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Cardiac troponin testing and the simplified Pulmonary Embolism Severity Index. The SWISS Venous ThromboEmbolic Registry (SWIVTER)

Spirk, D ; Aujesky, D ; Husmann, M ; Hayoz, D ; Baldi, T ; Frauchiger, B ; Banyai, M ; Baumgartner, I ; Kucher, N

Abstract: A low simplified Pulmonary Embolism Severity Index (sPESI), defined as age ≥ 80 years and absence of systemic hypotension, tachycardia, hypoxia, cancer, heart failure, and lung disease, identifies low-risk patients with acute pulmonary embolism (PE). It is unknown whether cardiac troponin testing improves the prediction of clinical outcomes if the sPESI is not low. In the prospective Swiss Venous Thromboembolism Registry, 369 patients with acute PE and a troponin test (conventional troponin T or I, highly sensitive troponin T) were enrolled from 18 hospitals. A positive test result was defined as a troponin level above the manufacturers assay threshold. Among the 106 (29%) patients with low sPESI, the rate of mortality or PE recurrence at 30 days was 1.0%. Among the 263 (71%) patients with high sPESI, 177 (67%) were troponin-negative and 86 (33%) troponin-positive; the rate of mortality or PE recurrence at 30 days was 4.6% vs. 12.8% ($p=0.015$), respectively. Overall, risk assessment with a troponin test (hazard ratio [HR] 3.39, 95% confidence interval [CI] 1.38-8.37; $p=0.008$) maintained its prognostic value for mortality or PE recurrence when adjusted for sPESI (HR 5.80, 95%CI 0.76-44.10; $p=0.09$). The combination of sPESI with a troponin test resulted in a greater area under the receiver-operating characteristic curve (HR 0.72, 95% CI 0.63-0.81) than sPESI alone (HR 0.63, 95% CI 0.57-0.68) ($p=0.023$). In conclusion, although cardiac troponin testing may not be required in patients with a low sPESI, it adds prognostic value for early death and recurrence for patients with a high sPESI.

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Cardiac troponin testing and the simplified Pulmonary Embolism Severity Index

The SWISS Venous ThromboEmbolism Registry (SWIVTER)

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Summary

A low simplified Pulmonary Embolism Severity Index (sPESI), defined as age ≤ 80 years and absence of systemic hypotension, tachycardia, hypoxia, cancer, heart failure, and lung disease, identifies low-risk patients with acute pulmonary embolism (PE). It is unknown whether cardiac troponin testing improves the prediction of clinical outcomes if the sPESI is not low. In the prospective Swiss Venous Thromboembolism Registry, 369 patients with acute PE and a troponin test (conventional troponin T or I, highly sensitive troponin T) were enrolled from 18 hospitals. A positive test result was defined as a troponin level above the manufacturers assay threshold. Among the 106 (29%) patients with low sPESI, the rate of mortality or PE recurrence at 30 days was 1.0%. Among the 263 (71%) patients with high sPESI, 177 (67%) were troponin-negative and 86 (33%) troponin-positive; the rate of mortality or PE recurrence at 30 days was 4.6% vs. 12.8% ($p=0.015$), respectively.

Overall, risk assessment with a troponin test (hazard ratio [HR] 3.39, 95% confidence interval [CI] 1.38–8.37; $p=0.008$) maintained its prognostic value for mortality or PE recurrence when adjusted for sPESI (HR 5.80, 95% CI 0.76–44.10; $p=0.09$). The combination of sPESI with a troponin test resulted in a greater area under the receiver-operating characteristic curve (HR 0.72, 95% CI 0.63–0.81) than sPESI alone (HR 0.63, 95% CI 0.57–0.68) ($p=0.023$). In conclusion, although cardiac troponin testing may not be required in patients with a low sPESI, it adds prognostic value for early death and recurrence for patients with a high sPESI.

Keywords

Pulmonary embolism, risk stratification, Pulmonary Embolism Severity Index, cardiac troponin

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Introduction

The most important factors for predicting clinical outcomes in patients with acute pulmonary embolism (PE) include haemodynamic parameters, such as the systemic pressure, the heart rate, and oxygen saturation (1, 2), advanced age or the presence of comorbidities including, cancer, heart failure, or respiratory disease (3), right ventricular dysfunction by echocardiography (4–6), and increased cardiac biomarker levels (7–14). Current consensus guidelines of the European Society of Cardiology (15) and the American College of Chest Physicians (16) recommend risk stratification for identifying PE patients at increased risk of adverse clinical events.

Through their high negative predictive value for mortality, clinical prediction rules identify low-risk patients with PE who are candidates for an abbreviated hospital stay or in whom outpatient management may be considered. The Pulmonary Embolism Severity Index (PESI), the most accurate and reproducible clinical risk assessment score to date (17–19), has recently been simplified using a seven-item instead of the original 11-item score (20). Patients with a low simplified Pulmonary Embolism Severity Index (sPESI), defined as an age ≤ 80 years and the absence of systemic hypotension, tachycardia, hypoxia, cancer, heart failure, and chronic lung disease, had a 30-day mortality rate of 1% (20).

As with the clinical prediction rules, the strength of cardiac biomarkers is the identification of low-risk PE patients due to their

high negative predictive value for adverse events (7–14). However, cardiac biomarker testing may lose its prognostic value when PE patients are risk stratified by a clinical prediction rule (21, 22). We aimed to investigate whether risk stratification by cardiac troponin testing improves the prediction of 30-day clinical outcomes in patients with a high sPESI.

Methods

Patients

In the prospective SWISS Venous ThromboEmbolic Registry (SWIVTER), four academic and 14 non-academic acute care hospitals prospectively enrolled 644 consecutive patients with acute PE between January 2009 and May 2010. Inclusion criteria were age ≥ 18 years and objectively confirmed acute PE, and there were no exclusion criteria. For the present analysis, 257 patients were excluded because no cardiac troponin test was available within 24 hours (h) of diagnosis, and 18 were excluded because no follow-up data was available. Overall, 369 patients were included. Eligible patients were enrolled at the time of PE diagnosis during clinical inpatient or outpatient visits. PE diagnosis had to be objectively confirmed by contrast-enhanced chest computed tomography according to the Prospective Investigation of Pulmonary Embolism (PIOPED) II criteria (23), by a high-probability ventilation-perfusion lung scan, or by an abnormal conventional pulmonary angiogram. SWIVTER did not issue guidelines or recommendations on the risk stratification (biomarkers, echocardiography) and treatment of patients with acute PE. According to local regulations, the study was approved by the local ethics committees of the participating hospitals.

Data acquisition and definitions

A standardised electronic case report form (e-CRF) was used for collecting anonymous data on patient age, sex, and outpatient or inpatient status at the time of PE diagnosis, clinical presentation, haemodynamic parameters, comorbidities, risk factors for venous thromboembolism (VTE) and bleeding, detailed risk stratification test results, and treatment modalities. In addition, clinical outcomes were captured, including mortality, symptomatic objectively confirmed recurrent PE, and bleeding requiring medical attention through 30 days after PE diagnosis. Overall, 332 (90%) had completed follow-up data through 30 days, and 37 (10%) had follow-up data for a minimum of 15 days.

A low sPESI was defined as an age ≤ 80 years and absence of systemic hypotension (systolic pressure < 100 mm Hg), tachycardia (heart rate ≥ 110 beats per minute), hypoxia (oxygen saturation $< 90\%$), cancer, heart failure, and chronic lung disease (20).

Cardiac troponin test results were considered only if they were obtained within 24 h after PE diagnosis. Point-of-care cardiac tro-

ponin tests were not allowed, and the following quantitative assays were used in the participating centers: conventional troponin I (Beckman Coulter TnI, cut-off $0.09 \mu\text{g/l}$), and conventional (Roche Elecsys cTnT, cut-off $0.1 \mu\text{g/l}$) or highly-sensitive (Roche Elecsys cTnT-hs, cut-off $0.014 \mu\text{g/l}$) troponin T. A positive troponin test result was defined as a troponin level above the manufacturers assay threshold for the diagnosis of myocardial injury. According to the results of risk stratification, patients were classified into three groups: patients with a low sPESI, patients with a high sPESI and negative troponin test, and patients with a high sPESI and positive troponin test.

Right ventricular dysfunction was defined as presence of at least one of the following echocardiographic findings within 24 h after PE diagnosis: right ventricular dimension of more than 30 mm in the parasternal long axis view, end-diastolic right-to-left ventricular dimension ratio (RV/LV) > 0.9 in the apical four-chamber view, moderate or severe systolic hypokinesis of the right ventricular free wall, tricuspid velocity > 2.6 m/s, septal flattening or paradoxical septal motion.

Clinical endpoints and statistical analysis

Continuous variables with a normal distribution are presented as means with standard deviations (SD), and group comparisons were performed with the t-test. Discrete variables are presented as frequencies and percentages, and group comparisons were performed using the Chi-square or Fisher's exact test. Kaplan-Meier graphs were created to compare by log-rank test the cumulative 30-day rates of the combined endpoint of mortality and recurrent PE for the three risk stratification groups. Univariate Cox regression analysis reporting hazard ratios (HR) with 95% confidence intervals (CI) was performed to explore whether dichotomised data for cardiac troponin and sPESI are associated with the combined endpoint of mortality and recurrent PE within 30 days. In addition, bivariate Cox regression analysis was used to investigate whether dichotomised data for cardiac troponin independently predict 30-day clinical outcomes, adjusting for the sPESI. For patients with completed follow-up, sensitivity, specificity, positive and negative predictive values, as well as areas under the receiver-operating characteristic curve (AUC) for sPESI, cardiac troponin, and the combination of sPESI and troponin were obtained. For the calculation of AUC by logistic regression analysis, the combination of sPESI and troponin resulted in a new categorical variable: 1) low sPESI plus negative troponin, 2) low sPESI plus positive troponin, 3) high sPESI plus negative troponin, and 4) high sPESI plus positive troponin. AUCs for sPESI alone and for the combination of sPESI and troponin were compared by the Chi-square test. All reported p-values are two-tailed. Data were analysed using STATA 10.1 software (STATACorp LP, College Station, TX, USA).

Results

Patient characteristics

Overall, 174 (47%) patients were female and 77 (21%) were older than 80 years, 78 (21%) patients had cancer, 39 (11%) chronic lung disease, 34 (9%) chronic heart failure, 321 (87%) dyspnea, and 50

(14%) syncope (► Table 1). A systolic blood pressure <100 mm Hg was present in 31 (8%), oxygen saturation in room air <90% in 116/330 (35%), and heart rate ≥110 beats/min in 113/358 (32%). One hundred six (29%) patients had a low sPESI. Among the 263 (71%) patients with high sPESI, 177 (67%) were troponin-negative and 86 (33%) troponin-positive.

	Low sPESI N = 106	High sPESI and positive troponin N = 86	High sPESI and negative troponin N = 177	P-value*
Demographics				
Age, mean years ± SD	59 ± 15	72 ± 13	70 ± 16	0.19
Age > 80 years, n (%)	0 (0.0)	23 (26.7)	54 (30.5)	0.53
Women, n (%)	40 (37.7)	46 (53.5)	88 (49.7)	0.57
Inpatient at the time of diagnosis, n (%)	57 (53.8)	34 (39.5)	102 (57.6)	0.006
Comorbidities				
Cancer, n (%)	0 (0.0)	21 (24.4)	57 (32.2)	0.20
Prior venous thromboembolism, n (%)	32 (30.2)	20 (23.3)	34 (19.2)	0.45
Chronic lung disease, n (%)	0 (0.0)	8 (9.3)	31 (17.5)	0.08
Bed rest for > 3 days within 30 days, n (%)	14 (13.2)	16 (18.6)	24 (13.6)	0.29
Obesity, n (%)	15 (14.2)	17 (19.8)	26 (14.7)	0.30
Congestive heart failure, n (%)	0 (0.0)	16 (18.6)	18 (10.2)	0.06
Surgery within 30 days, n (%)	11 (10.4)	10 (11.6)	26 (14.7)	0.50
Clinical findings				
Right ventricular dysfunction, n (%)	16/39 (41.0)	45/53 (84.9)	39/78 (50.0)	<0.001
Right heart strain by ECG, n (%) †	39/98 (39.8)	65/81 (80.3)	73/155 (47.1)	<0.001
Oxygen saturation in room air <90%, n (%)	0/89 (0.0)	57/81 (70.4)	59/160 (36.9)	<0.001
Heart rate ≥ 110 beats/min, n (%)	0/100 (0.0)	45/85 (52.9)	68/173 (39.3)	0.038
Systolic blood pressure < 100 mm Hg, n (%)	0 (0.0)	19 (22.1)	12 (6.8)	<0.001
Therapy				
Inpatient therapy, n (%)	93 (87.7)	86 (100.0)	168 (94.9)	0.033
Reperfusion therapy, n (%)	4 (3.8)**	17 (19.8)	5 (2.8)	<0.001
Systemic thrombolysis, n (%)	4 (3.8)	10 (11.6)	3 (1.7)	<0.001
Catheter intervention, n (%)	0 (0.0)	4 (4.7)	2 (1.1)	0.07
Surgical thrombectomy, n (%)	0 (0.0)	4 (4.7)	1 (0.6)	0.023
Inferior vena cava filter, n (%)	2 (1.9)	4 (4.7)	3 (1.7)	0.16
Initial parenteral anticoagulation, n (%)	105 (99.1)	82 (95.4)	171 (96.6)	0.62
Vitamin K antagonist, n (%)	97 (91.5)	70 (81.4)	146 (82.5)	0.83
Planned duration of anticoagulation				
≤ 3 months, n (%)	5 (4.7)	5 (5.8)	11 (6.2)	0.90
> 3–6 months, n (%)	41 (38.7)	27 (31.4)	61 (34.5)	0.62
> 6–12 months, n (%)	32 (30.2)	22 (25.6)	52 (29.4)	0.52
> 12 months or indefinite, n (%)	28 (26.4)	32 (37.2)	53 (29.9)	0.24

* for comparison of the two groups with a high sPESI. ** Among the four patients with low sPESI who underwent thrombolysis, two had a positive troponin test and two had embolism of the pulmonary main stem or main pulmonary arteries.
† Right heart strain by electrocardiography was defined as presence of at least one of the following signs: sinus tachycardia, incomplete or complete right bundle branch block, SI-QIII type, or negative T waves in V2, V3, or V4 within 24 hours of VTE diagnosis.
sPESI = simplified Pulmonary Embolism Severity Index.

Table 1: Patient characteristics.

Cardiac troponin was more often positive in patients with a high sPESI vs. low sPESI (33% vs. 12%; $p < 0.001$). Both the conventional troponin test (29% vs. 14%; $p = 0.016$) and the highly-sensitive troponin T test (40% vs. 9%; $p = 0.001$) were more often positive in patients with a high vs. low sPESI. Among 170 patients with echocardiographic data, right ventricular dysfunction was present in 100 (59%); it was more often found in patients with a high vs. low sPESI (64% vs. 41%; $p = 0.010$). Massive or haemodynamically unstable PE, defined as systolic blood pressure of less than 90 mm Hg, was present in 29 (8%) patients.

Overall, 347 (94%) patients were treated on an inpatient basis; patients with a high sPESI were more often hospitalised than patients with a low sPESI (97% vs. 88%; $p = 0.001$). Among the patients with a high sPESI, reperfusion therapy, including systemic fibrinolysis, catheter intervention, or surgical thrombectomy was less frequently used in troponin-negative vs. troponin-positive patients (3% vs. 20%; $p < 0.001$).

Clinical outcomes at 30 days

None of the patients with a low sPESI died within 30 days, and the 30-day mortality rate was 6.1% in the patients with high sPESI ($p = 0.010$). Among the patients with a high sPESI, the 30-day mortality rate was 4.6% if the troponin test was negative vs. 9.4% if it was positive ($p = 0.12$). The combined rate of 30-day mortality or recurrent PE was 1.0% in patients with a low sPESI vs. 7.3% in patients with a high sPESI, ($p = 0.016$). Among the patients with a high sPESI, the combined rate of 30-day mortality or recurrent PE was 4.6% if the troponin test was negative and 12.8% if it was posi-

tive ($p = 0.015$) (► Fig. 1). Bleeding complications requiring medical attention occurred in 1.9% vs. 6.9% patients with a low vs. high sPESI, respectively ($p = 0.06$), and in 3.3% patients with a high sPESI plus negative troponin test and 14.0% patients with a high sPESI plus positive troponin test ($p = 0.001$).

sPESI (HR 7.92, 95%CI 1.06–59.19; $p = 0.044$) and cardiac troponin (HR 4.23, 95%CI 1.73–10.35; $p = 0.002$) were univariate predictors of the combined endpoint of 30-day mortality or PE recurrence. The HR for the highly-sensitive troponin T assay was 5.75 (95% CI 1.12–29.64; $p = 0.037$), and for the conventional troponin, the HR was 3.71 (95% CI 1.25–11.04; $p = 0.018$).

Overall, risk assessment with a troponin test (HR 3.39, 95%CI 1.38–8.37; $p = 0.008$) maintained its prognostic value for 30-day mortality or PE recurrence when adjusted for sPESI (HR 5.80, 95%CI 0.76–44.10; $p = 0.09$). The combination of sPESI with a troponin test resulted in a greater AUC (0.72, 95% CI 0.63–0.81) than sPESI alone (0.63, 95% CI 0.57–0.68) ($p = 0.023$) (► Table 2).

Among the haemodynamically stable patients with a high sPESI, the combined rate of 30-day mortality or recurrent PE was 3.0% if the troponin test was negative and 10.3% if it was positive ($p = 0.023$). Risk assessment with a troponin test (HR 4.35, 95%CI 1.41–13.45; $p = 0.011$) maintained its prognostic value for 30-day mortality or PE recurrence when adjusted for sPESI (HR 4.00, 95%CI 0.51–31.40; $p = 0.19$). The combination of sPESI with a troponin test resulted in a greater AUC (HR 0.73, 95% CI 0.61–0.84) than sPESI alone (HR 0.62, 95% CI 0.54–0.70) ($p = 0.032$).

Among the haemodynamically unstable patients with massive PE, the combined rate of 30-day mortality or recurrent PE was 27.3% if the troponin test was negative and 22.2% if it was positive ($p = 0.78$).

Figure 1: Cumulative rate of the combined endpoint of mortality and recurrent pulmonary embolism through 30 days.

Table 2: Test characteristics for predicting death or recurrent pulmonary embolism at 30 days.

Characteristics	sPESI	Highly-sensitive troponin T	Conventional troponin T	Any troponin	sPESI plus highly-sensitive troponin T	sPESI plus conventional troponin T	sPESI plus any troponin
Test positive, n (%)	235/332 (71)	38/115 (33)	41/172 (24)	94/332 (28)	35/115 (30)	34/172 (20)	81/332 (24)
Specificity, % (95% CI)	31 (26–36)	69 (60–78)	79 (71–85)	74 (69–79)	72 (63–80)	82 (76–88)	78 (73–82)
Positive predictive value, % (95% CI)	8 (5–12)	13 (4–28)	17 (7–32)	13 (7–21)	14 (5–30)	18 (7–35)	14 (7–23)
Sensitivity, % (95% CI)	95 (75–100)	71 (29–96)	54 (25–81)	60 (36–81)	71 (29–96)	46 (19–75)	55 (32–77)
Negative predictive value, % (95% CI)	99 (94–100)	97 (91–100)	95 (90–98)	97 (94–99)	98 (91–100)	95 (90–98)	96 (93–98)
Area under the curve (95% CI)	0.63 (0.57–0.68)	0.70 (0.52–0.89)	0.66 (0.52–0.81)	0.67 (0.56–0.78)	0.76 (0.62–0.90)	0.71 (0.59–0.83)	0.72 (0.63–0.81)

sPESI = simplified Pulmonary Embolism Severity Index. Among the 45 patients with a positive conventional troponin I, none of the patients died or had recurrent PE at 30 days: specificity was 67% (95% CI 51–80%) and negative predictive value was 100% (95% CI 88–100%). The combination of sPESI plus conventional troponin I had a specificity of 73% (95% CI 58–85%) and a negative predictive value of 100% (95% CI 89–100%).

Discussion

The main finding of the present study is that the combination of the sPESI with a cardiac troponin test identified patients at risk of death or recurrent PE at 30 days more accurately than risk stratification with the dichotomised clinical prediction rule alone. Whereas troponin testing was not useful for risk stratifying patients with massive PE, it provided incremental prognostic information in haemodynamically stable patients with a high sPESI.

The 29% rate of patients with a low sPESI in our study compares favourably to the 31% rate from the validation study, as does the 30-day mortality rate in these patients (0% vs. 1%, respectively) (20). Therefore, additional risk assessment by cardiac troponin or echocardiography will not add prognostic information in patients with a low sPESI, and further research should determine whether management on an outpatient basis is feasible and safe.

Clinicians are particularly interested in identifying low-risk patients based on risk assessment strategies that provide very high negative predictive values. In clinical practice, it may be less important to obtain risk assessment strategies resulting in moderate increases in positive predictive values for adverse clinical events. However, more than two thirds of the PE patients have a high sPESI because they are elderly or they exhibit signs of haemodynamic impairment, including systemic hypotension, tachycardia, or hypoxia, or they suffer from comorbidities including cancer or cardiopulmonary disease. Our study proves that further risk stratification on top of a clinical prediction rule helps assessing PE severity. This finding is consistent with a previous study of haemodynamically stable PE patients in which conventional troponin I predicted adverse clinical events independently when adjusted to the PESI and the presence of right ventricular dysfunction (24). In SWIVTER, cardiac troponin testing using the manufacturers assay threshold was helpful for separating patients with a high sPESI into two similarly large groups: in the troponin-positive group, the risk of death or recurrent PE within 30 days was substantially greater

(12.8%) than in the troponin-negative group (4.6%). This prognostic information is important because it may affect the management strategy, including the need for cardiovascular monitoring or bed rest and initial treatment. In the future, troponin-negative patients may likely be treated on a regular ward, whereas troponin-positive PE patients may be candidates for observation on an intermediate or intensive care unit during the initial period. For the latter patients, clinical trials are also needed to investigate the efficacy and safety of reperfusion treatment, such as systemic fibrinolysis or pharmacomechanical catheter intervention, in comparison to management with anticoagulation alone.

Due to their high negative predictive value for adverse clinical events, conventional troponins (7) and highly sensitive troponin T (12) are helpful for identifying low-risk PE patients. Similarly to a recent study (21), the negative predictive value of the clinical score in our study was higher as compared to the negative predictive value of cardiac troponin testing. For the troponin tests, the cut-off values are identical to the manufacturers assay thresholds for the diagnosis of myocardial infarction. In total, 27% of the patients had increased troponin levels, and both the conventional and the highly-sensitive troponin assays were predictive of the combined endpoint. According to a recent study (12), highly sensitive troponin T may be capable of improving risk stratification in patients with acute non-massive PE as compared with conventional troponin T; however, our study was not powered to compare the performance of various troponin assays.

Strengths of SWIVTER include the prospective multicentric enrollment of patients with acute PE and cardiac troponin test results and the acquisition of detailed clinical data allowing the calculation of the seven-item sPESI score. We believe that it was important not to exclude patients with systemic hypotension on admission because blood pressure is an important component of the sPESI score, and systemic hypotension may rapidly improve with intravenous fluids and oxygen supplement. However, troponin testing did not further improve the prediction of early mortality or

PE recurrence in haemodynamically unstable patients. One weakness of the present study is that we could not assess the prognostic role of echocardiography on top of the clinical prediction rule because it was not systemically performed in the participating centres. We have chosen the well-validated high-sensitivity sPESI cut-off, differentiating between patients at low (0 sPESI points) and increased risk (≥ 1 sPESI points) (20). A recent study suggested a second high-specificity cut-off for identifying a subgroup of patients at high risk (25), but the use of more than one cut-off level for the sPESI score may hamper its usefulness for risk-stratifying PE patients in clinical practice. Another limitation is that various troponin assays were permitted in the present study. Our study was not designed to determine cut-off values for the various cardiac troponins but to investigate whether dichotomous data using the manufacturers assay thresholds from available troponin tests are helpful for predicting important clinical outcomes on top of a simple clinical prediction rule. Since various cardiac troponin tests were allowed in SWIVTER, it was not possible to account for the extent of troponin elevation. Dichotomisation of data for the cardiac troponin and the sPESI likely caused an underestimation of the true area under the receiver-operating characteristic curve but enabled a direct comparison of the predictive accuracy of both tests and their combination. Selection bias is likely because a large proportion (40%) of patients had no cardiac troponin test available. Finally, survival bias was potentially introduced because a non-negligible proportion (10%) of patients had hospital follow-up only and were lost between discharge and 30 days.

In conclusion, cardiac troponin testing may not be required for the minority of patients with a low sPESI but it adds prognostic information for patients with a high sPESI. Risk stratification with the combination of sPESI and cardiac troponin may also serve for designing clinical trials on novel PE treatment strategies.

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Conflict of interest

Dr. Spirk is an employee of Sanofi-Aventis (Suisse) SA, Meyrin, Switzerland. No other conflict of interest was reported from the authors regarding the content of this manuscript.

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What is known about this topic?

- A low simplified Pulmonary Embolism Severity Index (sPESI), defined as age ≤ 80 years and absence of systemic hypotension, tachycardia, hypoxia, cancer, heart failure, and lung disease, identifies low-risk patients with acute pulmonary embolism (PE).
- It is unknown whether cardiac troponin testing improves the prediction of clinical outcomes if the sPESI is not low.

What does this paper add?

- Although cardiac troponin testing may not be required in patients with a low sPESI, it adds prognostic value for early death and recurrence for patients with a high sPESI.
- Risk stratification with the combination of sPESI and cardiac troponin may also serve for designing clinical trials on novel PE treatment strategies.

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