Research article

# Predictors of medium- and long-term mortality in elderly patients with acute pulmonary embolism

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| ARTICLE INFO | ABSTRACT |
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| | *Introduction:* Data on medium- and long-term prognostic factors for death in elderly patients with acute Pulmonary Embolism (APE) are lacking. The present study aimed to assess sPESI score and the Charlson Comorbidity Index (CCI) as medium- and long-term predictors of mortality in elderly patients with haemodinamically stable APE.<br>*Methods:* All consecutive patients aged$\geq$65 years old, evaluated at the emergency department (ED) of our hospital from 2010 through 2014, with a final diagnosis of APE, were included in this retrospective cohort study.<br>*Results:* Study population:162 patients, female:36.5%, median age:79 years old, 74% presented a sPESI score$>$0, and 61% a CCI$\geq$ 1. All causes mortality: 19.8%, 23.5%, 26.5%, 32.1% and 48.2% at 3, 6 months, 1, 2 and 5 years after APE. Univariate regression analysis: CCI$\geq$1 was associated with a higher mortality at 3, 6 months, 1, 2 and 5 years. Multivariate Cox analysis: CCI$\geq$1 associated with increased mortality at 3 months (HR:4.29; IC95%:1.46–12.59), 6 months (HR:5.33; IC95%:1.84–15.44), 1 year (HR:4.87; IC95%:1.87–12.70), 2 years (HR:3.78; IC95%:1.74–8.25), and 5 years (HR:2.30; IC95%:1.33–3.99). sPESI score$\geq$1 was not found to be related to an increased medium-or long-term mortality. Negative predictive values (IC95%) of CCI$\geq$1 were 93.65% (87.61–99.69), 93.65% (87.61–99.69), 92.06% (85.37–98.76), 87.3% (79.05–95.55) and 71.61% (60.13–83.1) for mortality at 3, 6 months, 1, 2 and 5 years.<br>*Conclusion:* In elderly patients with a confirmed normotensive APE, unlike sPESI score, CCI showed to be an independent prognostic factor for medium- and long-term mortality. In these patients, after the acute phase following a PE event, the assessment of the comorbidities burden represents the most appropriate approach for predicting medium- and long-term mortality. |

## 1. Introduction

Pulmonary embolism (PE) is a major cause of mortality, morbidity, and hospitalization worldwide [1, 2]. Elderly subjects present a higher incidence of PE and a higher risk of recurrences and mortality, when compared with younger individuals [3, 4, 5].

Current European Society of Cardiology (ESC) guidelines for the diagnosis and management of acute PE [1] advocate for the risk stratification of haemodinamically stable acute PE patients using clinical decision rules such as the Pulmonary Embolism Severity Index

(PESI) score [6] and its simplified version (sPESI) [7], echocardiography and biomarkers [1]. PESI and sPESI have been validated as short-term (30-day) predictors of overall mortality, and are among the most extensively used prediction rules based on clinical parameters [1].

The development of tools for estimating the risk of medium- and long-term mortality may represent a substantial contribute for clinical decision making regarding treatment regimes, specific preventive screening programs, and follow-up duration. However, despite a great amount of evidence on short-term prognosis is available, only a few studies

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investigated the predictors of mortality beyond the first 30 days after acute PE [8, 9, 10], and in the elderly the prognostic value of clinical prediction rules and comorbidities burden has not been clearly established. The use of the sPESI score as may be interesting due to its simplicity and widespread use, and comorbidities may have a significant impact on long-term mortality [11, 12], especially in elderly subjects who are likely to have a higher comorbidity burden [13, 14].

The aim of the present study was to assess the performance of sPESI score and the comorbidity burden as medium- and long-term predictors of death in elderly patients with haemodinamically stable acute PE.

## 2. Materials and methods

All consecutive patients aged ≥65 years old, evaluated at the emergency department (ED) of the Vimercate Hospital - a 500 bed General Hospital - from 2010 through 2014, with a final diagnosis of acute PE by using discharge codes according to the 9th Clinical Modification International Classification of Diseases (ICD-9-CM 415.19 and 415.11), were included in this retrospective cohort study.

Patients with haemodinamic instability were excluded. A pulmonary computed tomography angiography (CTA) scan was performed to confirm PE. Electronic charts of all included patients were retrieved for evaluation. Trained study personnel retrospectively recorded patient characteristics at the time of the index event, including the variables for calculate the sPESI score [7] and Charlson Comorbidity Index (CCI) [15].

The sPESI score was calculated giving one point for the presence of every of the following parameters: (1) age >80 years; (2) history of cancer; (3) history of chronic cardiac or pulmonary disease (heart failure or chronic lung disease); (4) pulse rate >110 beats/minute; (5) systolic blood pressure <100 mmHg; and (6) arterial oxyhemoglobin saturation <90% measured at the time of PE diagnosis. Patients with none of the variables (0 points) were categorized as low-risk; and those with one to six the variables (1–6 points) as high-risk, as stated by the validation study and by international guidelines [1, 7]. CCI is a summation score based on 17 medical conditions with varying assigned weights (non-age adjusted) [15]. A score of 1 is given whether 1 of the following conditions is present: myocardial infarction, cardiac failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, connective tissue disease, peptic ulcer disease, mild liver disease, and diabetes (without organ damage); a score of 2 is given for hemiplegia, moderate to severe renal disease, any tumor (within last 5 years), lymphoma, leukemia, and diabetes with organ damage; a score of 3 for moderate to severe liver disease; and a score of 6 for metastatic solid tumor and acquired immunodeficiency syndrome. Although an specific cut-off of CCI to discriminate low and high risk in patients with PE has not been validated, we considered 0 as low risk and ≥1 for high risk following a clinical empiric criteria, given that a value of 0 indicates no comorbidity, while higher values represent at least some burden of comorbid illnesses.

Pulmonary embolism was confirmed on the basis of the presence of a filling defect in one or more pulmonary arteries up to subsegmental arteries in pulmonary CTA at the time of the acquisition of images, as stated by certified radiologists belonging to the hospital team. Helical CTA scans were performed on a Brilliance Philips CT scanner (Philips, Cleveland, OH, USA) which included 64-detector row capability.

Unique personal identifiers were checked for the follow-up concerning vital status (and mortality) using the regional demographic register updated at August 31th 2018, for all included subjects.

Permission for data analysis and to perform the study was asked to the Institutional Research Ethics Committee, albeit informed consent was not obtained from individual patients due to the retrospective design.

### 2.1. Statistical methods

The distributions of the clinical variables for patients with PE confirmed were reported as percentages for categorical variables and as median and range for continuous variables. CCI and sPESI score where dichotomized as follows: 0 vs ≥ 1. The number of deaths and Kaplan Meier estimated cumulative incidence were reported at 3, 6 months, 1, 2 and 5 years.

Kaplan Meier survival curves were fitted both for CCI and sPESI and the curves were compared by log rank test.

The prognostic role of clinical variables at 3, 6 months, 1,2, and 5 years was investigated in univariate analysis by Cox regression model. Results are reported as Hazard ratios with 95% Confidence intervals and p-values of Wald Statistics.

The joint prognostic role of the variables was evaluated by multivariate Cox regression models for mortality within 3, 6 months, 1,2 and 5 years. To obtain reliable estimates from multivariate analysis, the maximum number of the variables to be included in the models was decided according to the EPV rule suggested by Concato et al [16]. According to this rule 4 variables was allowed for 3 months model. Considering clinical opportunity Sex, Age, CCI and sPESI score were chosen and the same variables were included in Cox regression models for subsequent time periods. Results are reported as adjusted hazard ratios with 95% confidence intervals and Wald statistics p-values. Although age is a component of sPESI score (age >80 years), we preferred adjusting for age as a continuous variable to evaluate its prognostic effect for each 1 year increase.

To evaluate the diagnostic accuracy of sPESI score and CCI to predict mortality at 3 and 6 months, 1, 2 and 5 years, sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio, negative likelihood ratio and area under ROC curve (AUC) were calculated at each time point by a method specifically used for survival data [17]. Results are reported as estimated value and corresponding 95% confidence interval for sensitivity, specificity, positive and negative predictive values and AUC.

All analyses were performed using R software version 3.6.1, with packages survival and timeROC added.

## 3. Results

Study population was represented by 162 patients aged ≥65 years, consecutively evaluated in the ED of our hospital from 2010 through 2014, with a confirmed diagnosis of hemodynamically stable acute PE, female sex 36.5%, median age 79 years old, subjects aged ≥80 years 46.2%, Table 1. Three out of four patients presented a sPESI score >0, and more than a half (61%) a CCI score >1. All causes mortality was 19.8%, 23.5%, 26.5%, 32.1% and 48.2% at 3 months, 6 months, 1, 2 and 5 years after the index episode, respectively. Table 1 shows the main clinical baseline variables.

Figure 1 depicts Kaplan-Meier curve of overall survival probability, according to sPESI (0 vs ≥ 1) and CCI (0 vs ≥ 1). A significant difference is found by log-rank tests for both CCI (chi-square = 15.9, p-value<0.001) and sPESI score (chi square = 6.7, p-value = 0.009).

The univariate regression analysis showed that a CCI ≥1 was associated with a higher mortality at 3 months, 6 months, 1, 2 and 5 years, unlike a sPESI score ≥1 which did not show statistically significant differences, Table 2. The presence of a story of cancer, chronic cardiopulmonary disease, and an arterial oxygen saturation <90% at the index episode were also related to a higher risk of death.

Multivariate Cox analysis showed that CCI was strongly associated with a higher mortality at 3 and 6 months, 1, 2 and 5 years. Instead, an sPESI score ≥1 was not found to be related to an increased medium- or long-term mortality, Table 3.

In the medium- and long-term, CCI presented an AUC of 0.66 for predicting death, with high sensitivity, low specificity and high NPV.

**Table 1.** Main clinical baseline variables of elderly patients with haemodinamically stable acute PE.

| | N = 162 |
|---|---|
| Age, median (range) | 79.24 (65.52–98.5) |
| Age >80 years, n (%) | 78 (48.15) |
| Female n (%) | 52 (32.1) |
| CCI score median (range) | 1 (0–12) |
| CCI score >0 n (%) | 99 (61.11) |
| sPESI score median (range) | 1 (0–4) |
| sPESI score >0, n (%) | 120 (74.07) |
| Cancer, n (%) | 24 (14.81) |
| Chronic cardiopulmonary disease, n (%) | 13 (8.02) |
| Chronic cardiac disease, n (%) | 6 (3.7) |
| Chronic pulmonary disease, n (%) | 7 (4.32) |
| Cancer and/or chronic cardiac disease and/or chronic pulmonary disease, n (%) | 34 (20.99) |
| Pulse ≥110 beats per minute, n (%) | 42 (25.93) |
| Systolic blood pressure <100 mmHg, n (%) | 10 (6.17) |
| Arterial oxygen saturation <90 %, n (%) | 42 (25.93) |
| Overall Mortality at 3 months, n (%) | 32 (19.75%) |
| Overall Mortality at 6 months, n (%) | 38 (23.46%) |
| Overall Mortality at 1 year, n (%) | 43 (26.54%) |
| Overall Mortality at 2 years, n (%) | 52 (32.1%) |
| Overall Mortality at 5 years, n (%) | 77 (48.17%) |

PE: Pulmonary Embolism. CCI: Charlson Comorbidity Index. sPESI: simplified Pulmonary Embolism Severity Index.

Values of sensitivity, specificity, PPV, NPV and AUC were lower for sPESI, Table 4.

## 4. Discussion

The currently available prognostic tools to define the risk of death after acute PE have been validated only for the short-term follow-up [1, 6, 7]. Providing data on the medium- and long-term prognostic performance of clinical prediction rules and comorbidity burden should help clinicians to improve the management of these patients and to choice the more appropriated follow-up strategies, especially for elderly subjects.

The results of our study showed that among elderly patients with haemodinamically stable PE a CCI score ≥1 was associated with a higher risk of medium- and long-term mortality in the univariate and multivariate analysis, presenting a high sensitivity, a low specificity and a high negative predictive value for predicting death. A diagnosis of cancer, a story of chronic cardiopulmonary disease, and an arterial oxygen saturation <90% at the index episode in the univariate analysis and female sex and age in the multivariate analysis, were also associated with a higher risk of death. Instead, a sPESI score ≥1 did not provide significant information for predicting medium- and long-term mortality in that clinical setting.

To our best knowledge, the present study is the first investigation assessing the prognostic value of a clinical prediction rule (sPESI) along with the comorbidity burden (measured as a CCI ≥1) for predicting medium- and long-term mortality in elderly patients after an acute PE event. Our study confirms that elderly patients with PE present mortality rates markedly higher than those observed in younger subjects [3, 4, 5], and some other points are worthy of note.

Firstly, CCI, a measure of the burden of disease arising from multiple comorbidities, shows to be a strong, independent, predictor of death after the acute phase of PE. In an analysis from the RIETE registry, medical patients with previous acute VTE showed three-month mortality 3 times higher than surgical patients [18]. The two populations differed, besides
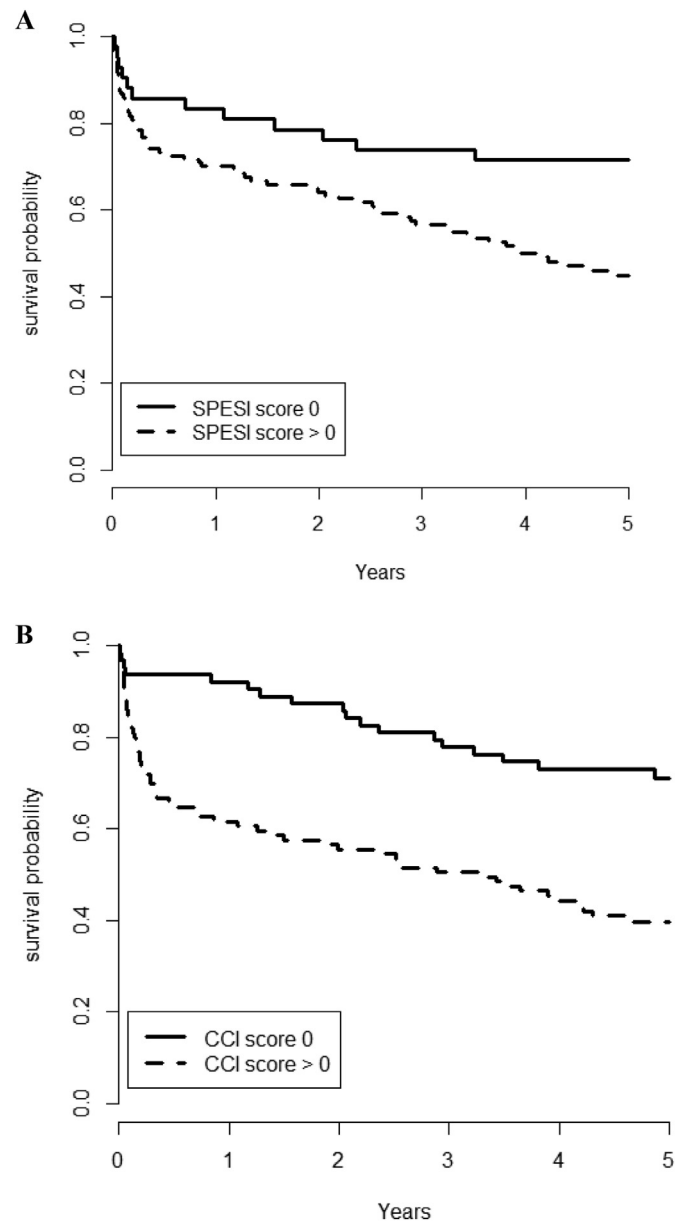
**Figure 1.** Kaplan-Meier curve of overall survival probability for elderly patients with acute PE, according to sPESI (A) and CCI (B) categories. PE: Pulmonary Embolism. sPESI: simplified Pulmonary Embolism Severity Index. CCI: Charlson Comorbidity Index.

the younger age of surgical subjects, for the greater frequency of comorbidities in medical patients. Other studies described higher 6-month mortality in patients with pre-existing heart failure and acute PE compared to patients without PE [19, 20] and in patients with pre-existing COPD [21, 22]. Although data on the prognostic performance of CCI in PE patients are scarce, a retrospective cohort found that long-term mortality of patients with a CCI score of 0 was similar to the population-derived age and sex-matched mortality rate, and was significantly better than for those with a CCI score ≥1 (12.5 vs 47.5%; P < 0.001) [11]. The present results extend those findings to an elderly population, for the medium-term and up to 5 years of follow-up.

Secondly, the sPESI score, an extensively used clinical rule validated as predictor of short-term (30-day) mortality, did not associate with a higher risk of death in the medium- and long-term follow-up after acute

**Table 2.** Univariate Cox regression analysis of the effect of different variables on mortality at 3 and 6 months, 1, 2 and 5 years, in elderly patients with PE.

| | Mortality at | 3 months | Mortality at | 6 months | Mortality at | 1 year | Mortality at | 2 years | Mortality at | 5 years |
|---|---|---|---|---|---|---|---|---|---|---|
| | HR (95% CI) | p | HR (95% CI) | p | HR (95% CI) | p | HR (95% CI) | p | HR (95% CI) | p |
| Sex (Female vs Male) | 1.72 (0.86–3.47) | 0.127 | 1.46 (0.76–2.8) | 0.255 | 1.63 (0.89–2.98) | 0.116 | 1.44 (0.82–2.51) | 0.203 | 1.13 (0.70–1.82) | 0.614 |
| Age, for each 1 year increase | 1.05 (1.00–1.10) | 0.055 | 1.05 (1.00–1.10) | 0.034 | 1.05 (1.01–1.09) | 0.026 | 1.05 (1.01–1.09) | 0.008 | 1.08 (1.05–1.12) | <0.001 |
| Age (>80 years vs ≤ 80 years) | 1.42 (0.71–2.86) | 0.325 | 1.38 (0.73–2.61) | 0.326 | 1.42 (0.78–2.59) | 0.256 | 1.56 (0.90–2.70) | 0.115 | 2.46 (1.53–3.95) | <0.001 |
| CCI score ≥1 vs 0 | 4.89 (1.71–13.95) | 0.003 | 6.15 (2.18–17.35) | 0.001 | 5.68 (2.2–14.44) | <0.001 | 4.31 (2.03–9.16) | <0.001 | 2.81 (1.65–4.77) | <0.001 |
| sPESI Score ≥1 vs 0 | 1.58 (0.65–3.84) | 0.313 | 1.97 (0.82–4.71) | 0.128 | 1.92 (0.86–4.32) | 0.113 | 1.82 (0.89–3.74) | 0.102 | 2.22 (1.20–4.11) | 0.011 |
| Cancer (Yes vs No) | 2.03 (0.91–4.51) | 0.084 | 1.93 (0.92–4.09) | 0.084 | 2.20 (1.11–4.37) | 0.024 | 2.00 (1.05–3.81) | 0.036 | 1.89 (1.09–3.28) | 0.024 |
| Chronic cardiopulmonary disease (Yes vs No) | 4.27 (1.84–9.89) | 0.001 | 3.59 (1.58–8.16) | 0.002 | 3.15 (1.40–7.10) | 0.006 | 2.57 (1.16–5.71) | 0.020 | 2.24 (1.11–4.48) | 0.024 |
| Chronic cardiac disease (Yes vs No) | 3.82 (1.16–12.54) | 0.027 | 3.22 (0.99–10.47) | 0.052 | 2.83 (0.88–9.16) | 0.082 | 2.31 (0.72–7.41) | 0.160 | 2.15 (0.78–5.88) | 0.137 |
| Chronic pulmonary disease (Yes vs No) | 2.54 (0.77–8.33) | 0.125 | 2.17 (0.67–7.07) | 0.197 | 1.93 (0.60–6.25) | 0.271 | 1.60 (0.50–5.13) | 0.431 | 1.39 (0.51–3.81) | 0.521 |
| Cancer and/or chronic cardiac disease and/or chronic pulmonary disease (Yes vs No) | 2.92 (1.44–5.92) | 0.003 | 2.57 (1.33–4.96) | 0.005 | 2.68 (1.44–4.97) | 0.002 | 2.27 (1.27–4.05) | 0.006 | 1.96 (1.19–3.22) | 0.008 |
| Pulse (≥110 beat per minute vs < 110 beats per minute) | 0.38 (0.13–1.08) | 0.069 | 0.59 (0.26–1.34) | 0.209 | 0.71 (0.34–1.49) | 0.367 | 0.71 (0.37–1.39) | 0.322 | 0.74 (0.43–1.26) | 0.266 |
| Systolic blood pressure (<100 mmHg vs ≥ 100 mmHg) | 1.61 (0.49–5.30) | 0.430 | 1.90 (0.67–5.35) | 0.226 | 2.19 (0.86–5.56) | 0.100 | 1.85 (0.73–4.65) | 0.192 | 1.24 (0.50–3.06) | 0.647 |
| Arterial oxygen saturation (<90% vs ≥ 90%) | 2.94 (1.47–5.89) | 0.002 | 2.75 (1.45–5.21) | 0.002 | 3.02 (1.66–5.51) | <0.001 | 2.64 (1.52–4.58) | 0.001 | 1.98 (1.23–3.17) | 0.005 |

PE: Pulmonary Embolism. CCI: Charlson Comorbidity Index. sPESI: simplified Pulmonary Embolism Severity Index.

**Table 3.** Multivariate Cox analysis of the effect of sPESI and CCI on mortality at 3 and 6 months, 1, 2 and 5 years in elderly patients with acute PE, adjusted by sex and age.

| | Mortality | at 3 months | Mortality | at 6 months | Mortality | at 1 year | Mortality | at 2 years | Mortality | at 5 years |
|---|---|---|---|---|---|---|---|---|---|---|
| | HR (95% CI) | p | HR (95% CI) | p | HR (95% CI) | p | HR (95% CI) | p | HR (95% CI) | p |
| Sex (Female vs Male) | 2.17 (1.00–4.68) | 0.049 | 1.79 (0.87–3.65) | 0.111 | 2.03 (1.05–3.95) | 0.037 | 1.84 (1.00–3.39) | 0.050 | 1.77 (1.06–2.98) | 0.030 |
| Age, for each 1 year increase | 1.06 (1.00–1.13) | 0.046 | 1.05 (1.00–1.11) | 0.068 | 1.05 (1.00–1.11) | 0.039 | 1.06 (1.01–1.11) | 0.015 | 1.09 (1.05–1.13) | <0.001 |
| sPESI score 0 vs ≥ 1 | 0.80 (0.28–2.27) | 0.681 | 0.98 (0.36–2.65) | 0.967 | 0.99 (0.39–2.49) | 0.978 | 0.90 (0.39–2.09) | 0.811 | 0.99 (0.48–2.05) | 0.981 |
| CCI score 0 vs ≥ 1 | 4.29 (1.46–12.59) | 0.008 | 5.33 (1.84–15.44) | 0.002 | 4.87 (1.87–12.70) | 0.001 | 3.78 (1.74–8.25) | 0.001 | 2.30 (1.33–3.99) | 0.003 |

sPESI: simplified Pulmonary Embolism Severity Index. CCI: Charlson Comorbidity Index. PE: Pulmonary Embolism.

PE. The performance of clinical prediction rules to predict medium- and long-term mortality has been investigated in just a few studies, with elderly patients often scarcely represented. In 105 general population PE patients the mortality at 12-month was 5.7% among subjects with a Geneva prognostic rule score of ≤2 and 47.1% among those with a score >2 (P < 0.0001), with a sensitivity, specificity, and NPV for overall mortality of 61.5% (95% CI 31.6–86.1%), 90.2% (95% CI 82.2–95.4%), and 94.3% (95% CI 87.2–98.1%), respectively [23]. In another study Dentali and colleagues [9] found that the sPESI score had an overall accuracy for predicting the risk of death similar to that of the original PESI at 3 and 6 months, whereas, interestingly, at 1 year the overall accuracy of the simplified PESI was significantly lower compared with the original PESI (AUC: 0.75; 95% CI, 0.71–0.79 vs. AUC: 0.79; 95% CI, 0.75–0.82; P = 0.011). Conversely, in our elderly population we did not find an association of sPESI score with medium- and long-term mortality. Differences in study population may account for these discrepancies. Indeed, our population was older (mean age 79 against 70 years) and the markedly high overall mortality rates found in the study by Dentali et may be explained by the very high prevalence of patients with cancer (27.9% vs. 14.8% in our study).

Finally, our data support the hypothesis that, due to the fact that after an acute episode of haemodinamically stable PE the short-term prognosis is mainly related to the acute event, the sPESI score (along with other clinical prediction rules mostly based on acute clinical parameters) has showed to be an useful predictor of death. Instead, since medium- and long-term follow-up mortality is mainly driven by comorbidities, CCI represent the most appropriate predictor of death, whith sPESI losing its prognostic value. These data are in keeping with other studies' results which found that in PE patients mortality was associated with variables not strictly related to the acute index event, such as plasma osmolality and nutritional indexes [24, 25].

Several limitations of our study should be mentioned, such as retrospective and monocentric design and a relative small sample size. In an attempt to limit these drawbacks we have included all consecutive elderly patients evaluated in the ED with a confirmed diagnosis of PE in 5 years' time. Thus, our study population represents a real world sample of elderly patients with normotensive PE. Yet, multicenter, prospective, larger cohort studies are needed to confirm our findings. Another limitation is the lack of data on the exact causes of death. Given the retrospective design of our study, the exact vital status (death or alive) was retrieved from the regional demographic register, albeit causes of death were not available for all patients.

## 5. Conclusions

The present study provides new insights into the prognostic assessment of PE patients after the first, short-term, follow up period. In elderly patients with a confirmed normotensive acute PE, comorbidity burden,

Table 4. Accuracy of sPESI score (0 vs $\geq$ 1) and CCI (0 vs $\geq$ 1) to predict mortality at 3 and 6 months, 1, 2 and 5 years in elderly patients with acute PE.

| | CCI | | | | | sPESI | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 3 months | 6 months | 1 year | 2 years | 5 years | 3 months | 6 months | 1 year | 2 years | 5 years |
| Sensitivity* | 87.50 (76.01–98.99) | 89.47 (79.69–99.26) | 88.37 (78.76–97.98) | 84.62 (74.78–94.45) | 76.46 (66.91–86.02) | 81.25 (67.68–94.82) | 84.21 (72.58–95.84) | 83.72 (72.65–94.79) | 82.69 (72.38–93.01) | 84.62 (76.58–92.66) |
| Specificity* | 45.38 (36.8–53.97) | 47.58 (38.76–56.4) | 48.74 (39.73–57.75) | 50 (40.63–59.37) | 55.17 (42.33–68.01) | 27.69 (19.98–35.41) | 29.03 (21.02–37.05) | 29.41 (21.2–37.62) | 30.00 (21.41–38.59) | 37.93 (25.41–50.46) |
| Positive Predictive Value* | 28.28 (19.38–37.18) | 34.34 (24.96–43.73) | 38.38 (28.77–47.99) | 44.44 (34.63–54.26) | 61.32 (50.83–71.8) | 21.67 (14.27–29.06) | 26.67 (18.73–34.6) | 30 (21.78–38.22) | 35.83 (27.23–44.44) | 55.89 (46.38–65.39) |
| Negative Predictive Value* | 93.65 (87.61–99.69) | 93.65 (87.61–99.69) | 92.06 (85.37–98.76) | 87.3 (79.05–95.55) | 71.61 (60.13–83.1) | 85.71 (75.1–96.33) | 85.71 (75.1–96.33) | 83.33 (72.03–94.64) | 78.57 (66.12–91.02) | 72.63 (58.89–86.37) |
| Positive Likelihood Ratio | 1.6 | 1.71 | 1.72 | 1.69 | 1.71 | 1.12 | 1.19 | 1.19 | 1.18 | 1.36 |
| Negative Likelihoor Ratio | 0.28 | 0.22 | 0.24 | 0.31 | 0.43 | 0.68 | 0.54 | 0.55 | 0.58 | 0.41 |
| Area Under the ROC Curve | 0.66 (59.27–73.62) | 0.69 (61.94–75.11) | 0.69 (61.97–75.14) | 0.67 (60.51–74.1) | 0.66 (57.82–73.82) | 0.54 (46.67–62.27) | 0.57 (49.56–63.68) | 0.57 (49.68–63.46) | 0.56 (49.63–63.06) | 0.61 (53.83–68.72) |

sPESI: simplified Pulmonary Embolism Severity Index. CCI: Charlson Comorbidity Index. PE: Pulmonary Embolism.
* Values expressed as % (CI 95%).

measured as a CCI score $\geq$1, showed to be an independent prognostic factor for medium- and long-term mortality. This was not true for the sPESI score, a 30-day validated prognostic tool, which did not demonstrate a significant predictive value for death after the short-term follow-up. These data suggest that, in elderly patients, since death is mainly determined by comorbidities after the acute phase following a PE event, the assessment of the comorbidities burden represent the most appropriate approach for predicting medium- and long-term mortality.

## Declarations

### Author contribution statement

H. Friz: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

C. Cimminiello: Conceived and designed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

P. Boracchi: Conceived and designed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data.

E. Gelfi: Performed the experiments; Analyzed and interpreted the data; Wrote the paper.

E. Motto, L. Primitz, L. d'Oro, C. Giannattasi and G. Vighi: Performed the experiments; Analyzed and interpreted the data.

A. Orenti: Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

### Competing interest statement

The authors declare no conflict of interest.

### Additional information

No additional information is available for this paper.

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