Review Article ISSN: 3065-5641

Global Journal of Critical Care and Emergency Medicine

Screening for Pulmonary Thromboembolism in Patients Presenting to the Emergency Department with Acute Exacerbation of Chronic Obstructive Pulmonary Disease: Clinical Case Series from a Corporate Healthcare System in India

Nisha Das, Nikita Makwana and Renaldo Pavrey*

Centre for Accident and Emergency Medicine, Nanavati Max Super Specialty Hospital, Mumbai, India.

***Correspondence:**
Renaldo Pavrey, Centre for Accident and Emergency Medicine, Nanavati Max Super Specialty Hospital, Mumbai, India.

Received: 02 May 2025; **Accepted:** 12 Jun 2025; **Published:** 20 Jun 2024

Citation: Das N, Makwana N, Pavrey R. Screening for Pulmonary Thromboembolism in Patients Presenting to the Emergency Department with Acute Exacerbation of Chronic Obstructive Pulmonary Disease: Clinical Case Series from a Corporate Healthcare System in India. Glob J Emerg Crit Care Med. 2024; 2(1); 1-7.

ABSTRACT

Objective: *In light of the rising global burden of chronic obstructive pulmonary disease (COPD), concurrent associated thrombo-embolic risk cannot be denied. Our objectives were to estimate the incidence of pulmonary embolism in patients presenting with acute exacerbation of COPD (AECOPD), to identify diagnostic shortcomings, and to suggest strategies for improved detection and management of pulmonary embolism in COPD patients, with the goal of enhancing emergency care protocols and patient survival.*

Methods: *This was a prospective observational study conducted at a tertiary level care corporate hospital in the city of Mumbai, India. We included consecutive patients who were hospitalized from the Emergency Department for an acute exacerbation of COPD (AECOPD) between January of 2023 and January of 2024. All patients underwent clinical risk assessment (Wells' and revised Geneva scores), arterial blood gas analyses, d-Dimer testing, bedside two-point compressibility test of both lower limbs, two-dimensional echocardiography, and computed tomography pulmonary angiography (CTPA) using a 16-detector system.*

Results: *Our study included 20 patients, with a mean age of 57 years, with 11 males (55%) and 9 females (45%). The distribution of GOLD (Global Initiative for Chronic Obstructive Lung Disease) stages was as follows: Stage I (5%), Stage II (50%), Stage III (25%), and Stage IV (20%). Approximately 80% of the patients had comorbidities such as obesity, diabetes mellitus, hypertension, and coronary artery disease. The prevalence of pulmonary embolism (PE) was 25%, and 15% of all patients had deep vein thrombosis (DVT). The thrombi were localized in the main pulmonary artery (5%), segmental (5%), unilateral (10%), and sub segmental (5%). Compression ultrasonography revealed thrombi in the popliteal vein (10%) and femoral vein (5%). The clinical probability of PE was assessed using the revised Geneva and Wells' scores. The revised Geneva score classified 45% of patients as low risk, 35% as moderate risk, and 20% as high risk. The Wells' score classified 40% as low risk, 25% as moderate risk, and 35% as high risk.*

Conclusion: *Our study underscores the importance of maintaining vigilance, ensuring early recognition, and conducting systematic diagnostic evaluations for pulmonary embolism in AECOPD cases. We acknowledge the value of careful clinical assessment and the appropriate use of predictive tools to enhance early detection of pulmonary embolism in AECOPD.*

Keywords
Chronic obstructive pulmonary disease, Acute exacerbation, Pulmonary embolism, Screening, Emergency department, Computed tomography pulmonary angiography.

Introduction
Overview of COPD
Chronic obstructive pulmonary disease (COPD) is a major global respiratory illness contributing significantly to morbidity and mortality. It primarily arises due to long-term exposure to harmful gases or particles, particularly tobacco smoke, causing progressive airflow limitation and chronic lung inflammation. Patients typically present with persistent symptoms like dyspnea, chronic cough, and sputum production [1].

COPD is vulnerable to acute exacerbations, commonly triggered by infections, pollutants, or systemic insults, leading to deterioration in respiratory function and increased hospitalizations [1]. These exacerbations carry a high risk of complications such as pulmonary embolism (PE), impacting patient outcomes severely. Therefore, understanding the mechanisms and consequences of COPD exacerbations is vital for optimizing management and improving survival [1,2].

Pulmonary embolism: definition and pathophysiology
Pulmonary embolism (PE) refers to the blockage of pulmonary arteries, most often caused by thrombi migrating from deep veins in the legs. This results in elevated pulmonary vascular resistance, right heart strain, and impaired oxygen exchange. Severity varies from asymptomatic small emboli to life-threatening massive PE causing shock [3].

The development of PE revolves around Virchow's triad: venous stasis, endothelial injury, and hypercoagulability [3]. COPD patients are particularly susceptible to PE due to chronic inflammation, reduced mobility during exacerbations, and hypoxia-induced clotting tendencies. Clinical presentations range widely, complicating timely diagnosis. Recognizing and managing PE promptly is crucial, especially in emergency settings for patients with underlying lung diseases [3,4].

Relevance of pulmonary embolism in acute COPD (AECOPD) exacerbations
Pulmonary embolism represents a significant but frequently overlooked contributor to acute respiratory deterioration in COPD exacerbations. Overlapping symptoms like worsening dyspnea, chest discomfort, and hypoxemia make differentiation difficult [5]. Studies reveal that PE occurs in a notable proportion of patients hospitalized for COPD exacerbations, often leading to delayed recognition and poor outcomes [6].

Given the reduced pulmonary reserve in COPD, the effects of PE are even more devastating. Despite its impact, standardized screening strategies for PE in COPD patients are lacking [7]. Emergency physicians must maintain heightened awareness, use validated risk assessment tools, and apply appropriate imaging protocols to improve detection and management.

Literature Review
Global burden of COPD
COPD stands among the leading causes of death worldwide, affecting millions and contributing to substantial healthcare burdens. Factors like smoking, aging populations, and environmental exposures drive its rising incidence. The burden is particularly heavy in low- and middle-income countries where preventive measures are less accessible [7].

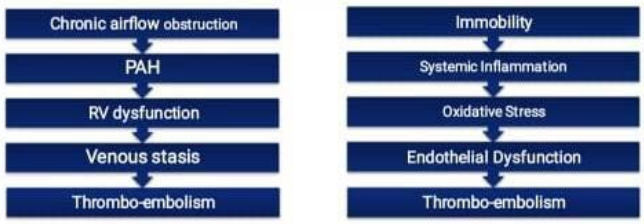
Acute exacerbations, often triggered by infections or pollutants, are critical events that accelerate disease progression and increase mortality risk. Recognizing the global magnitude of COPD is fundamental for devising prevention, early intervention, and emergency care strategies [8,9].

PE in COPD – is the association significant?
Causes of acute exacerbations
- Respiratory infections: 50-70%
- Environmental pollution: 10%
- Unknown aetiology: 30%
- Prevalence of PE in AECOPD of unknown aetiology: 16-30%
- Incidence of PE in post-mortem AECOPD: 28-51%
- Delayed & missed diagnosis of PE much higher in patients with severe COPD

Among exacerbations with no identified cause, pulmonary embolism has a reported prevalence of 16-30%. Post-mortem studies report PE in 28-51% of deceased COPD patients [10,11].

Hospital-based studies indicate PE presence in about 3-29% of COPD exacerbations requiring admission, depending on the diagnostic methods used. However, PE is often underdiagnosed due to symptom overlap. The absence of routine PE screening leads to missed cases and worsened patient outcomes. Emergency clinicians must maintain a high degree of suspicion and employ structured diagnostic strategies, using D-dimer testing, two-dimensional echocardiography screening, two-point compression ultrasound and imaging, to improve early detection and management [12,13].

Pathophysiology and Mechanisms
Is obstructive airway disease a risk factor for pulmonary embolism?



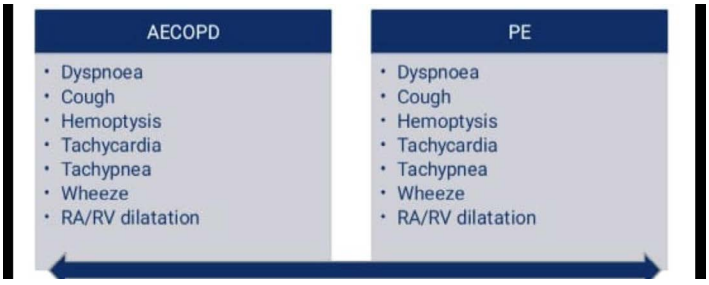
Patients with COPD frequently exhibit abnormalities in coagulation due to a combination of factors such as systemic inflammation, oxidative stress, hypoxemia, endothelial dysfunction, and an overall hypercoagulable state [3]. Inflammatory pathways significantly contribute to enhanced coagulability. For instance, serum levels of interleukin-6 and TNF alpha in COPD patients have been shown to activate coagulation via tissue factor (TF), initiating clot formation [3]. These cytokines may also reduce fibrinolytic activity by inhibiting plasminogen activators, fostering localized thrombus formation [4].

Growth differentiation factor-15 (GDF-15) is a key biomarker elevated in COPD, with evidence linking it to the severity of thrombosis and higher PE incidence. Research indicates that increased GDF-15 levels correlate with higher COPD exacerbation rates and may serve as a future therapeutic target for thromboembolic disease. Eosinophilia has also been implicated in COPD exacerbations, with elevated levels of eosinophil activation markers noted during acute episodes [3,4].

There are shared pathophysiological mechanisms between COPD and PE. Both involve chronic systemic inflammation, which disrupts endothelial integrity and promotes clot formation. Chronic hypoxia in COPD further promotes vasoconstriction, platelet aggregation, and impaired fibrinolysis, all contributing to thrombogenesis. Moreover, comorbidities like atrial fibrillation and heart failure are common in COPD patients, and enhance the risk of PE. This interplay between inflammation, vascular injury, and thrombosis creates a feedback loop, placing COPD patients at high risk for embolic complications, especially during exacerbations [14].

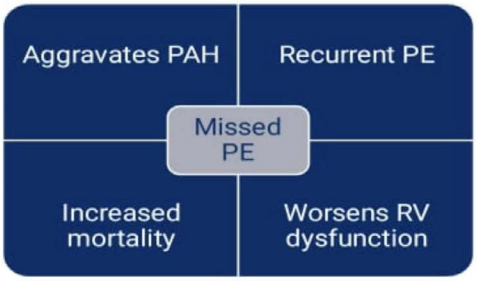
Challenges in diagnosis of pulmonary embolism in AECOPD

Can pulmonary embolism be overlooked?



- Clinical symptoms often overlap
- Limited availability of high-sensitivity, high-specificity diagnostic tools
- Similar presentations with other conditions like pneumonia, heart failure, pleural effusion, and pneumothorax

Consequences of missed pulmonary embolism



Overlapping symptoms of PE and AECOPD

The clinical features of PE and COPD exacerbations frequently resemble each other. Both may present with sudden breathlessness, tachypnea, chest tightness, and oxygen desaturation. While COPD flares often include cough, wheezing, and excess sputum, PE may involve pleurisy, haemoptysis, and evidence of shock [15]. However, these distinguishing signs are not always present, leading to frequent diagnostic delays or errors. Prompt identification is vital, as untreated PE can result in severe decompensation in already hypoxic COPD patients [16].

Clinical features suggestive of PE

Signs raising suspicion of PE in the context of AECOPD include:

- Acute, unexplained increase in dyspnea or oxygen requirement
- Pleurisy
- Haemoptysis or unilateral leg swelling
- Hypotension, raised JVP, or right ventricular strain/ McConnell's sign on echocardiogram
- Elevated D-dimer, respiratory alkalosis, or widened alveolar-arterial oxygen gradient on arterial blood gas

Identifying these warning signs in emergency scenarios is essential for differentiating PE from primary COPD exacerbations.

Impact of pulmonary embolism on patient outcomes

The coexistence of PE with COPD exacerbations is associated with worsened clinical outcomes [16]. These patients experience more frequent respiratory failure, often requiring mechanical ventilation and ICU admission. They are also prone to developing recurrent PE, worsening of RV dysfunction and aggravation of pre-existing pulmonary artery hypertension.

PE significantly increases hospital stay duration, risk of hemodynamic collapse, and short-term (30-day) as well as long-term (1-year) mortality [16].

Methods

Study Design and Population

This prospective, observational study was conducted over one year, from January 2023 to January 2024, at Nanavati Max Super Speciality Hospital, Mumbai, India. We enrolled adult patients presenting to the Emergency Department (ED) with an acute exacerbation of COPD. COPD was diagnosed according to GOLD (Global Initiative for Chronic Obstructive Lung Disease) criteria. An acute exacerbation was defined as a deviation from baseline respiratory symptoms (increased breathlessness, worsened cough, or sputum changes) requiring a change in treatment. Patients were included if they underwent computed tomography pulmonary angiography (CTPA) as part of their diagnostic workup. Patients were excluded if they had chronic kidney disease, a contrast allergy, hemodynamic instability, pre-existing chronic pulmonary embolism, or were unwilling to undergo CTPA. (Figure 1) depicts the design of the study.

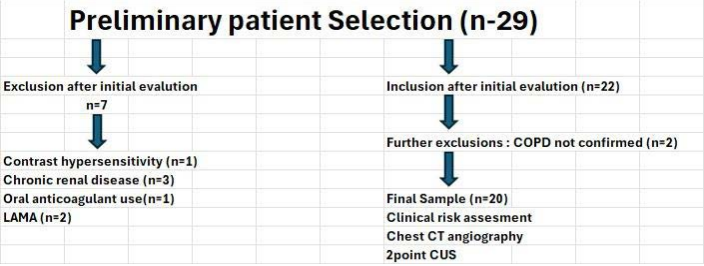


Figure 1: Study design.

Data Collection

Patient demographics, medical history, clinical presentation, laboratory results, and imaging findings were collected. The following data were specifically recorded:

- **Clinical Presentation:** Symptoms of COPD exacerbation, presence of pleurisy, and lower limb asymmetry.
- **Clinical Scoring Systems:** The Wells' Score and revised Geneva Score were calculated to estimate the pre-test probability of PE.
- **Arterial Blood Gas (ABG) Analysis:** pH, PaCO2, and PaO2 values were recorded using the Radiometer ABL80 FLEX blood gas analyser (Mumbai, India).
- **D-dimer Testing:** D-dimer levels were measured.
- **Bedside Compression Ultrasound (CUS):** Compression ultrasound of the bilateral lower limbs was performed to assess for deep vein thrombosis using the Sonosite Edge II ultrasound system (Fujifilm, Washington, United States).
- **2D Echocardiography:** 2-dimensional focused cardiac ultrasound findings (including right atrial/right ventricular dilatation and McConnell's sign) were recorded using the Sonosite M-Turbo (Fujifilm, Washington, United States).
- **Other Workup**: Chest radiographs, electrocardiography, complete blood count, and N-terminal pro-brain natriuretic peptide (NT-pro-BNP) levels.
- **Comorbidity Assessment:** Presence of obesity (Body Mass Index > 30 kg/m2), hypertension (blood pressure > 140/90 mm Hg on three occasions), type 2 diabetes mellitus (based on American Diabetes Association criteria or ongoing therapy), coronary artery disease (diagnosed by past echocardiograms or CT coronary angiography) and anaemia (haemoglobin <13.5 g/dL in males or <12.0 g/dL in females)
- **CT Pulmonary Angiography (CTPA):** CTPA was performed using a 16-detector CT system. Iodinated contrast was administered intravenously. CTPA images were reviewed for the presence of intraluminal filling defects or complete blockage of a pulmonary artery.

Ethical Considerations

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Institutional Ethics Committee (IEC) of Nanavati Max Super Speciality Hospital, Mumbai (ECR/566/Inst/MH/2014/RR-20). Given the retrospective nature of the data collection, the requirement for informed consent was waived by the IEC. All data were anonymised and handled with strict confidentiality.

Results

The study included 20 patients, with a mean age of 57 years. There were 11 male (55%) and 9 female (45%) participants. The prevalence of pulmonary embolism was 5 (25%) based on CTPA results. 3 of these (15%) had deep vein thrombosis (DVT). (Figure 2) shows the demographic properties and general clinical characteristics of the study populations.

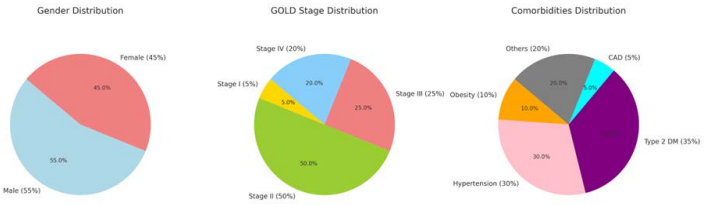


Figure 2: General demographic characteristics of the study population.

The localisation of thrombi in patients who had pulmonary embolism, and the results of bedside compression ultrasound are shown below in (Figure 3) and (Figure 4) respectively;

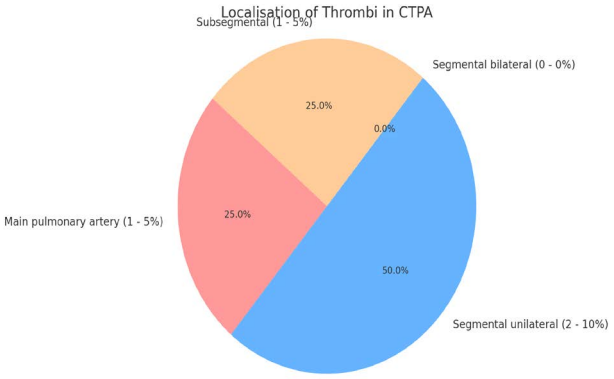


Figure 3: Localisation of thrombi based on CTPA.

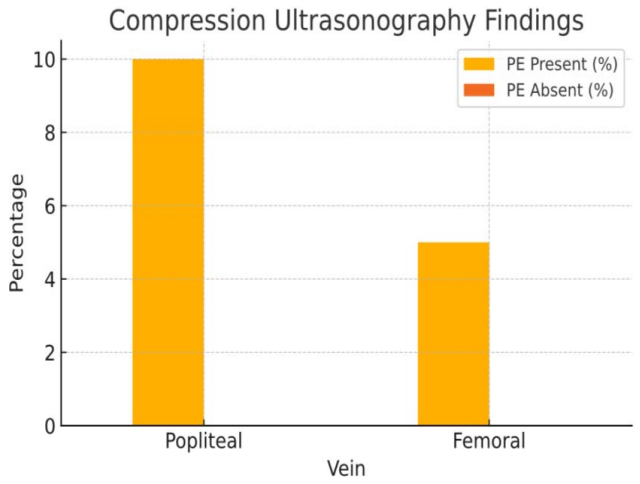


Figure 4: Two-point bedside compression ultrasound.

No statistically significant differences were noted between PE and non-PE groups regarding age, gender, or comorbidity burden. However, immobilization was significantly more frequent among those with PE. Risk factors like prior trauma, surgery, malignancy, or previous VTE history showed no statistical difference (Table 1). Pleurisy and asymmetry in lower limbs were more frequent among PE-positive patients (Table 2). Elevated D-dimer and NT-pro BNP levels were correlated with PE diagnosis (Table 3). Patients diagnosed with PE also had higher arterial pH values and reduced PaCO2 levels (Table 4).

Table 1: Clinical probability of 20 patients diagnosed with PE according to scoring systems used in study.

SCORING SYSTEM			
	LOW	MODERATE	HIGH
REVISED GENEVA	9 (45%)	7 (35%)	4 (20%)
WELL's	8 (40%)	5 (25%)	7 (35%)

Limitations

- Being a single-centre study, generalization remains limited.
- Small sample size necessitates larger multicentre studies for accurate prevalence estimation.
- Retrospective study design introduces possible selection bias.
- Two patients who left against medical advice were excluded, which could further impact the findings.

Table 2: Clinical presentations and symptomatology.

CLINICAL FEATURES	PE Present (5 patients)	PE Absent (15 patients)
Pleuritic chest pain	3 (60%)	2 (13.33%)
Lower limb asymmetry	2 (40%)	0
Hemoptysis	3 (60%)	6 (40%)
Shock	4 (80%)	3 (20%)

Table 3: Incidence of positive dimer and BNP levels.

LAB VALUE	PE Present (5 patients)	PE Absent (15 patients)
Positive D-DIMER	80%	5%
Positive NTproBNP	78%	52%

Table 4: Mean pH, PCO2, and PaO2 values.

ABG	PE Present (5 patients)	PE Absent (15 patients)
MEAN pH	7.52	7.23
Mean Pco2	29 mmhg	57 mmhg
Mean PaO2	68 mmhg	72 mmhg

Discussion

Our study identified pulmonary embolism (PE) in 25% of patients admitted for COPD exacerbation (AECOPD). Literature reports vary, showing prevalence rates between 2% and 29.1%. In their 2006 study, Tillie-Leblond et al. reported a 25% prevalence of PE in patients hospitalized in a single centre for COPD exacerbation [7]. Similar results were shown by Gunen et al. who showed prevalence at 29.1% [8. However, contrasting results were reported by Rutschmann et al. in 2007 who noted a significantly lower 3.3% prevalence, which was declared as such probably due to a selection bias [17]. A few studies from Asia, including studies from India and Korea showed PE prevalence of 2% and 5%, respectively.

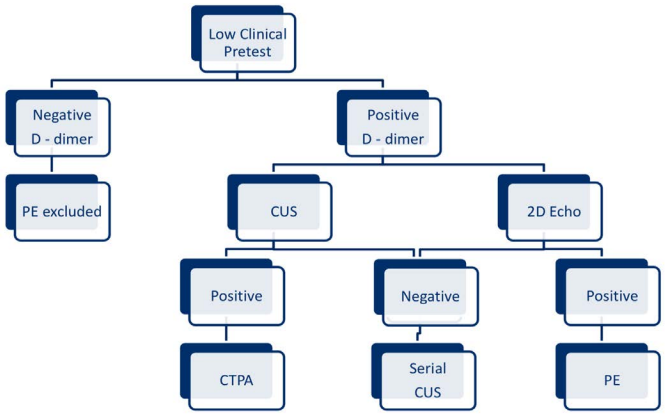
A meta-analysis incorporating seven studies reported a pooled PE prevalence of 16.1% in unexplained COPD exacerbations [2]. Variations across studies can be attributed to differences in sample size, patient selection, study methodologies, and diagnostic tools used (V/Q scans vs. CTPA). In our analysis, the revised Geneva Score better stratified PE risk in COPD exacerbations compared to Wells' Score. Key factors in patient history were immobility, pleurisy, and syncope. Leg asymmetry, severe hypoxemia, and shock stood out as the main clinical signs on examination. Arterial blood gas analysis showed that an elevated pH along with a reduction in PaCO2 levels > 5 mm Hg below baseline were significant for risk-prediction of pulmonary embolism in these patients.

Neither electrocardiography nor chest radiography proved reliable for diagnosing PE. We observed that a combination of low pre-test probability (based on scoring systems), negative D-dimer, and normal compression ultrasound offered an excellent negative predictive value for PE. Conversely, a high pre-test probability, alongside either a positive compression ultrasound or a positive McConnell's sign on two-dimensional echocardiography, demonstrated high positive predictive value. It was also noted that venous thromboembolism (VTE) and PE often coexist, with about 60% of PE patients also showing deep vein thrombosis (DVT) on compression ultrasound. Skilful clinical screening could potentially reduce the need for CTPA in selected patients.

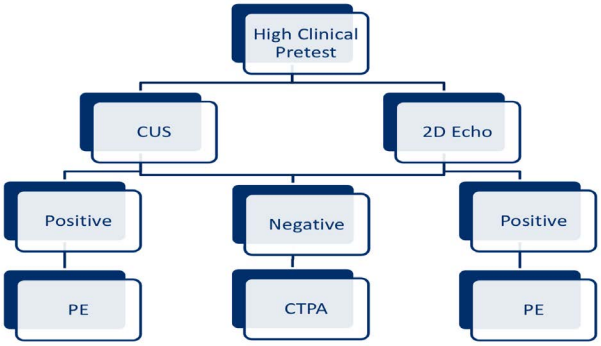
Recommendations

Based on our study, we propose integrating standardized diagnostic algorithms for evaluating suspected PE among patients presenting with AECOPD in emergency settings. However, clinical judgment, individualized patient assessment, and institutional capabilities must guide final decision-making.

Diagnostic algorithm recommendation – I



Diagnostic algorithm recommendation – II



Future Research Directions

While our results provide meaningful insights, further investigations are warranted:

1. Larger multicentre trials: broader studies across diverse populations are needed to establish the actual incidence of PE during COPD exacerbations.
2. Optimization of diagnostic protocols: future studies should focus on refining non-invasive diagnostic pathways, minimizing unnecessary radiation exposure, and reducing healthcare costs through more systematic screening.
3. Long-term research outcomes: additional research is required to explore the impact of PE on disease trajectory, rehospitalisation, and mortality rates in COPD patients.

Conclusion

There exists a notable prevalence of pulmonary embolism in acute COPD exacerbations, emphasizing the need for vigilance, early recognition, and systematic diagnostic evaluations. All patients presenting to the Emergency Department with acute exacerbation of COPD should be screened for presence of underlying pulmonary embolism.

While computed tomography pulmonary angiography (CTPA) remains the diagnostic gold standard, careful clinical assessment and appropriate use of predictive tools can enhance early detection. Prompt anticoagulation therapy upon diagnosis remains vital to patient outcomes.

Key Points

1. Pulmonary embolism continues to be an underdiagnosed, yet critical complication in the context of COPD exacerbations.
2. Despite advancements in diagnostics and therapeutics, early identification challenges persist.
3. Future emphasis must be placed on clinician education, implementation of clinical protocols, and ongoing research to improve detection rates and patient prognosis.

References

1. Bagot CN, Arya R. Virchow and his triad: a question of attribution. Br J Haematol. 2008; 143: 180-90.
2. Halbert RJ, Natoli JL, Gano A, et al. Global burden of COPD: systematic review and meta-analysis. Eur Respir J. 2006; 28:5 23-32.
3. Yang R, Liu G, Deng C. Pulmonary embolism with chronic obstructive pulmonary disease. Chronic Dis Transl Med. 2021; 7: 149-156.
4. Calverley PM, Walker P. Chronic obstructive pulmonary disease. Lancet 2003; 362: 1053-1061.
5. Akpinar EE, Hoşgün D, Akpinar S, et al. Incidence of pulmonary embolism during COPD exacerbation. J Bras Pneumol. 2014; 40: 38-45.
6. Couturaud F, Bertoletti L, Pastre J, et al. Prevalence of Pulmonary Embolism Among Patients With COPD Hospitalized With Acutely Worsening Respiratory Symptoms. JAMA. 2021; 325: 59-68.
7. Tillie-Leblond I, Marquette CH, Perez T, et al. Pulmonary embolism in patients with unexplained exacerbation of chronic obstructive pulmonary disease: Prevalence and risk factors. Ann Intern Med. 2006; 144: 390-396.
8. Gunen H, Gulbas G, In E, et al. Venous thromboemboli and exacerbations of COPD. Eur Respir J. 2010; 35:1243-1248.
9. Ra, S.W, Sin, D.D. Should We Screen for Pulmonary Embolism in Severe COPD Exacerbations? Not Just Yet, Primum Non Nocere. Chest. 2017; 151:523-524
10. Gregory Le Gal, Marc Righini, Pierre-Marie Roy, et al. Prediction of pulmonary embolism in the emergency department: the revised Geneva score. Ann Intern Med. 2006; 144: 165-71.
11. Michel L, Rassaf T, Totzeck M. Biomarkers for the detection of apparent and subclinical cancer therapy-related cardiotoxicity. J Thorac Dis. 2018; 10: S4282-S4295.
12. Le Gal G, Righini M, Sanchez O, et al. A positive compression ultrasonography of the lower limb veins is highly predictive of pulmonary embolism on computed tomography in suspected patients. Thromb Haemost. 2006; 95: 963-6.

13. Zantonelli G, Cozzi D, Bindi A, et al. Acute Pulmonary Embolism: Prognostic Role of Computed Tomography Pulmonary Angiography (CTPA). Tomography. 2022; 8: 529-539.
14. Doğan H, de Roos A, Geleijins J, et al. The role of computed tomography in the diagnosis of acute and chronic pulmonary embolism. Diagn Interv Radiol. 2015; 21: 307-16.
15. Naoum JJ. Anticoagulation Management Post Pulmonary Embolism. Methodist Debakey Cardiovasc J. 2024; 20: 27-35.
16. Aleva FE, Voets LW, Simons SO, et al. Prevalence and localization of pulmonary embolism in unexplained acute exacerbations of COPD: A systematic review and meta-analysis. Chest 2017; 151: 544-554.
17. Rutschmann OT, Cornuz J, Poletti PA, et al. Should pulmonary embolism be suspected in exacerbation of chronic obstructive pulmonary disease? Thorax. 2007; 62:121-5.