DEM Journal Club

Article Appraisal

Article: Prandoni, Lensing, Prins et al. Prevalence of pulmonary embolism among patients hospitalized for syncope. N Engl J Med 2016;375:1524-31. doi:10.1056/NJEMoa1602172.

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Resident Reviewer Name(s) and Residency Affiliation: Paola Camorlinga (PGY-2) and Daniel Ting (PGY-3), FRCP Residency Program

Faculty Methodology/Bio-statistics Resource Person: Garth Hunte

Background and Study Objective(s):

Syncope is a common patient presentation in the emergency department (ED). Most patients have benign ED workups and can be safely discharged home, whereas some will require additional monitoring and admission. In previous studies, admitted patients with poor outcomes have primarily been patients with structural heart disease or arrhythmias. Another potential underlying, serious, and treatable cause in syncopal patients is pulmonary embolism (PE). Previous studies have diagnosed only 0-0.5% of their cohorts with PEs, but have also not indiscriminately worked patients up for PE [Quinn et al., Ann Emerg Med 2006(47)5; Birnbaum et al., Ann Emerg Med 2008 (52)2].

Study Design:

Multicenter, cross-sectional study conducted between March 2012 and October 2014. The study took place in 11 Italian hospitals (2 academic, 9 non-academic). Inclusion criteria were patients ≥ 18 years old presenting to ED with their first episode of syncope and admitted to hospital. Exclusion criteria were patients with previous syncope, anticoagulated, or who were pregnant. Patients were interviewed and evaluated by trained study physicians who were also investigators in the Pulmonary Embolism in Syncope Italian Trial (PESIT) team. This included a standardized history and physical that evaluated venous thromboembolism (VTE) symptoms and signs outlined by the Wells score, and a standard workup based on European cardiology clinical guidelines. As part of this workup, all patients received D-dimer testing. Patients with a Wells score ≥4 or positive D-dimer levels underwent CT pulmonary angiography (CTPA) or V/Q scan to test for PE. The primary outcome was the presence or absence of PE. A positive PE diagnosis was a patient with either: (a) intraluminal filling defect on CT; (b) perfusion defect of at least 75% of a segment with corresponding normal ventilation on V/Q scan; or (c) PE identified on autopsy. A negative PE diagnosis was considered in patients with a Wells score ≤4 and a negative D-dimer. Baseline characteristics between the groups with and without PE were compared with chi square (categorical variables) and student t tests (continuous variables). 95% confidence intervals and odds ratios were calculated with logistic regression.

Results:

The final study cohort included 560 patients. PE was diagnosed in 42.2% (97/230), and ruled out in 58.9% (330/560). Therefore the prevalence of PE in patients admitted with syncope is 17.3% (97/560). Many of the PEs represented large thromboses, as 68.9% (31/45) had a lobar or more proximal location of the thrombuson CTPA or a defect >25% of total lung area on V/Q scan. Significant differences between patients who were diagnosed with PE vs those who were not were identified. Patients in the PE group were more likely to have: previous VTE: OR 2.83 (95% CI 1.31-6.13); respiratory rate >20 breaths per minute: OR 10.80 (95% CI 6.34-18.45); HR >100 bpm: OR 2.55 (95% CI 1.56-4.19); systolic blood pressure < 110 mmHg: OR 1.90 (95% CI 1.19-3.04); signs of DVT: OR 14.20 (95%CI 7.79-25.71); active cancer: OR 2.21 (95% CI 1.23-3.97); and undetermined cause of syncope: OR 2.34 (95%CI 1.59-3.65).

Validity of Results:

The prevalence of PE in this study was higher than in previous studies of syncope. The precision of the result is reasonable, 17.3% (95% CI 14.2-20.5). Although the prevalence of PE is high, the clinical importance of these PEs is uncertain. Thrombotic burden itself does not directly correlate with symptoms or outcomes. It is possible many PEs were incidentalomas after indiscriminate use of D-dimer and subsequent imaging (detection bias). Furthermore, age-adjusted D-dimer was not used, which would have increased the amount of testing in a predominantly elderly population. In the PIOPED-2 study, CTPAs done in a low probability population yielded a PPV of 58% (i.e., false positives = 42%). The group with PE diagnosis excluded did not undergo imaging; having done so might also have identified a proportion of PEs that are clinically unimportant. The group diagnosed with PEs had a high rate of classic risk factors for VTE (75.3%, 73/97) suggesting that history and physical examination would have identified many of these patients.

Generalizability of Results:

In the ED, our patient population includes all patients who present, and who may or may not be admitted to hospital. From an ED perspective, the prevalence of PE among all patients presenting to the ED during the study period is 3.9% (97/2427). The subjects in this study were elderly (>75% older than 70 years of age) with multiple comorbidities. They study was conducted in Italy, and European cohorts studying PE have shown a higher rate of PE (~20%) compared with North American settings (e.g., ADJUST-PE, Christopher, Revised Geneva). Lastly, our local settings rarely use V/Q scanning for PE.

The Bottom Line:

First time syncope in an elderly population with comorbidities is generally a harbinger of serious underlying pathology. Indiscriminate use of D-dimer testing and subsequent imaging will identify a high prevalence of PE in elderly patients who are admitted to hospital for syncope. Although only admitted patients were studied, all of these patients transited through an ED. In our patient population, the prevalence of PE could be interpreted as ~4%, although the clinical importance of such a diagnosis is uncertain, including whether the identified PE was the cause of syncope or an incidental finding that would not affect prognosis. Therefore, a decision to anticoagulate patients should carefully consider risks and benefits. This study found that patients with PE generally show symptoms and signs classically associated with the diagnosis. We suspect that most of the clinically important PEs would have also been clinically apparent, meaning that we ought not change our practice based solely on these study findings.