA) is a congenital defect of heart in which aorta arises from morphologic right ventricle and pulmonary artery arises from morphologic left ventricle. The relationship between aorta and the pulmonary artery also changes: in the majority of cases (60%) the aorta lies anterior and to the right of the pulmonary artery (i.e, dextro-transposition of the great arteries, d-TGA).

TGA was first described by Baillie in 1797. TGA is the most common cyanotic heart defect in infancy and accounts for almost 5 to 9.9% of all cases of congenital heart disease. TGA is more common in diabetic mothers.

TGAs are subdivided into those with intact ventricular septum (TGA/IVS ~ 50%), with ventricular septal defect (TGA/VSD ~ 40-45%) and VSD with LV outflow tract obstruction (LVOTO) or pulmonary stenosis (TGA/VSD/PS ~10%) and very rarely TGA/IVS with LVOTO in about 5% . In about 30% of the patients with TGA, coronary artery abnormality can be detected. Other frequently found cardiac anomalies include patent ductus arteriosus and coarctation of aorta.

In TGA, pulmonary and systemic circulation work in parallel, rather than in series, which results in a compromised oxygen supply to the tissue and in augmented work load to right and left ventricles. In absence of an atrial, ventricular or arterial level mixing, there will be circulation only with de-

saturated blood which worsens with every other cardiac cycle, accompanied by progressive acidosis and the kid may die shortly after the birth. Overall, only half of the TGA patients survive for month, 90% of all the kids with TGA die before the age of 1 year.

Diagnosis

Clinical presentation may vary according to the associated defects. Cyanosis is prevalent during first day of life in patient with TGA and intact ventricular septum, whereas cyanosis may be less or not noticed in those with VSDs. Infact severe cyanosis without murmur is the hallmark in TGA-IVS. However, signs and symptoms of congestive heart failure (tachypnea, tachycardia, failure to thrive) may be evident after 3 to 6 weeks. Second heart sound is loud and single.

Chest x-ray may show cardiomegaly, increased pulmonary vascularity and a narrow mediastinum. In the case of TGA-IVS with adequate atrial mixing, CXR can be normal, but classical "egg on the string" phenomenon can be noted in up to 30% of patients.

Echocardiography is usually diagnostic with posterior great vessel dividing into right and left pulmonary arteries arising from left ventricle. Echocardiography may also demonstrate the anatomy of the coronary arteries. It will also show any associated cardiac anomalies.

Initial Management

TGA is a pediatric urgency and needs quick attention. All kids with cyanosis in infancy should have an echocardiography. If the TGA is associated with sizable ASD, VSD or a PDA the kid may be stable because of the good mixing of the blood.

Prostaglandin E1 may be administered to keep the ductus open and increase the pulmonary blood flow.

In the case of severe hypoxemia due to insufficient atrial level shunts, balloon atrial septostomy may be done to increase atrial level mixing, for children who are not undergoing immediate arterial switch operation.

Management of acidosis and or other associated medical conditions should be done promptly so that they can be offered an arterial switch operation. Mechanical ventilation may be needed.

Prompt consultation and transfer required to the specialized center with diagnostic, therapeutic and surgical intervention possibility.

Surgical Management

Surgery is the only definitive treatment of all TGAs and the timing of surgery is within first few weeks of life. The choice of operation depends upon the timing of presentation and whether or not the left ventricle has regressed in its mass. Arterial Switch operation (ASO), where the aorta and the pulmonary arteries are transected and re-anastomosed to left ventricular outflow and the right ventricular outflow respectively with relocation of the coronary arteries to the "neo-aorta", is performed in case of TGA/IVS. In children with TGA with VSD the surgery can be little delayed, because the LV mass remains adequate for longer period of time due to pressure and volume overload on the ventricle.

For children presenting late, arterial switch can be considered when LV mass is normal for the age or calculated LV mass is greater than 35 gm/m2. If the LV has already regressed in its mass, then an atrial switch operation (rerouting of the pulmonary venous blood to the right ventricle; IVC and SVC blood to the left ventricle) can be performed. Two-stage arterial switch operation namely, a preliminary pulmonary artery banding with or without systemic-pulmonary artery shunt to prepare the left ventricle, followed by the arterial switch operation after an interval is also a good option for late presenters. The low risk of the atrial switch and favorable long-term results in infants with isolated transposition of the great arteries support its consideration in this situation.

Some patients may ultimately require cardiac transplantation. Sinus node dysfunction is increasingly common with longer follow-up, and some patients need pacemaker implantation.

Summary

TGA is a complex congenital heart defect with potentially lethal outcome, if untreated however the reverse is equally true that if surgery (ASO) is performed in experienced centre in appropriate time, the outcome is excellent. Any suspicion of this condition should be a reason for early referral to a specialist center with pediatric cardiologist and cardiothoracic surgeon. If the kid is severely cyanosed, infusion of prostaglandin E1 can be started even in the peripheral setup till the kid reaches the specialized center. All patients should be seen periodically in a center where expertise in the clinical evaluation, imaging, and hemodynamic assessment is available.

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X. 6. COARCTATION OF AORTA

Introduction

Coarctation of the aorta is narrowing of the aorta that obstructs blood flow between the upper and lower body. Coarctation most often occurs as an isolated defect, but may occur with a ventricular septal defect, mitral valve abnormalities, or complex congenital heart defects. Aortic valve abnormalities most commonly bicuspid aortic valve (≤85%), often accompany this condition.

Coarctation of the aorta accounts for 6 to 8% of congenital heart anomalies. It occurs in 10 to 20% of patients with Turner syndrome. The prevalence is more in males with a male: female ratio of 2:1. However, most cases are sporadic.

The average survival age of individuals with un-operated coarctation was approximately 35 years of age, with 75 percent mortality by 46 years of age. Common complications in unoperated patients or in those operated on during later childhood or adulthood were systemic hypertension, accelerated coronary artery disease, stroke, aortic dissection, and heart failure. Causes of death include heart failure, aortic rupture, aortic dissection, endocarditis, endarteritis, intracerebral hemorrhage, and myocardial infarction.

Morphology

The morphology of CoA is a spectrum, and varies widely based on the age at presentation. For example, preductal coarctation is most commonly seen in the newborn period which is generally associated with hypoplastic transverse

arch. If severe, blood flow to the aorta distal (to lower body) to the narrowing is dependent on a patent ductus arteriosus, and hence its closure can be life-threatening. Other types of CoA include juxtaductal and posductal which are often encountered in older children and adults.

Presentation

Clinical presentation depends on the age at presentation. The age at presentation is primarily dependent upon the degree of stenosis across the coarcted segment, associated cardiac defects and presence of extensive collateral vessels that bypass the area of CoA. For example, severe CoA can lead to heart failure, shock, renal insufficiency and metabolic acidosis upon closure of the ductus arteriosus in neonatal period. Late presentation is commonly seen with milder form which may be diagnosed incidentally due to presence of murmur or hypertension in young adult.

Diagnosis

Diagnosis of a coarctation can be suspected just by clinical examination. But the following test will help establish a diagnosis.

Chest x-ray reveals normal sized heart, but sometimes cardiomegaly may be seen due to cardiac dilatation. In older children rib notching may be present and is a definite sign of coarctation. Post-stenotic dilation of the aorta results in a classic 'reverse 3 sign' on x-ray. ECG usually shows left ventricular hypertrophy but may be normal. In neonates and small infants, ECG usually shows right ventricular hypertrophy rather than left ventricular hypertrophy. Echocardiography is usually diagnostic. It can visualize the anatomic narrowing of the aorta and the pressure difference between the proximal and the distal parts of the coarctation. It will also demonstrate any associated anomalies in the heart.

While diagnosis of coarctation may be made by a clinical examination and echocardiography, computed tomography angiography (CTA) /cardiac magnetic resonance imaging (CMR) may be required in select cases, especially in adults when anatomy is unclear on echocardiography and for

follow-up after surgical or catheter intervention. Cardiac catheterization is primarily limited for catheter intervention.

Treatment

In Early presentation of coarctation of aorta treatment in patients with congestive heart failure (CHF) includes the use of diuretics and inotropic drugs. Prostaglandin E1 is infused intravenously to open the ductus arteriosus.

Indications for intervention

The following are the indications for intervention:

I. Patients with CoA gradient ≥20 mmHg (class I).
II. Patients with CoA presenting with left ventricular dysfunction, even though the CoA gradient is < 20 mmHg, where left ventricular dysfunction is considered to be due to tight CoA (class I).
III. Patients with gradient <20 mmHg but having upper limb hypertension, left ventricular hypertrophy, or significant collateral formation (class IIa).
IV. Patients with hypertension who have >50% narrowing at the site of CoA, relative to the aortic diameter at the level of diaphragm on CTA/CMR/angiography, irrespective of pressure gradient (class IIa).
V. Intervention is not indicated if the Doppler gradient across the coarctation segment is < 20 mmHg with normal left ventricular function and no upper limb hypertension (class III).

Mode of intervention

I. For neonatal presentation, surgery is the preferred mode of intervention. Aortic arch hypoplasia, if associated, should also be repaired.
II. For critically ill neonates who are considered high risk for surgery (shock-like syndrome and severe left ventricular dysfunction), balloon angioplasty may be performed to tide over the crisis (class IIa).
III. For infants with native coarctation, surgery (class I) or balloon angioplasty (class IIa) may be performed.
IV. For infants with recoarctation, balloon angioplasty

(class I) is the preferred mode of intervention.

V. For children weighing <25 kg with native coarctation balloon angioplasty (class I) or surgery (class IIa), may be performed

VI. For children weighing <25 kg with recoarctation, balloon angioplasty ± stenting (class I) is the preferred mode of intervention.

VII. For children weighing >25 kg and adults, with native coarctation, catheter-based stenting (class IIa) is the preferred mode of intervention.

VIII. For children weighing >25 kg and adults, with recoarctation, catheter-based stenting (class I) is the preferred mode of intervention

Indications of using a covered stent (provided the anatomy is suitable)

The following are the indications:

I. Native coarctation where risk of rupture of the aorta is high (BAV with ascending aorta dilation, nearly atretic isthmus [<3-mm diameter], Turner syndrome, age >60 years, Marfan syndrome).

II. Recoarctation with aneurysm or pseudoaneurysm at the site of CoA.

Prognosis

The risk of residual hypertension and early atherosclerotic cardiovascular disease is increased with late repair. The prevalence of residual hypertension is only 6% in patients who undergo repair between 1 and 5 years of age in comparison with 30- 50% in patients who undergo repair at an older age.

Postoperative hypertension can be treated short-term with vasodilators, such as sodium nitroprusside, and intravenous beta-blockers, such as esmolol. When longer-term antihypertensive therapy is required, beta-blockers may be continued, and if no residual arch obstruction exists, ACE inhibitors or angiotensin II antagonists may be added if hypertension persists despite beta-blocker therapy.

Residual or recurring coarctation, status of the aortic valve (if bicuspid), aneurysms of the ascending aorta or aneurysm at the intervention site, premature coronary artery disease, and berry aneurysms of the circle of Willis are important determinants of long-term prognosis.

Most women with repaired coarctation shouldn't have any difficulties with pregnancies, unless there's residual aortic obstruction or generalized high blood pressure.

Follow-up recommendations

I. Lifelong follow-up is required.

II. Annual follow-up is required initially, later every 2-3 years if there are no residual lesions.

III. Clinical assessment should include measuring upper and lower limb blood pressure. Echocardiography should be done at each follow-up to exclude any residual issues and to assess for other abnormalities, such as BAV.

IV. Beyond 5 years of age, echocardiography alone may not be sufficient for evaluation. CMR or CTA is recommended every 3-5 years or earlier. CMR is preferable in postsurgical and post-balloon angioplasty patients whereas CTA is preferred after endovascular stenting.

IE prophylaxis is needed for 6 months after surgery and intervention. However, all patients are advised to maintain good orodental hygiene after this period also.

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