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ORIGINAL ARTICLE

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Diagnostic yield of pulmonary embolism testing in patients presenting to the emergency department with syncope

Christopher Kelly MD[1] | Joseph R. Bledsoe MD[2,3] | Scott C. Woller MD[1,2] | Scott M. Stevens MD[1,2] | Jason R. Jacobs PhD[2] | Allison M. Butler MStat[2] | James Quinn MD[3]

[1]University of Utah, Salt Lake City, Utah

[2]Intermountain Medical Center, Murray, Utah

[3]Stanford University, Stanford, California

Correspondence
Christopher Kelly, University of Utah, Salt Lake City, Utah.
Email: christopher.kelly@hsc.utah.edu

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Abstract

Background: Syncope occurs in 1 in 4 people during their lifetime and accounts for 1% to 1.5% of emergency department (ED) visits. Most causes of syncope are benign, but syncope may be caused by life-threatening conditions including pulmonary embolism (PE) in up to 2% of cases. A recent publication reported the prevalence of PE in patients with syncope to be over 17%.

Aims: We sought to determine the frequency and diagnostic yield of testing for PE in patients presenting to the ED with syncope in our large, integrated health care system.

Methods: We performed a retrospective, longitudinal cohort study of patients who presented with syncope to EDs within a 21-hospital integrated health care system from 2010 to 2015 to find the frequency and diagnostic yield of testing for PE in patients with syncope at index ED visit and within 180 days afterward.

Results: We screened 2 749 371 ED encounters to find 32 440 (1.2%) with syncope. Median age was 52 (interquartile range, 31-71), 57.5% were female, and 90% were Caucasian. PE was diagnosed on the index ED visit in 259 (0.8%; 95% confidence interval [CI], 0.7%-0.9%) cases. Assessment for suspected PE with D-dimer occurred in 5089 (15.7%) patients, and 2338 (7.2%) underwent computed tomography pulmonary angiography (CTPA). The yield of CTPA was 7.9%. PE was detected in 2.2% in whom a D-dimer was performed. From index visit to 180 days, 467 (1.4%; 95% CI, 1.3%-1.6%) patients were diagnosed with a PE, and 1051 (3.2%, 95% CI, 3.0%-3.4%) patients died.

Conclusion: Diagnostic testing for PE is frequent in patients with syncope presenting to the EDs of a large, integrated health care system. The yield of diagnostic testing is low.

KEYWORDS

CT pulmonary angiogram, emergency medicine, pulmonary embolism, retrospective study, syncope

Essentials

- Syncope is a common presenting symptom in emergency department (ED) patients, with pulmonary embolism (PE) often considered as an etiology.
- We present a retrospective study conducted in a 24-hospital integrated health care network.
- Testing rates for PE are high in patients presenting to the ED with syncope.
- In patients presenting to the ED with syncope, PE is an uncommon diagnosis.

1 | INTRODUCTION

Syncope is a common symptom encountered in the emergency department (ED) and occurs in an estimated 1.5% of ED visits.[1–5] The American College of Cardiology/American Heart Association/Heart Rhythm Society 2017 guidelines define *syncope* as "a symptom that presents with an abrupt, transient, complete loss of consciousness, associated with inability to maintain postural tone, with rapid and spontaneous recovery."[6] The etiologies of syncope range from benign to potentially life-threatening pathologies.[5,7,8] Pulmonary embolism (PE) is often considered as an etiology for syncope, but the likelihood of finding PE in patients presenting with syncope has varied substantially across studies.[5,9–13] The Pulmonary Embolism in Syncope Italian Trial (PESIT) evaluated patients admitted to the hospital after their first syncopal episode and reported an overall prevalence of PE of 17.3%.[9] This reported prevalence rate was significantly higher than previous studies. Costantino et al conducted a multinational retrospective, observational study and found an overall rate of PE in patients presenting with syncope to range from 0.06% to 0.55% (a subgroup analysis of patients with similar characteristics to those enrolled in the PESIT trial revealed a rate of only 0.15%-2.10%).[10] An additional study published by Verma et al[13] found rates of 1.4% for venous thromboembolism (VTE), which included diagnosed PE or isolated deep venous thrombosis. A prospective single-center cohort study by Frizell et al,[12] found an overall rate of PE diagnosis at 30 days of 1.4% in ED patients presenting with syncope.

None of these trials evaluated rates of diagnostic testing for suspected PE in patients presenting to the ED following syncope. Therefore, the rate of testing for PE, and the diagnostic yield of testing in ED patients with syncope, remains largely unknown. We hypothesized that the rate of PE diagnosis among patients with syncope in our integrated health network would be closer aligned to previous studies and substantially lower than that of PESIT. We designed a study to determine this rate, as well as the rate of testing for PE in patients with syncope and the diagnostic yield of testing. We measured the rate of D-dimer testing and computed tomography pulmonary angiography (CTPA), as well as the rate of PE diagnosis at the index ED visit for syncope. We then assessed the rate of PE and death for 180 days following the index visit.

2 | METHODS

This was a retrospective, longitudinal cohort study that included all patients, age 18 or older, presenting with syncope to any of the 21 EDs in an integrated health system from January 1, 2010, through December 31, 2015. Intermountain is a 24-hospital integrated health care network with an incorporated health insurance company caring for >60% of patients in the state of Utah that allows for a roughly 90% follow-up rate. Data from 3 hospitals within the system were unable to be obtained. For each identified case, we assessed whether testing for PE was performed and whether PE was diagnosed. Finally, clinically overt PE occurring within 180 days of the index ED presentation was evaluated by electronic health record EHR interrogation for all patients. We determined the diagnostic yield of testing for PE by dividing the number of confirmed cases by the number of patients tested in the initial ED encounter (diagnostic testing for PE in subsequent encounters was not counted in this measure). The integrity of EHR interrogation for capture of extracted data elements was confirmed through manual chart review by one author (JB) prior to data extraction from the EHR.

Syncope was determined using International Classification of Diseases (ICD) codes at discharge (ICD-9: 780.2, ICD-10: R55). D-dimer (internal code) and CTPA (CPT: 71 275) testing was assessed using a query of the enterprise data warehouse (EDW) matched to the encounter identifier of the identified syncope cases. Confirmed PE was determined using ICD codes (ICD-9: 415, ICD-10: I26). Only the first encounter at which a patient presented with syncope was included, and subsequent encounters were used to identify 180-day events during the follow-up period. Unique patients were identified on index visit by enterprise master patient index, and any subsequent encounters were excluded in our analysis. We reviewed 1959 randomly selected charts through a combination of a validated natural language processing (NLP) tool continuously screening CT scans for PE diagnoses and hand review for accuracy of PE diagnoses.[14] Deaths were confirmed by use of the EDW master death file, which is derived from the State of Utah Mortality Registry.

Descriptive statistics were performed for patient data and are reported as means with standard deviation, unless specified as median and interquartile range. Logistic regression modeling was performed to identify the odds ratios associated with the predictor variables and the primary outcome. The study was approved by the Intermountain Healthcare Institutional Review Board (no. 1050574).

3 | RESULTS

From January 1, 2010, to December 31, 2015, a total of 2 749 371 ED visits were screened, and 32 440 (1.2%) adult patients met the inclusion criteria of presentation to the ED for syncope. Study population demographics are listed in Table 1. The median age

TABLE 1 Characteristics of patients presenting to the emergency department with syncope from 2010-2015, according to pulmonary embolism status

Variable	All patients	PE confirmed	PE ruled out
N	32 440	467	31 973
Age			
Median (IQR)	52 (31-71)	65 (49-76)	51 (31-71)
Sex, n (%)			
Male	13 778 (42.5)	225 (48.2)	13 553 (42.4)
Female	18 661 (57.5)	242 (51.8)	18 419 (57.6)
Missing	1 (0)	0 (0)	1 (0)
Race, n (%)			
Other	3010 (9.3)	29 (6.2)	29 871 (9.3)
White	29 430 (90.7)	438 (93.8)	28 992 (90.7)
Heart rate >95 beats/min, n (%)	4333 (13.4)	102 (21.8)	4231 (13.2)
Troponin >0.04 ng/mL, n (%)	1098 (3.4)	107 (22.9)	991 (3.1)
BNP elevated, n (%)	1136 (3.5)	54 (11.6)	1082 (3.4)
Systolic blood pressure <90 mm Hg, n (%)	1360 (4.2)	32 (6.9)	1328 (4.2)
Previous VTE, n (%)	2007 (6.2)	191 (40.9)	1816 (5.7)
Previous cancer, n (%)	1751 (5.4)	63 (13.5)	1688 (5.3)
Previous cardiac disease, n (%)	5235 (16.1)	162 (34.7)	5073 (15.9)
Venous thrombosis in ED, n (%)	382 (1.2)	266 (57)	116 (0.4)
Congestive heart failure, n (%)	2414 (7.4)	67 (14.3)	2347 (7.3)
Coronary artery disease, n (%)	2595 (8)	57 (12.2)	2538 (7.9)
Ventricular heart disease, n (%)	582 (1.8)	11 (2.4)	571 (1.8)

Abbreviations: BNP, brain natriuretic peptide; ED, emergency department; IQR, interquartile range; PE, pulmonary embolism; VTE, venous thromboembolism.

of patients in the study was 52 years (interquartile range, 31-71). Most (57.5%) patients were female, and the majority (90.7%) were Caucasian (reflecting demographics in the geographic area) (Table 1).

Pulmonary embolism was diagnosed during the initial encounter in 259 patients; 0.8% (95% confidence interval [CI], 0.7%-0.9%) of the population with syncope (Table 2). PE in the ED was diagnosed in 66 patients, with 60 confirmed by a combination of NLP and manual chart review (91%). An additional 208 patients were diagnosed with PE within 180 days after the initial ED visit. Therefore, the total number of patients diagnosed with a PE (at presentation or during 180-day follow-up) was 467 (1.4%; 95% CI, 1.3%-1.6%). At 180-day follow-up, 1051 (3.2%; 95% CI, 3.0%-3.4%) patients had died.

TABLE 2 Outcomes of patients presenting to the ED with syncope on initial presentation and up to 180 days' follow-up

	Total	N	Percent (95% CI)
PE in ED	32 440	259	0.8 (0.7-0.9)
PE from ED to 180 days' follow-up	32 440	467	1.4 (1.3-1.6)
Death up to 180 days' follow-up	32 440	1051	3.2 (3-3.4)

Abbreviations: CI, confidence interval; ED, emergency department; PE, pulmonary embolism.

Of the 32 440 encounters, PE testing was conducted in 5964 (18.4%) during the index ED visit. D-dimer testing was performed without subsequent imaging in 3626 (11.2%) encounters. CTPA was performed without a D-dimer test in 875 (2.7%) encounters. Both D-dimer testing and CTPA were performed in 1463 (4.5%) encounters. The yield of CTPA was 7.9% (184 of 2338 patients imaged) (Table 3). PE was detected in 2.2% (113 of 5089 patients) using imaging strategies other than CTPA. Of the total included cohort, 74% (n = 23 923) had a subsequent ED or hospital visit within 365 days of the index visit.

We identified patient characteristics associated with a higher likelihood of PE. The odds of PE were 8.58 times higher in patients

TABLE 3 Diagnostic testing yield in patients presenting to the ED with syncope

	N	PE confirmed	Testing yield, % (95% CI)
Other[a]	26 476	52	0.2 (0.1-0.3)
D-dimer only	3626	23	0.6 (0.4-1)
CTPA only	875	94	10.7 (8.8-13)
D-dimer and CTPA	1463	90	6.2 (5-7.5)
Total	32 440	259	
PESIT[b]	560	97	17.3 (14.2-20.5)

Abbreviations: CI, confidence interval; CTPA, computed tomography pulmonary angiography; ED, emergency department; PE, pulmonary embolism; PESIT, Pulmonary Embolism in Syncope Italian Trial.

[a]Identified based on combination of ventilation-perfusion scan or comprehensive lower extremity ultrasound with high clinical suspicion for concomitant PE.

[b]Based on PESIT CONSORT diagram, 560 patients were included in their study; 330 of these patients had PE ruled out by low pretest probability and negative D-dimer; 230 patients had high pretest probability and/or positive D-dimer. Of 560 patients, the total number of PEs diagnosed was 97.

with a prior VTE; 5.67 times higher in patients with a positive troponin; 1.75 times higher in patients with initial heart rate >95 beats per minute; 1.69 times higher in patients with a current or previous diagnosis of cancer; 1.52 times higher in patients of white race, and 1.37 times higher in patients with a previous cardiac history. For every 10 years above the median age of 52, the odds of a PE diagnosis increases by 10% (Table 4). CTPA yield for patients ≤60 years is 8.3%. CTPA yield for patients >60 years is 7.6%. A 2-sample test of proportions is not significant, showing that CTPA yield is not different by age category (P = .589).

4 | DISCUSSION

Our study used a large, integrated hospital health care system database to evaluate PE diagnostic testing for patients presenting to the ED with an episode of syncope. We demonstrated a low diagnostic rate of PE at both index ED visit and over a 180-day follow-up. This result was in line with previous studies, which found the rate of PE to be <1.5%.[12,13,15] Despite the low prevalence, 15.7% of all patients underwent D-dimer testing, and 7.2% had CTPA performed. The diagnostic yield of testing for PE with CTPA was 7.9%. While ED clinicians appear to be selective in targeting patients with syncope for diagnostic testing for PE, the low diagnostic yield suggests that further efforts are needed to better identify the subpopulation of syncope patients likely to have PE, so that the risk and expense of unnecessary imaging can be avoided.

The rate of PE in patients with syncope in our study is in agreement with several other studies[10–13,15] and is much lower than the rate found in the PESIT trial. However, the rates of testing for PE were not reported in these studies, suggesting the possibility of underascertainment.

TABLE 4 Factors associated with PE diagnosis from initial ED presentation to 180-day follow-up

Variable	Odds ratio (95% CI)	*P* value
Age	1.01 (1.00-1.01)	.03
Sex		
Female vs. male	0.94 (0.78-1.14)	.51
Race		
White vs. other	1.52 (1.05-2.29)	.04
Heart rate >95 beats/min	1.75 (1.37-2.22)	<.001
Troponin >0.04 ng/mL	5.87 (4.53-7.58)	<.001
BNP elevated	1.31 (0.93-1.80)	.11
Systolic blood pressure <90 mm Hg	1.14 (0.76-1.66)	.50
Previous VTE	8.58 (6.99-10.52)	<.001
Previous cancer	1.69 (1.26-2.25)	<.001
Previous cardiac disease	1.37 (1.10-1.70)	.005

Abbreviations: BNP, brain natriuretic peptide; CI, confidence interval; ED, emergency department; PE, pulmonary embolism; VTE, venous thromboembolism.

Importantly, the rates of testing for PE in the PESIT study appear to be similar to ours (after accounting for subjects screened for PESIT but not hospitalized), yet we found a much lower rate of PE. Assuming D-dimer testing was not performed in the PESIT patients discharged from the ED or excluded from the study, the D-dimer testing rate in that study was 21.6% (557/2584) compared to 15.7% in our study. CTPA was performed in 6.9% (180/2584) of patients in PESIT, compared to 7.2% in our study, yet the rate of PE at index ED visit in PESIT was >4.5 times that in our study (3.75% vs. 0.8%). The reason for this difference in PE diagnostic rate is not clear. It is possible that the PESIT trial overestimated the prevalence of PE in patients presenting with syncope due to high rates of testing and selecting a higher-risk population (only those subsequently hospitalized following syncope). A recent study of 9091 patients with syncope showed overall PE testing rates of 6%, with 56 of 386 (14.5%) receiving imaging diagnosed with a PE. Despite the lower rate of testing, their reported PE prevalence is 0.6%.[15] We believe that the prevalence of PE we report among patients who present to the ED with syncope aligns with the majority of studies and is supportive of the true rate of PE among patients with syncope assessed in the ED.

In addition to index visit PE diagnoses in the ED, we also conducted a 180-day follow-up and found the prevalence of subsequent diagnosis of PE to be only 1.4%. Previous studies have had shorter follow-up intervals (30-90 days).[10,12] Therefore, taking into consideration the follow-up timeline and our ability to capture encounters in our integrated health care system, we feel it is unlikely that we missed any clinically significant PE cases, yet we acknowledge that a small proportion of these patients likely experienced de novo PE independent of the initial ED visit.

Our findings demonstrate an overall low diagnostic yield of PE in patients presenting with syncope. We acknowledge that this likely includes a patient population of obvious benign etiologies of syncope and may represent a falsely low PE diagnostic rate. With this, if a patient presenting with syncope does not fit a benign etiology or there is clinical concern for PE, considering further workup is reasonable.

4.1 | Limitations

Given that our study included multiple hospitals, practice patterns may vary, and there was no standardized diagnostic pathway used in evaluating patients for syncope. While this may have led to differential use of diagnostic testing, it may make our findings more generalizable. In addition, given that our data were obtained retrospectively using ICD codes, it is possible that there were missed cases due to other applicable codes that were not used in data collection. Former reports suggest a rate of syncope as the chief complaint for an ED visit of approximately 1% to 3%.[16–18] We may have missed outcome events if patients reported to outside institutions following their initial ED visit in our system. However, the geographic isolation of the mountain West, and our integrated 21-hospital health care system which cares for about half of all

Utah residents creates an environment where most patients receive in-network follow-up care.

The homogeneity of our patient population (90% Caucasian) limits generalizing our results to more heterogeneous patient populations.

We were not able to ascertain the cause of the 1051 (3.2%) deaths, which occurred during the 180-day follow-up. It is possible that some of these were attributable to undiagnosed PE. Additionally, our 180-day follow-up period was longer than some previous studies, which may raise questions regarding the temporality of PE diagnosis to the patient's initial syncopal event. We feel that this would likely result in an overestimation rather than an underestimation of PE prevalence and, given our overall low rate, further supports the low yield of PE workup in patients presenting with syncope.

Additionally, some patients may have been missed due to our usage of ICD-10 codes. This includes those with other forms of syncope or loss of consciousness such as vasovagal reaction, transient loss of consciousness, and the like. This is, however, partially in line with PESIT, as patients with diagnoses such as "vasovagal reaction" would not have been admitted to the hospital for further testing and therefore would not have been included in their data set. Adding these diagnostic codes would have likely lowered our diagnostic yield of PE even further. We acknowledge that a limitation of using ICD codes inherently means that some patients with classic vasovagal syncope were included in our analysis and likely lowers the overall diagnostic rate of PE.

5 | CONCLUSION

The diagnosis of PE is frequently pursued in patients presenting to the ED with syncope, but the overall prevalence of PE at presentation and at 180-day follow-up is low. Improved strategies are needed to identify syncope patients at high probability of PE to avoid the risk and waste of low-yield diagnostic testing.

RELATIONSHIP DISCLOSURE

JRB has received investigator-initiated grant funding from Bristol-Myers-Squibb/Pfizer paid to his employer, Intermountain Healthcare, without financial benefit distributed to him. SCW has received investigator-initiated grant funding from Bristol-Myers-Squibb/Pfizer paid to his employer, Intermountain Healthcare, without financial benefit distributed to him. SMS has received investigatorinitiated grant funding from Bristol-Myers-Squibb/Pfizer paid to his employer, Intermountain Healthcare, without financial benefit distributed to him.

AUTHOR CONTRIBUTIONS

CK, JRB SCW, SMS, and JQ contributed to the writing of the draft manuscript. CK, JRB SCW, SMS, JQ, JRJ, and AMB contributed to the editing of the manuscript. JRJ and AMB contributed to the statistical analysis. CK was responsible for journal submission.

ORCID

Scott C. Woller https://orcid.org/0000-0002-2522-2705

TWITTER

Christopher Kelly @stEMi_CK

Joseph R. Bledsoe @jbledsoeslc

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