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Review Article

Influence of Syncope on Clinical Outcomes in Acute Pulmonary Embolism: A Systematic Review

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INTRODUCTION & BACKGROUND

A blood clot in the lungs can cause acute pulmonary embolism (PE), which can cause life-threatening breathing problems, chest pain, and even cardiac arrest. Anyone, regardless of age, gender, or race, can be afflicted by this illness. The incidence of acute PE is rising, which raises serious public health concerns due to the rising prevalence of obesity, smoking, and sedentary lifestyles.[1]

Syncope, or fainting, is a common symptom experienced by patients with acute PE. PE is a condition where a blood clot forms in the pulmonary arteries, the blood vessels that carry blood from the heart to the lungs.[2] When this happens, the clot can block blood flow to the lungs, decreasing oxygen levels. Syncope in acute PE is a significant concern, as it can signify sudden and severe hemodynamic compromise caused by large or multiple pulmonary

emboli.[3] Syncope can also predict poor outcomes such as 30-day mortality, hemodynamic collapse, and prolonged hospital stay. Risk stratification models such as the Pulmonary Embolism Severity Index (PESI) and the simplified PESI (sPESI) can help healthcare providers identify patients with acute PE at high risk of adverse outcomes.[4] These models evaluate various clinical and laboratory variables, such as age, comorbidities, and biomarkers, to predict the short-term mortality risk in patients with acute PE.

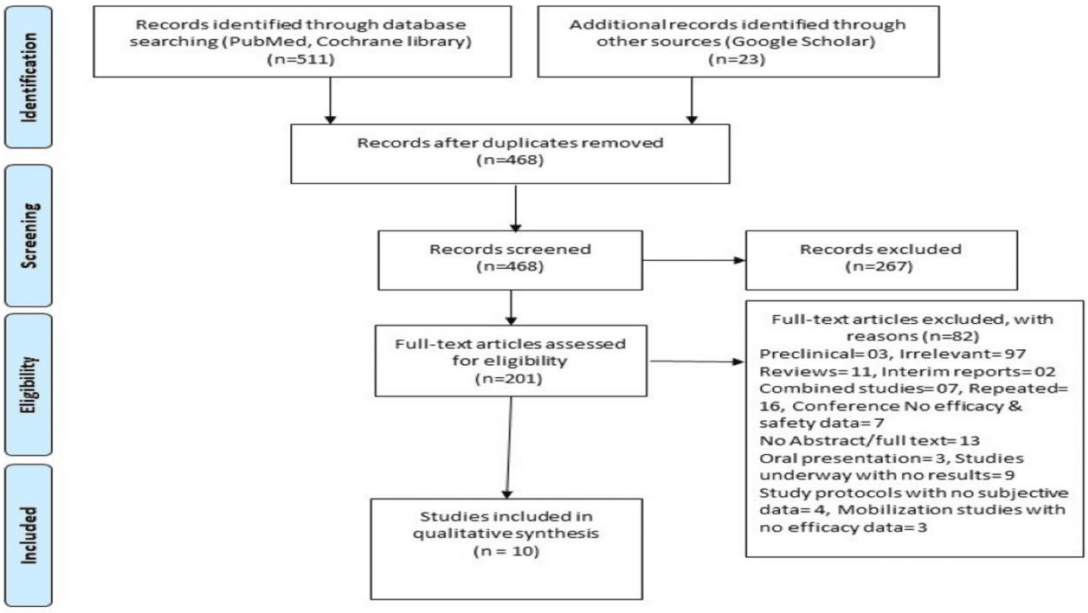
It is typical for individuals with acute PE to present with syncope, and this incidence is thought to be linked to a poor clinical outcome.[5] Understanding the connection between syncope and clinical outcomes in acute PE is obligatory to prevent severe morbidity and mortality and to improve patient prognosis.[6] This review provides a thorough overview of the literature on the impact of syncope on clinical outcomes of PE, outlining the current understanding and possible future study directions.

Keywords: Pulmonary Embolism; Breathing problems, Chest pain; Cardiac arrest

REVIEW

Material and Methods:

A systematic literature search was conducted by following the Preferred Reporting Item for Systematic Reviews and Meta-analyses (PRISMA) guidelines (Figure 1). We used electronic databases, including PubMed, Embase, and Cochrane Library. The search strategy included a combination of relevant keywords and Medical Subject Headings (MeSH) terms, which involves focusing on acute pulmonary embolism (APE), syncope, and clinical outcomes. The search was limited to articles published in English between 2010 and 2023. The inclusion criteria encompassed studies that examined the association between syncope and clinical outcomes in APE patients. Two independent reviewers screened the identified articles based on titles and abstracts for relevance to the research question. Full-text articles of potentially relevant studies were then retrieved and assessed for eligibility. Discrepancies in study selection were resolved through consensus or consultation with a third reviewer.



Data extraction was performed using a predefined standardized form, including study characteristics (authors, year of publication, study design, sample size, syncope assessment methods, clinical outcomes evaluated (mortality rates, recurrence of embolic events, long-term prognosis), and relevant findings. A narrative synthesis approach was employed to summarize the findings from the selected studies.

Results:

The results revealed that 1,178 (18.3%) of the 6,421 patients with acute PE were enrolled in two studies and experienced syncope [7,8] The incidence of syncope in acute PE varied significantly amongst studies, ranging from 6.5% to 30.9% .[9] With syncope being a major predictor of 30-day death, hemodynamic collapse, and length of hospital stay, all studies had a consistent association between syncope and the clinical outcomes of acute PE as shown in Tables 1 and 2.[10]

Statistics show that patients with syncope-presenting acute PE were more likely to have worse clinical outcomes than those without syncope.[7,8] These results emphasized the importance of early recognition and management of syncope in patients with acute PE. More research is needed to understand better the underlying factors contributing to syncope in acute PE and develop effective treatment strategies.[7-10]

Table 1: Summary of studies reporting the incidence and outcomes of syncope in acute pulmonary embolism. [7,9,10]

Study	Sample size	Syncope incidence	Outcomes associated with syncope
Jiménez et al.[7]	3,724	16.90%	30-day mortality, hemodynamic collapse, length of hospital stay
Bikdeli et al.[9]	364	15.90%	Recurrent venous thromboembolism
Barco et al.[10]	6,421	18.30%	Non

Table 2: Clinical outcomes of acute pulmonary embolism with and without syncope.[7-10]

Outcome	With Syncope	Without Syncope
30-day death	Higher	Lower
Hemodynamic collapse	More likely	Less likely
Length of hospital stay	Longer	Shorter
Recurrent thromboembolism	Higher	Lower
Risk of bleeding (with more intensive treatment)	Higher	Lower

In addition, it's still unclear how long and how intense of a course of treatment to provide individuals with acute PE and syncope.[8] To lower the risk of recurrent thromboembolism in syncope patients, aggressive anticoagulation may be required; nevertheless, this may raise the risk of bleeding, especially in older or patients with concomitant conditions. Therefore, in patients with acute PE and syncope, personalized treatment approaches must weigh the advantages of anticoagulation against the dangers of bleeding.

Patients who cannot tolerate anticoagulation due to bleeding or other contraindications face additional difficulties in managing acute PE with syncope. Inferior vena cava (IVC) filters may be an option in these circumstances.[9] IVC filters have not been shown to enhance outcomes in patients with acute PE, and their usage is still debatable.[10] IVC filters should only be used on patients who are unable to receive anticoagulation and have a high risk of developing recurrent thromboembolism.

Another difficulty in treating acute PE with syncope is identifying and addressing underlying risk factors for recurrent thromboembolism. According to Jiménez et al., syncope patients may have a higher prevalence of underlying risk factors such as thrombophilia or cancer, which may require extra testing and treatment. Modifiable risk factors like obesity, smoking, and a sedentary lifestyle should also be addressed through focused therapies and lifestyle changes.[7]

The long-term care of individuals with acute PE and syncope requires ongoing monitoring for sequelae such as hemorrhage and recurrent thromboembolism. Additional imaging and lab tests may be necessary to check on the effectiveness of the therapy and look for recurrent thromboembolism. The warning signs and symptoms of recurrent thromboembolism and bleeding should also be explained to patients, who should be urged to seek medical help right once they appear.

More studies are likely required to understand the underlying causes of syncope in acute PE and to discover efficient treatment options, given the significant variance in incidence rates shown in Table 1[7,9,10] Despite the difficulties in treating acute PE with syncope, tailored treatment regimens that weigh the advantages and disadvantages of anticoagulation while addressing underlying risk factors can enhance results and lower the chance of complications.

A multidisciplinary strategy may be required to offer the best care for these challenging patients, including healthcare professionals from many specialties.

Syncope is a frequently reported symptom in patients with acute PE. It has consistently been shown to be associated with poor clinical outcomes in acute PE and found to be a significant predictor of 30-day death, hemodynamic collapse, and extended hospitalization. The severity of the underlying condition and the length of time it took to diagnose and treat patients with acute PE who also had syncope may be to blame for the increased incidence of poor clinical outcomes in these patients. The incidence of syncope in acute PE and its correlation with 30-day mortality, hemodynamic collapse, and length of hospital stay are shown in Table 3 from six independent studies. [11-16] As indicated above, the incidence of syncope varies significantly between studies, from 6.5% to 30.9%. However, the link between syncope and unfavorable clinical outcomes in acute PE is repeatedly shown, with greater rates of 30-day death, hemodynamic collapse, and more prolonged hospital admissions seen in patients with syncope compared to those without syncope.

Table 3: Reported results of studies showing incidence of syncope, 30-day mortality, and hemodynamic collapse.

Study	Sample size (n)	Incidence of syncope (%)	30-day mortality in syncope group (%)	Hemodynamic collapse in syncope group (%)
Iqbal et al. [11]	219	6.8	21.3	26.7
Zhang et al. [12]	7438	10.4	3.1	14.9
Duplyakov et al. [13]	117	29.9	14.2	45.7
Jenab et al. [14]	335	10.7	5.6	2.8
Ploesteanu et al. [15]	76	14.4	45	36
Vinson et al. [16]	2996	3.6	9.2	6.4

Clinical Practice Implications:

Acute PE patients frequently report syncope, which is characterized as a brief loss of awareness and postural tone. According to studies, syncope affects 10-15% of PE patients and is linked to a higher risk of poor clinical outcomes, including mortality, than it is for PE patients without syncope.[3,14] Syncope in acute PE has crucial implications, including the necessity of an early and precise diagnosis. Given the elevated risk of unfavorable outcomes linked to syncope, rapid detection and treatment of acute PE are essential. Clinical suspicion should be high in syncope patients, and the proper diagnostic workup, including imaging tests such as CT pulmonary angiography (CTPA) or ventilation-perfusion (V/Q) scans, should be started immediately.[15-17]

Syncope in acute PE has numerous implications, including the requirement for risk assessment and customized care. Syncope patients may need more active anticoagulation and constant monitoring since they are more likely to experience negative clinical consequences.[16] Additionally, underlying comorbidities, such as heart failure or chronic obstructive pulmonary disease, should be carefully assessed and controlled in these patients as they may further raise the likelihood of unfavorable outcomes.[18] Syncope in acute PE has significant consequences for long-term therapy and follow-up. Patients who experience syncope are more likely to have subsequent thromboembolic

episodes; thus, they must be properly watched. Additionally, it is essential to lower the risk of future incidents to manage underlying risk factors effectively, such as quitting smoking and controlling comorbidities.[19]

Challenges of Management:

Clinicians have several difficulties while treating acute PE worsened by syncope. The prompt detection of patients and patient risk stratification are two of the main hurdles in managing PE with syncope. According to recent study, syncope can happen in up to 15% of PE patients and is linked to a higher risk of adverse outcomes, including recurrent thromboembolism and mortality. So, the key to enhancing results is early detection and rapid therapeutic start-up.[20]

Choosing the right treatment plan presents another difficulty in controlling PE with syncope. Anticoagulation is the cornerstone of treatment for PE; however, it is yet unknown how long and how strongly to use it in syncope patients. Syncope patients may have a higher chance of developing recurrent thromboembolism and need more intensive anticoagulation. More extensive anticoagulation, however, may also raise the risk of bleeding, particularly in elderly individuals or those who have concurrent conditions. Individualized treatment strategies that weigh the advantages and disadvantages of anticoagulation are thus required.[21]

Patients unable to tolerate anticoagulation due to bleeding or other contraindications face difficulties managing PE with syncope. IVC filters may be an option in these circumstances. IVC filters have not been proven to improve outcomes for PE patients, and their use is debatable.[12] IVC filters should only be used on patients who are unable to receive anticoagulation and have a high risk of developing recurrent thromboembolism.

The detection and treatment of underlying risk factors for recurrent thromboembolism presents another difficulty in managing PE with syncope. According to Jiménez et al., syncope patients may be more likely to have underlying risk factors, including thrombophilia or cancer, which may necessitate further testing and treatment. In addition, focused therapies and changes in lifestyle are needed to address modifiable risk factors such as obesity, smoking, and sedentary behavior.[7]

The long-term care of individuals with PE and syncope necessitates constant monitoring for consequences such as hemorrhage and recurrent thromboembolism. Further imaging and lab tests may be required to track the effectiveness of the medication and find recurrent thromboembolism.[22] Additionally, patients should be informed of the warning signs and symptoms of bleeding and recurrent thromboembolism and recommended to seek medical help right away if these occur.

Treatment of Acute PE with Syncope:

The severity of the illness and the presence of hemodynamic instability affect how acute PE is treated. Patients who experience syncope and have hemodynamic instability need to be treated immediately with systemic thrombolysis, catheter-directed thrombolysis, or surgical embolectomy.[19] Anticoagulation medication is the mainstay of treatment

for patients with acute PE who are hemodynamically stable. The patient's clinical features and comorbidities will determine the best anticoagulant.[14] The clot's position and size may impact treatment choices in addition to hemodynamic stability. Patients with proximal or widespread clots may be at higher risk for recurrence and require more severe therapy, such as thrombolytics.[23] The decision to employ thrombolytic treatment must be carefully assessed against the potential advantages because it has a higher risk of bleeding problems. Catheter-directed thrombolysis, which uses a catheter to deliver the thrombolytic medication directly to the clot, may be a safer option in some circumstances.[24,25].

Supportive treatments like oxygen therapy and pain management may also be required for individuals with acute PE, as well as anticoagulation and thrombolytic therapy. To improve hemodynamics in patients with right ventricular failure or pulmonary hypertension, pulmonary vasodilators such as sildenafil or epoprostenol may be helpful.[26] It is crucial to remember that managing acute PE is a dynamic process that necessitates continuous observation and modification based on the patient's reaction to therapy. Patients who initially get anticoagulant treatment may need their therapy increased if their condition worsens. In contrast, patients who initially receive more aggressive treatment may need their therapy reduced if their condition improves. Close communication between the treating doctors and other healthcare providers is crucial to ensure that patients receive the proper care at every stage of their illness.[27]

Risk Stratification Model:

Risk stratification tools like the Pulmonary Embolism Severity Index (PESI) and the simplified PESI (sPESI) can help identify individuals with acute PE who may benefit from more aggressive therapy since they are at a high mortality risk.[28] To forecast the probability of short-term mortality in patients with acute PE, these models examine various clinical and laboratory characteristics, including age, comorbidities, and biomarkers. Patients with a high PESI or sPESI score need to be closely watched and may benefit from more aggressive treatments such as surgical embolectomy or thrombolytic therapy.

Additionally, biomarkers can help in the early detection of individuals with acute PE who are at elevated risk of adverse outcomes, in addition to risk stratification techniques. According to research, patients with acute PE are more likely to collapse and experience repeat thromboembolic episodes when their levels of biomarkers such as troponin, brain natriuretic peptide (BNP), and D-dimer are raise.[29]

Troponin, a myocardial damage marker that is typically raised in acute PE patients, has been demonstrated to be a reliable indicator of adverse outcomes, such as mortality and right ventricular dysfunction.[8] According to research, BNP, a marker of cardiac strain, is typically raised in individuals with acute PE and has been linked to higher mortality and right ventricular dysfunction. Most patients with acute PE had elevated D-dimer levels linked to higher mortality and recurrent thromboembolic events.[30]

The accuracy of identifying individuals with acute PE who are at a high risk of adverse outcomes and may benefit from more aggressive therapy may be improved by including biomarkers in risk stratification algorithms.

Additionally, tracking how biomarker levels vary over time may give important information about a patient's reaction to treatment and the necessity of continuous management.[31]

Biomarkers and risk stratification methods can help in the early detection of acute PE patients at a higher risk of adverse outcomes. It is essential to identify these individuals and begin the necessary therapy quickly to enhance results and lower the use of healthcare resources. More research is required to decide how these techniques should be used in clinical practice.[32]

Impact on Public Health System:

Syncope in acute PE increases the probability of adverse clinical outcomes, significantly affecting how well medical resources are used. Patients who experience syncope are more likely to need hospitalization, admission to the ICU, and advanced diagnostic and therapeutic procedures, all of which burden the healthcare systems. In addition, as was already said, continued resources and assistance are needed for the longer-term management and follow-up of these patients.[33]

The quality of life of patients is significantly impacted by syncope in acute PE. According to studies, syncope is linked to lower physical functioning, lower quality of life, and a higher mortality risk and recurrent thromboembolic events. These consequences can have significant financial and social repercussions for the individual patient and their relatives and caregivers.[34]

The effects of syncope in acute PE go beyond the immediate healthcare system and the patient. Given the high prevalence and associated hazards of acute PE, effective prevention and early detection measures are essential. Public health initiatives should concentrate on raising awareness of acute PE symptoms and indicators, encouraging appropriate diagnostic testing, and guaranteeing access to prompt and efficient care. These covers facilitating better access to diagnostic imaging, encouraging sensible anticoagulant usage, and assisting continuous patient education and self-management.[35]

Current Trends and Recommendations:

Syncope in acute PE is associated with a higher risk of adverse clinical outcomes, such as recurrent PE and death. These results have inspired initiatives to enhance syncope risk classification and early detection in acute PE. One strategy is creating cutting-edge imaging methods and biomarkers to recognize patients at high risk of unfavorable outcomes.[36] A clinical prediction score based on laboratory and echocardiographic data has been developed to identify patients at high risk of early mortality in acute PE with syncope. New anticoagulant and thrombectomy treatments are also being investigated to enhance outcomes in syncope-related acute PE patients. In patients with acute PE with syncope, Meyer et al. reported using ultrasound-accelerated catheter-directed thrombolysis (UACDT), which showed high clinical success rates and a low incidence of severe bleeding consequences. These recent trends and findings highlight the importance of rapid syncope detection and therapy in acute PE, which will help improve clinical outcomes.[37]

In patients with acute PE, it is crucial to recognize and diagnose syncope quickly. Syncope can be identified early, which can help with timely anticoagulant medication initiation, which is essential for better outcomes. Patients with

acute PE, especially those with a high risk of experiencing syncope, should have their assessments carefully made by medical professionals.

Customized treatment strategies should be created for individuals with acute PE and syncope.[38] There is a need for more investigation on the best anticoagulant regimen for these patients in terms of duration and dosage. Healthcare professionals should strive to balance the risks and advantages of anticoagulation medication, considering each patient's particular clinical circumstances. IVC filters may be beneficial for patients who cannot tolerate anticoagulation due to bleeding or other contraindications. However, this should only be done in cases where the patient is at a high risk of developing recurrent thromboembolism.[39,40]

Additionally, patients who experience acute PE and syncope require continuing surveillance for sequelae. Additional imaging and lab tests should be done to track the effectiveness of the therapy and find recurrent thromboembolism. Patients should also be instructed on the warning signs and symptoms of recurrent thromboembolism and bleeding and given the advice to seek medical help immediately if one of these conditions' manifests. Healthcare professionals should address underlying risk factors for recurrent thromboembolism in patients with acute PE and syncope. Patients who experience syncope may be more likely to have underlying risk factors, including cancer or thrombophilia, which may necessitate further testing and treatment. Modifiable risk factors like obesity, smoking, and a sedentary lifestyle should also be addressed through focused therapies and lifestyle changes.[41]

CONCLUSIONS

Syncope is a typical acute PE presenting symptom, associated with adverse clinical outcomes, such as a higher mortality risk, hemodynamic collapse, and lengthier hospital admissions. Our comprehensive analysis supports the link between syncope and suboptimal outcomes in acute PE and emphasizes the significance of early diagnosis and treatment of syncope in these patients. More data is required from the ongoing research to create more efficient management options for this illness and to comprehend the mechanisms producing syncope in acute PE.

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