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Original article

How to recognize pulmonary embolism in syncope patients: A simple rule

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ABSTRACT

Background: Syncope can be the presenting symptom of Pulmonary Embolism (PE). It is not known wether using a standardized algorithm to rule-out PE in all patients with syncope admitted to the Emergency Departments (ED) is of value or can lead to overdiagnosis and overtreatment.
Methods: We tested if simple anamnestic and clinical parameters could be used as a rule to identify patients with syncope and PE in a multicenter observational study. The rule's sensitivity was tested on a cohort of patients that presented to the ED for syncopal episodes caused by PE. The clinical impact of the rule was assessed on a population of consecutive patients admitted for syncope in the ED.
Results: Patients were considered rule-positive in the presence of any of the following: hypotension, tachycardia, peripheral oxygen saturation $\leq$ 93 % (SpO2), chest pain, dyspnea, recent history of prolonged bed rest, clinical signs of deep vein thrombosis, history of previous venous thrombo-embolism and active neoplastic disease. The sensitivity of the rule was 90.3 % (95 % CI: 74.3 % to 98.0 %). The application of the rule to a population of 217 patients with syncope would have led to a 70 % reduction in the number of subjects needing additional diagnostic tests to exclude PE.
Conclusions: Most patients with syncope due to PE present with anamnestic and clinical features indicative of PE diagnosis. A clinical decision rule can be used to identify patients who would benefit from further diagnostic tests to exclude PE, while reducing unnecessary exams that could lead to over-testing and over-diagnosis.

1. Introduction

Pulmonary embolism (PE) is a known and potentially serious cause of syncope but the prevalence of PE in patients presenting with syncope remains unclear. In particular, while PE is reported as a rare cause of syncope in some studies, with a frequency below 1.5 % [1–5], its prevalence was as high as 10–17 % in others [6,7]. These broad differences highlight the need for a standardized approach to identify patients at high risk of PE that warrant further evaluation.

A clinical framework to easily recognize patients at high risk of PE is particularly relevant in Emergency Departments (ED) where syncope is a common condition, accounting for 1–3 % of the presenting symptoms [8–10]. In this context, physicians face the challenge of promptly identifying those patients who should be screened for PE through additional testing, while preventing unnecessary exams and clinically not relevant diagnoses [11–13].

The objective of our study was to evaluate whether the use of simple anamnestic and clinical parameters could help ED physicians to identify those patients with syncope that warrant further exams to exclude the presence of PE.

Abbreviations: PE, pulmonary embolism; ED, emergency department; DVT, deep venous thrombosis; VTE, venous thrombo-embolism; CTPA, computed tomography pulmonary angiogram; AF, atrial fibrillation; COPD, chronic obstructive pulmonary disease, SpO2, peripheral oxygen saturation.

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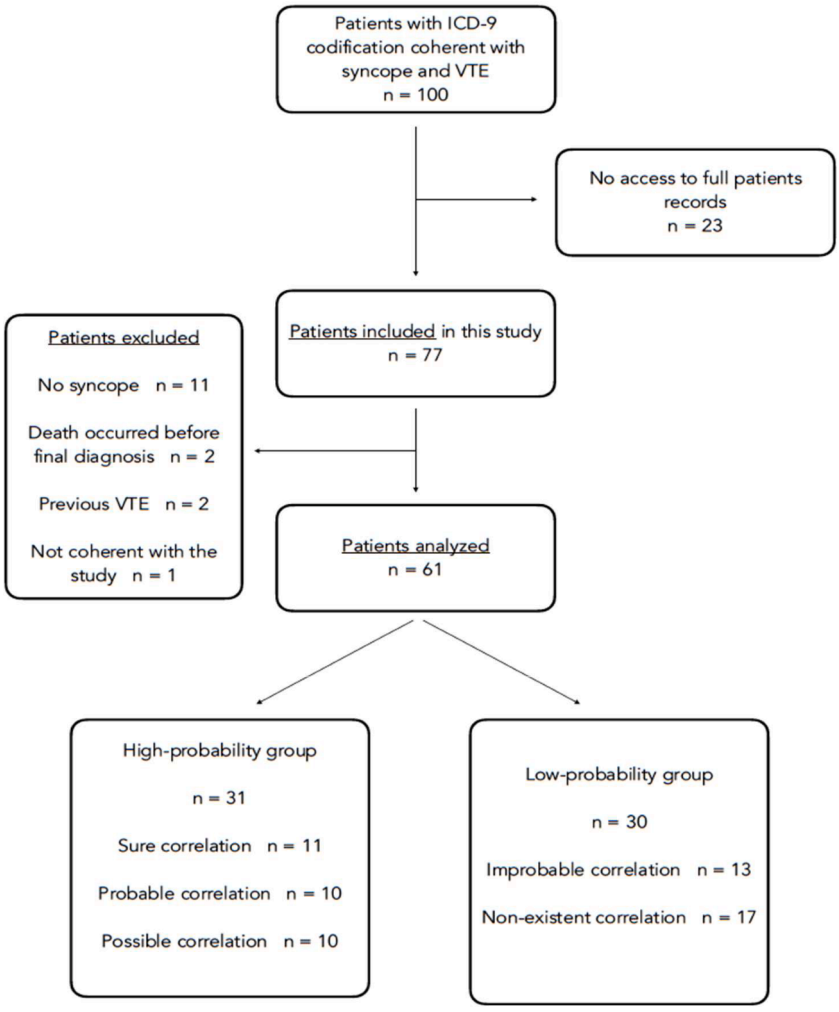

Fig. 1. Flow diagram of study population (Phase 2).

2. Study design and methods

We conducted a multicenter observational study based on a three phases design.

- *Phase 1. Identification of the relevant clinical parameters – Clinical rule.*

Three expert physicians (GCos, MB, MS), with clinical expertise in cardiology, emergency medicine and internal medicine, collegially selected clinical variables that could lead to suspect PE in patients with syncope.

We first performed a comprehensive review of the published literature, which was analyzed independently by each clinician to identify relevant variables. Next, a consensus on the most relevant clinical/anamnestic parameters was reached among the three experts by discussion. Finally, the selected variables were used as a clinical rule to identify patients most likely to have PE; therefore, subjects with at least one of these clinical parameters identified by the three experts were considered as patients in which PE should be excluded through further evaluations.

- *Phase 2. Assessment of the accuracy of the rule.*

Medical records of patients with PE and syncope were retrospectively collected from administrative databases and used to test the clinical decision rule. Clinical data were retrieved from the databases of ED visits and hospital discharges maintained by the Agency for Health Protection (Agenzia Tutela della Salute, ATS) of Milan (Italy), where diagnoses are stratified according to the International Classification of Diseases, Ninth Revision (ICD-9). We identified all adult patients (>18 years) who presented to the ED for syncope (ICD-9 code 780.2) in 22 different Emergency Departments of the metropolitan area of Milan between January 1st, 2014 and September 30th, 2016. Only patients with venous thromboembolism (VTE) (ICD-9 codes 415, 453.4, 453.5, 453.8, 453.9) diagnosed at the time of the ED access or in the following 90 days were included in the study. Additionally, patients were excluded based on the following criteria: (i) death before a final diagnosis of VTE could be made; (ii) incomplete medical records; (iii) wrongly attributed ICD code (e.g. not a real syncope event, or VTE referring to past medical history). The following data were collected: demographical characteristics (age and sex), medical history (neoplasia, prolonged bed rest, previous VTE), vital signs (blood pressure, heart rate and arterial oxygen saturation, SpO2), blood gas analysis, symptoms associated with the syncope, presence of VTE at the time of EDs admission or in the 90 days follow-up and PE pre-test probability using the simplified Geneva score [14]. Three ED physicians, who were blind to the rule, independently evaluated all the clinical records and, using their clinical judgment and expertise, estimated the probability that the syncopal episode was caused by PE. As a result, patients were classified in 5 distinct categories of PE probability: sure, probable, possible, improbable or non-existent. Conflicts between the physicians were resolved through discussion, and cases that could not be attributed to a specific category were

Table 1
Baseline characteristics of the Phase 1 Population ($N = 61$) and of the High - probability group ($N = 31$).

	Analyzed population ($n = 61$)	High probability group ($n = 31$)
Demographic features		
Age - median (IQR)	82	81
Male - N (%)	22 (36)	9 (29)
Female - N (%)	39 (64)	22 (71)
Vital signs		
Systolic Blood Pressure - median (IQR)	130 (110–150)	130 (110–150)
Systolic Blood Pressure < 100 - N (%)	8 (13)	3 (9.7)
Diastolic Blood Pressure - median (IQR)	70 (60–80)	70 (60–80)
Heart Rate - median (IQR)	84 (70–95)	87
Heart Rate > 100 - N (%)	14 (22.9)	9 (29)
Respiratory Rate > 18 - N (%)	4 (6.6)	2 (6.4)
SpO2 - median (IQR)	95 (92–98)	95 (92–98)
SpO2≤93 - N (%)	20 (32.8)	16 (51.6)
Hemogasanalysis		
pH - *mean*	7.4	7.4
pO2 - median	67.5	63.5
pCO2 - median	33	33.5
HCO3 - mean	23.3	23
Lactates - mean	1.8	1.8
Base Excess - mean	- 0.5	- 1.2
Alveolar-arterial gradient - mean	46.5	47.7
sO2 - mean	92.9	92
Features of syncope - N (%)		
Chest pain	5 (8.2)	4 (12.9)
Dyspnea	13 (21.3)	10 (32.3)
Presence of prodrome	22 (36)	12 (38.7)
Type of VTE - N (%)		
DVT	24 (39.3)	15 (48.4)
PE	52 (85.2)	29 (93.5)
- Saddle	4 (6.6)	4 (15.4)
- Lobar	8 (13)	6 (23)
- Segmental	15 (24.6)	4 (15.4)
- Bilateral	18 (29.5)	11 (42.3)
- Subsegmental	5 (8.2)	1 (3.8)
Risk factors for VTE - N (%)		
Signs of DVT	10 (16.4)	7 (22.6)
Previous PE/DVT	10 (16.4)	6 (19.3)
Recent lower limb fracture	3 (4.9)	2 (6.4)
Recent immobilization	10 (16.4)	8 (25.8)
Active cancer	10 (16.4)	4 (12.9)
Simplified Geneva score - N (%)		
High probability subjects (score ≥ 3)	28 (45.9)	14 (45)
Low probability subjects (score < 3)	33 (54)	17 (55)

assigned to the most likely probability class. Based on this approach, patients were divided in two groups: the low-probability group that included cases for which a causal relationship between VTE and syncope was reasonably excluded (indicated as improbable or non-existent by physicians); and the high-probability group that included patients with a sure, probable or possible correlation between VTE and syncope. Patients were then classified as being at high/non-high risk of PE according to the clinical rule identified in Phase 1.

- *Phase 3. Assessment of the clinical impact of the rule.*

To estimate clinical impact of the approach, defined as the number of patients for which an algorithm to exclude PE could be avoided, we applied the clinical rule (Phase 1) to a second cohort of patients with syncope enrolled in the SyMoNE prospective multicenter study [15]. As done for the population in Phase 2, all clinical charts were evaluated retrospectively, and data on clinical and demographical variables were collected, including the characteristics of the syncopal episode and the presence of the clinical parameters identified in Phase 1. Exclusion criteria are available in the original publication [15]. and include age < 18 years, pregnancy and syncope as an underlying symptom of an acute condition diagnosed in the ED as the most relevant ones for the present study. Patients on anticoagulant therapy, with known atrial fibrillation (AF) or with chronic pulmonary diseases such as chronic obstructive pulmonary disease (COPD) were also excluded.

Table 2
Prevalence of the nine clinical variables in the high-probability group ($N = 31$).

	N *n% (IC 95%)*
SpO2 ≤93	16 51.6 (33.1–69.9)
Dyspnea	10 32.3 (16.7–51.4)
Heart Rate > 100bpm	9 29.0 (14.2–48.0)
Recent immobilization	8 25.8 (11.9–44.6)
Signs of DVT	7 22.6 (9.6–42.1)
Previous PE/DVT	6 19.3 (7.5–37.5)
Chest pain	4 12.9 (3.6–29.8)
Active cancer	4 12.9 (3.6–29.8)
BP < 100 mmHg	3 9.7 (2.0–25.8)

Data are presented as total number (N) and percentages of patients (IC 95%). SpO2= Peripheral Saturation of Oxygen BP= Blood Pressure; DVT= Deep Venous Thrombosis.

2.1. Statistical analysis

Quantitative variables are expressed as mean (standard deviation, SD) or median (interquartile range, IQR) values depending on their distribution; qualitative variables are expressed as counts and percentages. To assess the ability of the *a priori* selected variables identified in Phase 1 to predict VTE as the underlying cause of syncope, we performed a very simple decision-tree analysis. Considering only patients in the high-probability group (Phase 2), we introduced the variables in the tree one at a time according to their prevalence in our cohort. Starting from the variable with the highest prevalence, patients scoring positive for the variable were considered true positives (TP), while patients scoring negative for the variable were classified as false negatives (FN) and moved to the next step, where the second most prevalent variable was introduced in the tree. If positive to the second variable, patients were classified as TPs, while those negative moved to the third step. This stepwise approach was applied until all the identified variables were included. Patients who resulted negative to all the variables were the FNs of our rule. We then calculated the sensitivity of our rule with 95 % confidence interval (CI).

To evaluate the clinical impact of the rule (Phase 3), we estimated the proportion of patients with syncope that should be further evaluated for PE exclusion, with 95 % CI, by calculating the percentage of rule-positive patients (patients with at least one positive variable).

This study complied with the Declaration of Helsinki and received approval from the institutional review board of the L. Sacco Hospital (approval number 608/2015).

3. Results

- *Phase 1: Identification of the variables - Clinical rule*

The following nine clinical/anamnestic variables were concordantly identified by the panel, mostly extracted from PE pretest probability scores [14,16,17]:

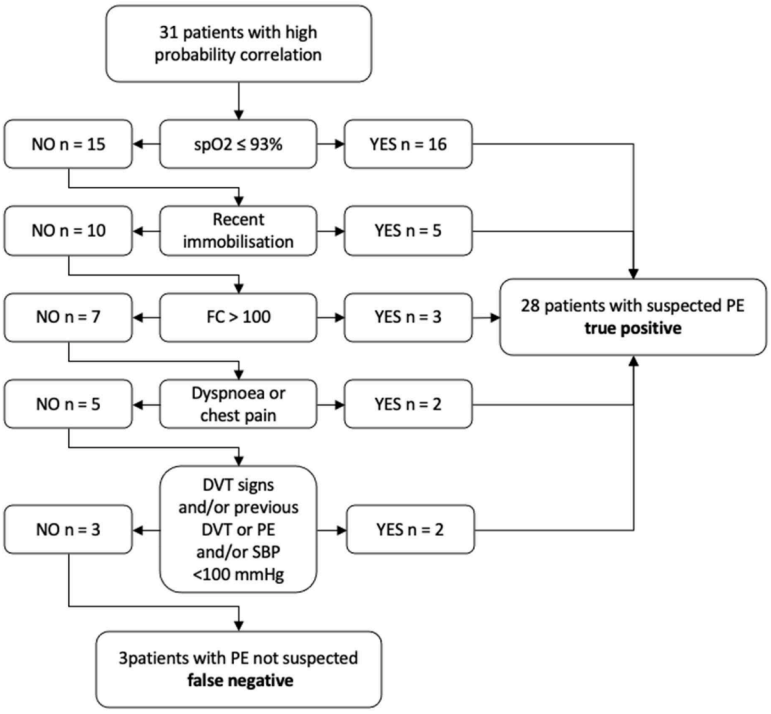

Fig. 2. Assessment of the sensitivity of the rule.

- hypotension, defined as systolic blood pressure (SBP) lower than 100 mmHg
- tachycardia, defined as a cardiac rate higher than 100 beats per minute (bpm)
- peripheral oxygen saturation $\leq$ 93 %
- presence of chest pain during syncope event
- presence of dyspnea during syncope event
- a recent history of prolonged bed rest
- clinical signs of DVT
- history of previous VTE
- active neoplastic disease

Patients with at least one of the nine characteristics were considered rule-positive.

- *Phase 2. Assessment of the accuracy of the rule.*

In the defined period, 100 subjects were screened for inclusion. Of these, 61 had complete clinical records and were considered eligible for further analysis. Among these patients, a causal relationship between PE and syncope was excluded for 30 (49 %) patients (low-probability group), while the remaining 31 (51 %) were considered in the high-probability group (Fig. 1). Descriptive characteristics and the prevalence of the nine risk factors identified in the high-probability group are reported in Tables 1 and 2.

Of the 31 subjects considered in the high-probability group, 16 had oxygen saturation lower than or equal to 93 % and were considered with suspect PE diagnosis (true positives, TP). Five patients had a history of recent immobilization and were classified as true positives. Of the remaining 10 patients, three were found to have a heart rate greater or equal to 100 bpm, and thus were also moved to the TP group, and two additional ones were classified as TP at the next step, based on the presence of dyspnea, with chest pain in one case. Importantly, since the number of patients with dyspnea and the number of patients with previous VTE was overlapping, we decided to consider dyspnea/chest pain as the next node of the tree as it appeared more likely for those symptoms to be reported in the clinical charts. Finally, two of the 5 remaining potential false negative (FN) patients had either active signs or a previous history of VTE that was also associated, in one case, with systolic blood pressure lower than 100 mmHg. Of note, we did not include active cancer in the decision tree because all subjects with this condition were also positive for at least one other parameter. Therefore, based on our nine clinical features rule, only 3 out of 31 patients were classified as FN (false negative ratio 9.7 %, 95 % CI: 2.0 % to 25.8 %) and would have not been suspected of PE (Fig. 2). One of these patients had a low PE pre-test probability and the syncope was initially considered due to arrythmia (sinus bradycardia with frequent ventricular ectopic beats). In this case, PE was diagnosed nine days after his access to the ED, and was suspected because the patient developed chest pain after being immobilized due to a malleolar fracture that followed the syncopal event. The second FN patient had been considered negative for the variable “recent immobilization”, but a recent history of ischemic stroke had severely limited his daily activity. Finally, the third patient, although not having a history of previous PE, was found to have post-embolic pulmonary arterial hypertension upon computed tomography pulmonary angiogram (CTPA) performed in the ED, despite being negative for a history of previous PE. The sensitivity of the anamnestic and clinical parameters resulted as 90.3 % (95 % CI: 74.3 % to 98.0 %).

- *Phase 3. Assessment of the clinical impact of the rule.*

Between September 2015 and February 2017, 414 patients were screened for inclusion [15]. Of them, 69 were excluded from the study because of missing follow-up data (n = 43 patients), carotid sinus massage positivity (n = 11 patients) and syncope recognized as a symptom of an acute condition diagnosed in the ED (n = 15 patients). Twenty additional patients were excluded because they were on anticoagulant therapy and/or had a history of atrial fibrillation or COPD. Of the remaining 325 eligible patients, 108 (33.2 %) could not be considered for further analysis due to the lack of anamnestic data regarding the variables "recent rest, signs of DVT, and previous DVT". Thus, 217 patients with complete medical records were available to assess the clinical impact of the rule. Descriptive characteristics of the analyzed population are reported in Table 3. When applying our clinical decision rule,

Table 3
Baseline characteristics of the Phase 3 Population ($N = 217$).

Demographic features	Number (%) or median (IQR)
Patients enrolled	217
Age - median	71 (50–82)
Male - N (%)	109 (50.2)
Female - N (%)	108 (49.8)
Vital signs	
Systolic Blood Pressure	130 (115–150)
Systolic Blood Pressure < 100 - N (%)	13 (6.0)
Heart Rate	75 (65–85)
Heart Rate > 100 - N (%)	9 (4.1)
SpO2	98 (97–99)
SpO2≤93% - N (%)	14 (6.5)
Risk factors for VTE	
Signs of DVT	0
Previous PE/DVT	1 (0.5)
Recent lower limb fracture	NA
Recent immobilization	3 (1.4)
Active cancer	10 (4.6)
Hemoglobin < 9 g/dL (available for 214)	4 (1.9)
Past medical history	
Syncope in the previous year	62 (28.6)
Congestive heart failure	2 (0.9)
Ischemic cardiomyopathy	28 (12.9)
Structural heart disease	14 (6.5)
Aortic stenosis	4 (1.8)
Left ventricular outflow obstruction	0
Left ventricular hypertrophy	1 (0.5)
Left ventricular ejection fraction < 40%	1 (0.5)
Pulmonary hypertension	4 (1.8)
Valvular heart disease	4 (1.8)
Arrhythmia	16 (7.4)
Previous PM implantation	5 (2.3)
Previous ICD implantation	0
Sick sinus syndrome	1 (0.5)
Mobitz 2 s- or third-degree AV block	0
Arterial hypertension	109 (50.2)
Stroke/TIA	15 (6.9)
Chronic kidney disease (serum creatinine ≥ 2 mg/dL)	6 (2.8)
Abnormal ECG findings (ECG results available for 213 patients)	
Bradycardia < 50 beats/min	7 (3.2)
First-degree AV block	23 (10.8)
Right bundle branch block 3	26 (12)
Left bundle branch block	6 (2.8)
Left anterior fascicular block	15 (6.9)
Previous myocardial infarction	13 (6.0)
Left ventricular hypertrophy	3 (1.4)
Ventricular ectopic beats	9 (4.1)
Supraventricular ectopic beats	11 (5.2)
Atrial fibrillation (not previously known)	12 (5.6)
Prolonged QT interval	1 (0.5)

AV = atrioventricular; COPD = chronic obstructive pulmonary disease; ECG = electrocardiography; ICD = implantable cardioverter defibrillator; IQR = interquartile range; PM = pacemaker; TIA = transient ischemic attack.

60/217 patients (27.6 %, IC95 % 21.8 % to 34.1 %) would have been suspected of PE and further evaluated for PE exclusion.

4. Discussion

Our study shows that most patients with syncope and PE have anamnestic and clinical features that could raise a suspect diagnosis of pulmonary embolism. Here, we derived a clinical decision rule to identify patients with syncope that would benefit from further diagnostic algorithms to exclude PE as a cause of syncope. Importantly, the application of the rule to an independent large population of patients revealed that only 27.6 % (IC95 % 21.8 % to 34.1 %) of subjects presenting to the ED for a syncopal event would be suspected of pulmonary embolism and would undergo additional diagnostic tests. We believe that our findings have relevant clinical utility. Decreasing the number of patients who would be evaluated with a diagnostic PE algorithm will reduce the risk of over-testing and over-diagnosing, optimizing patient's management in the ED.

While several clinical decision tools such as the Wells and the Geneva scores have been developed and validated to exclude PE and reduce the number of unnecessary radiologic exams, their use in patients with syncope might not be appropriate [14,16–19]. This is because most of the available scores, with the exception of the PERC score, include D-dimer testing as part of the decision algorithm. However, measurement of D-dimer in every patients with syncope has limited utility because of its very low specificity and positive predictive value, which might lead to over-diagnosis and over-treatment [20–22].

Pulmonary embolism is a potentially serious cause of syncope, and the prompt identification of patients who need a treatment for this condition represents a priority for ED physicians. Clinical suspect and pretest probability assessments are not sufficiently accurate, and the definitive diagnosis of PE mostly relies on CTPA. Importantly, the broad availability of CTPA in EDs and the concern of misdiagnosing PE have led in recent years to an increase in the use of this exam, which is often unnecessary, is costly, and exposes patients to radiations and contrast reactions [23]. Of note, while the widespread use of CTPA is associated with a rise in diagnosis and reported incidence of PE, the mortality has not significantly changed, thus reflecting an increase in detection and treatment of clinically not significant PE events [19,24–26].

The risk of over-testing, over-diagnosing and over-treating PE is especially relevant in patients presenting to the ED for syncope. Syncope is a frequent clinical condition that accounts for about 1–3 % of ED visits [8,10]. A careful selection of patients who need further testing to exclude PE is key not only to avoid embolism complications but also to limit unnecessary and potentially harmful exams and treatments. Jimenez et al. showed that adding an active strategy of PE detection in patients hospitalized for exacerbation of chronic obstructive pulmonary disease who are at high risk for PE increases the rate of PE diagnosis, but did not improve the clinical outcome [27].

Furthermore, data on the prevalence of PE in patients with syncope are still controversial, with different studies reporting percentages of PE ranging from less than 1.5 % to greater than 17 % [2,6,7]. This high variability in PE prevalence reflects, at least in part, the absence of a gold standard approach to the diagnostic workup of patients with syncope. Prandoni et al. conducted a cross-sectional study aimed at defining PE prevalence in patients hospitalized for a first episode of syncope. Patients with a high clinical pre-test probability, as defined by the Simplified Wells score >4 and D-dimer measurement (d-dimer cutoff value> 250 ug/ml or 500 ug/ml), underwent CTPA or ventilation perfusion scan to rule out PE. Using this algorithm, PE was confirmed in 17 % of the screened patients [7]. Interestingly, and in contrast with this finding, a systematic review and metanalysis conducted by Ogab and colleagues reported an estimated pooled PE prevalence < 1 % in subjects accessing EDs for syncope [4].

Overall, syncope represents a challenge for ED physicians, who must identify patients who are at high risk for adverse outcomes needing to be hospitalized. While there is a general consensus in the initial diagnostic workup (medical history, electrocardiogram and physical examination) [11,12,28], a gold-standard approach to exclude PE without running the risk of over-testing and over-diagnosing is still undefined. In this context, the clinical decision rule that we proposed in our study can provide a simple rational and rapid strategy to identify patients who need further testing to rule out PE.

4.1. Limitations

The main limitation of our study is that we used administrative databases to select patients with PE and syncope. Therefore, some patients with syncope and PE might have been missed.

The evaluation of the causal relationship between syncope and PE could have been affected by the subjective judgment of the two clinicians in charge of the analysis. Nonetheless, their independent

evaluation should have partially resolved this limitation.

In addition, since the clinical variables were chosen on the basis of clinical experience and literature, we cannot exclude that different parameters could have led to similar or even better results. Our aim was to show that clinical factors alone can guide the physicians' suspect of PE in patients with syncope.

Importantly, the analysis was conducted on a population of patients where PE was confirmed; therefore, we could only assess the sensitivity of the rule but not the specificity. In addition, the small sample size resulted in rather wide 95 % confidence intervals.

Finally, in the Phase 3 population (the population of the SyMoNE study), variables that were not available in the clinical charts were considered negative and this could represent a possible bias. Of note, none of the patients included in Phase 3 had non low-risk syncopal episodes; therefore the number of patients for whom an algorithm to exlcude PE could be avoided might have been higher if the rule was applied to a more heterogenous population.

We did not evaluate the specificity of the rule in the phase 3 population, because we did not adopt a structured algorithm to exclude PE; thus, our results could have been biased toward an over estimation of specificity. Our results should be replicated in prospective studies to be generalized.

5. Conclusions

Our study shows that most of the patients with syncope and PE present anamnestic and clinical factors that may suggest this diagnosis. We have proposed a rule to identify patients with PE among patients with syncope, and the evaluation of its general applicability allowed us to see that this would be applied to the minority of patients presenting to the ED with syncope. Further studies are needed to validate this score in a larger population and to allow calculating of the specificity of the rule.

Declaration of Competing Interest

All the authors have no conflict of interest to declare

Acknowledgments

G.Cos. is the guarantor of the content of the manuscript, have full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. G. Cos., M. S., G. Cas. conceived and designed this study. G. Cas. performed the statistical analysis. A.R. provided data from administrative database. F.G., G. Cas, M.S, Gio. Col. interpreted the data and drafted the manuscript. M.B, A.J., G.D., Giu. Col. aquired the data. All the authors contributed to manuscript revision, important intellectual content, and final version approval.

References

[1] Badertscher P, et al. Prevalence of pulmonary embolism in patients with syncope. J Am Coll Cardiol 2019;74(6):744–54.
[2] Costantino G, et al. Prevalence of pulmonary embolism in patients with syncope. JAMA Intern Med 2018;178(3):356–62.
[3] Frizell A, et al. Prevalence of pulmonary embolism in patients presenting to the emergency department with syncope. Am J Emerg Med 2018;36(2):253–6.
[4] Oqab Z, Ganshorn H, Sheldon R. Prevalence of pulmonary embolism in patients presenting with syncope. A systematic review and meta-analysis. Am J Emerg Med 2018;36(4):551–5.
[5] Verma AA, et al. Pulmonary embolism and deep venous thrombosis in patients hospitalized with syncope: a multicenter cross-sectional study in Toronto, Ontario, Canada. JAMA Intern Med 2017;177(7):1046–8.
[6] Pop C, et al. Prospective study of pulmonary embolism presenting as syncope. Am J Ther 2019;26(3):e301–7.
[7] Prandoni P, et al. Prevalence of pulmonary embolism among patients hospitalized for syncope. N Engl J Med 2016;375(16):1524–31.
[8] Blanc JJ, et al. Prospective evaluation and outcome of patients admitted for syncope over a 1 year period. Eur Heart J 2002;23(10):815–20.
[9] Huff JS, et al. Clinical policy: critical issues in the evaluation and management of adult patients presenting to the emergency department with syncope. Ann Emerg Med 2007;49(4):431–44.
[10] Kapoor WN. Evaluation and outcome of patients with syncope. Medicine 1990;69(3):160–75 (Baltimore).
[11] Brignole M, et al. 2018 ESC Guidelines for the diagnosis and management of syncope. Eur Heart J 2018;39(21):1883–948.
[12] Costantino G, et al. Syncope clinical management in the emergency department: a consensus from the first international workshop on syncope risk stratification in the emergency department. Eur Heart J 2016;37(19):1493–8.
[13] Konstantinides SV, et al. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS). Eur Heart J 2020;41(4):543–603.
[14] Klok FA, et al. Simplification of the revised Geneva score for assessing clinical probability of pulmonary embolism. Arch Intern Med 2008;168(19):2131–6.
[15] Solbiati M, et al. Predictive accuracy of electrocardiographic monitoring of patients with syncope in the emergency department: the SyMoNE multicenter study. Acad Emerg Med 2020;27(1):15–23.
[16] Le Gal G, et al. Prediction of pulmonary embolism in the emergency department: the revised Geneva score. Ann Intern Med 2006;144(3):165–71.
[17] Wells PS, et al. Derivation of a simple clinical model to categorize patients probability of pulmonary embolism: increasing the models utility with the SimpliRED D-dimer. Thromb Haemost 2000;83(3):416–20.
[18] Ceriani E, et al. Clinical prediction rules for pulmonary embolism: a systematic review and meta-analysis. J Thromb Haemost 2010;8(5):957–70.
[19] Roussel M, et al. Temporal trends in the use of computed tomographic pulmonary angiography for suspected pulmonary embolism in the emergency department: a retrospective analysis. Ann Intern Med 2023;176(6):761–8.
[20] Stockley CJ, et al. The utility of routine D-dimer measurement in syncope. Eur J Emerg Med 2009;16(5):256–60.
[21] Freund Y, et al. Effect of the pulmonary embolism rule-out criteria on subsequent thromboembolic events among low-risk emergency department patients: the PROPER randomized clinical trial. JAMA 2018;319(6):559–66.
[22] Kline JA, et al. Clinical criteria to prevent unnecessary diagnostic testing in emergency department patients with suspected pulmonary embolism. J Thromb Haemost 2004;2(8):1247–55.
[23] Kline JA, et al. Over-testing for suspected pulmonary embolism in American emergency departments: the continuing epidemic. Circ Cardiovasc Qual Outcomes 2020;13(1):e005753.
[24] Dobler CC. Overdiagnosis of pulmonary embolism: definition, causes and implications. Breathe 2019;15(1):46–53 (Sheff).
[25] Wiener RS, Schwartz LM, Woloshin S. Time trends in pulmonary embolism in the United States: evidence of overdiagnosis. Arch Intern Med 2011;171(9):831–7.
[26] DeMonaco NA, et al. Pulmonary embolism incidence is increasing with use of spiral computed tomography. Am J Med 2008;121(7):611–7.
[27] Jiménez D, et al. Effect of a pulmonary embolism diagnostic strategy on clinical outcomes in patients hospitalized for COPD exacerbation: a randomized clinical trial. JAMA 2021;326(13):1277–85.
[28] Shen WK, et al. 2017 ACC/AHA/HRS Guideline for the evaluation and management of patients with syncope. J Am Coll Cardiol 2017;70(5):e39–110.