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Diagnosis and Management of Pulmonary Embolism Through Nursing Assessment, Coagulation Biomarkers, and Radiological Imaging

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Abstract

Background: Acute pulmonary embolism (PE) is a potentially life-threatening cardiovascular condition caused by obstruction of the pulmonary arterial circulation, most commonly by thrombi originating from the deep veins of the lower extremities. Its clinical presentation ranges from asymptomatic disease to severe hemodynamic instability and cardiac arrest. Early diagnosis and appropriate management are essential to reduce complications and mortality.

Aim: This review examines the clinical features, etiology, epidemiology, pathophysiology, diagnostic evaluation, and management of acute PE, with emphasis on the complementary roles of nursing, laboratory investigations, and radiological imaging.

Methods: A narrative review approach was used to discuss the available evidence concerning PE, including its risk factors, clinical manifestations, diagnostic strategies, treatment options, and prevention of recurrence. Particular attention was given to laboratory biomarkers, imaging modalities, clinical assessment tools, and multidisciplinary patient care.

Results: PE develops through interactions among venous stasis, endothelial injury, and hypercoagulability. Diagnosis requires integration of clinical probability assessment with laboratory tests, including D-dimer, blood gas analysis, and cardiac biomarkers, alongside imaging techniques such as computed tomography pulmonary angiography, ventilation-perfusion scanning, and echocardiography. Anticoagulation remains the mainstay of treatment, while thrombolysis, catheter-directed interventions, and surgical embolectomy are considered in selected high-risk patients. Nursing assessment and continuous monitoring support early recognition of deterioration, treatment safety, and recovery.

Conclusion: Effective PE management requires coordinated clinical, laboratory, radiological, and nursing assessment to facilitate timely diagnosis, risk stratification, treatment selection, and prevention of recurrence.

Keywords: Pulmonary embolism; nursing assessment; coagulation biomarkers; D-dimer; computed tomography pulmonary angiography; ventilation–perfusion scanning; echocardiography; anticoagulation; thrombolytic therapy; prevention of recurrence.

Introduction

Acute pulmonary embolism (PE) is a potentially life-threatening cardiovascular and respiratory condition characterized by the obstruction of one or more pulmonary arteries by an embolus, most commonly originating from a thrombus in the deep veins of the lower extremities. This process typically occurs when a portion of a deep vein thrombus detaches, travels through the venous circulation, passes through the right side of the heart, and lodges within the pulmonary arterial system. Although thrombotic emboli represent the predominant cause, pulmonary vascular obstruction may occasionally result from other materials, including air, fat, amniotic fluid, or tumor cells [1]. PE and deep vein thrombosis (DVT) are collectively classified as venous thromboembolism (VTE), which represents a major cause of preventable morbidity and mortality worldwide. The development of PE is associated with several predisposing factors, including

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inherited thrombophilia, advanced age, obesity, malignancy, pregnancy, prolonged immobilization, previous VTE, major surgery, and hospitalization. These factors contribute to venous stasis, endothelial injury, and hypercoagulability, which collectively increase the likelihood of thrombus formation. The clinical presentation of acute PE varies considerably according to the extent of pulmonary vascular obstruction, the patient's cardiopulmonary reserve, and the presence of associated cardiovascular conditions. Common manifestations include sudden-onset dyspnea, pleuritic chest pain, tachypnea, tachycardia, cough, hemoptysis, and syncope. In severe cases, extensive pulmonary arterial obstruction may increase pulmonary vascular resistance, resulting in right ventricular pressure overload, reduced cardiac output, systemic hypotension, obstructive shock, and sudden cardiac death. However, these manifestations are frequently nonspecific and may resemble other respiratory and cardiovascular disorders, including pneumonia, acute coronary syndromes, and heart failure. Consequently, clinical recognition remains challenging, particularly in patients presenting with atypical symptoms or multiple underlying comorbidities. Early identification of clinical warning signs and predisposing factors is therefore essential to facilitate timely diagnostic evaluation and treatment.

The diagnosis of acute PE requires an integrated approach involving clinical assessment, laboratory investigations, and radiological imaging. Clinical probability assessment using validated tools, particularly the Wells criteria and revised Geneva score, helps determine the need for further diagnostic testing. Laboratory investigations play an important complementary role, with D-dimer testing commonly used to exclude PE in patients with low or intermediate clinical probability. Cardiac biomarkers, including troponin and B-type natriuretic peptide (BNP), may also provide information regarding right ventricular myocardial injury and disease severity. Computed tomography pulmonary angiography (CTPA) represents the principal imaging modality for confirming PE in most clinically suitable patients, while ventilation-perfusion scanning and lower-extremity venous ultrasonography provide alternative or complementary diagnostic information [1,2]. Management depends primarily on hemodynamic stability, clinical risk classification, and the presence of contraindications to specific treatments. Anticoagulation remains the cornerstone of therapy, whereas systemic thrombolysis, catheter-directed interventions, or surgical embolectomy may be considered in selected patients with high-risk PE. Nursing care is equally important throughout the clinical course, encompassing continuous monitoring of vital signs and oxygen saturation, assessment of respiratory and cardiovascular status, administration of prescribed anticoagulants, recognition of bleeding complications, and patient education. Effective coordination between nursing professionals, laboratory specialists, and radiology teams supports timely diagnosis, appropriate risk stratification, and treatment monitoring. Despite advances in diagnostic technologies and therapeutic strategies, variations in clinical practice and delays in recognizing PE continue to affect patient outcomes. Therefore, an integrated multidisciplinary approach is essential to improve diagnostic accuracy, optimize treatment decisions, prevent complications, and reduce PE-associated mortality [1,2].

Etiology

Risk Factors for Pulmonary Embolism

Pulmonary embolism (PE) most commonly develops as a consequence of deep vein thrombosis (DVT), particularly thrombosis involving the deep veins of the lower extremities. Therefore, the predisposing factors for PE largely overlap with those associated with DVT and venous thromboembolism (VTE). The pathophysiological basis of thrombus formation is explained by Virchow's triad, which comprises three major mechanisms: venous stasis, endothelial injury, and hypercoagulability. These mechanisms may occur independently or simultaneously, increasing the likelihood of venous thrombus formation, subsequent embolization, and pulmonary arterial obstruction. Risk factors for PE can be broadly classified into genetic and acquired factors. Genetic predispositions primarily involve inherited abnormalities affecting the coagulation and anticoagulation systems. These include factor V Leiden mutation, prothrombin gene mutation, antithrombin deficiency, protein C deficiency, and protein S deficiency. These abnormalities increase the tendency toward excessive coagulation and recurrent thrombus formation. Hyperhomocysteinemia has also been associated with vascular and thrombotic complications. Individuals with inherited thrombophilia may remain asymptomatic for years but become susceptible to VTE when additional acquired risk factors are present.

Acquired risk factors are more diverse and frequently involve circumstances that promote venous stasis, vascular injury, or increased coagulation activity. Prolonged immobilization, including bed rest exceeding three days and extended travel lasting more than four hours, can reduce venous blood flow and facilitate thrombus formation. Major orthopedic procedures, particularly hip and knee replacement, lower-extremity fractures, major trauma, and recent surgical interventions, represent important risk factors because of vascular injury and postoperative immobility. Other contributing factors include hospitalization, central venous catheterization, chemotherapy, obesity, cigarette smoking, and advanced age. Pregnancy and the postpartum period are also associated with increased thrombotic risk because of physiological hypercoagulability, venous compression, and changes in venous circulation. Hormonal exposure, particularly oral contraceptive use and hormone replacement therapy, may further

increase the likelihood of VTE [2–5]. Malignancy represents another important acquired risk factor for PE. Cancer-associated thrombosis results from several mechanisms, including tumor-related activation of coagulation pathways, inflammatory responses, endothelial dysfunction, and reduced mobility. Pancreatic, hematological, lung, gastric, and brain malignancies are particularly associated with an increased incidence of VTE, with metastatic disease carrying a substantial thrombotic burden. In addition, acute infections, including pneumonia, urinary tract infections, and human immunodeficiency virus infection, may promote coagulation through systemic inflammation and endothelial activation [8,9]. Cardiovascular conditions, particularly congestive heart failure, atrial fibrillation, atrial flutter, and recent myocardial infarction, may also contribute to thrombotic risk, especially among hospitalized patients with reduced mobility and multiple comorbidities. A previous history of DVT or PE is another important predictor of recurrence and requires consideration during clinical assessment [10,11].

Types and Classification of Pulmonary Embolism

Pulmonary embolism is primarily classified according to its hemodynamic consequences because cardiovascular stability provides important information regarding disease severity, prognosis, and therapeutic requirements. This classification distinguishes high-risk PE from intermediate-risk and low-risk PE. High-risk PE, previously referred to as massive PE, is characterized by hemodynamic instability rather than the anatomical size of the embolus. It is generally defined by cardiac arrest, obstructive shock, or persistent hypotension, including systolic blood pressure below 90 mmHg or a sustained reduction of at least 40 mmHg from baseline. Patients may require vasopressor or inotropic support to maintain adequate systemic circulation. The principal mechanism of deterioration involves acute pulmonary arterial obstruction, increased pulmonary vascular resistance, right ventricular pressure overload, and subsequent right ventricular failure. Reduced left ventricular filling and cardiac output may ultimately result in circulatory collapse and death. These patients require immediate assessment and consideration of advanced reperfusion strategies, including systemic thrombolysis, catheter-directed treatment, or surgical embolectomy. Intermediate-risk PE, previously termed submassive PE, occurs in patients who maintain systemic blood pressure but demonstrate evidence of right ventricular dysfunction, myocardial injury, or both. Echocardiography and computed tomography pulmonary angiography may identify right ventricular enlargement or impaired ventricular function, while laboratory investigations such as cardiac troponin and BNP may indicate myocardial injury or ventricular strain. Intermediate-risk patients require close clinical monitoring because some may deteriorate despite initially preserved blood pressure.

Low-risk PE refers to patients without hemodynamic instability or significant evidence of right ventricular dysfunction. These individuals generally have a more favorable short-term prognosis, although the clinical presentation may range from mild respiratory symptoms to incidental or asymptomatic pulmonary embolism. Validated prognostic tools, including the Pulmonary Embolism Severity Index (PESI) and simplified PESI, help identify patients who may be suitable for outpatient management. Understanding the etiology, predisposing factors, and hemodynamic classification of PE is essential for clinical decision-making. Integrating nursing assessment, laboratory investigations, and radiological findings enables healthcare professionals to identify high-risk patients, recognize early deterioration, and select appropriate diagnostic and therapeutic interventions.

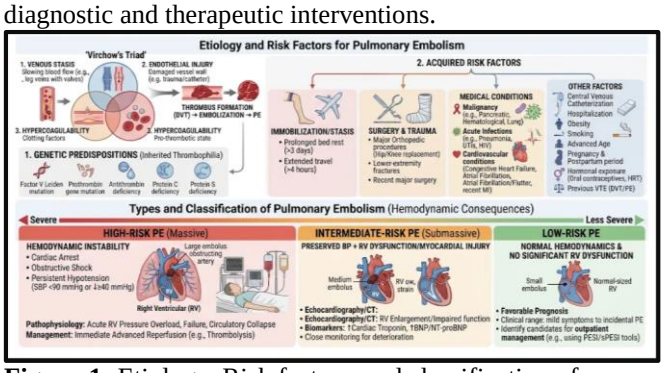


Figure-1: Etiology, Risk factors, and classification of pulmonary embolism.

Epidemiology

Acute pulmonary embolism (PE) represents a major public health concern and an important cause of cardiovascular morbidity and mortality worldwide. Its epidemiological burden is closely associated with the incidence of deep vein thrombosis (DVT), as both conditions constitute the two principal manifestations of venous thromboembolism (VTE). The estimated annual incidence of acute PE ranges from 39 to 115 cases per 100,000 individuals, whereas the incidence of DVT ranges from 53 to 162 cases per 100,000 individuals. These estimates demonstrate the substantial burden of thromboembolic disorders across different populations and healthcare settings [12]. Following coronary artery disease and stroke, PE is considered the third most common cardiovascular disease, highlighting its clinical and epidemiological significance [13]. The occurrence of PE varies according to several demographic and clinical characteristics, including age, sex, comorbidities, and exposure to predisposing factors. Epidemiological observations indicate a higher incidence of acute PE among males than females, although sex-related differences may vary across age groups and clinical populations [14]. Advanced age is an important determinant of PE occurrence because older individuals are more likely to have multiple predisposing conditions, including cardiovascular disease, malignancy, reduced mobility, previous

hospitalization, and surgical interventions. Nevertheless, PE can occur at any age, particularly in individuals with inherited thrombophilia, pregnancy-related risk factors, hormonal exposure, or prolonged immobilization.

Pulmonary infarction represents another important complication of acute PE, occurring in approximately 16% to 31% of affected patients. It develops when pulmonary arterial obstruction compromises blood supply to a portion of lung tissue, particularly when the bronchial circulation cannot adequately compensate for reduced pulmonary perfusion. Clinically, pulmonary infarction may present with pleuritic chest pain, hemoptysis, fever, and radiological abnormalities, potentially complicating the differential diagnosis of respiratory infections and other pulmonary disorders [7]. Despite improvements in diagnostic technologies and therapeutic approaches, PE continues to account for a considerable number of preventable deaths. In the United States, PE is estimated to cause approximately 100,000 deaths annually [14]. However, determining its actual mortality burden remains challenging because some cases may be misclassified as sudden cardiac death or other cardiovascular events without definitive postmortem confirmation. Furthermore, patients with severe PE may experience rapid hemodynamic deterioration before receiving appropriate diagnostic evaluation or treatment. Importantly, PE-related case-fatality rates have declined over time, reflecting advances in clinical recognition, risk stratification, computed tomography pulmonary angiography, anticoagulant therapy, and reperfusion interventions. Early identification of patients at increased risk and timely initiation of appropriate treatment remain essential for reducing mortality. These epidemiological findings emphasize the importance of coordinated nursing assessment, laboratory investigations, and radiological evaluation in improving early diagnosis, monitoring disease progression, and reducing the clinical burden of acute PE.

Pathophysiology

Pulmonary embolism (PE) develops when a thrombus or other embolic material enters the pulmonary circulation and obstructs one or more branches of the pulmonary arterial system. In most cases, the embolus originates from a deep vein thrombosis (DVT), particularly in the lower extremities, and travels through the inferior vena cava and right side of the heart before reaching the pulmonary arteries. The anatomical distribution of pulmonary emboli varies according to their size, number, and origin. Multiple emboli are frequently observed, with a greater tendency to involve the lower lung lobes than the upper lobes. Bilateral pulmonary involvement is also more common than isolated unilateral involvement [15]. Large emboli may lodge within the main pulmonary artery or at its bifurcation, producing a saddle embolus that can cause substantial obstruction of pulmonary blood flow and severe cardiovascular consequences. In contrast, smaller emboli generally obstruct peripheral pulmonary arterial branches and may produce localized ischemia, intra-alveolar hemorrhage, and pulmonary infarction. One of the primary physiological consequences of PE is impaired pulmonary gas exchange. Obstruction of the pulmonary vascular bed reduces blood flow to ventilated alveoli, producing an imbalance between ventilation and perfusion (V/Q mismatch). Although alveolar ventilation may remain relatively preserved, pulmonary capillary perfusion decreases substantially in the affected regions. Consequently, some alveoli receive adequate ventilation but insufficient blood flow, resulting in increased physiological dead space. This impairment reduces the efficiency of oxygen transfer and contributes to arterial hypoxemia. The redistribution of pulmonary blood flow toward unaffected regions may also increase ventilation-perfusion abnormalities because compensatory perfusion does not always correspond to the distribution of alveolar ventilation.

In addition to mechanical vascular obstruction, the release of vasoactive and inflammatory mediators contributes to pulmonary circulatory disturbances. Substances such as serotonin and other thrombus-associated mediators may induce pulmonary vasoconstriction, further increasing pulmonary vascular resistance and reducing blood flow in both affected and relatively unaffected pulmonary regions. Inflammatory responses associated with ischemic lung tissue can also alter pulmonary surfactant function, impair alveolar stability, and promote localized atelectasis. Furthermore, stimulation of respiratory drive commonly produces tachypnea and increased alveolar ventilation. This compensatory hyperventilation reduces arterial carbon dioxide concentration, resulting in hypocapnia and respiratory alkalosis [16]. A major pathophysiological consequence of acute PE is the sudden increase in pulmonary vascular resistance. This increase results from the combined effects of mechanical obstruction by thrombotic material and hypoxic pulmonary vasoconstriction. When thromboembolic obstruction involves approximately 30% to 50% of the total cross-sectional area of the pulmonary arterial bed, pulmonary artery pressure may rise substantially. The resulting increase in pulmonary vascular resistance places an excessive pressure load on the right ventricle, which is normally adapted to function under relatively low pulmonary arterial pressures. Consequently, the right ventricle experiences acute pressure overload and may become progressively dilated as it attempts to maintain pulmonary blood flow. Right ventricular dilation produces several important structural and functional abnormalities. The interventricular septum may flatten or shift toward the left ventricle, reducing the available space for left ventricular filling. In severe cases, right ventricular ischemia and impaired contractility may

develop because myocardial oxygen demand increases while coronary perfusion becomes compromised. Electrical conduction abnormalities, including right bundle branch block, may also occur and contribute to impaired coordination between ventricular contractions [17].

The deterioration in right ventricular function has direct consequences for systemic circulation. As right ventricular outflow becomes impaired, the volume of blood reaching the pulmonary circulation and subsequently the left atrium decreases. This reduces left ventricular preload and limits left ventricular filling during diastole. Consequently, stroke volume and cardiac output decline, leading to systemic hypotension and reduced tissue perfusion. In severe cases, progressive right ventricular failure results in obstructive shock, cardiovascular collapse, and cardiac arrest. Acute right ventricular failure secondary to pressure overload represents the principal mechanism of death in patients with severe PE. Therefore, clinical findings indicating right ventricular dysfunction, particularly hypotension, persistent tachycardia, syncope, and signs of circulatory compromise, are important indicators of increased early mortality risk. Pulmonary infarction represents another pathological consequence of PE, although it does not occur in every affected patient. Historically, patients with pre-existing cardiopulmonary disease were considered particularly susceptible to pulmonary infarction because impaired cardiovascular function was thought to reduce the effectiveness of collateral circulation. However, subsequent studies have suggested that younger patients without underlying cardiopulmonary disease may experience pulmonary infarction more frequently [7,18]. One proposed explanation is that chronic cardiopulmonary disorders promote the development of an extensive bronchial vascular collateral network. This adaptation may provide alternative oxygen delivery to pulmonary tissues when pulmonary arterial blood flow becomes obstructed, thereby reducing the likelihood of tissue necrosis.

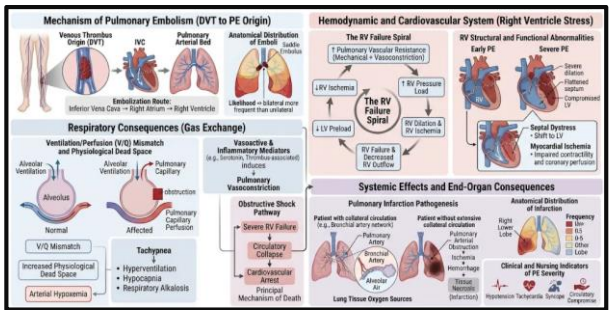


Figure-2: Pathophysiology of Pulmonary Embolism.

The lung parenchyma receives oxygen through three principal sources: pulmonary arterial blood, bronchial arterial circulation, and direct diffusion of oxygen from alveolar air [19]. These sources provide a degree of physiological protection against ischemic injury. However, when pulmonary embolism compromises the pulmonary circulation and the remaining oxygen supply becomes insufficient, tissue ischemia may progress to hemorrhage and infarction. The resulting inflammatory response can further aggravate pulmonary dysfunction through the release of mediators that promote vasoconstriction and bronchoconstriction. These changes reduce regional ventilation and perfusion, further compromising gas exchange [20]. The anatomical distribution of pulmonary infarction is also clinically relevant. Approximately 77% to 87% of pulmonary infarctions are unilateral, with the right lower lobe showing a particularly frequent involvement. Lower pulmonary lobes are affected more often than upper lobes, a distribution that may be influenced by gravitational effects on pulmonary blood flow and the physiological relationships between alveolar, pulmonary arterial, and bronchial arterial pressures [7,21]. Pulmonary infarction may manifest clinically through pleuritic chest pain, hemoptysis, fever, and localized radiological abnormalities. Understanding these pathophysiological mechanisms is essential for the multidisciplinary assessment and management of acute PE. Nursing professionals contribute through continuous monitoring of respiratory rate, oxygen saturation, heart rate, blood pressure, and signs of right ventricular failure. Laboratory investigations, including arterial blood gas analysis, D-dimer, cardiac troponin, and BNP, provide information about gas exchange abnormalities, thrombotic activity, and myocardial strain. Radiological investigations, particularly computed tomography pulmonary angiography and echocardiography, help establish the diagnosis, identify the anatomical extent of embolic obstruction, and assess its cardiovascular consequences. Integrating these findings facilitates early recognition of clinical deterioration, appropriate risk stratification, and timely therapeutic intervention.

History and Physical

Clinical History

Early recognition of pulmonary embolism (PE) is essential because delayed diagnosis and treatment are associated with increased morbidity and mortality. Approximately 30% of patients with untreated PE may die, compared with approximately 8% of those receiving timely treatment [22,23]. However, clinical diagnosis remains challenging because PE presents with variable and frequently nonspecific symptoms that may overlap with other cardiovascular and respiratory disorders. The most common clinical manifestations include dyspnea, pleuritic chest pain, cough, hemoptysis, presyncope, and syncope. Dyspnea is frequently the initial symptom and varies according to the location and extent of pulmonary vascular obstruction. Patients with central PE may experience sudden and severe respiratory distress, whereas smaller peripheral emboli may produce mild or transient breathlessness. In individuals with pre-existing cardiac or pulmonary diseases, worsening dyspnea may represent the only clinical indication of PE. Chest pain is another

frequent manifestation, particularly in patients with peripheral emboli associated with pulmonary infarction and pleural irritation. In central PE, chest discomfort may result from right ventricular ischemia and requires differentiation from acute coronary syndrome and aortic dissection [24]. Less common presentations include cardiac arrhythmias, particularly atrial fibrillation, syncope, and hemodynamic collapse [25]. Syncope may indicate significant pulmonary vascular obstruction and is associated with an increased likelihood of right ventricular dysfunction and hemodynamic instability [26]. Importantly, PE may also remain asymptomatic or be discovered incidentally during investigations performed for other conditions. Therefore, clinical assessment should incorporate the patient's medical history, previous venous thromboembolism, recent surgery, immobilization, malignancy, and other established thrombotic risk factors.

Physical Examination Findings

Physical examination may reveal tachypnea and tachycardia, which represent common but nonspecific findings. Other manifestations include hypoxemia, calf swelling, localized tenderness, erythema, palpable venous cords, and peripheral edema, particularly when associated DVT is present. Pulmonary examination may demonstrate crackles, reduced breath sounds, or other abnormalities. Signs of pulmonary hypertension and right ventricular strain include elevated jugular venous pressure, an accentuated pulmonary component of the second heart sound (P2), right-sided third heart sound, and a parasternal right ventricular lift. Massive PE may cause acute right ventricular failure, presenting with jugular venous distension, cyanosis, hypotension, and cardiogenic or obstructive shock. PE is also an important cause of sudden cardiac arrest, accounting for approximately 8% of cases [27]. Sudden bradycardia or the development of broad-complex tachycardia with right bundle branch block in a patient with suspected PE may indicate worsening right ventricular dysfunction and impending cardiovascular collapse. Hypotension accompanied by jugular venous distension should raise suspicion of PE, particularly after excluding acute myocardial infarction, cardiac tamponade, and tension pneumothorax [28]. Integrating clinical history with physical examination findings and thrombotic risk assessment supports early recognition and guides subsequent laboratory investigations and radiological evaluation.

Evaluation

The diagnostic evaluation of acute pulmonary embolism (PE) requires an integrated approach combining clinical probability assessment, laboratory investigations, electrocardiography, and radiological imaging. Because the clinical manifestations of PE are frequently nonspecific, no single clinical finding or laboratory test is sufficient to establish or exclude the diagnosis in all patients. Therefore, validated clinical prediction tools, particularly the Wells criteria and revised Geneva score, are used to estimate the pretest probability of PE and guide the selection and interpretation of subsequent investigations. The diagnostic strategy also depends on the patient's hemodynamic condition, as unstable patients may require immediate bedside assessment and emergency intervention, whereas stable patients can undergo a systematic diagnostic pathway [29]. Arterial blood gas (ABG) analysis provides information about respiratory function and gas exchange in patients with suspected PE. Unexplained hypoxemia, particularly when accompanied by a normal chest radiograph, should raise clinical suspicion of pulmonary vascular obstruction. Common ABG abnormalities include an increased alveolar-arterial oxygen gradient, respiratory alkalosis, and hypocapnia. These findings primarily result from ventilation-perfusion mismatch, increased physiological dead space, and compensatory hyperventilation. Although these abnormalities support the clinical assessment, they are not specific to PE and may also occur in other respiratory and cardiovascular disorders. Respiratory or lactic acidosis is relatively uncommon but may develop in patients with massive PE, particularly when associated with obstructive shock, severe respiratory compromise, or cardiac arrest [29].

Brain natriuretic peptide (BNP) and N-terminal pro-BNP are additional laboratory markers that provide information about cardiac involvement in PE. Their diagnostic value for confirming PE is limited; however, they have prognostic importance because increased pulmonary vascular resistance produces acute right ventricular pressure overload and myocardial stretching. This mechanical stress stimulates the release of natriuretic peptides into the circulation. Consequently, elevated BNP and NT-proBNP concentrations may reflect the severity of right ventricular dysfunction and help identify patients at increased risk of adverse clinical outcomes [30,31]. Cardiac troponin, particularly troponin I, is another important biomarker in the assessment of patients with acute PE. Although troponin testing does not establish the diagnosis, it provides prognostic information regarding myocardial injury and right ventricular dysfunction. Increased pulmonary arterial pressure places excessive strain on the right ventricle, potentially resulting in myocardial ischemia and the release of cardiac troponins. Approximately 30% to 50% of patients with moderate to large PE demonstrate elevated troponin concentrations. These elevations have been associated with clinical deterioration and increased mortality, making troponin measurement useful for risk stratification and monitoring patients with intermediate- or high-risk PE [32–34]. D-dimer testing is one of the most frequently used laboratory investigations in the diagnostic evaluation of suspected PE. D-dimer represents a fibrin degradation product released when cross-linked fibrin undergoes enzymatic breakdown. Its

concentration increases during acute thrombotic processes because coagulation and fibrinolysis are activated simultaneously. The main clinical value of D-dimer testing is its high negative predictive value, meaning that a normal result can effectively exclude PE or DVT in patients with an appropriate low or intermediate pretest probability. However, elevated D-dimer concentrations have limited positive predictive value because they may occur in several other conditions, including infection, malignancy, pregnancy, inflammation, recent surgery, and advanced age. Therefore, an elevated result cannot independently confirm PE [35].

The diagnostic performance of D-dimer depends on the assay used. Quantitative enzyme-linked immunosorbent assay (ELISA) demonstrates a sensitivity of at least 95% and is particularly useful for excluding PE in patients with low or intermediate clinical probability. A negative ELISA D-dimer result, combined with low clinical probability, may exclude PE in approximately 30% of patients with suspected disease without requiring further diagnostic imaging. However, D-dimer specificity decreases with advancing age and may reach approximately 10% in individuals older than 80 years. Age-adjusted D-dimer thresholds can improve diagnostic efficiency among older adults. For patients older than 50 years, the age-adjusted threshold is calculated by multiplying age in years by 10 ng/mL. For example, the threshold for a 75-year-old patient is 750 ng/mL. Evidence indicates that this approach can increase the proportion of patients in whom PE can be excluded without additional false-negative findings [36]. Electrocardiography (ECG) is routinely performed in patients presenting with acute chest pain, dyspnea, or suspected PE. Although ECG abnormalities are generally nonspecific, they may provide useful evidence of right ventricular strain and help identify alternative cardiovascular diagnoses. Sinus tachycardia is among the most frequent ECG findings. Other abnormalities include nonspecific ST-segment and T-wave changes, the S1Q3T3 pattern, right ventricular strain, and incomplete or complete right bundle branch block. These findings are associated with increased right ventricular pressure and electrical disturbances resulting from acute pulmonary vascular obstruction. However, their absence does not exclude PE, and ECG should be interpreted alongside clinical findings and other diagnostic investigations [37].

Chest radiography is another important initial investigation in patients with suspected PE, particularly those presenting with acute respiratory symptoms. A chest radiograph is frequently normal or demonstrates nonspecific abnormalities, including atelectasis, pleural effusion, and focal consolidation. Although conventional chest radiography cannot reliably confirm or exclude PE, it is valuable for identifying alternative explanations for dyspnea and chest pain. It may also provide the first radiological indication of pulmonary infarction. Specific radiographic signs include Hampton hump, which appears as a peripheral wedge-shaped opacity associated with pulmonary infarction; Westermark sign, characterized by regional oligemia or increased pulmonary lucency; and Fleischer sign, which involves prominence of the pulmonary artery. Despite their association with PE, these findings have limited sensitivity. Hampton hump, for example, has a reported sensitivity of approximately 22% and specificity of 82%. Westermark sign is uncommon and occurs in approximately 2% of cases. Other findings, such as atelectasis and localized consolidation, are neither sufficiently sensitive nor specific to establish the diagnosis [38,39]. Computed tomography pulmonary angiography (CTPA) is the preferred imaging modality for diagnosing acute PE in most patients. Multidetector CTPA provides direct visualization of pulmonary arterial branches and can identify emboli extending to the subsegmental level. The PIOPED II study reported a sensitivity of 83% and specificity of 96% for CTPA in diagnosing PE [40,41]. In addition to identifying intravascular filling defects, CTPA provides information about the anatomical distribution and extent of pulmonary emboli and may demonstrate associated pulmonary infarction. Radiological features of pulmonary infarction include a feeding vessel sign, central lucency, and semicircular configuration. The presence of air bronchograms makes pulmonary infarction less likely. The combination of a vessel sign, central lucency, and absence of air bronchograms has been associated with a specificity of approximately 99% for pulmonary infarction [7,42].

The diagnostic accuracy of CTPA must be interpreted in relation to the patient's pretest clinical probability. According to PIOPED II findings, a negative CTPA has a negative predictive value of approximately 96% in patients with low clinical probability and 89% in those with intermediate probability. However, this value decreases to approximately 60% in patients with high clinical probability. Conversely, the positive predictive value of CTPA ranges from 92% to 96% in patients with intermediate or high clinical probability but decreases to approximately 58% in those with low clinical probability [41]. Therefore, discrepancies between clinical assessment and CTPA findings may require additional diagnostic investigations rather than relying exclusively on imaging results. Certain clinical conditions may limit the use of CTPA. Moderate to severe allergy to iodinated contrast media and significant renal impairment, particularly an estimated glomerular filtration rate below 30 mL/min/1.73 m², represent important considerations. The potential risks should be balanced against the clinical necessity of obtaining a definitive diagnosis. Alternative imaging, particularly ventilation-perfusion scanning, may be appropriate in patients with contraindications to iodinated contrast. CTPA also provides information about cardiovascular involvement, including right

ventricular enlargement. A right ventricular-to-left ventricular diameter ratio of at least 0.9 has been associated with increased risk of severe in-hospital outcomes, including among patients who remain hemodynamically stable [43].

Ventilation-perfusion (V/Q) scanning is an established alternative imaging technique for evaluating suspected PE, particularly when CTPA is contraindicated, inconclusive, or unsuitable. The investigation compares pulmonary ventilation with regional pulmonary perfusion to identify areas receiving adequate ventilation but reduced or absent blood flow. A normal chest radiograph is generally preferred before performing planar V/Q scanning because underlying radiographic abnormalities may increase the likelihood of false-positive or nondiagnostic findings. V/Q scanning is particularly useful in pregnant patients with a normal chest radiograph and individuals with severe renal impairment or previous severe hypersensitivity reactions to iodinated contrast media [44]. V/Q scan findings are generally categorized into three groups: normal, high probability, and nondiagnostic. A normal perfusion scan effectively excludes PE, whereas a high-probability scan strongly supports the diagnosis in patients with compatible clinical findings. However, an intermediate or nondiagnostic result requires additional investigations. The PIOPED II study demonstrated that the predictive value of a high-probability V/Q scan depends on the patient's clinical probability. Therefore, a high-probability result should be interpreted cautiously when the pretest clinical probability is low. A major limitation of planar V/Q scanning is the relatively high frequency of nondiagnostic results, which may necessitate additional imaging or lower-extremity venous ultrasonography [44–47].

Pulmonary angiography was historically considered the reference standard for diagnosing PE. The procedure involves introducing a catheter through the venous circulation into the right side of the heart and pulmonary arteries under fluoroscopic guidance, followed by the injection of contrast material. The diagnosis is established by identifying an intravascular filling defect or abrupt termination of a pulmonary arterial branch. However, the widespread availability of CTPA has substantially reduced the routine use of conventional pulmonary angiography. It is now generally reserved for selected patients in whom clinical suspicion remains high despite inconclusive CTPA or V/Q scanning. Its use may also be justified when catheter-based treatment is planned because the procedure can provide diagnostic information while facilitating therapeutic interventions, including catheter-directed thrombolysis [48,49]. Magnetic resonance angiography (MRA) has also been investigated as an imaging alternative for patients with suspected PE. Its main advantage is the absence of ionizing radiation, making it a potential option in selected clinical circumstances. However, MRA is not recommended as a first-line diagnostic investigation because of its relatively low sensitivity, limited availability in emergency settings, and considerable proportion of technically inadequate or inconclusive examinations. In a prospective study involving 371 adults with suspected PE, magnetic resonance pulmonary angiography demonstrated a sensitivity of 78% and specificity of 99% among patients with technically adequate images. Combining pulmonary angiography with magnetic resonance venography improved diagnostic performance in the evaluated subgroup. Nevertheless, its use remains limited to selected patients in whom CTPA and V/Q scanning cannot be performed [50].

Transthoracic echocardiography is particularly valuable for assessing right ventricular function and identifying cardiovascular consequences of acute PE. Although direct visualization of thrombi within the proximal pulmonary arteries or right heart may occasionally establish the diagnosis, echocardiography is primarily used for risk stratification rather than definitive exclusion or confirmation. Findings suggestive of PE include right ventricular dilation, impaired right ventricular contractility, septal flattening, and increased right-sided cardiac pressures. These findings are particularly important in hemodynamically unstable patients because they may support an emergency presumptive diagnosis and justify immediate reperfusion treatment when definitive imaging cannot be performed safely [51–53]. Right ventricular dilation is observed in at least 25% of patients with PE and provides important prognostic information. Additional echocardiographic findings include the McConnell sign, characterized by reduced contractility of the right ventricular free wall with relative preservation of apical contraction, and the 60/60 sign, involving a pulmonary ejection acceleration time below 60 milliseconds combined with a peak systolic tricuspid valve gradient below 60 mmHg. A right ventricular-to-left ventricular diameter ratio of at least 1 and tricuspid annular plane systolic excursion (TAPSE) below 16 mm are also associated with unfavorable outcomes. Nevertheless, a negative echocardiographic examination cannot exclude PE because its negative predictive value is approximately 40% to 50%. Furthermore, right ventricular dysfunction may result from pre-existing cardiac or respiratory disease [54–56].

Compression ultrasonography of the lower extremities is another important investigation because most pulmonary emboli originate from lower-limb DVT. Upper-extremity DVT represents a less common source and is frequently associated with central venous catheterization. Compression ultrasound identifies thrombi through the inability of affected veins to collapse under external pressure. Studies have demonstrated a sensitivity exceeding 90% and specificity of approximately 95% for detecting proximal symptomatic DVT. In patients

with suspected PE, identification of proximal DVT may provide sufficient evidence to initiate anticoagulant treatment without further pulmonary imaging when appropriate. However, because ultrasonography has limited sensitivity for detecting all cases of DVT, it is particularly useful when CTPA or V/Q scanning is contraindicated or inconclusive [57–60]. Clinical probability scoring systems are essential components of the diagnostic evaluation. The revised Geneva score and Wells criteria are widely used to estimate the likelihood of PE before definitive imaging. The revised Geneva score incorporates previous PE or DVT, heart rate, recent surgery or fracture, hemoptysis, active malignancy, unilateral lower-limb pain, pain on deep venous palpation, unilateral edema, and age above 65 years. The three-level classification identifies low, intermediate, and high probability, whereas the two-level classification categorizes patients as PE unlikely or PE likely. The Wells criteria include clinical symptoms of DVT, the likelihood of alternative diagnoses, heart rate above 100 beats/minute, recent immobilization or surgery, previous DVT or PE, hemoptysis, and malignancy. Traditional Wells scoring classifies patients into low, moderate, and high probability, while modified Wells scoring distinguishes PE likely from PE unlikely [61].

The Pulmonary Embolism Rule-Out Criteria (PERC) provide another clinical decision tool for excluding PE in selected emergency department patients with an initially low clinical probability. The eight criteria include age below 50 years, heart rate below 100 beats/minute, oxygen saturation of at least 95%, absence of hemoptysis, absence of estrogen use, no previous DVT or PE, absence of unilateral leg swelling, and no surgery or trauma requiring hospitalization during the preceding four weeks. When all eight criteria are satisfied in an appropriately selected low-risk patient, further diagnostic testing may be unnecessary. However, PERC should only be applied in populations with a low prevalence of PE and should not be used in patients with intermediate or high clinical suspicion or in hospitalized patients [62–64]. The diagnostic pathway for hemodynamically stable patients generally begins with clinical probability assessment using the Wells criteria or revised Geneva score. In patients with low probability, all eight PERC criteria may be applied. If these criteria are satisfied, PE can be excluded without additional testing. If PERC criteria are not fulfilled, D-dimer testing is recommended. A negative result using the appropriate standard or age-adjusted threshold excludes PE in patients with low or intermediate clinical probability. A positive result requires further investigation, usually with CTPA. For intermediate-probability patients, the same D-dimer-based approach is applied, followed by CTPA when the result is positive. If CTPA is contraindicated or inconclusive, V/Q scanning provides an alternative diagnostic option.

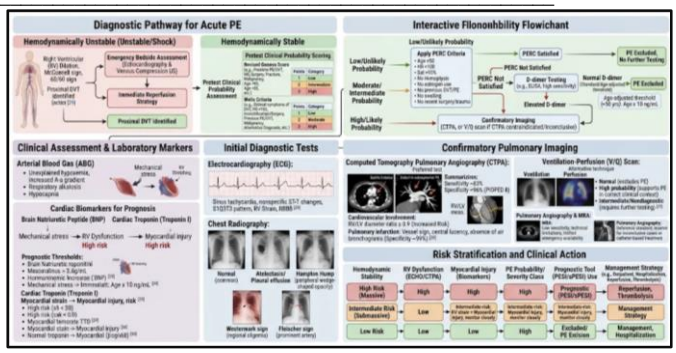


Figure-3: Evaluation of Pulmonary Embolism.

In patients with high clinical probability, urgent CTPA is generally recommended without relying on D-dimer testing to exclude PE. If CTPA cannot be performed or provides inconclusive findings, V/Q scanning should be considered. A normal V/Q scan excludes PE, whereas a high-probability result supports the diagnosis in an appropriate clinical context. Intermediate-probability findings may require additional evaluation with lower-extremity compression ultrasonography. In hemodynamically unstable patients who cannot safely undergo definitive imaging, bedside echocardiography and venous compression ultrasonography may provide sufficient supporting evidence for an emergency presumptive diagnosis and facilitate timely administration of life-saving treatment [51]. Overall, accurate diagnosis of acute PE depends on integrating clinical probability, laboratory findings, and radiological evidence. Nursing professionals contribute through initial assessment, monitoring of vital signs and oxygen saturation, recognition of clinical deterioration, and preparation of patients for diagnostic procedures. Laboratory specialists support diagnosis and risk stratification through D-dimer, cardiac biomarkers, and ABG analysis, while radiology teams provide definitive imaging and assessment of pulmonary vascular obstruction and right ventricular involvement. Coordinated interpretation of these findings improves diagnostic decision-making and supports timely treatment.

Treatment and Management

The management of acute pulmonary embolism (PE) aims to restore pulmonary circulation, prevent thrombus extension and recurrence, support right ventricular (RV) function, and reduce mortality. Treatment depends on hemodynamic stability, clinical probability, bleeding risk, and the presence of underlying risk factors. Initial management focuses on supportive measures. Supplemental oxygen is indicated when oxygen saturation falls below 90%. Noninvasive or invasive mechanical ventilation may be required in unstable patients, although positive-pressure ventilation can adversely affect cardiac output and RV function. Acute RV failure represents the leading cause of death in patients with hemodynamically unstable PE. Excessive intravenous

fluid administration can worsen RV dilation, increase ventricular interdependence, and reduce cardiac output. Therefore, fluid resuscitation should be considered mainly in patients with intravascular depletion or a collapsible inferior vena cava. Vasopressors may provide additional hemodynamic support, while extracorporeal membrane oxygenation may be considered in selected patients with severe circulatory or respiratory failure. Anticoagulation represents the mainstay of acute PE treatment. Low-molecular-weight heparin (LMWH) and fondaparinux are generally preferred because they are associated with lower risks of major bleeding and heparin-induced thrombocytopenia than unfractionated heparin (UFH). UFH remains appropriate for patients with hemodynamic instability who may require urgent reperfusion or those with significant renal impairment. Direct oral anticoagulants and vitamin K antagonists are also established treatment options.[65,66]

Treatment decisions depend on hemodynamic status and clinical probability, assessed using tools such as the revised Geneva or Wells scores. In hemodynamically stable patients with high clinical suspicion, anticoagulation should begin before diagnostic imaging. For patients with low or intermediate suspicion, treatment may be deferred briefly when imaging is expected within the recommended timeframes, allowing diagnostic confirmation before anticoagulation. When anticoagulation is absolutely contraindicated in a patient with confirmed PE, inferior vena cava (IVC) filter placement may be considered. Patients with suspected high-risk PE and hemodynamic instability require urgent assessment using computed tomography pulmonary angiography (CTPA), portable perfusion scanning, or bedside transthoracic echocardiography when feasible. Primary reperfusion, usually systemic thrombolysis, is the preferred treatment for unstable PE. Surgical pulmonary embolectomy and catheter-directed interventions are alternatives when thrombolysis is contraindicated or unsuccessful. After successful reperfusion and stabilization, patients can transition from parenteral to oral anticoagulation. Thrombolytic therapy reduces pulmonary artery pressure and vascular resistance and improves RV dilation. Its greatest benefit is generally observed when administered within 48 hours of symptom onset, although benefit may remain when symptoms began within the preceding 14 days.[67–70] The Pulmonary Embolism Thrombolysis (PEITHO) trial demonstrated that thrombolysis in selected patients with intermediate-risk PE reduced hemodynamic deterioration and cardiovascular collapse. However, this benefit was accompanied by an increased risk of severe bleeding.[71,72] Absolute contraindications include previous intracranial hemorrhage, intracranial vascular abnormalities or malignant tumors, recent ischemic stroke, suspected aortic dissection, active bleeding, bleeding disorders, recent intracranial or spinal surgery, and significant recent head or facial trauma.

Catheter-directed treatment provides an alternative reperfusion approach through pulmonary arterial catheterization. Techniques include ultrasound-assisted thrombolysis, suction or rotational embolectomy, thrombus aspiration, and mechanical fragmentation combined with local thrombolytic administration. Reported success rates reach approximately 87% in selected studies.[73,74] However, complications include pulmonary artery perforation, massive hemoptysis, and cardiac tamponade. Although uncommon, these complications may be fatal. Surgical pulmonary embolectomy is generally reserved for patients with hemodynamically unstable PE who cannot receive thrombolysis or who have not responded to it.[75–77] Available comparisons have not demonstrated a clear mortality difference between thrombolysis and surgical embolectomy, although thrombolysis has been associated with higher risks of stroke and repeated intervention. IVC filters prevent venous thrombi from reaching pulmonary circulation. Their use is mainly indicated when anticoagulation is absolutely contraindicated or when recurrent venous thromboembolism occurs despite appropriate anticoagulant treatment. Retrievable filters are preferred because they can be removed once the contraindication resolves, allowing anticoagulation to resume. The PREPIC study demonstrated that permanent filter placement reduced recurrent PE but increased DVT risk, without a substantial reduction in overall recurrent VTE or mortality.[78]

Long-term anticoagulation aims to complete treatment of the acute episode and prevents recurrent VTE. At least three months of anticoagulant therapy is recommended for patients with PE. Although extending treatment beyond three to six months reduces recurrence during therapy, it also increases bleeding risk. Extended anticoagulation can reduce recurrent VTE by up to 90%, but protection does not persist after treatment discontinuation. [79–81] Treatment duration should therefore reflect the cause of PE, persistence of risk factors, and individual bleeding risk. Approximately 30% of PE cases are unprovoked, and these patients have a two- to threefold higher recurrence risk than patients with provoked PE.[82] Persistent risk factors, including active cancer and antiphospholipid antibodies, also increase recurrence risk compared with temporary factors such as surgery, trauma, and immobilization.[83] Consequently, anticoagulation should be reassessed after three months. Extended treatment is generally considered unprovoked PE or persistent risk factors when bleeding risk remains acceptable. In patients with cancer-associated PE, LMWH and direct oral anticoagulants, including apixaban and rivaroxaban, are preferred over vitamin K antagonists.[84]

Conclusion:

Acute pulmonary embolism remains a major clinical challenge because of its variable presentation, potential for rapid deterioration, and risk of mortality. Accurate diagnosis requires integration of clinical findings, validated probability scores, laboratory investigations, and radiological imaging. D-dimer testing assists in excluding PE in appropriately selected patients, while cardiac biomarkers provide information about right ventricular injury and prognosis. Computed tomography pulmonary angiography remains the principal imaging modality, supported by echocardiography, ventilation-perfusion scanning, and venous ultrasonography when indicated. Anticoagulation forms the foundation of treatment, whereas thrombolysis, catheter-directed therapy, and surgical embolectomy provide additional options for selected patients. Nursing professionals contribute through systematic assessment, monitoring, medication administration, and recognition of complications. Effective collaboration among nursing, laboratory, radiology, and medical teams improves diagnostic accuracy, supports timely intervention, and promotes patient safety. Individualized anticoagulation and follow-up are also essential to reduce recurrence and improve long-term outcomes.

References:

1. COON WW, WILLIS PW. Deep venous thrombosis and pulmonary embolism: prediction, prevention and treatment. Am J Cardiol. 1959 Nov;4:611-21.
2. Goldhaber SZ, Grodstein F, Stampfer MJ, Manson JE, Colditz GA, Speizer FE, Willett WC, Hennekens CH. A prospective study of risk factors for pulmonary embolism in women. JAMA. 1997 Feb 26;277(8):642-5.
3. Gohil R, Peck G, Sharma P. The genetics of venous thromboembolism. A meta-analysis involving approximately 120,000 cases and 180,000 controls. Thromb Haemost. 2009 Aug;102(2):360-70.
4. Rogers MA, Levine DA, Blumberg N, Flanders SA, Chopra V, Langa KM. Triggers of hospitalization for venous thromboembolism. Circulation. 2012 May 01;125(17):2092-9.
5. Anderson FA, Spencer FA. Risk factors for venous thromboembolism. Circulation. 2003 Jun 17;107(23 Suppl 1):I9-16
6. Kaptein FHJ, Kroft LJM, Hammerschlag G, Ninaber MK, Bauer MP, Huisman MV, Klok FA. Pulmonary infarction in acute pulmonary embolism. Thromb Res. 2021 Jun;202:162-169.
7. Islam M, Filopei J, Frank M, Ramesh N, Verzosa S, Ehrlich M, Bondarsky E, Miller A, Steiger D. Pulmonary infarction secondary to pulmonary embolism: An evolving paradigm. Respirology. 2018 Mar 25;
8. Blom JW, Doggen CJ, Osanto S, Rosendaal FR. Malignancies, prothrombotic mutations, and the risk of venous thrombosis. JAMA. 2005 Feb 09;293(6):715-22.
9. Clayton TC, Gaskin M, Meade TW. Recent respiratory infection and risk of venous thromboembolism: case-control study through a general practice database. Int J Epidemiol. 2011 Jun;40(3):819-27.
10. Prandoni P, Pesavento R, Sørensen HT, Gennaro N, Dalla Valle F, Minotto I, Perina F, Pengo V, Pagnan A. Prevalence of heart diseases in patients with pulmonary embolism with and without peripheral venous thrombosis: findings from a cross-sectional survey. Eur J Intern Med. 2009 Sep;20(5):470-3.
11. Sørensen HT, Horvath-Puho E, Pedersen L, Baron JA, Prandoni P. Venous thromboembolism and subsequent hospitalisation due to acute arterial cardiovascular events: a 20-year cohort study. Lancet. 2007 Nov 24;370(9601):1773-9.
12. Wendelboe AM, Raskob GE. Global Burden of Thrombosis: Epidemiologic Aspects. Circ Res. 2016 Apr 29;118(9):1340-7.
13. Raskob GE, Angchaisuksiri P, Blanco AN, Buller H, Gallus A, Hunt BJ, Hylek EM, Kakkar A, Konstantinides SV, McCumber M, Ozaki Y, Wendelboe A, Weitz JI., ISTH Steering Committee for World Thrombosis Day. Thrombosis: a major contributor to global disease burden. Arterioscler Thromb Vasc Biol. 2014 Nov;34(11):2363-71.
14. Horlander KT, Mannino DM, Leeper KV. Pulmonary embolism mortality in the United States, 1979-1998: an analysis using multiple-cause mortality data. Arch Intern Med. 2003 Jul 28;163(14):1711-7.
15. Moser KM. Venous thromboembolism. Am Rev Respir Dis. 1990 Jan;141(1):235-49.
16. Nakos G, Kitsiouli EI, Lekka ME. Bronchoalveolar lavage alterations in pulmonary embolism. Am J Respir Crit Care Med. 1998 Nov;158(5 Pt 1):1504-10.
17. Morrone D, Morrone V. Acute Pulmonary Embolism: Focus on the Clinical Picture. Korean Circ J. 2018 May;48(5):365-381.
18. Miniati M. Pulmonary Infarction: An Often Unrecognized Clinical Entity. Semin Thromb Hemost. 2016 Nov;42(8):865-869.
19. Tsao MS, Schraufnagel D, Wang NS. Pathogenesis of pulmonary infarction. Am J Med. 1982 Apr;72(4):599-606.
20. Kroegel C, Reissig A. Principle mechanisms underlying venous thromboembolism: epidemiology, risk factors, pathophysiology and pathogenesis. Respiration. 2003 Jan-Feb;70(1):7-30.
21. Choi SH, Cha SI, Shin KM, Lim JK, Yoo SS, Lee SY, Lee J, Kim CH, Park JY, Lee DH. Clinical Relevance of Pleural Effusion in Patients with Pulmonary Embolism. Respiration. 2017;93(4):271-278.
22. Carson JL, Kelley MA, Duff A, Weg JG, Fulkerson WJ, Palevsky HI, Schwartz JS,

Thompson BT, Popovich J, Hobbins TE. The clinical course of pulmonary embolism. N Engl J Med. 1992 May 07;326(19):1240-5.
23. Nijkeuter M, Söhne M, Tick LW, Kamphuisen PW, Kramer MH, Laterveer L, van Houten AA, Kruip MJ, Leebeek FW, Büller HR, Huisman MV., Christopher Study Investigators. The natural course of hemodynamically stable pulmonary embolism: Clinical outcome and risk factors in a large prospective cohort study. Chest. 2007 Feb;131(2):517-23.
24. Stein PD, Henry JW. Clinical characteristics of patients with acute pulmonary embolism stratified according to their presenting syndromes. Chest. 1997 Oct;112(4):974-9.
25. Stein PD, Beemath A, Matta F, Weg JG, Yusen RD, Hales CA, Hull RD, Leeper KV, Sostman HD, Tapson VF, Buckley JD, Gottschalk A, Goodman LR, Wakefied TW, Woodard PK. Clinical characteristics of patients with acute pulmonary embolism: data from PIOPED II. Am J Med. 2007 Oct;120(10):871-9.
26. Barco S, Ende-Verhaar YM, Becattini C, Jimenez D, Lankeit M, Huisman MV, Konstantinides SV, Klok FA. Differential impact of syncope on the prognosis of patients with acute pulmonary embolism: a systematic review and meta-analysis. Eur Heart J. 2018 Dec 14;39(47):4186-4195.
27. Courtney DM, Sasser HC, Pincus CL, Kline JA. Pulseless electrical activity with witnessed arrest as a predictor of sudden death from massive pulmonary embolism in outpatients. Resuscitation. 2001 Jun;49(3):265-72.
28. Kucher N, Goldhaber SZ. Management of massive pulmonary embolism. Circulation. 2005 Jul 12;112(2):e28-32.
29. Wood KE. Major pulmonary embolism: review of a pathophysiologic approach to the golden hour of hemodynamically significant pulmonary embolism. Chest. 2002 Mar;121(3):877-905.
30. Kiely DG, Kennedy NS, Pirzada O, Batchelor SA, Struthers AD, Lipworth BJ. Elevated levels of natriuretic peptides in patients with pulmonary thromboembolism. Respir Med. 2005 Oct;99(10):1286-91.
31. Henzler T, Roeger S, Meyer M, Schoepf UJ, Nance JW, Haghi D, Kaminski WE, Neumaier M, Schoenberg SO, Fink C. Pulmonary embolism: CT signs and cardiac biomarkers for predicting right ventricular dysfunction. Eur Respir J. 2012 Apr;39(4):919-26.
32. Meyer T, Binder L, Hruska N, Luthe H, Buchwald AB. Cardiac troponin I elevation in acute pulmonary embolism is associated with right ventricular dysfunction. J Am Coll Cardiol. 2000 Nov 01;36(5):1632-6.
33. Konstantinides S, Geibel A, Olschewski M, Kasper W, Hruska N, Jäckle S, Binder L. Importance of cardiac troponins I and T in risk stratification of patients with acute pulmonary embolism. Circulation. 2002 Sep 03;106(10):1263-8.
34. Horlander KT, Leeper KV. Troponin levels as a guide to treatment of pulmonary embolism. Curr Opin Pulm Med. 2003 Sep;9(5):374-7.
35. Stein PD, Hull RD, Patel KC, Olson RE, Ghali WA, Brant R, Biel RK, Bharadia V, Kalra NK. D-dimer for the exclusion of acute venous thrombosis and pulmonary embolism: a systematic review. Ann Intern Med. 2004 Apr 20;140(8):589-602.
36. Righini M, Van Es J, Den Exter PL, Roy PM, Verschuren F, Ghuysen A, Rutschmann OT, Sanchez O, Jaffrelot M, Trinh-Duc A, Le Gall C, Moustafa F, Principe A, Van Houten AA, Ten Wolde M, Douma RA, Hazelaar G, Erkens PM, Van Kralingen KW, Grootenboers MJ, Durian MF, Cheung YW, Meyer G, Bounameaux H, Huisman MV, Kamphuisen PW, Le Gal G. Age-adjusted D-dimer cutoff levels to rule out pulmonary embolism: the ADJUST-PE study. JAMA. 2014 Mar 19;311(11):1117-24.
37. Rodger M, Makropoulos D, Turek M, Quevillon J, Raymond F, Rasuli P, Wells PS. Diagnostic value of the electrocardiogram in suspected pulmonary embolism. Am J Cardiol. 2000 Oct 01;86(7):807-9, A10.
38. Bird SH, Leng RA. Further studies on the effects of the presence or absence of protozoa in the rumen on live-weight gain and wool growth of sheep. Br J Nutr. 1984 Nov;52(3):607-11.
39. Worsley DF, Alavi A, Aronchick JM, Chen JT, Greenspan RH, Ravin CE. Chest radiographic findings in patients with acute pulmonary embolism: observations from the PIOPED Study. Radiology. 1993 Oct;189(1):133-6.
40. Ghaye B, Szapiro D, Mastora I, Delannoy V, Duhamel A, Remy J, Remy-Jardin M. Peripheral pulmonary arteries: how far in the lung does multi-detector row spiral CT allow analysis? Radiology. 2001 Jun;219(3):629-36.
41. Stein PD, Fowler SE, Goodman LR, Gottschalk A, Hales CA, Hull RD, Leeper KV, Popovich J, Quinn DA, Sos TA, Sostman HD, Tapson VF, Wakefield TW, Weg JG, Woodard PK., PIOPED II Investigators. Multidetector computed tomography for acute pulmonary embolism. N Engl J Med. 2006 Jun 01;354(22):2317-27.
42. Revel MP, Triki R, Chatellier G, Couchon S, Haddad N, Hernigou A, Danel C, Frija G. Is It possible to recognize pulmonary infarction on multisection CT images? Radiology. 2007 Sep;244(3):875-82.
43. Becattini C, Agnelli G, Vedovati MC, Pruszczyk P, Casazza F, Grifoni S, Salvi A, Bianchi M, Douma R, Konstantinides S, Lankeit M, Duranti M. Multidetector computed tomography for acute pulmonary embolism: diagnosis and risk stratification in a single test. Eur Heart J. 2011 Jul;32(13):1657-63.

44. Reid JH, Coche EE, Inoue T, Kim EE, Dondi M, Watanabe N, Mariani G., International Atomic Energy Agency Consultants' Group. Is the lung scan alive and well? Facts and controversies in defining the role of lung scintigraphy for the diagnosis of pulmonary embolism in the era of MDCT. Eur J Nucl Med Mol Imaging. 2009 Mar;36(3):505-21.
45. Glaser JE, Chamarthy M, Haramati LB, Esses D, Freeman LM. Successful and safe implementation of a trinary interpretation and reporting strategy for V/Q lung scintigraphy. J Nucl Med. 2011 Oct;52(10):1508-12.
46. Anderson DR, Kahn SR, Rodger MA, Kovacs MJ, Morris T, Hirsch A, Lang E, Stiell I, Kovacs G, Dreyer J, Dennie C, Cartier Y, Barnes D, Burton E, Pleasance S, Skedgel C, O'Rouke K, Wells PS. Computed tomographic pulmonary angiography vs ventilation-perfusion lung scanning in patients with suspected pulmonary embolism: a randomized controlled trial. JAMA. 2007 Dec 19;298(23):2743-53.
47. Sostman HD, Stein PD, Gottschalk A, Matta F, Hull R, Goodman L. Acute pulmonary embolism: sensitivity and specificity of ventilation-perfusion scintigraphy in PIOPED II study. Radiology. 2008 Mar;246(3):941-6.
48. PIOPED Investigators. Value of the ventilation/perfusion scan in acute pulmonary embolism. Results of the prospective investigation of pulmonary embolism diagnosis (PIOPED). JAMA. 1990 May 23-30;263(20):2753-9.
49. Wittram C, Waltman AC, Shepard JA, Halpern E, Goodman LR. Discordance between CT and angiography in the PIOPED II study. Radiology. 2007 Sep;244(3):883-9.
50. Stein PD, Chenevert TL, Fowler SE, Goodman LR, Gottschalk A, Hales CA, Hull RD, Jablonski KA, Leeper KV, Naidich DP, Sak DJ, Sostman HD, Tapson VF, Weg JG, Woodard PK., PIOPED III (Prospective Investigation of Pulmonary Embolism Diagnosis III) Investigators. Gadolinium-enhanced magnetic resonance angiography for pulmonary embolism: a multicenter prospective study (PIOPED III). Ann Intern Med. 2010 Apr 06;152(7):434-43, W142-3.
51. Grifoni S, Olivotto I, Cecchini P, Pieralli F, Camaiti A, Santoro G, Conti A, Agnelli G, Berni G. Short-term clinical outcome of patients with acute pulmonary embolism, normal blood pressure, and echocardiographic right ventricular dysfunction. Circulation. 2000 Jun 20;101(24):2817-22.
52. Torbicki A, Kurzyna M, Ciurzynski M, Pruszczyk P, Pacho R, Kuch-Wocial A, Szulc M. Proximal pulmonary emboli modify right ventricular ejection pattern. Eur Respir J. 1999 Mar;13(3):616-21.
53. Bova C, Greco F, Misuraca G, Serafini O, Crocco F, Greco A, Noto A. Diagnostic utility of echocardiography in patients with suspected pulmonary embolism. Am J Emerg Med. 2003 May;21(3):180-3.
54. Wolfe MW, Lee RT, Feldstein ML, Parker JA, Come PC, Goldhaber SZ. Prognostic significance of right ventricular hypokinesis and perfusion lung scan defects in pulmonary embolism. Am Heart J. 1994 May;127(5):1371-5.
55. Kurzyna M, Torbicki A, Pruszczyk P, Burakowska B, Fijałkowska A, Kober J, Oniszh K, Kuca P, Tomkowski W, Burakowski J, Wawrzyńska L. Disturbed right ventricular ejection pattern as a new Doppler echocardiographic sign of acute pulmonary embolism. Am J Cardiol. 2002 Sep 01;90(5):507-11.
56. Pruszczyk P, Goliszek S, Lichodziejewska B, Kostrubiec M, Ciurzyński M, Kurnicka K, Dzikowska-Diduch O, Palczewski P, Wyzgal A. Prognostic value of echocardiography in normotensive patients with acute pulmonary embolism. JACC Cardiovasc Imaging. 2014 Jun;7(6):553-60.
57. Hull RD, Hirsh J, Carter CJ, Jay RM, Dodd PE, Ockelford PA, Coates G, Gill GJ, Turpie AG, Doyle DJ, Buller HR, Raskob GE. Pulmonary angiography, ventilation lung scanning, and venography for clinically suspected pulmonary embolism with abnormal perfusion lung scan. Ann Intern Med. 1983 Jun;98(6):891-9.
58. Kearon C, Ginsberg JS, Hirsh J. The role of venous ultrasonography in the diagnosis of suspected deep venous thrombosis and pulmonary embolism. Ann Intern Med. 1998 Dec 15;129(12):1044-9.
59. Le Gal G, Righini M, Sanchez O, Roy PM, Baba-Ahmed M, Perrier A, Bounameaux H. A positive compression ultrasonography of the lower limb veins is highly predictive of pulmonary embolism on computed tomography in suspected patients. Thromb Haemost. 2006 Jun;95(6):963-6.
60. van Rossum AB, van Houwelingen HC, Kieft GJ, Pattynama PM. Prevalence of deep vein thrombosis in suspected and proven pulmonary embolism: a meta-analysis. Br J Radiol. 1998 Dec;71(852):1260-5.
61. Wells PS, Ginsberg JS, Anderson DR, Kearon C, Gent M, Turpie AG, Bormanis J, Weitz J, Chamberlain M, Bowie D, Barnes D, Hirsh J. Use of a clinical model for safe management of patients with suspected pulmonary embolism. Ann Intern Med. 1998 Dec 15;129(12):997-1005.
62. Kline JA, Mitchell AM, Kabrhel C, Richman PB, Courtney DM. Clinical criteria to prevent unnecessary diagnostic testing in emergency department patients with suspected pulmonary embolism. J Thromb Haemost. 2004 Aug;2(8):1247-55.

63. Coutance G, Cauderlier E, Ehtisham J, Hamon M, Hamon M. The prognostic value of markers of right ventricular dysfunction in pulmonary embolism: a meta-analysis. Crit Care. 2011;15(2):R103.
64. Hugli O, Righini M, Le Gal G, Roy PM, Sanchez O, Verschuren F, Meyer G, Bounameaux H, Aujesky D. The pulmonary embolism rule-out criteria (PERC) rule does not safely exclude pulmonary embolism. J Thromb Haemost. 2011 Feb;9(2):300-4.
65. Stein PD, Hull RD, Matta F, Yaekoub AY, Liang J. Incidence of thrombocytopenia in hospitalized patients with venous thromboembolism. Am J Med. 2009 Oct;122(10):919-30.
66. Cossette B, Pelletier ME, Carrier N, Turgeon M, Leclair C, Charron P, Echenberg D, Fayad T, Farand P. Evaluation of bleeding risk in patients exposed to therapeutic unfractionated or low-molecular-weight heparin: a cohort study in the context of a quality improvement initiative. Ann Pharmacother. 2010 Jun;44(6):994-1002.
67. Goldhaber SZ, Haire WD, Feldstein ML, Miller M, Toltzis R, Smith JL, Taveira da Silva AM, Come PC, Lee RT, Parker JA. Alteplase versus heparin in acute pulmonary embolism: randomised trial assessing right-ventricular function and pulmonary perfusion. Lancet. 1993 Feb 27;341(8844):507-11.
68. Dalla-Volta S, Palla A, Santolicandro A, Giuntini C, Pengo V, Visioli O, Zonzin P, Zanuttini D, Barbaresi F, Agnelli G. PAIMS 2: alteplase combined with heparin versus heparin in the treatment of acute pulmonary embolism. Plasminogen activator Italian multicenter study 2. J Am Coll Cardiol. 1992 Sep;20(3):520-6.
69. Daniels LB, Parker JA, Patel SR, Grodstein F, Goldhaber SZ. Relation of duration of symptoms with response to thrombolytic therapy in pulmonary embolism. Am J Cardiol. 1997 Jul 15;80(2):184-8.
70. Marti C, John G, Konstantinides S, Combescure C, Sanchez O, Lankeit M, Meyer G, Perrier A. Systemic thrombolytic therapy for acute pulmonary embolism: a systematic review and meta-analysis. Eur Heart J. 2015 Mar 07;36(10):605-14.
71. Meyer G, Vicaut E, Danays T, Agnelli G, Becattini C, Beyer-Westendorf J, Bluhmki E, Bouvaist H, Brenner B, Couturaud F, Dellas C, Empen K, Franca A, Galiè N, Geibel A, Goldhaber SZ, Jimenez D, Kozak M, Kupatt C, Kucher N, Lang IM, Lankeit M, Meneveau N, Pacouret G, Palazzini M, Petris A, Pruszczyk P, Rugolotto M, Salvi A, Schellong S, Sebbane M, Sobkowicz B, Stefanovic BS, Thiele H, Torbicki A, Verschuren F, Konstantinides SV., PEITHO Investigators. Fibrinolysis for patients with intermediate-risk pulmonary embolism. N Engl J Med. 2014 Apr 10;370(15):1402-11.
72. Konstantinides SV, Meyer G, Becattini C, Bueno H, Geersing GJ, Harjola VP, Huisman MV, Humbert M, Jennings CS, Jiménez D, Kucher N, Lang IM, Lankeit M, Lorusso R, Mazzolai L, Meneveau N, Áinle FN, Prandoni P, Pruszczyk P, Righini M, Torbicki A, Van Belle E, Zamorano JL., The Task Force for the diagnosis and management of acute pulmonary embolism of the European Society of Cardiology (ESC). 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS): The Task Force for the diagnosis and management of acute pulmonary embolism of the European Society of Cardiology (ESC). Eur Respir J. 2019 Sep;54(3)
73. Tafur AJ, Shamoun FE, Patel SI, Tafur D, Donna F, Murad MH. Catheter-Directed Treatment of Pulmonary Embolism: A Systematic Review and Meta-Analysis of Modern Literature. Clin Appl Thromb Hemost. 2017 Oct;23(7):821-829.
74. Bajaj NS, Kalra R, Arora P, Ather S, Guichard JL, Lancaster WJ, Patel N, Raman F, Arora G, Al Solaiman F, Clark DT, Dell'Italia LJ, Leesar MA, Davies JE, McGiffin DC, Ahmed MI. Catheter-directed treatment for acute pulmonary embolism: Systematic review and single-arm meta-analyses. Int J Cardiol. 2016 Dec 15;225:128-139.
75. Lee T, Itagaki S, Chiang YP, Egorova NN, Adams DH, Chikwe J. Survival and recurrence after acute pulmonary embolism treated with pulmonary embolectomy or thrombolysis in New York State, 1999 to 2013. J Thorac Cardiovasc Surg. 2018 Mar;155(3):1084-1090.e12.
76. Keeling WB, Sundt T, Leacche M, Okita Y, Binongo J, Lasajanak Y, Aklog L, Lattouf OM., SPEAR Working Group. Outcomes After Surgical Pulmonary Embolectomy for Acute Pulmonary Embolus: A Multi-Institutional Study. Ann Thorac Surg. 2016 Nov;102(5):1498-1502.
77. Pasrija C, Kronfli A, Rouse M, Raithel M, Bittle GJ, Pousatis S, Ghoreishi M, Gammie JS, Griffith BP, Sanchez PG, Kon ZN. Outcomes after surgical pulmonary embolectomy for acute submassive and massive pulmonary embolism: A single-center experience. J Thorac Cardiovasc Surg. 2018 Mar;155(3):1095-1106.e2.
78. PREPIC Study Group. Eight-year follow-up of patients with permanent vena cava filters in the prevention of pulmonary embolism: the PREPIC (Prevention du Risque d'Embolie Pulmonaire par Interruption Cave) randomized study. Circulation. 2005 Jul 19;112(3):416-22.
79. Agnelli G, Prandoni P, Becattini C, Silingardi M, Taliani MR, Miccio M, Imberti D, Poggio R, Ageno W, Pogliani E, Porro F, Zonzin P., Warfarin Optimal Duration Italian Trial Investigators. Extended oral anticoagulant therapy after a first episode of pulmonary embolism. Ann Intern Med. 2003 Jul 01;139(1):19-25.

80. Campbell IA, Bentley DP, Prescott RJ, Routledge PA, Shetty HG, Williamson IJ. Anticoagulation for three versus six months in patients with deep vein thrombosis or pulmonary embolism, or both: randomised trial. BMJ. 2007 Mar 31;334(7595):674.
81. Schulman S, Rhedin AS, Lindmarker P, Carlsson A, Lärfars G, Nicol P, Loogna E, Svensson E, Ljungberg B, Walter H. A comparison of six weeks with six months of oral anticoagulant therapy after a first episode of venous thromboembolism. Duration of Anticoagulation Trial Study Group. N Engl J Med. 1995 Jun 22;332(25):1661-5.
82. Boutitie F, Pinede L, Schulman S, Agnelli G, Raskob G, Julian J, Hirsh J, Kearon C. Influence of preceding length of anticoagulant treatment and initial presentation of venous thromboembolism on risk of recurrence after stopping treatment: analysis of individual participants' data from seven trials. BMJ. 2011 May 24;342:d3036.
83. Poli D, Miniati M. The incidence of recurrent venous thromboembolism and chronic thromboembolic pulmonary hypertension following a first episode of pulmonary embolism. Curr Opin Pulm Med. 2011 Sep;17(5):392-7.

Young AM, Marshall A, Thirlwall J, Chapman O, Lokare A, Hill C, Hale D, Dunn JA, Lyman GH, Hutchinson C, MacCallum P, Kakkar A, Hobbs FDR, Petrou S, Dale J, Poole CJ, Maraveyas A, Levine M. Comparison of an Oral Factor Xa Inhibitor With Low Molecular Weight Heparin in Patients With Cancer With Venous Thromboembolism: Results of a Randomized Trial (SELECT-D). J Clin Oncol. 2018 Jul 10;36(20):2017-2023.