CJEM Journal Club

Prevalence of pulmonary embolism in syncope patients

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Clinical question
How often is pulmonary embolism (PE) found in patients admitted for syncope?
Article chosen
Prandoni P, Lensing A, Prins M, et al. Prevalence of pulmonary embolism among patients hospitalized for syncope (PESIT). *N Engl J Med* 2016;375:1524-31, doi: 10.1056/NEJMoa1602172.
Objective
To determine the prevalence of PE in patients hospitalized for a first episode of syncope.

Keywords: pulmonary embolism, syncope, venous thromboembolism

BACKGROUND

Syncope is defined as an abrupt and transient loss of consciousness with complete and sudden spontaneous recovery.[1] Episodes of syncope are a common reason for presentation to emergency departments (EDs), comprising up to 3% of visits.[2] The differential diagnosis for the etiology of syncope is wide and consists of neurologic, volume depletion, and cardiovascular causes such as pulmonary embolism (PE).[1] Due to more frequent etiologies for syncope, PE is considered to be an uncommon cause.[1]

Although PE is not a common cause of syncope, a syncopal episode can be an important symptom of PE.[3,4] Syncope as an initial presentation of PE has been reported to be as high as 10%.[5,6] However, accurate diagnosis of PE can be challenging because the most common clinical features – such as dyspnea, shock, syncope, and hemoptysis – have minimal diagnostic value in isolation.[4,7] The diagnosis of PE is exceptionally important because it is a common cause of hospital admission and mortality.[7,8] The Pulmonary Embolism in Syncope Italian Trial (PESIT) reviewed in this article was conducted to determine the prevalence of PE in patients hospitalized through the ED for syncope.

POPULATION STUDIED

Patients older than 18 years who presented to the ED and subsequently admitted to the medical ward for their first episode of syncope were enrolled in this study. Any patient with previous episodes of syncope or who received anticoagulants or was pregnant was excluded.

STUDY DESIGN

PESIT was a multicentre cross-sectional study with the primary objective of determining the frequency of PE in hospitalized patients. Once admitted to hospital, patients were assessed by physicians trained in the study protocol, according to the 2014 European Society of Cardiology (ESC) Syncope Guidelines and Simplified Wells Score.[1,9,10] All patients underwent chest radiography, arterial blood gas, and blood testing, including a D-dimer assay.

Patients with a high pretest probability based on the Wells Score and/or a positive D-dimer were sent for a computed tomography pulmonary angiogram (CTPA). If patients had a history of kidney impairment or contrast allergy, ventilation-perfusion (V-Q) scanning was used. An autopsy was used if patients died before imaging. For patients with a low pretest probability and a negative D-dimer, no further testing was done.

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OUTCOME MEASURED

The primary outcome was the presence of PE with an intraluminal filling defect on CTPA or a defect of at least 75% of a segment with corresponding normal ventilation.

RESULTS

Patients totalling 2,584 presented to the ED with syncope, of whom 717 were admitted to hospital; 118 patients were excluded due to current anticoagulation therapy for atrial fibrillation or unspecified reasons, 35 for recurrent syncope, and 4 refused consent. This left 560 patients with first episode of syncope to be included in the study. For 330 patients, PE was ruled out based on low pretest probability and a negative D-dimer. Of the remaining 230, 135 had a positive D-dimer only, 3 patients had a high pretest probability only, and 92 patients had both. PE was confirmed in 97 of the 230 patients. In patients hospitalized with syncope, the prevalence of PE was 17.3% (95% confidence interval, 14.2-20.5).

COMMENTARY

It is important to remember that the 17% prevalence of PE in syncope patients reported in PESIT was only for the patients admitted to the hospital and did not include all syncope patients who presented to the ED. From the ED, 72% were discharged with benign causes of syncope such as vasovagal or orthostatic. Patients with PE represented only 3.7% of the original ED syncope patients. However, this may underestimate the prevalence of PE in discharged patients because they were not systematically screened or followed for PE. The total number of syncope patients with PE in the ED in PESIT was still higher than the 1% prevalence of PE in syncope patients reported from previous studies.[11]

In the PESIT study, 27% of syncope patients from the ED were admitted to the hospital. A 27% admission rate for syncope was appropriate considering the wide variation in rates worldwide. For example, the 27% in PESIT was double the 13% in Canada, but less than the elevated 50% admission rate in the United States and Europe.[12-14] However, the criteria to admit to the hospital were not standardized, and the decision was made by physicians aware of the goals of the study. The cohort admitted to the hospital had multiple comorbidities such as cardiac disease and cancer and a median age of 80 years. This older and sicker cohort likely may have contributed to a higher estimation of prevalence of PE.

One reassuring finding is that many of the diagnosed PE patients had risk factors and clinical features consistent with PE. For example, 45% of patients with PE were tachypneic, 33% were tachycardic, 40% had signs of deep vein thrombosis (DVT), and 20% had active cancer. Consequently, many of these patients would have been considered high risk and would have been identified in the ED using common screening tools.[1,9,15,16] Screening for PE in patients with clinical signs of PE is appropriate; however, the blanket approach used in PESIT, where all syncope patients were screened, is not. This is especially relevant because 135 of the 235 hospitalized patients were imaged with a low pretest probability and a positive D-dimer only. In the case of low pretest probability, the Pulmonary Embolism Rule Out Criteria (PERC) rule should have been used to decrease the use of D-dimer testing and prevent over-imaging.[17]

Over-imaging in PE also increases the risk of false-positive imaging results. False-positive imaging rates are not insignificant with CTPA having 26% false-positive rate and V-Q scanning having up to 12% false-positive rate for high probability scans.[18,19] These rates may be due to a tendency for radiology to favor a positive result due to the consequences of a false-negative or "missed" PE. However, false-positive PEs are not benign and expose the patient to the unnecessary cost and bleeding risk of prolonged anticoagulation. Falsely diagnosed patients may also experience the stigma and anxiety associated with a label of PE.[20] For example, they may no longer qualify for travel insurance and often seek future medical aid for the mildest of symptoms.

Increased imaging with CTPA can also unveil asymptomatic PE or PE of uncertain clinical significance.[4,20] In PESIT, 25% of PE patients had no symptoms other than syncope. Other studies have shown that up to 3% of PEs are asymptomatic.[21,22] Therefore, many of the PEs may have been pre-existing and not the cause of syncope. From the results, it was impossible to determine the time of onset of the PE and whether PE was the cause of the syncope. In addition, some of the PEs found in PESIT may not have clinically significant or required treatment. For example, 6.9% of PEs diagnosed with a CT in PESIT were subsegmental, in which anticoagulation treatment is controversial.[23]

PESIT begs the question of whether all patients with syncope require a full workup to rule out PE.

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Systematic screening for PE in syncope patients with laboratory and radiographic investigation would lead to unnecessary testing, risks, and costs. Considering that PE is an uncommon etiology in ED syncope patients, continuing with the safe, cost-effective manner of using validated screening tools, such as the Wells Score and PERC rule, to assess pretest probability and decide D-Dimer testing is sufficient to rule out PE.[9,17]

CONCLUSION

The findings of the PESIT trial came as a surprise to many physicians who consider PE too low on the differential diagnosis for syncope. It is important to reiterate that the prevalence of PE in PESIT reflects older and multiple comorbid hospitalized patients and not the ED patient population. The findings may help bring PE to the front of the minds of ED physicians in the workup of unexplained syncope. This is a positive development considering the seriousness of PE; however, this could lead to increased costs and harm due to less discriminating CTPA use.

Competing interests: None declared.

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