SAFETY

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SIMULATION APPROACH FOR EDUCATION AND TRAINING IN EMERGENCY

Pulmonary emergencies

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Summary

Pulmonary embolism

1. Abstract/ introduction

Pulmonary embolism is the most dangerous form of venous thromboembolism (VTE), ranking high among the causes of cardiovascular mortality (1). PE is caused by fragments of venous thrombi that travel to the right cavities of the heart and subsequently occlude segments of the pulmonary artery.
VTE is the result of the interaction between patient-related (permanent) risk factors and setting-related (temporary) risk factors. Predisposing factors can be classified in strong risk factors (major trauma, hip or knee replacement, fracture of lower limb, previous VTE, recent myocardial infarction, spinal cord injury), moderate risk factors (including arthroscopic knee surgery, intravenous catheters, congestive heart failure, hormone replacement therapy, post-partum period, infection, autoimmune or inflammatory diseases, cancer, superficial vein thrombosis, thrombophilia) and weak risk factors (prolonged immobility, increasing age, obesity, pregnancy, varicose veins, diabetes, arterial hypertension).
Acute PE indices changes in both lungs and heart. Hypoxemia and respiratory failure are a result of ventilation/ perfusion mismatch caused by reduced blood flow in obstructed pulmonary capillaries and overflow in patent capillaries. In acute high-risk PE, when more than 30-50% of the total cross-sectional area of the pulmonary arterial bed is occluded by thromboemboli, the pulmonary artery pressure (PAP) increases and the acute pressure overload results in right ventricle (RV) dysfunction. Hypoxic vasoconstriction in the affected lung area further increases pulmonary vascular resistance (PVR). The increase in RV pressure and volume leads to RV dilation with leftward displacement of the interventricular septum, development of right bundle branch block and reduction of left ventricle (LV) filling. In turn, this results in reduction of cardiac output (CO), systemic hypotension and hemodynamic instability. The increased pressure gradient between the right and the left atrium may lead to right-to-left shunting through a patent foramen ovale and severe hypoxia or paradoxical embolization. Mixed venous blood oxygen saturation also decreases because of low arterial oxygen saturation and low CO. Although rare, acute high-risk PE is a life-threatening situation that can present with cardiac arrest, obstructive/ cardiogenic shock or persistent hypotension.

2. Symptoms and clinical signs

The clinical signs and symptoms of PE are non-specific.

- Breathing: dyspnoea at rest or with exertion, tachypnoea, pleuritic pain, cough, syncope, desaturation, haemoptysis.
- Chest pain, palpitations, tachycardia
- Signs of DVT: leg swelling, pain, warn red skin in the painful area, swollen vein.
- In cases of high-risk acute PE, signs of low CO: cold extremities, sweating, hemodynamic instability with hypotension, tachycardia, oliguria, altered mental status, syncope, signs of congestion (distended jugular veins, enlarged liver, epigastric tenderness).

In addition to signs and symptoms, predisposing factors for VTE are important in determining the clinical probability of PE. The most commonly used prediction rules are the revised Geneva rule and the Wells rule, which are presented in subsection 4. Diagnosis.

3. Differential diagnosis

Differential diagnosis with:	**Work up:**
Acute coronary syndrome	ECG, cardiac echocardiography and coronarography showing segmental kinetics disorders and coronary artery occlusion/ obstruction, coronary angiography
Acute valvular dysfunction	cardiac echocardiography showing valvular regurgitation/stenosis
Dissection of the thoracic aorta	transesophageal cardiac ultrasound and/or CT angiography of aorta showing intimal tear
Acute Respiratory Distress Syndrome	Berlin definition of ARDS
Anxiety Disorders	neurologic/ neuropsychiatric examination
Acute atrial fibrillation/ arrhythmias	ECG showing absence P wave, abnormal rhythm, irregular rhythm
Cardiogenic Shock/ Acute pulmonary Oedema	cardiac echocardiography, ECG and pulmonary artery catheter showing reduced LV ejection fraction, cardiac index < 2.2 L/min, and pulmonary wedge pressure > 18 mm Hg, chest X-ray
Fat Embolism	triad of respiratory insufficiency, neurological impairment, and a petechial rash
Acute Pericarditis	chest pain, pericardial friction-rub, characteristic ECG changes (new widespread ST-elevation or PR depression), pericardial effusion
Pneumothorax	chest X-ray or CT scan
Pneumonia	fever, tachycardia, lung pulmonary opacities located at the level of a lobe
Pulmonary emphysema	Chest X-Ray or CT scan
Hypersensitivity pneumonitis	cough, dyspnea following exposure to environmental antigens, the presence of characteristic changes in CT scan: bilateral, mosaic, ground glass opacities in the middle and lower lung zones, ill-defined centrilobular nodules

4. Diagnosis

4.1. Routine panel

Electrocardiogram (ECG):

- May be non-specific
- Sinus tachycardia, atrial arrythmias, most commonly atrial fibrillation
- Changes indicative of RV strain: inversion of T waves in V1-V4, QR pattern in V1, S1Q3T3 pattern, incomplete or complete right bundle branch block – usually in severe cases of acute PE

Chest X-Ray:

- Frequently abnormal, but the changes are non-specific for PE
- cardiomegaly, atelectasis, elevated hemi diaphragm, pleural effusion, pulmonary infarction, parenchymal areas of increased opacity

Gas-exchange:

- Pulse oximetry (SpO_2) – usually decreased
- Arterial blood gases (ABG) – arterial partial pressure of oxygen (PaO_2) is typically low but may be normal in 40% of patients. Arterial partial pressure of carbon dioxide ($PaCO_2$) may be either low (hyperventilation) (usually low)
- Venous blood gases (central venous oxygen saturation or mixed venous oxygen saturation) is decreased in patients with low CO

4.2. Pretest probability assessment

Prediction rules use the combination of clinical finding with the presence of VTE risk factors to classify the patients with suspected PE in distinct categories of clinical or pre-test probability. The proportion of patients with confirmed PE can be expected to be 10% in the low-probability category, 30% in the moderate-probability category and 65% in the high- probability category. The most used prediction rules are the revised Geneva rule and the Wells rule.

Wells criteria		
Presence of active malignancy: +1 Haemoptysis :+1 History of previous DVT of PE: +1.5 Heart rate >100 bpm:+1.5 Surgery or bed rest ≥ 3 days in 1 month:+1.5 Clinical signs or symptoms of DVT:+3 No presence of alternative diagnosis as likely as or more likely than PE:+3		
Pretest probability	**Points**	**Prevalence of PE (%; 95% CI)**
Low	<2	5.7 (3.7-8.2)
Intermediate	2-6	23.2 (18.3-28.4)
High	>6	49.3 (42.6-56.0)
Unlikely	≤4	8.4 (6.4-10.6)
Likely	>4	34.4 (29.4-39.7)

Revised Geneva score		
Age >65 years:+1 Presence of active malignancy:+2 Haemoptysis:+2 History of previous DVT of PE: +3 Surgery of lower limb fracture within previous month:+2 Unilateral oedema and pain at palpation:+4 Spontaneously reported calf pain:+3 Heart rate between 75 and 94 bpm:+3 Heart rate ≥95 bpm :+3		
Pretest probability	**Points**	**Prevalence of PE (%; 95% CI)**
Low	0-3	9.0 (7.6-10.6)
Intermediate	4-10	26.2 (24.4-28.0)
High	≥11	75.7 (69.0-81.8)

4.3. Lab testing

- D-dimer testing: high negative predictive value, low positive predictive value (a few more, and more explanatory words on d-dimers)
- Biochemical markers of myocardial injury (CK, CK-MB, troponins) and stretch (BNP, NT-proBNP).
- Full blood count (FBC), e.g., leucocytosis
- Urea and electrolytes (U&Es) may indicate renal impairment, electrolyte imbalances, particularly if on diuretics.
- Liver function tests (LFTs): Abnormal transaminases are usually associated with hypoperfusion and RV dysfunction.
- Lactate measurement: Increased lactate levels are indicators of low CO/ shock
- Thrombophilia profile assessment

4.4. CT pulmonary angiography (CTPA)

- The method of choice for imaging of the pulmonary vasculature in patients with suspected PE, allowing visualization up to subsegmental level.
- High negative predictive value in patients with low or intermediate clinical probability of PE
- High positive predictive value in patients with intermediate or high clinical probability of PE

4.5. Echocardiography

- Not mandatory in patients without hemodynamic instability with suspected PE.
- Mandatory in patients with hemodynamic instability with suspected PE, in which the absence of sign of RV dysfunction excludes PE as cause of hemodynamic instability.
- Focused on the evaluation of right heart cavities:
    - Enlarged RV
    - Dilated RV with basal RV/ LV ratio > 1 and McConnell sign (akinesia of the mid free wall and hyper contractility of the apical wall of the RV)

- Flattened interventricular septum
- Distended inferior vena cava with diminished inspiratory collapse
- 60/ 60 sign: coexistence of acceleration time of pulmonary ejection < 60 ms and midsystolic notch with mildly elevated (<60 mmHg) peak systolic gradient at the tricuspid valve
- Mobile thrombus detected in the right heart cavities
- Decreased tricuspid annular plane systolic excursion
- Decreased peak systolic velocity of tricuspid annulus (< 9.5 cm/s)

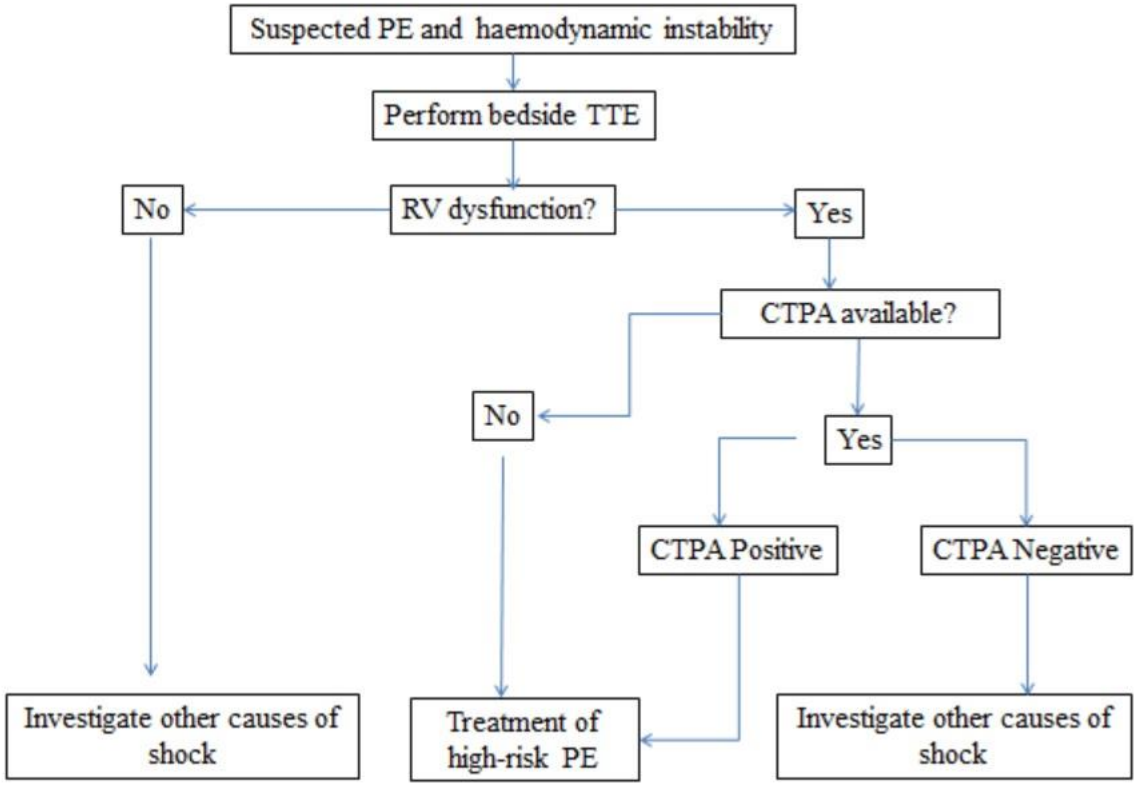
4.6. Supplementary investigations to be considered

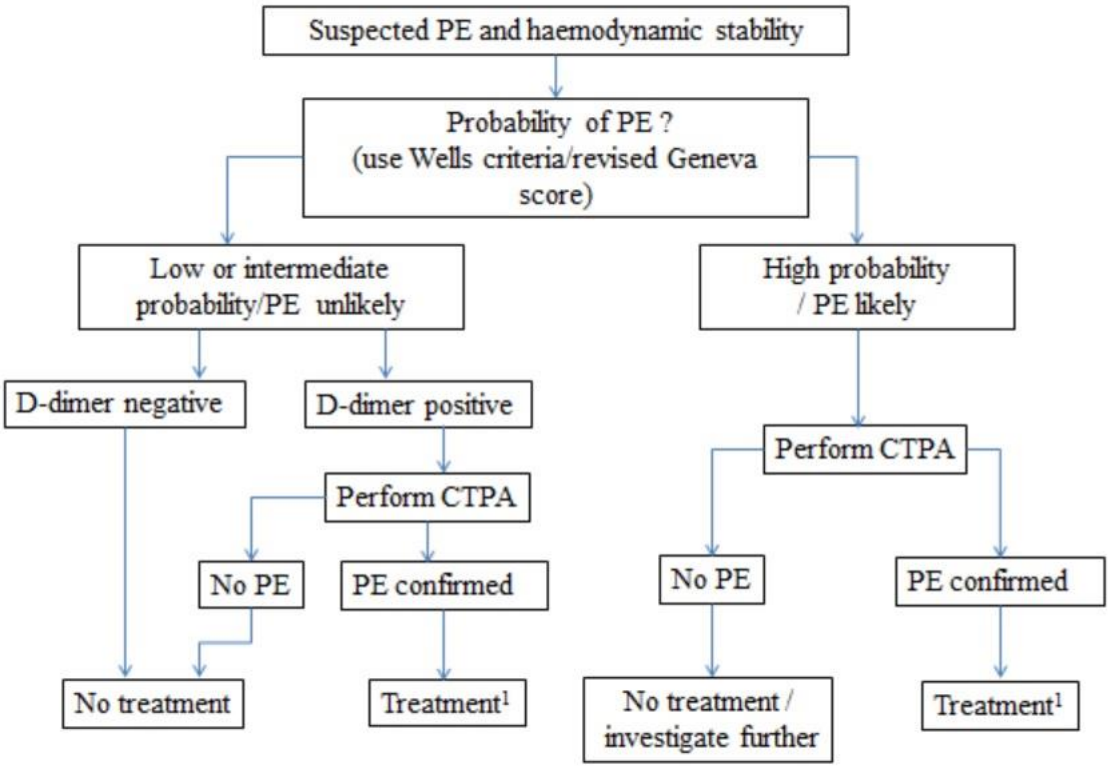
- Lung scintigraphy: may be applied in patients with low clinical probability, pregnant women, history of contrast-medium induced anaphylaxis, severe renal failure.
- Magnetic resonance angiography: low sensitivity, scarce availability.
- Pulmonary angiography: rarely used, as CTPA has similar diagnosis accuracy.
- Compression ultrasonography: for DVT diagnosis

4.7. Assessment of PE severity and diagnosis strategies

Different diagnosis strategies are used in patients with suspected PE, according to their hemodynamic status. In patients with suspected PE without hemodynamic instability, assessing clinical probability of PE, D-dimers testing and CTPA indicate the appropriate line of treatment. In patients with suspected PE presenting with hemodynamic instability (shock), echocardiography is the first method used to assess RV and global cardiac function. In patients with RV dysfunction and positive CTPA, treatment for high-risk PE should be initiated. In patient without RV dysfunction or with RV dysfunction but negative CTPA, alternative shock causes should be evaluated.

The Pulmonary Embolism Severity Index (PESI) integrates PE severity and comorbidities to evaluate 30-days mortality risk in patients with PE.





Note: Treatment refers to anticoagulation treatment for PE.

4.8. Skills needed for diagnosis

Basic skills:

- Peripheral venous cannulation to secure vascular access and provide blood samples for lab testing.
- Arterial puncture to provide ABG. Arterial cannulation may be needed to enable continuous invasive blood pressure (BP) monitoring and follow its response with treatment.
- ECG lead placement, SpO_2 and respiratory rate monitoring, non-invasive BP measurement and interpretation.
- Urinary catheter insertion to monitor urine output and, if indicated, take cultures.
- Interpretation of Wells criteria and the revised Geneva score, interpretation of D-Dimer and other lab result values

Advanced skills:

- Central venous cannulation – US real-time guidance is advised whenever performing central cannulation. The endpoint can be either a central venous catheter, or a pulmonary artery catheter. In either case, adequate interpretation and not the monitor itself will improve clinical outcomes.
- US examination of the heart, CTPA interpretation

5. Therapy

5.1. Monitoring

- ECG (place ECG electrodes).
- Respiratory rate.
- Peripheral oxygen saturation (place SpO_2 sensor).
- Non-invasive BP (place inflatable cuff).
- Invasive BP in patients with hemodynamic instability
- Central venous pressure/ Pulmonary artery pressure in patients with shock and low CO
- Urine output (insert urinary catheter).
- ABG and/or VBG (arterial puncture, secure venous access).

5.2. Respiratory support

- Supplemental oxygen on nasal cannula/ facial mask for patient with $SpO_2 < 94\%$
- High-flow oxygen on nasal cannula for severe hypoxemic patients
- Indications for further ventilatory support include:
    - Physical exhaustion and/or US evidence of severely depressed diaphragm function.
    - Rising $PaCO_2$ with stabilization measures.
    - Persistent or worsening hypoxemia ($PaO_2 < 60$ mmHg) and/or acidosis (pH < 7.25) despite administration of supplemental oxygen

- Methods to apply ventilatory support include:
    - Non-invasive: continuous positive airway pressure (CPAP) if patients are cooperative, able to protect their airway, and have adequate diaphragm function.

- Invasive mechanical ventilation when at least one of the above criteria is not met; precautions should be taken before intubation in patients with hemodynamic instability and RV dysfunction as positive pressure ventilation could aggravate RV dysfunction (starting vasopressors and/ or inotropes infusion, choosing the appropriate induction agents)

5.3. Hemodynamic support

- Hemodynamic instability is caused by RV failure resulting in low CO
- Pharmacological treatment of RV failure is necessary in parallel with pharmacological, surgical or interventional reperfusion treatment for PE.
- Volume optimization can be used in preload dependent patients, after careful evaluation of RV preload tolerance, as it can aggravate RV dysfunction.
- If systolic BP < 100 mmHg and/or arterial lactate ≥ 2 mmol/l, then incipient or overt shock is possible and would require advanced management.
    - These patients often exhibit altered mental status, cool peripheries, low urine output, and low pulse volume.
    - A general approach includes a combination of inodilators, vasopressors, fluid removal and, ultimately, circulatory mechanical support.
    - Vasodilators decrease PAP and PVR but may worsen hypotension and systemic hypoperfusion
    - Nitric oxide may improve hemodynamic status and gas exchange.

5.4. Anticoagulation

- In patients with high or intermediate probability of PE, anticoagulation should be initiated while waiting for tests' results.
- Low-molecular weight heparin and fondaparinux are preferred over non-fractioned heparin for initial anticoagulation, due to a lower risk of major bleeding and heparin-induced thrombocytopenia. (how long?)

5.5. Reperfusion treatment

- Systemic thrombolysis – in intermediate or high-risk PE
- Percutaneous catheter-directed therapy – mechanical reperfusion by catheter-based embolectomy of pulmonary artery – in patients with intermediate or high-risk PE
- Surgical embolectomy – under cardiopulmonary bypass without cardiac arrest, in high-risk PE

5.6. Skills needed to carry out treatment:

- Perform non-invasive mask ventilation.
- Invasive airway management.

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Acute Pulmonary Oedema

1. Abstract/Introduction

Acute pulmonary oedema (APE) is a common and potentially fatal cause of respiratory failure that requires timely diagnosis, precise management, and usually hospital admission.
APE may be associated with many clinical conditions, including cardiovascular, pulmonary, renal, and cerebral disturbances. APE is classically divided into cardiogenic (CAPE) and noncardiogenic pulmonary oedema (NCAPE). A high pulmonary capillary pressure (PCP) of cardiac origin causes abnormal fluid redistribution in CAPE. In contrast, factors other than elevated PCP usually are responsible for NCAPE, of which increased pulmonary capillary permeability is the most common. However, in many instances, APE may stem from a combination of several mechanisms, as predicted by the Starling relationship.
CAPE most often results from acute decompensated heart failure generated by left ventricular (LV) systolic or diastolic impairment with or without additional aggravating hemodynamic factors, including valve abnormalities, fluid overload, and severe hypertension[1].
The major cause of NCAPE is the acute respiratory distress syndrome (ARDS). Other noncardiogenic forms include transfusion-related acute lung injury (TRALI), eclampsia, immersion, high altitude, neurogenic, reperfusion, re-expansion, and drug-related pulmonary oedema.
A focused history and physical examination, ultrasound or chest radiograph, and lab analysis should distinguish CAPE from NCAPE as further treatment is different between the two groups (see Figure 1). Only CAPE will be addressed in this chapter.

2. Symptoms and clinical signs

- Breathing: acute and worsening breathlessness, tachypnoea, cough, and frothy blood-stained sputum.
- Auscultation: pulmonary rales or crackles and cardiac S3 gallop or murmurs.
- Signs of congestion: leg swelling, epigastric tenderness, abdominal fullness, enlarged liver and distended jugular veins.
- Chest pain or palpitations, oliguria, headaches, insomnia or altered mental status.
- Essential hemodynamic profiles: 1) normotensive or hypertensive CAPE with preserved perfusion, and 2) cool “shut-down” peripheries with diminished pulse pressure signalling shock or impending cardiac arrest.

3. Differential diagnosis

Symptoms and clinical signs are highly heterogeneous amongst patients. Therefore, securing a correct diagnosis relies on an initially broad differential diagnosis.
The chief differential is NCAPE (see Figure 1). However, consideration should also be given to:

- acute (infective) exacerbation of chronic obstructive pulmonary disease (COPD).
- acute asthma.
- pericardial tamponade or constriction.
- pulmonary embolism.

4. Diagnosis

4.1. Urgent investigations for all patients include:

4.1.1. Electrocardiogram (ECG):

- sinus tachycardia is the most common presentation, but any other cardiac arrhythmia may be found, e.g., atrial fibrillation (AF), supraventricular tachycardia (SVT).
- look for evidence of acute ST segment change, e.g., STEMI, NSTEMI or unstable angina (UA).
- look for underlying heart disease, e.g., LV hypertrophy, right or left atrial enlargement.

4.1.2. Ultrasound (US) within an **ABC** approach (see Figure 1).:

- **A**eration: lung ultrasound to confirm and differentiate CAPE.
- **B**reathing: diaphragm ultrasound to assess efficiency of diaphragm contraction.
- **C**irculation: cardiac ultrasound to assess LV function, valve and regional wall motion abnormalities, preload reserve, interventricular interdependence, fluid overload and venous congestion.

4.1.3. Chest X ray to confirm and differentiate CAPE (see Figure 1).

4.1.4. Gas-exchange:

- Pulse oximetry (SpO_2) – if peripherally shut down or oedematous, this may prove inaccurate.
- Arterial blood gases (ABG) – arterial partial pressure of oxygen (PaO_2) is typically low. However, arterial partial pressure of carbon dioxide ($PaCO_2$) may be either low (hyperventilation) or high (hypoventilation) depending on CAPE severity.
- Venous blood gases (VBG) – multiple sampling sites are available, depending on monitoring extent, including peripheral (venipuncture), central (central venous catheter) and mixed (pulmonary venous catheter). Adequate interpretation of results requires correlation with clinical context and ABG.

4.1.5. Biochemical markers of myocardial injury (CK, CK-MB, troponins) and stretch (BNP, NT-proBNP).

4.1.6. Full blood count (FBC), e.g., leucocytosis, may indicate precipitants or aggravating factors.

4.1.7. Urea and electrolytes (U&Es) may indicate renal impairment, electrolyte imbalances, particularly if on diuretics.

4.1.8. Liver function tests (LFTs):

- Abnormal transaminases are usually associated with hypoperfusion and herald short-term excess mortality.
- Abnormal alkaline phosphatase is usually associated with systemic congestion and elevated right-sided filling pressure.

4.2. Supplementary investigations to consider when appropriate:

4.2.1. Septic screen to find infectious precipitants or aggravating factors (sputum, blood cultures, urine).

4.2.2. Coronary angiography to enable early revascularization.

4.3. Skills needed to carry out diagnostic tests:

4.3.1. Basic skills:

- Peripheral venous cannulation to secure vascular access and provide VBG, FBC, U&Es, LFTs, cardiac markers and, if indicated, blood cultures.
- Arterial puncture to provide ABG. Arterial cannulation may be needed to enable continuous invasive blood pressure (BP) monitoring and follow its response with treatment.
- ECG lead placement, SpO_2 and respiratory rate monitoring, non-invasive BP measurement.
- Urinary catheter insertion to monitor urine output and, if indicated, take cultures.

4.3.2. Advanced skills:

- Central venous cannulation – US real-time guidance is advised whenever performing central cannulation. The endpoint can be either a central venous catheter, or a pulmonary artery catheter. In either case, adequate interpretation and not the monitor itself will improve clinical outcomes.
- US examination of the lung, heart, and diaphragm.

5. Therapy

5.1. Basic monitoring:

- ECG (place ECG electrodes).
- Respiratory rate.
- Non-invasive BP (place inflatable cuff).
- Peripheral oxygen saturation (place SpO_2 sensor).
- Urine output (insert urinary catheter).
- ABG and/or VBG (arterial puncture, secure venous access).

Therapeutic management includes three phases: stabilization, optimization, and systematization (**S.O.S.**).

5.2. **S**tabilization:

- Position the patient up in bed.
- Provide 60-100% oxygen by facemask.
- Administer morphine 2-4 mg iv. However, caution is advised with severely abnormal ABG as it may set off respiratory depression requiring intubation.
- Administer frusemide 0.5-1 mg/kg iv. Lower doses may suffice if patient is diuretic naïve.
- Start iv glyceryl trinitrate (GTN) infusion (10-100 micrograms/min) aiming to keep systolic BP ≥ 100 mmHg in patients with concomitant myocardial ischaemia, severe hypertension, and regurgitant aortic or mitral valve disease. Avoid it in patients with known aortic stenosis or hypertrophic cardiomyopathy. If possible, apply invasive BP monitoring to prevent accidental hypotension.

- If already systolic BP < 100 mmHg, manage the patient as cardiogenic shock (see below).
- Treat all hemodynamically unstable arrhythmias.

5.3. Optimization

5.3.1. This patient exhibits wheezing. Does this patient have a history of asthma/COPD? If yes, then administer:

- Nebulized salbutamol 2.5-5 mg.
- Hydrocortisone 200 mg iv.

5.3.2. Is this patient in need of ventilatory support?

➢ Indications for further ventilatory support include:
- Physical exhaustion and/or US evidence of severely depressed diaphragm function.
- Rising $PaCO_2$ with stabilization measures.
- Persistent or worsening hypoxemia (PaO_2 < 60 mmHg) and/or acidosis (pH < 7.25) 30 minutes following onset of stabilization measures.

➢ Methods to apply ventilatory support include:
- Non-invasive: continuous positive airway pressure (CPAP) if patients are cooperative, able to protect their airway, and have adequate diaphragm function.
- Invasive mechanical ventilation when at least one of the above criteria is not met.

5.3.3. Is this patient in circulatory shock?

➢ If systolic BP ≥ 100 mmHg and arterial lactate < 2 mmol/l, then probably not.
- Continue GTN infusion and titrate against blood pressure as shown above.
- Further add to or replace the GTN infusion with arteriolar vasodilators, e.g., nicardipine.
- Consider nesiritide 2 micrograms/kg bolus IV followed by 0.01 micrograms/kg/min for refractory symptoms.
- Switch to a continuous infusion of frusemide if fluid overload is probable (10 – 60 mg/h).
- Resume beta-blockers and ACE inhibitors.

➢ If systolic BP < 100 mmHg and/or arterial lactate ≥ 2 mmol/l, then incipient or overt shock is possible and would require advanced management.
- These patients often exhibit altered mental status, cool peripheries, low urine output, and low pulse volume.
- A general approach includes a combination of inodilators, vasopressors, fluid removal and, ultimately, circulatory mechanical support.

5.4. Systematization:

- Identify and treat precipitants or aggravating factors, e.g., fever or infection, noncompliance of heart failure medication, hyperthyroidism.
- Identify specific hemodynamic profiles in need of a specific intervention, e.g., fluid overload, valve regurgitation, poor diastolic LV function.

5.5. Skills needed to carry out treatment:

- Perform non-invasive mask ventilation.
- Invasive airway management.

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FIGURES

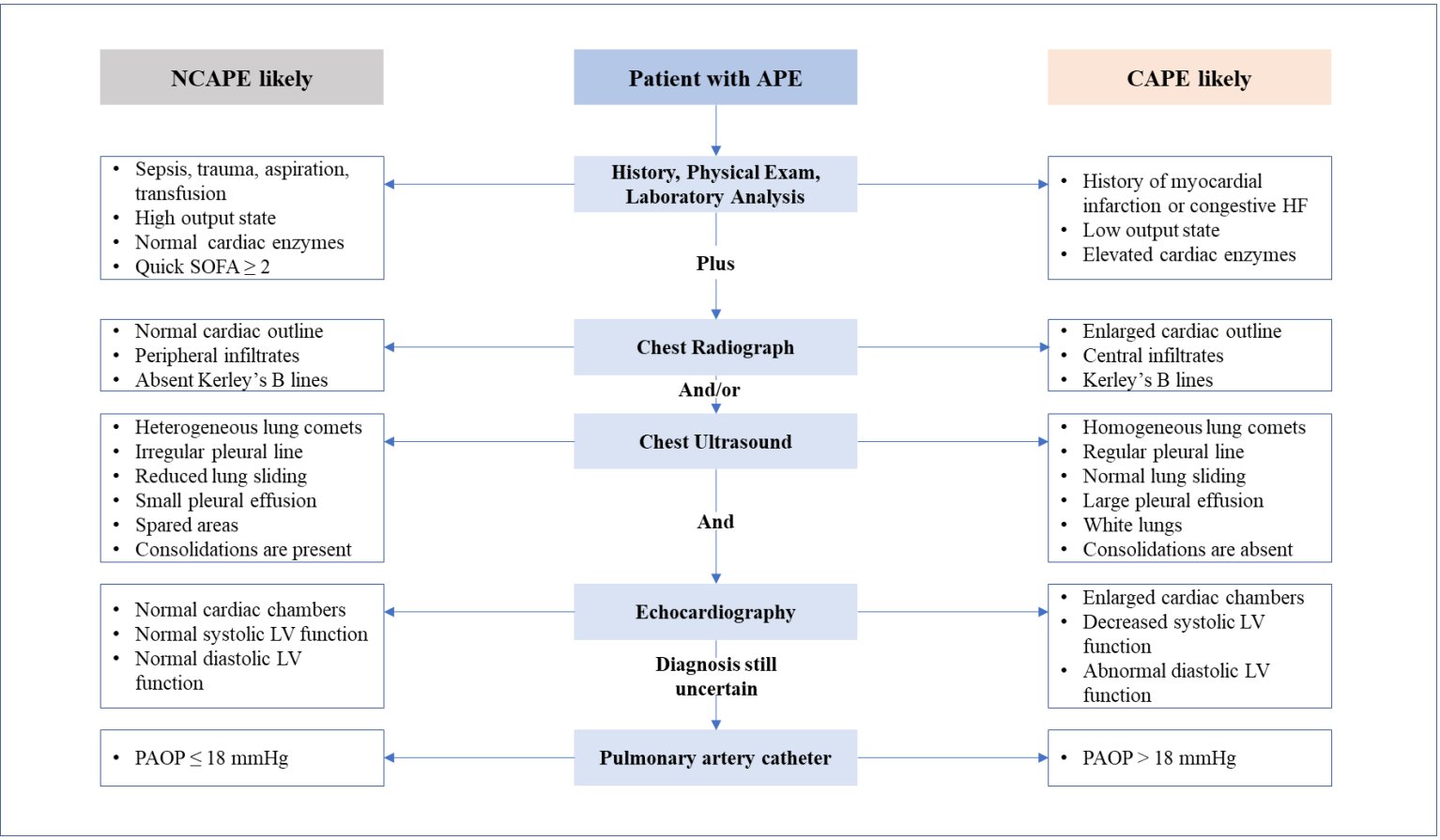

Figure 1: Flowchart to differentiate between cardiogenic pulmonary oedema (CAPE) and non-cardiogenic pulmonary oedema (NCAPE). HF, heart failure; LV, left ventricle; PAOP, pulmonary artery occlusion pressure.

Asthma and Chronic Obstructive Pulmonary Disease (COPD)

1. Introduction

Asthma and chronic obstructive pulmonary disease (COPD) are frequent obstructive pulmonary diseases in the general population, constituting major public health problems.

Asthma is an allergic condition that most commonly affects children, although it can also affect adults. It is characterized by airway hyper-responsiveness (AHR), which leads to intermittent and usually reversible airway obstruction. In contrast, COPD is a chronic respiratory disease typically linked to tobacco use, affecting people over the age of forty, and is characterized by progressive and irreversible airway obstruction.

Acute severe asthma is defined as a rapid-onset exacerbation (hours or days) that remains unresponsive to initial treatment with bronchodilators. It represents a medical emergency associated with significant morbidity and mortality and requires immediate recognition and treatment.

COPD is one of the most common reasons for intensive care unit (ICU) admissions and a leading cause of death and disability worldwide. An exacerbation of COPD is currently defined as a sustained worsening of the patient's condition from a stable state that is acute in onset and necessitates a change in regular medication.

The pathophysiological mechanism underlying the two conditions is a chronic inflammation of the small airways leading to increased mucus production and bronchoconstriction, thus limiting pulmonary airflow. Whilst there are several similarities between the two, some differences exist, and perhaps the most important one is the nature of inflammation which is primary eosinophilic and CD4-driven in asthma and neutrophilic and CD8-driven in COPD.

A significant proportion of patients who present with symptoms of a chronic airways disease have features of both asthma and COPD. This condition has been described as asthma- chronic obstructive pulmonary disease overlap syndrome (ACOS)

2. Symptoms and clinical signs

- Airway: shortness of breath, wheezing, chest tightness, and cough (dry cough for asthma, productive cough for COPD).
- Breathing: increased work of breathing, tachypnoea, involvement of accessory respiratory muscles, increased mucus production and/or color (COPD).
- Circulation: tachycardia, bradycardia, hypotension, pulsus paradoxus, cyanosis, cold extremities, right-side congestive heart failure (COPD), cardiorespiratory arrest.
- Disability: headaches, fever (if a respiratory infection is associated), altered mental state (confusion, impaired consciousness, coma) in patients with severe hypoxemia and/or hypercarbia.
- Exposure: positive smoking history (COPD), allergen, aspirin-induced, exercise, cold air exposure (asthma), infective exacerbations (most commonly viral respiratory tract infections).
- Other: symptom variability - daily changes in symptom frequency or intensity are common in asthma; COPD symptoms are less variable.

3. Differential diagnosis

Asthma and chronic obstructive pulmonary disease (COPD) are common respiratory disorders with overlapping clinical features. Distinguishing asthma from COPD can be challenging, particularly in smokers or older adults. Differentiation between the two is crucial since several aspects of the

guideline-recommended therapy differ. There is, however, a subset of patients in which both asthma and COPD coexist, a condition described as asthma-COPD overlap syndrome (ACOS)
The main differential for asthma is COPD and vice-versa. Apart from distinguishing between the two, the differential for dyspnea alone must be considered. Consider objectifying airflow limitation.
Respiratory causes include:

- acute asthma.
- acute exacerbation of chronic obstructive pulmonary disease COPD.
- interstitial lung disease (infectious, auto-immune, environmental).
- chest wall disease.
- pulmonary embolism.
- idiopathic anaphylaxis with predominant respiratory manifestations.
- drug-induced bronchospasm.
- upper/lower airway disorders.

Cardiac causes include:

- congestive heart failure.
- pericardial disease (restrictive pericarditis, cardiac tamponade).
- pulmonary hypertension.

Other causes of dyspnea, chronic cough, and chest pain include gastroesophageal reflux disease (GERD).

4. Diagnosis

A stepwise approach to diagnosis is recommended, including detection of a chronic airways disease, syndromic categorization as asthma, COPD, or the overlapping of asthma and COPD (ACOS), confirmation by spirometry, and, if required, referral to further investigations. (Figure 1)
A positive diagnosis is based upon clinical history, physical examination, and objective tests (spirometry, peak flow variability, DLCO, fractional exhaled nitric oxide [FeNO]-in asthma).
Investigations for all patients presenting with acute exacerbation of either asthma or COPD include:

4.1 Arterial Blood Gas analysis (ABG)

- In an acute asthma attack: initially, both partial pressure of oxygen (PaO_2) and partial pressure of carbon dioxide ($PaCO_2$) are low with an associated respiratory alkalosis (due to hyperventilation) and a mild non-anion gap acidosis (serum bicarbonate 20-24 mmol/L). However, in severe attacks, a normal or increased $PaCO_2$ suggests respiratory failure due to exhaustion. Another feature present in severe attacks is lactic acidosis.
- In COPD exacerbation: patients may present with:
    - respiratory failure type 1 (low PaO_2, normal $PaCO_2$).
    - respiratory failure type 2 (low PaO_2, increased $PaCO_2$).
- Patients in treatment with high doses of beta-agonists may have low K^+ levels.

4.2 Pulse-oximetry (SpO_2):

- continuous oximetry is mandatory; aim for 94-98% SpO_2. Consider the removal of a COPD patient's hypoxic respiratory drive when administering high levels of O_2.

4.3 Electrocardiogram (ECG):

- may be normal in mild to moderate asthma attacks; consider severe attack if elevated heart rate and near-fatal attack if bradycardia.
- look for signs of right-sided heart failure, e.g., right axis deviation, R/S ratio >1 in V1, p pulmonale in severe asthma or COPD.

- look for evidence of myocardial ischemia, e.g., acute ST-segment change in COPD.
- arrhythmias may be present in both asthma and COPD exacerbation.

4.3 PoCUS (point of care ultrasound) assessment - for evaluation and diagnosis of acute dyspnea

- LUS (lung ultrasound) - the presence or absence of B-lines, lung sliding, consolidation, pleural effusions, and diaphragm assessment.
- ECHO (emergency echocardiography) - asses LV, RV function; valve and regional wall motion abnormalities; fluid overload.
- IVC (inferior vena cava ultrasound) - diameter and collapsibility; mainly used for differential diagnosis.

In asthma attack or COPD exacerbation:

- LUS: absence of B-lines, normal lung sliding, consolidation may be present (if atelectasis or associated pneumonia), diaphragmatic assessment may show reduced mobility and thickness (correlated with air-trapping).
- ECHO:
  - may be normal or may show increased right-sided strain in severe asthma attacks.
  - typical findings for COPD are: signs of right +/- left-sided heart failure, pulmonary hypertension, regional wall motion abnormalities (if myocardial ischemia is associated).

4.4 Chest x-ray: to exclude other causes of dyspnea

- Asthma: usually normal.
- COPD: signs of hyperinflation (dark lung fields, low set diaphragm, increased anteroposterior diameter); signs of pulmonary consolidation.

4.5 Pulmonary function tests - spirometry, peak expiratory flow rate

- Consider performing spirometry as long as the equipment is readily available and testing will not compromise the treatment of an acute episode.
- FEV1/FVC < 0.7 - positive test for obstructive airway disease ;
- Post-bronchodilator FEV1/FVC < 0.7 positive for COPD - indicating irreversible or partial reversible airflow limitation.
- Evidence for reversible airflow limitation post-bronchodilator administration- suggestive of asthma.
- In severe asthma attack: PEFR< 200 l/min, FEV1 <1L.

4.6 Thoracic CT scan

- to investigate symptoms that seem disproportionate to the spirometry findings.
- to investigate signs that may suggest another pulmonary diagnosis (fibrosis, bronchiectasis).
- to further investigate abnormalities seen on chest X-ray.

4.7 Full blood count (FBC), urea and electrolytes (U&Es), C reactive protein (CRP), liver function tests (LFTs):

- asses for signs of infection: leukocytosis (COPD) and eosinophilia (asthma).
- asses for electrolyte disturbances, dehydration, and renal impairment (especially in COPD).
- elevated LFTs in case of congestive heart failure or alpha 1 antitrypsin deficiency.

4.8 Septic screen: blood and sputum culture (in case of suspected pneumonia and/or febrile patient).

4.9 Skill required to carry out diagnostic tests:

1. Basic skills:
    - Peripheral venous cannulation to secure vascular access and provide VBG, FBC, U&Es, LFTs, and, if indicated, blood cultures.
    - Arterial puncture to provide ABG analysis.
    - ECG lead placement, SpO_2, and respiratory rate monitoring, non-invasive BP measurement, $EtCO_2$ sensor placement.
    - Urinary catheter insertion to monitor urine output and, if indicated, take cultures.
2. Advanced skills:
    - Arterial catheter insertion may be needed to enable continuous invasive blood pressure (BP) monitoring.
    - Central venous cannulation – US real-time guidance is advised whenever performing central cannulation.
    - US examination of the lung, heart, and diaphragm.

5. Therapy

Monitoring:

- ECG (place ECG electrodes).
- Respiratory rate.
- Non-invasive BP (place inflatable cuff).
- Peripheral oxygen saturation (place pulse-oximetry sensor).
- Urine output (insert a urinary catheter).
- Temperature.
- End-tidal CO_2 monitoring ($EtCO_2$ sensor placement).
- ABG and/or VBG (arterial puncture, secure venous access).

Consider the placement of an arterial catheter for continuous blood pressure monitoring and serial ABG analysis, as well as central venous line insertion depending on the severity of the clinical presentation.

5.1 Initial treatment in acute exacerbations of asthma and COPD

- Position the patient up in bed.
- Administer O_2 as follows:

In asthma: FiO_2 of at least 60% or 15 L/min with a high flow mask. Maintain O_2 saturation above 92%.

In COPD:

- Type 1 respiratory failure: FiO_2 of 28-40%. Maintain O2 saturation of 88-92%.
- Type 2 respiratory failure: FiO_2 of 24-28% and consider ventilatory support. Non-invasive ventilation (NIV) is the first-line treatment for COPD exacerbation and type 2 respiratory failure as it allows administration of higher O2 concentrations without an uncontrolled increase in $PaCO_2$.

- Administer nebulized salbutamol 2.5 mg or terbutaline 10 mg and repeat up to every 15-30 min if needed. Consider continuous nebulization of salbutamol 5-10 mg/h if inadequate response to initial treatment.
- Perform serial ABG analysis.
- If the initial response to beta-agonists is poor, add nebulized ipratropium bromide 0.5 mg every 4-6 hours.

- Start steroids: 200 mg of hydrocortisone iv.
- Administer antibiotics if there is evidence of chest infection (purulent sputum, abnormal CXR, raised WBC, fever). Antibiotics should not be prescribed routinely to individuals with acute asthma attacks in the absence of an infectious precipitant.
- Adequate hydration is essential and may help prevent mucus plugging. Ensure an intake (IV or PO) of 30 ml/kg per day of water, taking care to avoid overload.
- Supplement K^+ as required.

5.2 Inadequate response to initial treatment or if the patient's condition is deteriorating:

- Continue O2 administration and nebulized beta-agonist every 15 min.
- Start administering bronchodilators by intravenous route:
  - Magnesium sulfate 1.2-2 g infused over 20 min. Give as a single dose only. Repeated doses may lead to hypermagnesaemia with muscle weakness and further aggravation of respiratory failure.
  - Salbutamol : loading dose 100-200 micrograms in 10 min; maintenance infusion: 5-20 micrograms/min.
  - Aminophylline: loading dose 4-5 mg/kg infused over 20 min; maintenance infusion: 0.5-0.7 mg/kg/h.

5.3 Further management

- NIV/CPAP- may reduce work of breathing and improve oxygenation.
- Ketamine- may be used in ventilated patients (1-3 mg/kg) as it exerts bronchodilatory effects.
- Inhalational anesthetic agents (e.g., sevoflurane, isoflurane) have been shown to improve bronchospasm and may be helpful in the setting of mechanical ventilation.
- Mechanical ventilation is life-saving in severe or near-fatal asthma attacks and in COPD patients with poor tolerance to NIV and inadequate response.

General principles of mechanical ventilation include:

- Provide adequate humidification and warming of inspired gases.
- Low-frequency ventilation.
- Low tidal volumes (6-8 ml/kg).
- Long expiratory phase (I: E ratio 1:3).
- Minimize airway pressures.
- Maintain adequate PaO2 and PaCO2, and provide a pH> 7.2. Consider permissive hypercapnia in COPD.
- Adequate sedation and paralysis (avoid atracurium as it may lead to histamine release) to overcome the respiratory drive.

5.4 Skills required for carrying out treatment:

- Perform non-invasive mask ventilation.
- Perform invasive airway management.

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STEP 1 DIAGNOSE CHRONIC AIRWAYS DISEASE
Do symptoms suggest chronic airways disease?

Yes → **STEP 2 SYNDROMIC DIAGNOSIS IN ADULTS**
(i) Assemble the features for asthma and for COPD that best describe the patient
(ii) Compare number of features in favor of each diagnosis and select a diagnosis

No → Consider other disease first

Features:	ASTHMA	COPD
Age of onset	☐Before age 20 y	☐After age 40 y
Pattern of symptoms	☐Variation over minutes, hours or days ☐Worse during the night or early morning ☐Triggered by exercise, emotions including laughter, dust or exposure to allergens	☐Persistent despite treatment ☐Good and bad days but always daily symptoms and exertional dyspnea ☐Chronic cough and sputum proceeded onset of dyspnea, unrelated to triggers
Lung function	☐record of variable airflow limitation (spirometry or peak flow)	☐Record of persistent airflow limitation (FEV1/FVC<0.7 post-BD)
Lung function between symptoms	☐Normal	☐Abnormal
Past history or family history	☐Previous doctor diagnosis of asthma ☐Family history of asthma, and other allergic conditions (allergic rhinitis or eczema)	☐Previous doctor diagnosis of COPD ☐Heavy exposure to risk factor: tobacco smoke, biomass fuels
Time course	☐No worsening of symptoms over time. Variation in symptoms either seasonally or from year to year ☐May improve spontaneously or have an immediate response to bronchodilators or to ICS over weeks	☐Symptoms already worsening over time (progressive course over years) ☐Rapid-acting bronchodilator treatment provides only limited relief
Chest X-ray	☐Normal	☐Severe hyperinflation

Note: •These features, if present, best distinguish between asthma and COPD •Several positive features (3 or more) for either asthma or COPD suggest that diagnosis •If there are a similar number for both asthma and COPD, consider diagnosis of ACOS

DIAGNOSIS	Asthma	Some features of asthma	Features of both	Some features of COPD	COPD
CONFIDENCE IN DIAGNOSIS	Asthma	Possible asthma	Could be ACOS	Possibly COPD	COPD

STEP 3 PERFORM SPIROMETRY

Marked reversible airflow limitation (pre-post bronchodilator) or other proof of variable airflow limitation

FEV1/FVC < 0.7
Post-BD

STEP 4 INITIAL TREATMENT*

Asthma drugs No LABA monotherapy	Asthma drugs No LABA monotherapy	ICS, and usually LABA and/or LAMA	COPD drugs	COPD drugs

*Consult GINA and GOLD documents for recommended treatments

STEP 5 SPECIALIZED INVESTIGSTIONS Or RELIEF:

- Persistent symptoms and/or exacerbations despite treatment
- Diagnostic uncertainty (e.g. suspected pulmonary hypertension, cardiovascular disease and other causes of respiratory symptoms)
- Suspected asthma or COPD with atypical or additional symptoms or signs (e.g. haemoptysis, weight loss, night sweat, fever, signs of bronchiectasis or other structural lung disease)
- Few features of either asthma or COPD
- Comorbidities present
- Reasons for referral for either diagnosis as outlined in the GINA and GOLD strategy reports.

FIGURES

Figure 1. Summary of syndromic approach to diseases of chronic airflow limitation. Global Initiative for Asthma (GINA) Global Strategy for Asthma Management and Prevention 2019