Utilisation of the simplified pulmonary embolism severity index in prognostication of pulmonary embolism – a retrospective study in a regional hospital in Hong Kong

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Utilisation of the Simplified Pulmonary Embolism Severity Index in Prognostication of Pulmonary Embolism — A Retrospective Study in a Regional Hospital in Hong Kong

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Abstract

Introduction: Pulmonary embolism is the most severe form of venous thromboembolism that can result in significant morbidity and mortality, especially if left untreated. Guidelines suggested the use of clinical scoring systems to stratify patients’ risk of mortality, which helps to guide subsequent management strategy. Simplified pulmonary embolism severity index is a well-validated prognostic score that predicts the risk of short-term mortality of pulmonary embolism and studies showed that low-risk patients could be safely managed as outpatients. However, local studies on the use of prognostic scores including simplified pulmonary embolism severity index in management of pulmonary embolism are lacking.

Method: This is a single-centre retrospective cohort study. All patients who were diagnosed with pulmonary embolism and admitted to Caritas Medical Centre between 1st January 2007 to 31st December 2017 were included. The ability of simplified pulmonary embolism severity index in predicting 30-day and in-hospital mortality was assessed. Besides, we tried to look into other independent predicting factors for 30-day and in-hospital mortality.

Result: Totally 267 patients were included in the study, 48 of them had simplified pulmonary embolism severity index 0 while 219 had simplified pulmonary embolism severity index ≥1. Simplified pulmonary embolism severity index ≥1 was associated with increased risk of 30-day mortality ($\chi^2$ 7.076, p = 0.008) and in-hospital mortality ($\chi^2$ 7.570, p = 0.006).

Besides, on univariate and multivariate Cox regression analysis, history of substance abuse (hazard ratio: 5.431, 95% confidence interval: 1.685–17.504, P = 0.005) and history of cancer (hazard ratio: 3.691, 95% confidence interval 1.799–7.571, P < 0.001) were found to be independent predictors for 30-day mortality. Whereas for in-hospital mortality, age (odds ratio 1.040, 95% confidence interval 1.005–1.075, P = 0.024), history of substance abuse (odds ratio 11.774, 95% confidence interval 2.067–67.052, P = 0.005) and history of cancer (odds ratio 4.965, 95% confidence interval 2.093–11.778, P < 0.001) were found to be independent predictors on multivariate binary logistic regression.

Kaplan–Meier analysis showed lower survival rates over 30 days among patients with simplified pulmonary embolism severity index ≥1.

Conclusion: Simplified pulmonary embolism severity index ≥1 predicted a higher risk of 30-day and in-hospital mortality among patients with acute pulmonary embolism. History of substance abuse and cancer are independent predictors of 30-day and in-hospital mortality, while age is an independent predictor of in-hospital mortality.

Keywords: Simplified pulmonary embolism severity index, Risk stratification, Prognosis, Thirty-day mortality, In-hospital mortality
Introduction

Venous thromboembolism (VTE), comprised of deep vein thrombosis (DVT) and pulmonary embolism (PE), are well-known important clinical entities. They can occur sporadically without obvious identifiable causes or as complications of other conditions such as prolonged immobility, malignancy and autoimmune diseases. They can result in potentially high morbidity and mortality, yet they are treatable and preventable.

It is traditionally believed that VTE is more common among Western populations who have higher thrombotic tendency, and is uncommon among Asian or Chinese counterparts. However, there are local epidemiological data suggestive of increasing incidence of VTE among Chinese populations, with estimated annual incidence of DVT and PE being 30 per 100,000 population (0.03%) and 11.7 per 100,000 population (0.012%) respectively in 2010–2011, compared with 17.1 per 100,000 population (0.017%) for DVT and 3.9 per 100,000 population (0.0039%) for PE in 2000–2001 [1,2].

PE is a severe form of VTE with potentially high morbidity and mortality. The mortality of PE in Hong Kong was 17.4% according to a local study [2]. In worldwide, the mortality of untreated PE was estimated to be 30%, while with treatment, the mortality rate could be lowered to around 4–8% [3–8]. However, patients with PE do present in a broad spectrum of severities, ranging from asymptomatic or minimally symptomatic haemodynamically stable disease to severe haemodynamically unstable disease and sudden death. Undoubtedly, unstable patients warrant inpatient close monitoring and intensive treatment with anticoagulation, thrombolysis, catheter-based interventions, or even open surgery. In contrast, for stable, low-risk patients, brief in-hospital treatment or even outpatient treatment were shown to be safe and effective [9–12].

There are several validated clinical prognostic scores which can be used to predict the short-term risk of mortality from PE, they help to guide physicians in making decisions on the management of patients with newly diagnosed PE in inpatient or outpatient settings. The most well-known validated prognostic scores are the Pulmonary Embolism Severity Index (PESI) and its simplified version – the Simplified Pulmonary Embolism Severity Index (sPESI). The use of PESI or sPESI for risk stratification of PE was recommended in the guidelines from the European Society of Cardiology and British Thoracic Society [13,14].

PESI consists of 11 clinical variables with different weighing, and the scores of all variables are added up to give the total score (Table 1). Patients can be classified into different risk classes using the total score, with class I and II indicating low-risk and class III to V indicating high-risk (Table 2) [15]. PESI is a well-validated prognostic score for predicting 30-day mortality in PE [16–26]. However, owing to its complexity, PESI is difficult and cumbersome to apply in day-to-day busy clinical practice.

On the other hand, sPESI consists of 6 clinical variables with equal weighing, and each item is assigned 1 point if presents (Table 3). Patients with sPESI of 0 belong to the low-risk group (30-day mortality rate of 1.0%), while those with sPESI of 1 or above are classified as high-risk (30-day mortality rate of 10.9%) [27]. The simplicity of sPESI makes it much easier to use compared with PESI.

<table>
<thead>
<tr>
<th>Table 1. PESI [15]</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical variables</strong></td>
</tr>
<tr>
<td>Age</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>History of cancer</td>
</tr>
<tr>
<td>History of heart failure</td>
</tr>
<tr>
<td>History of chronic lung disease</td>
</tr>
<tr>
<td>Pulse &gt;110 beats per minute</td>
</tr>
<tr>
<td>Systolic blood pressure &lt;100 mmHg</td>
</tr>
<tr>
<td>Respiratory rate ≥30 breaths per minute</td>
</tr>
<tr>
<td>Temperature &lt;36 °C</td>
</tr>
<tr>
<td>Altered mental status</td>
</tr>
<tr>
<td>Arterial oxyhaemoglobin saturation &lt;90%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 2. PESI risk classes [15].</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total PESI</strong></td>
</tr>
<tr>
<td>≤65</td>
</tr>
<tr>
<td>66–85</td>
</tr>
<tr>
<td>86–105</td>
</tr>
<tr>
<td>106–125</td>
</tr>
<tr>
<td>≥125</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 3. sPESI [27]</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical variables</strong></td>
</tr>
<tr>
<td>Age &gt;80 years</td>
</tr>
<tr>
<td>History of cancer</td>
</tr>
<tr>
<td>History of chronic cardiopulmonary diseases</td>
</tr>
<tr>
<td>Pulse ≥110 per minute</td>
</tr>
<tr>
<td>Systolic blood pressure &lt;100 mmHg</td>
</tr>
<tr>
<td>Arterial oxyhaemoglobin saturation &lt;90%</td>
</tr>
</tbody>
</table>
PESI and sPESI were shown to be accurate in predicting 30-day mortality in patients with acute PE, and data suggested their prognostic accuracies were comparable [27–31]. Besides, PESI and sPESI were found to have good predictive value for inhospital mortality [34,36]. After risk stratification with PESI or sPESI, low-risk cases can be managed in brief inpatient or outpatient settings while high-risk ones should be hospitalised for inpatient management.

The use of prognostic scores in clinical management of PE is rare despite their validated accuracies, and most PE patients are managed as inpatients throughout their clinical courses, even for stable cases. In a retrospective cohort study conducted in the United States, among 746 low-risk PE patients who were potentially eligible for outpatient treatment, only 13 (1.7%) of them were treated in outpatient setting and 119 (16%) were discharged from hospitals within 2 days [39]. Similar situation is observed in Hong Kong, where prognostic scores are seldom used to stratify patients diagnosed with PE into high-risk or low risk, and virtually all of them are managed as inpatients regardless of disease severity. If prognostic scores such as sPESI are used to predict early mortality risk, suitable low-risk patients may be selected and managed in brief inpatient or even full outpatient settings. Such practice may have implication in reducing unnecessary hospital stays, which may in turn help preventing complications of prolonged hospitalisation and cutting hospital costs. However, local studies and data on the use of prognostic scores in PE management are lacking.

This retrospective study aims to review a group of local patients diagnosed with acute PE and to correlate their short-term outcome, i.e. 30-day and in-hospital mortality, with sPESI.

Methods

Study design and patient population

This is a single-centre retrospective cohort study. All adult patients of 18 years or above diagnosed with acute PE who were admitted to Caritas Medical Centre at any time within the period from 1st January 2007 to 31st December 2017 were included. Patients were identified by searching with diagnosis code of “pulmonary embolism and infarction” (415.1) according to the Ninth Revision of International Classification of Diseases (ICD-9) through the Clinical Data Analysis and Reporting System (CDARS).

Inclusion criteria included age of 18 years or above and acute PE diagnosed by positive computed tomography pulmonary angiography (CTPA). Exclusion criteria included age below 18 years old, doubtful PE diagnosis and incomplete medical records. Subjects with PE diagnosed by ventilation/perfusion (V/Q) scan were not included since V/Q scan was not available in Caritas Medical Centre.

All included patients had their sPESI retrospectively calculated by adding up points assigned for each item (1 point for each): age >80 years, history of cancer, chronic cardiopulmonary disease, pulse >110 beats per minute, systolic blood pressure <100 mmHg and arterial oxygen saturation <90%.

Also, background demographics were recorded, including age, gender, ethnicity, premorbid mobility, history of cigarette smoking, alcoholism, substance abuse, thromboembolism, hypertension, diabetes mellitus, thrombophilia, cancer, chronic cardiopulmonary diseases, pulse (<110 or ≥110 beats per minute), systolic blood pressure (≥100 or <100 mmHg), arterial oxygen saturation i.e. SpO2 (≥90% or <90%), recent lower limb fractures or orthopaedic surgery, recent non-orthopaedic surgical procedures, and recent stroke within the same hospitalisation. Besides, any anticoagulant use prior to PE diagnosis, conversion from heparin or warfarin to novel oral anticoagulants (NOAC) and requirement of thrombolytics, interventional procedures or surgery were also recorded.

This study was approved by the Kowloon West Cluster Research Ethics Committee (KWC REC No. KW/EX-18-092 (125-08)). It was conducted with adherence to the Declaration of Helsinki and the policies and procedures required by the Research Ethics Committee of the Hospital Authority. All the research data were handled in strict accordance with the policies of the Hospital Authority and the hospital on handling and storage of patients’ medical records.

Statistical analysis

Baseline demographics and categorical variables were shown as standard descriptive summaries with counts and percentages. Continuous variables were expressed as means and standard deviations.

Patients had their sPESI calculated and divided into low-risk (sPESI = 0) and high-risk groups (sPESI ≥1). Thirty-day and in-hospital mortality rates in the two groups were compared using the Chi-square test or Fisher's exact test. Furthermore, univariate analysis for 30-day mortality was
performed and factors with P-value of <0.2 were included in multivariate analysis. Multivariate binary logistic regression analysis was done for in-hospital mortality.

Log rank test was used to compare Kaplan–Meier survival curves of patients with sPESI of 0 and sPESI ≥1.

All tests were two-sided, p-values <0.05 are regarded as statistically significant. All statistical analyses were conducted using IBM® SPSS® Statistics Version 21.

Results

Patient demographics

Totally 270 patients with computed tomography pulmonary angiography-confirmed acute pulmonary embolism were identified during the period of 1st January 2007 to 31st December 2017. Three patients were excluded from the study as one walked away from hospital while two ended up with discharge against medical advice during their index hospitalisations and were subsequently lost to follow up. Therefore 267 patients were included in statistical analysis.

The mean age of subjects in the study was 69.5 years (±15.3 years). Female accounted for more than half of the cases (57.3%, n = 153). Other background characteristics are as shown in Table 4.

Thirty-day mortality

Totally 38 patients died within 30 days, therefore the 30-day mortality rate among the whole study population was 14.2%. When dividing the patients into sPESI low or high-risk categories, forty-eight patients were classified as low-risk with sPESI of 0, and 219 were classified as high-risk with sPESI of 1 or above. Only 1 patient in the sPESI low-risk group died within 30 days, so the 30-day mortality rate in the sPESI low-risk group was 2.1%, whilst 37 sPESI high-risk patients died within 30 days, therefore the

<table>
<thead>
<tr>
<th>Table 4. Patient demographics</th>
<th>All</th>
<th>sPESI = 0</th>
<th>sPESI ≥1</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≤80 years</td>
<td>189</td>
<td>48</td>
<td>141</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&gt;80 years</td>
<td>78</td>
<td>0</td>
<td>78</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>114</td>
<td>21</td>
<td>93</td>
<td>0.871</td>
</tr>
<tr>
<td>Female</td>
<td>153</td>
<td>27</td>
<td>126</td>
<td></td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>266</td>
<td>48</td>
<td>218</td>
<td>0.639</td>
</tr>
<tr>
<td>Caucasian</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Premorbid mobility</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Walking unaided</td>
<td>160</td>
<td>35</td>
<td>125</td>
<td>0.116</td>
</tr>
<tr>
<td>Walking with aids or assistance</td>
<td>67</td>
<td>9</td>
<td>58</td>
<td></td>
</tr>
<tr>
<td>Chair-bound or bed-bound</td>
<td>40</td>
<td>4</td>
<td>36</td>
<td></td>
</tr>
<tr>
<td>History of smoking</td>
<td>87</td>
<td>16</td>
<td>71</td>
<td>0.903</td>
</tr>
<tr>
<td>History of alcoholism</td>
<td>30</td>
<td>7</td>
<td>23</td>
<td>0.417</td>
</tr>
<tr>
<td>History of substance abuse</td>
<td>9</td>
<td>1</td>
<td>8</td>
<td>0.585</td>
</tr>
<tr>
<td>History of venous thromboembolism</td>
<td>8</td>
<td>3</td>
<td>5</td>
<td>0.144</td>
</tr>
<tr>
<td>History of hypertension</td>
<td>121</td>
<td>18</td>
<td>103</td>
<td>0.230</td>
</tr>
<tr>
<td>History of diabetes mellitus</td>
<td>57</td>
<td>8</td>
<td>49</td>
<td>0.382</td>
</tr>
<tr>
<td>History of thrombophilia</td>
<td>6</td>
<td>5</td>
<td>1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>History of cancer</td>
<td>116</td>
<td>0</td>
<td>116</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>History of chronic cardiopulmonary disease</td>
<td>50</td>
<td>0</td>
<td>50</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pulse ≥110 per minute</td>
<td>51</td>
<td>0</td>
<td>51</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Systolic blood pressure &lt;100 mmHg</td>
<td>17</td>
<td>0</td>
<td>17</td>
<td>0.046</td>
</tr>
<tr>
<td>SpO2 &lt; 90%</td>
<td>90</td>
<td>0</td>
<td>90</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Recent lower limb fractures or orthopaedic surgery within the same hospitalisation</td>
<td>11</td>
<td>2</td>
<td>9</td>
<td>0.996</td>
</tr>
<tr>
<td>Recent stroke within the same hospitalisation</td>
<td>12</td>
<td>3</td>
<td>9</td>
<td>0.517</td>
</tr>
<tr>
<td>On anticoagulants prior to PE diagnosis</td>
<td>7</td>
<td>3</td>
<td>4</td>
<td>0.082</td>
</tr>
<tr>
<td>Put on NOAC or switched from warfarin to NOAC after diagnosis of PE</td>
<td>35</td>
<td>13</td>
<td>22</td>
<td>0.002</td>
</tr>
<tr>
<td>Advanced treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>240</td>
<td>44</td>
<td>196</td>
<td></td>
</tr>
<tr>
<td>Thrombolytic</td>
<td>13</td>
<td>3</td>
<td>10</td>
<td>0.506</td>
</tr>
<tr>
<td>Interventional procedure (e.g. IVC filter)</td>
<td>14</td>
<td>1</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>Surgery</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>
The 30-day mortality rate in the sPESI high-risk group was 16.9%. Simplified PESI of 1 or above was found to be significantly associated with higher risk of 30-day mortality ($\chi^2 = 7.076$, p = 0.008) (Table 5).

Additionally, on univariate and multivariate Cox regression analysis, history of substance abuse (hazard ratio: 5.431, 95% confidence interval: 1.685–17.504, P = 0.005) and history of cancer (hazard ratio: 3.691, 95% confidence interval: 1.799–7.571, P < 0.001) were found to be independent predictors of 30-day mortality.

On the other hand, age, gender, premorbid mobility, history of smoking, alcoholism, VTE, hypertension, DM, chronic cardiopulmonary diseases did not independently predict increased risk of 30-day mortality (Table 6).

**In-hospital mortality**

Forty-eight patients died during their index hospitalisation, thus the in-hospital mortality rate was 18%. When analysing by sPESI low or high-risk categories, 2 out of 48 sPESI low-risk patients died during their hospital stay, so the in-hospital mortality rate among sPESI low-risk patients was 4.2%. Whereas 46 out of 219 sPESI high-risk patients died as inpatients, therefore the in-hospital mortality rate among sPESI high-risk patients was 21%. High-risk sPESI $\geq 1$ was found to be significantly associated with in-hospital mortality ($\chi^2 = 7.570$, P = 0.006) (Table 7).

On multivariate binary logistic regression analysis, age (odds ratio 1.040, 95% confidence interval 1.005–1.075, P = 0.024), history of substance abuse (odds ratio 11.774, 95% confidence interval 2.067–67.052, P = 0.005) and history of cancer (odds ratio 4.965, 95% confidence interval 2.093–11.778, P < 0.001) were found to be independent predictors of in-hospital mortality.

Gender, premorbid mobility, history of smoking, alcoholism, VTE, hypertension, DM, chronic cardiopulmonary diseases did not independently predict in-hospital mortality (Table 8).

**Survival analysis**

Kaplan–Meier analysis showed that the 30-day survival among patients with sPESI of 0 was higher than those with sPESI of 1 or above, with the survival curves separated early (Fig. 1).

---

### Table 5. Thirty-day mortality.

<table>
<thead>
<tr>
<th>All patients</th>
<th>Thirty-day mortality</th>
<th>Chi-square, p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>sPESI = 0</td>
<td>48</td>
<td>Yes: 1 (2.1%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No: 47 (97.9%)</td>
</tr>
<tr>
<td>sPESI $\geq 1$</td>
<td>219</td>
<td>Yes: 37 (16.9%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No: 182 (83.1%)</td>
</tr>
<tr>
<td>Total</td>
<td>267</td>
<td>Yes: 38 (14.2%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No: 229 (85.8%)</td>
</tr>
</tbody>
</table>

### Table 6. Univariate and multivariate Cox regression model for 30-day mortality.

<table>
<thead>
<tr>
<th></th>
<th>Univariate P-value</th>
<th>Multivariate Hazard ratio</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.278</td>
<td>1.178</td>
<td>0.376–1.916</td>
<td>0.694</td>
</tr>
<tr>
<td>Gender</td>
<td>0.158</td>
<td>1.065</td>
<td>0.439–2.587</td>
<td>0.889</td>
</tr>
<tr>
<td>Premorbid mobility</td>
<td>0.494</td>
<td>1.746</td>
<td>0.691–4.417</td>
<td>0.239</td>
</tr>
<tr>
<td>History of smoking</td>
<td>0.067</td>
<td>5.431</td>
<td>1.685–17.504</td>
<td>0.005</td>
</tr>
<tr>
<td>History of alcoholism</td>
<td>0.101</td>
<td>3.691</td>
<td>1.799–7.571</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>History of substance abuse</td>
<td>0.003</td>
<td>1.463</td>
<td>0.684–3.130</td>
<td>0.327</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.300</td>
<td>3.691</td>
<td>1.799–7.571</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>0.953</td>
<td>1.463</td>
<td>0.684–3.130</td>
<td>0.327</td>
</tr>
<tr>
<td>History of cancer</td>
<td>0.002</td>
<td>1.463</td>
<td>0.684–3.130</td>
<td>0.327</td>
</tr>
<tr>
<td>History of cardiopulmonary disease</td>
<td>0.178</td>
<td>1.463</td>
<td>0.684–3.130</td>
<td>0.327</td>
</tr>
</tbody>
</table>

### Table 7. In-hospital mortality.

<table>
<thead>
<tr>
<th></th>
<th>All patients</th>
<th>In-hospital mortality</th>
<th>Chi-square, p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>sPESI = 0</td>
<td>48</td>
<td>Yes: 2 (4.2%)</td>
<td>No: 46 (97.9%)</td>
</tr>
<tr>
<td>sPESI $\geq 1$</td>
<td>219</td>
<td>Yes: 46 (21.0%)</td>
<td>No: 173 (79.0%)</td>
</tr>
<tr>
<td>Total</td>
<td>267</td>
<td>Yes: 48 (18.0%)</td>
<td>No: 219 (82.0%)</td>
</tr>
</tbody>
</table>
In this study, sPESI of 1 or above was found to be associated with 30-day and in-hospital mortality among patients diagnosed with PE. Besides, history of substance abuse and history of cancer were also found to independently predict 30-day mortality in PE. Furthermore, age, history of substance abuse and history of cancer were independent predictors of in-hospital mortality.

There was one patient with sPESI of 0 who died within 30 days of PE diagnosis. He suffered a massive ischaemic stroke with right middle cerebral artery territory infarct complicated with DVT and PE, and further complicated with haemorrhagic transformation of the infarct after initiation of anticoagulation.

In this study, only patients with positive CTPA were included. On the contrary, in many other PE studies, patients with high probability V/Q scan, positive lower limb venous compression Doppler ultrasound in case of inconclusive V/Q scan were also included. It was because CTPA was highly sensitive in detecting PE and was the standard of

| Table 8. Multivariate binary logistic regression model for in-hospital mortality |
|-----------------|--------------|-----------------|
|                | P-value      | Odds ratio      | 95% CI          |
| Age             | 0.024        | 1.040           | 1.005–1.075     |
| Gender          | 0.568        | 0.759           | 1.005–1.075     |
| Premorbid morbidity |            |                 |                 |
| Unaided        | 0.477        | 0.650           | 0.234–1.806     |
| Walk with aids or assistance | | |
| Chair or bed-bound | 0.261        | 0.488           | 0.139–1.705     |
| History of smoking | 0.933        | 0.995           | 0.354–2.799     |
| History of alcoholism | 0.161        | 2.279           | 0.720–7.216     |
| History of substance abuse | | |
| History of previous VTE  | 0.575        | 1.919           | 0.197–18.730    |
| Hypertension    | 0.467        | 0.737           | 0.323–1.678     |
| Diabetes mellitus | 0.893        | 0.940           | 0.380–2.323     |
| History of cancer | <0.001       | 4.965           | 2.093–11.778    |
| History of cardiopulmonary disease | | |

Discussion

In this study, sPESI of 1 or above was found to be associated with 30-day and in-hospital mortality among patients diagnosed with PE. Besides, history of substance abuse and history of cancer were also found to independently predict 30-day mortality in PE. Furthermore, age, history of substance abuse and history of cancer were independent predictors of in-hospital mortality.

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![Fig. 1. Kaplan–Meier survival curve for cumulative 30-day survival of patients with sPESI of 0 and sPESI of 1 or above. The 30-day survival of patients with sPESI of 0 is significantly better than those with 1 or above (97.9% vs. 83.1%), \( p = 0.01 \) by log-rank test.](image-url)
care for PE diagnosis [36]. Besides, V/Q scan was not available in Caritas Medical Centre. Furthermore, lower limb venous compression Doppler ultrasound per se could not reliably diagnose PE and was not done in almost one-third of the patients in this study (28.5%).

Prognostic scores and models

Several serum biomarkers and scoring systems were developed for prognostication of acute PE. Commonly used serum biomarkers included brain natriuretic peptide (BNP), N-terminal prohormone of brain natriuretic peptide (NT-proBNP) and cardiac troponin. Unfortunately, these biomarkers were shown to have poor predictive accuracy for adverse outcome when used individually. Major guidelines such as European Society of Cardiology (ESC) and British Thoracic Society (BTS) guidelines suggested the use of validated clinical scoring systems to predict the prognosis of acute PE patients [13,14]. Examples of clinical scoring systems included PESI, sPESI, Hestia criteria, Geneva score, and ESC model [32,35,40]. These scores comprised clinically available parameters or combinations of clinical, biochemical and imaging parameters. They were validated for identification of PE patients with low, intermediate or high-risk of mortality. PESI and sPESI are well-validated scores that serve such purpose and were recommended by the ESC and BTS [13–31].

Furthermore, in a recent meta-analysis of 21 studies, right ventricular dysfunction on echocardiogram or CTPA was found to predict early all-cause mortality and PE-related adverse events in patients with low clinical risk scores (PESI, sPESI and Hestia) [33]. Therefore, incorporating right ventricular dysfunction into the risk stratification process of PE may further improve prognostic accuracy.

Pulmonary embolism severity index – PESI

PESI is a clinical scoring system developed to predict 30-day mortality in acute PE [15]. It consists of 11 clinical variables carrying different weights, the corresponding score of each clinical variable can then be added up to obtain the total score (Table 4). After obtaining the total score, patients can be divided into class I to V. Classes I and II belong to the low-risk groups, while classes III, IV and V are the high-risk groups (Table 5).

The predictive accuracy and generalisability of PESI were supported by derivation and validation in more than 17,000 patients from more than 300 hospitals in the United States and Europe [15–19].

In a study by Choi et al. in 2008, it was found that the in-hospital and overall mortality rates of patients in PESI classes II, III and IV were similar, but higher than that of class I and lower than that of class V. Therefore, they suggested to further divide PESI risk categories into low (class I), intermediate (classes II-IV) and high (class V), and to exercise caution when managing class II patients as low-risk [34].

PESI was well established as a reliable prognostic scoring system for acute PE [15–26], which helps classifying patients into various risk categories so that physicians could provide appropriate management accordingly. Nevertheless, given the number of parameters and calculations needed, PESI may be difficult and cumbersome to apply under busy daily clinical settings.

Simplified pulmonary embolism severity index – sPESI

In 2010, David et al. developed a simplified version of PESI (Table 6) via a derivation cohort of around 1000 patients from a major hospital in Madrid, Spain. The sPESI was then externally validated on a cohort of patients from an international registry – Registro Informatizado de la Enfermedad Tromboembolica (The RIETE) [27].

The sPESI consists of only 6 equally weighed variables, all are readily available clinically. Each variable is given a score of 1 if presents. Patients with an overall score of 0 are regarded as low-risk (30-day mortality rate of 1.0%), while those scored 1 or above belong to the high-risk category (30-day mortality rate of 10.9%) [27]. The simplicity of sPESI makes it much easier to use than PESI in daily clinical practice.

Despite its relative simplicity compared with PESI, the prognostic accuracy of sPESI is maintained. Righini et al. [28], Venetz et al. [29], Sam et al. [30], Lankeit et al. [35] and Spirk et al. [37] demonstrated good prognostic accuracy of sPESI in their studies. In a pooled meta-analysis conducted by Zhou et al. in 2012, sPESI was shown to have similar accuracy in predicting all-cause mortality when compared with PESI, with good negative predictive value of 97–98% [31].

Apart from 30-day mortality, sPESI was investigated for its ability in predicting in-hospital, midterm and long term mortality among PE patients. In a study by Lankeit et al. in 2011, sPESI predicted 30-day and 6-month PE mortality [35]. While in another study by Kilic et al. in 2014, sPESI was found to be accurate in predicting in-hospital, 6-month and even 6-year mortality among PE patients [36]. In our study, high-risk sPESI category (i.e. 1 or above) was
significantly associated with in-hospital and 30-day mortality in local patients.

Furthermore, there were studies investigating the potential additive value of cardiac troponins on improving the prognostic accuracy of sPESI. Lankeit et al. showed the combination of high sensitivity troponin T and sPESI improved accuracy in identifying low-risk patients potentially eligible for outpatient treatment [35]. In a study by Spirk et al., it was shown that cardiac troponin I added prognostic value in predicting risk of early mortality and PE recurrence in high sPESI patients [37]. In another study, Sanchez et al. demonstrated cardiac troponin I predicted only 30-day PE-related mortality while sPESI predicted both 30-day PE-related and all-cause mortality [38].

In conclusion, there were robust data supporting sPESI as a simple yet accurate tool in predicting short term and probably long term outcome, with the addition of cardiac troponin potentially increasing its prognostic utility and accuracy.

Application of sPESI

There were studies showing that sPESI low-risk patients could be managed effectively and safely in outpatient settings and that outpatient treatment was non-inferior to inpatient treatment [9–12]. Clinical prognostic scores like sPESI facilitate the identification of low-risk PE patients. As suggested by international guidelines, those low-risk patients with PE as the only reason for hospitalisation, good family and social support and easy access to healthcare services in case of deterioration are candidates eligible for brief inpatient or even outpatient treatment. By managing low-risk patients in outpatient settings, unnecessary hospital stays and related costs can be reduced, so are the complications related to hospitalisation, such as hospital-acquired infections, delirium, falls and bedsores, etc.

However, the use of clinical prognostic scores in PE management is rare in daily clinical practice [39]. In Hong Kong, this is probably due to poor awareness of these scores among physicians and the lack of local studies and data supporting their use. This should call for further local studies to enrich local evidence and experience in using these scores.

In the management of PE, traditionally, most patients are treated by parenteral anticoagulants such as low molecular weight heparin for few days, followed by bridging to warfarin, with a period of overlapping use of both agents. Upon initiation of warfarin, loading doses are needed and frequent blood taking for monitoring of International Normalised Ratio (INR) is necessary for subsequent dose titration. Such practice essentially precludes early discharge or outpatient treatment of PE. Another potential choice is to use parenteral anticoagulants that allow once-daily dosing, by which patients can be discharged early and managed at day ward, outpatient clinic or even at home. However, this may still be cumbersome and involve extra costs and resources. Besides, needle phobia is not uncommon especially when injection is required on a daily basis.

The emergence of NOACs marks an important breakthrough in the management of thromboembolic diseases. With the availability of NOACs, patients can have simpler, more effective, and yet safer choices of anticoagulant therapies over traditional vitamin K antagonists. NOACs were first studied and used in ischaemic stroke prophylaxis for non-valvular atrial fibrillation, while subsequent further studies expanded their indications to the field of VTE with promising results. There were landmark randomised trials demonstrated non-inferiority of therapeutic effects of NOACs yet lower major bleeding risks when compared with warfarin [41–45]. The use of NOACs eliminates the need for frequent blood taking for dose titration especially during the initiation phase, and some of the NOACs such as rivaroxaban and apixaban can be used as agents for both initial and maintenance treatment for PE, without the need for prior use of low molecular weight heparin. Therefore, NOACs are particularly suitable for low-risk PE patients who are to be discharged early and managed on an outpatient basis. In a recently published study, the HoT-PE (Home Treatment of Patients with Low-risk Pulmonary Embolism with the Oral Factor Xa Inhibitor Rivaroxaban) study, it was shown that early discharge within 2 days of hospitalisation and treatment with rivaroxaban was effective and safe for low-risk PE patients without right ventricular dysfunction and intracardiac thrombus on echocardiogram, with no significant increase in recurrent VTE and mortality for up to 3 months [46].

Therefore, PE patients who are stratified as low-risk may be discharged early and offered outpatient treatment with NOACs. Such workflow renders great convenience to patients and physicians, and may potentially become the new paradigm for the management of low-risk PE.

Furthermore, in local practice, a substantial proportion of outpatients have their PE incidentally found on computed tomography performed for other reasons. These patients are usually referred to hospital and then admitted for inpatient treatment. Many of these patients, however, are stable and with no high-risk features, and are good candidates for outpatient management if their sPESI scores are found to be 0. Nonetheless, some of these patients may still require inpatient management to facilitate
early arrangement of certain investigations such as lower limb compression Doppler ultrasound to exclude DVT, serum tumour markers and computed tomography for malignancy screening.

**Substance abuse**

In our study, apart from sPESI of 1 or above, history of substance abuse was also found to be an independent predictor of 30-day and in-hospital mortality of PE. Of the 9 patients with history of intravenous abuse, 4 of them died within 30 days because of PE. Possible reasons for this included poor general health and physique, delayed presentation to medical service, poor disease insight, poor drug compliance and loss to follow up. Perhaps it is worthwhile to manage these patients as high-risk under inpatient setting and extra effort should be put on education to ensure good adherence to therapy and subsequent follow up.

The above results should be interpreted with caution given the small number of substance abusers in our study. However, this may still provide some insight into the relationship between substance abuse and PE-related mortality and may stimulate larger-scale studies to further investigate.

**Cancer**

History of cancer was found to be an independent predictor of 30-day and in-hospital mortality of PE. This is readily explicable. First of all, history of cancer is a part of the sPESI. Also, patients with cancer who are diagnosed with VTE or PE usually have their cancer evolved to advanced stage or metastatic disease, therefore their prognosis are generally poor.

**Limitation of this study**

This is a single centre, retrospective study with relatively small sample size. Larger-scale retrospective or prospective local studies on sPESI are highly desirable in evaluating its performance in predicting mortality among local PE patients, which may raise awareness among physicians and facilitate incorporation of sPESI into local PE management guidelines or protocols.

Although latest studies and international guidelines supported incorporation of echocardiographic assessment of RV function in the risk stratification process of PE, it was not included in this retrospective study since only a small proportion of subjects had echocardiogram done (34.5%).

Besides, there are important breakthroughs in treatment modalities for PE in recent years such as NOACs and ultrasound-assisted catheter-based thrombolysis [47,48], which resulted in great impact on improving the clinical outcome of PE patients. Since sPESI does not take into account the treatment strategy adopted, it cannot be used to predict the effect of treatment on patients’ outcome.

**Conclusion**

Simplified PESI predicts 30-day and in-hospital mortality of acute PE in a group of local patients, with a score of 1 or above predicts high-risk while a score of 0 predicts low risk. History of substance abuse and cancer are independent predictors for 30-day and in-hospital mortality. Age is an independent predictor of in-hospital mortality. Early discharge and outpatient treatment may be considered for low-risk patients, whereas for high-risk patients, hospital admission and inpatient management strategy should be adopted.

**Conflict of interest**

None declared.

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