Thrombosis Research 129 (2012) 710–714

Contents lists available at SciVerse ScienceDirect

Thrombosis Research

journal homepage: www.elsevier.com/locate/thromres

Regular Article

Does the Pulmonary Embolism Severity Index accurately identify low risk patients eligible for outpatient treatment?☆

Petra M.G. Erkens [a], Esteban Gandara [b], Philip S. Wells [b], Alex Yi-Hao Shen [b], Gauruv Bose [b], Gregoire Le Gal [c], Marc Rodger [b], Martin H. Prins [d], Marc Carrier [b,*]

[a] Department of General Practice, School for Public and Primary Care (CAPHRI) and Cardiovascular Research Institute Maastricht (CARIM), Maastricht University, The Netherlands
[b] Department of Medicine, Ottawa Hospital, Ottawa, Canada
[c] Departement de Medicine Interne et de Pneumologie, CHU de la Cavale Blanche, Brest, France
[d] Department of Epidemiology, Maastricht University, The Netherlands

ARTICLE INFO

Article history:
Received 27 May 2011
Received in revised form 4 August 2011
Accepted 18 August 2011
Available online 9 September 2011

Keywords:
pulmonary embolism severity index
outpatient treatment

ABSTRACT

Introduction: The pulmonary embolism severity index (PESI) and the recently derived simplified PESI prognostic model have been developed to estimate the risk of 30-day mortality in patients with acute PE. We sought to assess if the PESI and simplified PESI prognostic models can accurately identify adverse events and to determine the rates of events in patients treated as outpatients.
Methods: A retrospective cohort study of patients with acute pulmonary embolism (PE) presenting at the Ottawa Hospital (Canada) was conducted between 1 January 2007 and 31 December 2008.
Results: Two hundred and forty three patients were included. A total of 118 (48.6%) and 81 (33.3%) were classified as low risk patients using the original and simplified PESI prognostic models respectively. None of the low risk patients died within the 3 months of follow-up. One hundred and fifteen (47.3%) patients were safely treated as outpatients with no deaths or bleeding episodes and only 1 recurrent event within the first 14 days or after 30 days of follow-up. Thirty four (29.6%) of these outpatients were classified as high risk patients according to the original PESI and 54 (47.0%) to the simplified PESI prognostic model.
Conclusion: Both PESI strategies accurately identify patients with acute PE who are at low risk and high risk for short-term adverse events. However, 30 to 47% of patients with acute PE and a high risk PESI score were safely managed as outpatients. Future research should be directed at developing tools that predict which patients would benefit from inpatient management.

Introduction

The mortality and morbidity of pulmonary embolism (PE) may vary considerably depending on the severity of the event and co-morbidities. Predicting patient outcomes may enable different management strategies and may inform the clinician which patients can be treated as outpatients [1,2].

Over the last decade, several studies have suggested that outpatient treatment in a selected group of hemodynamically stable patients with acute PE is safe [3–7] . Benefits include: 1) cost savings from a decrease in hospitalizations; 2) fewer patients at risk for hospital acquired infections; and 3) an improvement in quality of life, increased physical activity and social functioning [3,8–11]. However, physicians are reluctant to treat patients with PE at home due to uncertainty on how to safely identify patients who are at low risk for short-term adverse events [8], irrespective of whether the adverse events could be averted by hospitalization.

Prognostic models that will accurately predict short-term adverse outcomes may help identify patients with acute PE at low-risk of adverse events that can be safely treated as outpatients. Several prognostic models have been developed to assess the risk of death, recurrent venous thromboembolism (VTE) or major bleeding in patients with acute PE [12]. The most extensively validated prognostic models are the Geneva Prognostic Score (GPS) and the Pulmonary Embolism Severity Index (PESI) [12]. The GPS predicts the combined adverse outcomes of death, recurrent VTE and major bleeding episodes during the first three months following the index PE. However, the GPS prognostic model is not frequently used since it requires the use of ultrasound variables and arterial blood gas which decrease

Abbreviations: PE, Pulmonary Embolism; VTE, Venous ThromboEmbolism; GPS, Geneva Prognostic Score; PESI, Pulmonary Embolism Severity Index; CTPA, Computed Tomography Pulmonary Angiography; V/Q scan, Ventilation / Perfusion scan; LMWH, Low Molecular Weight Heparin; CI, Confidence Interval; COPD, Chronic obstructive Pulmonary Disease; UFH, Unfractionated Heparin; CAD, Coronary Artery Disease.

☆ The results from this study were presented as an oral presentation at the ISTH meeting in Kyoto.

* Corresponding author at: Ottawa Hospital General Campus, Department of Medicine, 501 Smyth Road, Box 201, Ottawa, ON, K1H 8L6. Tel.: +1 613 729 7433; fax: +1 613 761 5351.
E-mail address: mcarrier@Ottawahospital.on.ca (M. Carrier).

0049-3848/$ – see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.thromres.2011.08.025

feasibility. Moreover, a comparison of GPS low-risk patients with PESI low-risk patients in a cohort of 599 consecutive patients with acute symptomatic PE showed that the PESI low-risk patients had a significantly lower mortality [13].

The PESI prognostic model stratifies patients in five risk classes with increasing risk of all cause short term mortality without any need for ultrasonography or laboratory studies [14]. The use of the PESI prognostic model requires computation of a score based on 11 variables each with a different weight (Table 1). Recently, a PESI-derived simplified model with a less complex scoring system has been proposed and seems to have a similar prognostic accuracy as the original PESI (Table 1) [15].

We sought to evaluate if the original and the simplified PESI prognostic models could identify patients with acute PE at low risk of short term adverse outcome who can be safely managed as outpatients.

Materials and methods

Study population

We performed a retrospective cohort study including consecutive patients with high risk and non-high risk acute PE [16,17] presenting at the Ottawa Hospital between 1 January 2007 and 31 December 2008 [4]. PE was defined as an intraluminal filling defect on CTPA or a high probability V/Q scan. Patients diagnosed with PE during hospitalization, patients with chronic PE and patients in whom anticoagulation was not initiated (e.g. palliative care patients, small clinical non-significant PE) were excluded from the analyses. Patients were also excluded if they were followed-up by a health care professional out of the Ottawa Hospital [4]. Patients were considered for outpatient management if they were hemodynamically stable, did not require supplemental oxygenation and had no contraindications to Low Molecular Weight Heparin (LMWH) or significant comorbidities. The decision to manage the patients as an outpatient or an inpatient was ultimately left to the discretion of the emergency room physician. Outpatients were followed in the Outpatient Thrombosis Assessment and Treatment Unit within 24–48 hours of diagnosis, then again at 7 days and 3 months. Admitted patients were followed in the Thrombosis Unit after discharge.

Table 1
[15]: Pulmonary Embolism Severity Index (PESI).

Predictors	Original score*	Simplified score¶
Demographic characteristics		
Age>80 years	Age, in years	1
Male sex	+10	
Comorbid illnesses		
Cancer†	+30	1
Heart failure	+10	1**¶
Chronic lung disease	+10	
Clinical findings		
Pulse≥110/min	+20	1
Systolic blood pressure<100 mm Hg	+30	1
Respiratory rate≥30/min	+20	
Temperature<36 °C	+20	
Altered mental status‡	+60	
Arterial oxygen saturation<90%§	+20	1

* A total point score for a given patient is obtained by summing the patient's age in years and the points for each predictor when present. The score corresponds with the following risk classes: < 65, class I; 66 – 85, class II; 86 – 105, class III; 106 – 125, class IV; and ≥ 125, class V. Patients in risk class I and II are defined as being at low risk.
† Cancer defined as a history of cancer or active cancer;‡ Defined as disorientation, lethargy, stupor or coma;§ With and without the administration of supplemental oxygen.
¶ A total point score for a given patient is obtained by summing the points. The score corresponds with the following risk classes: 0, low risk; ≥ 1, high risk. Empty cells indicate that the variable was not included.
** The variables were combined into a single category of chronic cardiopulmonary disease.

Risk-prognostic models

The original PESI prognostic model stratifies patients into five severity classes of increasing risk of mortality within 30 days after the diagnosis PE [16]. The model includes 11 routinely available clinical parameters at the time of presentation: age, male sex, cancer, heart failure, chronic lung disease, pulse≥110 beats/min, systolic blood pressure less than 100 mm Hg, respiratory rate 30≥breaths/min, temperature<36 °C, altered mental status and arterial oxygen saturation<90%. The model assigns points for each applicable characteristic and calculates a total point score by summing these points and the patient's age in years (Table 1). Point assignments correspond with the following risk classes: 65 or less, class I, very low risk; 66 – 85, class II, low risk; 86 – 105, class III, intermediate risk; 106 – 125, class IV, high risk; greater than 125, class V, very high risk [18].

The simplified PESI prognostic model consists of 6 variables: one demographic variable (age>80 years), two comorbid conditions (cancer, chronic pulmonary disease), and three physical examination findings (pulse ≥110 beats/min, systolic blood pressure<100 mmHg and arterial oxygen saturation<90%) (Table 1). Patients with none of these factors were defined as being at low risk [15].

Outcomes

Charts of all included patients were reviewed to extract the data necessary for computation of the original PESI and the simplified PESI prognostic models. All included patients were followed for 3 months.

The following variables were also specified prior to data collection: i) patient demographics; ii) reasons for hospitalization; iii) recurrent VTE and bleeding episodes; and iv) death (date and cause). Data were extracted from paper charts at the emergency department, hospital discharge reports and consultation notes from the Thrombosis Assessment and Treatment Unit. All outcomes were reviewed independently by two reviewers (E. G., P.M.G.E.). Disagreements on the variables were resolved by consensus or retrieving further information from other medical records.

The primary outcomes used to validate the risk-prediction models were overall mortality and fatal PE. The cause of death was identified by discharge summaries or other medical records. Secondary outcomes included recurrent VTE and major hemorrhage. Recurrent PE was defined as a new arterial filling defect on CTPA or high probability V/Q-scan and recurrent DVT was defined as a new non-compressible venous segment on an ultrasound of the extremities. Major hemorrhage was defined according to the definition of the Control of Anticoagulation Subcommittees (ISTH SSC 2004) [19].

Statistical analysis

Descriptive statistics were used to describe the patient characteristics and outcomes. Ninety-five percent confidence intervals (95% CI) and p-values were calculated for each event rate by using Fisher's exact test. The statistical analyses were performed using the Statistical Package for the Social Sciences software (version 17; SPSS; Chicago, IL, USA).

Results

A total of 243 patients presenting at the Ottawa Hospital with confirmed PE were included in this study. One hundred and fifteen (47.3%) patients were directly discharged from the Emergency Department and were treated out of the hospital, while 128 (52.7%) patients were admitted. According to the original PESI prognostic

model, 118 (48.6%; 95% CI, 42.1 – 55.0) patients were classified as low risk (class I and II) and 125 (51.4%; 95% CI, 45.0 – 58.0) were classified as high risk (class III to V). According to the simplified PESI prognostic model, 81 (33.3%; 27.4 – 39.6) patients were classified as low risk patients and 162 (66.7%; 60.4 – 72.6) were classified as high risk patients.

Baseline characteristics of patients in different PESI risk groups are shown in Table 2. High risk patients were older than low risk patients. High risk patients were more likely to have had a previous diagnosis of cancer, heart failure or chronic obstructive pulmonary disease (COPD) whereas low risk patients were more likely to have presented with chest pain and hemoptysis. Most low risk patients were treated with LMWH, while 16% to 22% of the high risk patients were treated with unfractionated heparin (UFH). Two (0.8%; 95% CI; 0.1 – 2.9) patients were treated with thrombolysis.

Overall mortality and fatal PE

No low risk patients, in either group, died within 14 days, 30 days or 3 months (Table 3). In the original PESI high risk group, 7 (5.6%; 95% CI, 2.3 – 11.2) patients died within 14 days, 10 (8%; 95% CI, 3.9 – 14.2) within 30 days and 32 (25.6%; 95% CI, 18.2 – 34.2) patients died within 3 months. The overall mortality in the simplified PESI high risk group was 7 (4.3%; 95% CI, 1.8 – 8.7) within 14 days, 10 (5.5%; 95% CI; 2.7 – 9.9) within 30 days and 32 (19.8%; 95% CI 13.9 – 26.8) within 3 months (Table 3). None of the patients died from PE. The majority (84.4%; 95% CI, 67.2 – 94.7) of the patients died from disease progression of an underlying cancer.

Recurrent VTE and major bleeding episodes

None of the low risk patients, in either group, had a recurrent event within 14 days (Table 3). At 3 months follow-up, 5 (4.2%; 95% CI, 1.4 – 9.6) and 2 (2.5%; 95% CI, 0.3 – 8.6) low risk patients from the original PESI and simplified PESI prognostic models developed recurrent VTE respectively. The rates of recurrent VTE in the high risk groups at 14 days and 3 months follow-up were 3 (2.4%; 95% CI, 0.5 – 6.9) and 5 (4%; 95% CI, 1.3 – 9.1) in the original PESI and 3 (1.9%; 0.4 – 5.3) and 8 (4.9%; 2.2 – 9.5) in the simplified PESI prognostic model (Table 3). The incidence of recurrent events did not differ significantly between the low and high risk groups at 14 days and 3 months (original PESI $P = 0.248$ and 1.000, simplified PESI $P = 0.553$ and 0.503).

There were no major hemorrhages in the low risk groups within 14 days (Table 3). At 3 months follow-up 2 (1.7%; 95% CI, 0.2 – 6.0) patients in the original PESI low risk group had a major hemorrhage, while no (0%; 95% CI, 0.0 – 4.5) patients in the simplified PESI low risk group had a major bleed. The rates of major bleeding in the high risk groups were 8 (6.4%; 95% CI, 2.8 – 12.2) at 14 days and 10 (8%; 95% CI, 3.9 – 14.2) at 3 months follow-up using the original PESI prognostic model and 8 (4.9%; 95% CI, 2.2 – 9.5) at 14 days and 12 (7.4%; 95%

Table 2
Demographic and clinical characteristics of the patients in the cohort.

	Original PESI Low Risk* (n = 118)	Original PESI High Risk† (n = 125)		Simplified PESI Low risk‡ (n = 81)	Simplified PESI High risk§ (n = 162)	
Demographics						
Male, *n* (%)	57 (48.3%)	59 (47.2%)		46 (56.8%)	70 (43.2%)	
Age, mean years (SD)	45.9 (17.0)	68.1 (11.7)		48.6 (17.0)	61.7 (17.3)	
	n (%; 95%CI)	*n* (%; 95%CI)	*p*-value	*n* (%; 95%CI)	*n* (%; 95%CI)	*p*-value
Risk factors for VTE						
Immobilization(≥ 3 days)	21 (17.8%; 11.4-25.9)	18 (14.4%; 8.8-21.8)	NS	15 (18.5%; 10.8-27.7)	24 (14.8%; 9.7-21.2)	NS
Recent surgery (≤ 4 weeks)	18 (15.3%; 9.3- 23.0)	15 (12%; 6.9-19.0)	NS	14 (17.3%; 9.8-27.3)	19 (11.7%; 7.2-17.7)	NS
VTE in history	25 (21.2%; 14.2-29.7)	15 (12%; 6.9-19.0)	NS	16 (19.8%; 11.7-30.1)	24 (14.8%; 9.7-21.2)	NS
Comorbidity						
Cancer¶	12 (10.2%;5.4-17.1)	91 (72.8%; 64.1-80.4)	0.000	0 (0%; 0.0-4.5)	103 (63.6%; 55.7-71.0)	0.000
Heart Failure	1 (0.8%; 0.0-4.6))	12 (9.6%; 5.1-16.2)	0.003	0 (0%; 0.0-4.5)	13 (8.0%; 4.3-13.3)	0.006
COPD	3 (2.5%; 0.5-7.3)	13 (10.4%; 5.7-17.1)	0.018	0 (0%; 0.0-4.5)	16 (9.9%; 5.8-15.5)	0.002
CAD	7 (5.9%; 2.4-11.8)	17 (13.6%; 8.1-20.9)	NS	4 (4.9%; 1.4-12.2)	20 (12.3%; 7.7-18.4)	NS
Stroke	3 (2.5%; 0.5-7.3)	9 (7.2%; 3.3-13.2)	NS	2 (2.5%; 0.3-8.6)	10 (6.2%; 3.0-11.1)	NS
Altered mental status**	0 (0%; 0.0-3.1)	5 (4%; 1.3-9.1)	NS	1 (1.2%; 0.0-6.7)	4 (2.5%; 0.7-6.2)	NS
Clinical presentation						
Dyspnea	90 (76.3%; 67..6-83.6)	102 (81.6%; 73.7-88.0)	NS	60 (74.1%; 63.1-83.2)	132 (81.5%; 74.6-87.1)	NS
Chest pain	89 (75.4% 66.7-82.9)	56 (44.8%; 35.9-54.0)	0.000	63 (77.8%; 67.2-86.3)	82 (50.6%; 42.7-58.6)	0.000
Hemoptysis	10 (8.5%; 4.1-15.0)	4 (3.2%; 0.9-8.0)	NS	9 (11.1%; 5.2-20.1)	5 (3.1%; 1.0-7.1)	0.018
Syncope	3 (2.5%; 0.5-7.3)	4 (3.2%; 0.9-8.0)	NS	1 (1.2%; 0.0-6.7)	6 (3.7%; 1.4-7.9)	NS
Heart rate ≥ 110 b/min	17 (14.4%; 8.6-22.1)	40 (32%; 23.9-40.9)	0.001	0 (0%; 0.0-4.5)	57 (35.2%; 27.9-43.1)	0.000
SBP < 100 mmHg	4 (3.4%; 0.9-8.5)	11 (8.8%; 4.5-15.2)	NS	0 (0%; 0.0-4.5)	15 (9.3%; 5.3-14.8)	0.003
Arterial oxygen saturation <90%††	5 (4.2%; 1.4-9.6)	29 (23.2%; 16.1-31.6)	0.000	0 (0%; 0.0-4.5)	34 (21.0%; 15.0-28.1)	0.000
Respiratory rate ≥ 30/min	4 (3.4%; 0.9-8.5)	12 (9.6%; 5.1-16.2)	NS	2 (2.5%; 0.3-8.6)	14 (8.6%; 4.8-14.1)	NS
Temperature < 36 °C	0 (0%; 0.0-3.1)	11 (8.8%; 4.5-15.2)	0.001	3 (3.7%; 0.8-10.4)	8 (4.9%; 2.2-9.5)	NS
Initial treatment						
LMWH	112 (94.9%; 89.3-98.1)	97 (77.6%; 69.3-84.6)	0.000	75 (92.6%; 84.6-97.2)	134 (82.7%; 76.0-88.2)	NS
UFH	5 (4.2%; 1.4-9.6)	27 (21.6%; 14.7-29.9)		6 (7.4%; 2.8-15.4)	26 (16.0%; 10.8-22.6)	
Other treatment‡‡	1 (0.8%; 0.0-4.6)	1 (0.8%; 0.0-4.4)		0 (0%; 0.0-4.5)	2 (1.2%; 0.1-4.4)	

Abbreviations: VTE, venous thromboembolism; COPD, chronic obstructive pulmonary disease; CAD, coronary artery disease; LMWH, low molecular weight heparin; UFH, unfractionated heparin.
* Original PESI Class I – II; † Original PESI Class III – V;
‡ Simplified PESI no risk factors; § Simplified PESI ≥ 1 risk factor;
¶ Cancer defined as a history of cancer or active cancer; ** Defined as disorientation, lethargy, stupor or coma; †† Saturation assessed with and without the administration of supplemental oxygen. ‡‡ Patients with thrombolysis.

Table 3
Main outcomes within risk strata derived from the original PESI and simplified PESI.

	Original PESI Low Risk* (n = 118)	Original PESI High Risk† (n = 125)		Simplified PESI Low risk‡ (n = 81)	Simplified PESI High risk§ (n = 162)	
	n (%; 95%CI)	*n* (%; 95%CI)	*p*-value	*n* (%; 95%CI)	*n* (%; 95%CI)	*p*-value
14 days follow up						
Overall mortality	0 (0%; 0.0 - 3.1)	7 (5.6%; 2.3 – 11.2)	0.015	0 (0%; 0.0 – 4.5)	7 (4.3%; 1.8 – 8.7)	0.099
Fatal PE	0 (0%; 0.0 - 3.1)	0 (0%; 0.0 – 2.9)	-	0 (0%; 0.0 – 4.5)	0 (0%; 0.0 – 2.3)	-
Recurrent VTE	0 (0%; 0.0 - 3.1)	3 (2.4%; 0.5 – 6.9)	0.248	0 (0%; 0.0 – 4.5)	3 (1.9%; 0.4 – 5.3)	0.553
Major bleeding	0 (0%; 0.0 - 3.1)	8 (6.4%; 2.8 – 12.2)	0.007	0 (0%; 0.0 – 4.5)	8 (4.9%; 2.2 – 9.5)	0.055
Any adverse outcome	0 (0%; 0.0 - 3.1)	17 (13.6%; 8.1 – 20.9)	0.000	0 (0%; 0.0 – 4.5)	17 (10.5%; 6.2 – 16.3)	0.001
30 days follow up						
Overall mortality	0 (0%; 0.0 - 3.1)	10 (8%; 3.9 – 14.2)	0.002	0 (0%; 0.0 – 4.5)	10 (6.2%; 3.0 – 11.1)	0.033
Fatal PE	0 (0%; 0.0 - 3.1)	0 (0%; 0.0 – 2.9)	-	0 (0%; 0.0 – 4.5)	0 (0%; 0.0 – 2.3)	-
Recurrent VTE	0 (0%; 0.0 - 3.1)	4 (3.2%; 0.9 – 8.0)	0.123	0 (0%; 0.0 – 4.5)	4 (2.5%; 0.7 – 6.2)	0.304
Major bleeding	1 (0.8%; 0.0 – 4.6)	9 (7.2%; 3.3 – 13.2)	0.019	0 (0%; 0.0 – 4.5)	10 (6.2%; 3.0 – 11.1)	0.033
Any adverse outcome	1 (0.8%; 0.0 – 4.6)	21 (16.8%; 10.7 – 24.5)	0.000	0 (0%; 0.0 – 4.5)	22 (13.6%; 8.7 – 19.8)	0.000
3 months follow up						
Overall mortality	0 (0%; 0.0 – 3.1)	32 (25.6%; 18.2 – 34.2)	0.000	0 (0%; 0.0 – 4.5)	32 (19.8%; 13.9 – 26.8)	0.000
Fatal PE	0 (0%; 0.0 – 3.1)	0 (0%; 0.0 – 2.9)	-	0 (0%; 0.0 – 4.5)	0 (0%; 0.0 – 2.3)	-
Recurrent VTE	5 (4.2%; 1.4 – 9.6)	5 (4%; 1.3 – 9.1)	1.000	2 (2.5%; 0.3 – 8.6)	8 (4.9%; 2.2 – 9.5)	0.503
Major bleeding	2 (1.7%; 0.2 – 6.0)	10 (8%; 3.9 – 14.2)	0.035	0 (0%; 0.0 – 4.5)	12 (7.4%; 3.9 – 12.6)	0.010
Any adverse outcome	7 (5.9%; 2.4 – 11.8)	41 (32.8%; 24.7 – 41.7)	0.000	2 (2.5%; 0.3 – 8.6)	46 (28.4%; 21.6 – 36.0)	0.000

* Original PESI Class I – II; † Original PESI Class III – V; ‡ Simplified PESI no risk factors; § Simplified PESI ≥ 1 risk factor.

CI, 3.9 – 12.6) at 3 month follow-up within the simplified PESI prognostic group (Table 3).

Any adverse outcome

None of the low risk patients had any adverse outcome within the first 14 days after the index PE (Table 3). The difference in adverse events between the low risk and high risk patients at 14 days and 3 months follow-up were statistically significant (original PESI $P = 0.000$ and 0.000, simplified PESI $P = 0.001$ and 0.000).

Outpatients versus inpatients

In our sample of 243 patients, 115 (47.3%; 95% CI, 40.9 – 53.8) patients were safely treated out of the hospital with no deaths or bleeding episodes and only 1 recurrent event within the first 14 days or 30 days of follow-up. Thirty four (29.6%) of these outpatients were classified as high risk patients according to the original PESI (19 patients in class III, 13 in class IV and 2 patients in class V) and 54 (47.0%) were classified as high risk patients according to the simplified PESI prognostic model. In the majority of these patients (74.5%) a malignancy contributed to the high PESI scores. On the contrary, thirty seven (28.9%) out of the 128 admitted patients were classified as low risk patients according to the original PESI (19 patients in class I and 18 in class II) and 20 (15.6%) were classified as low risk patients according to the simplified PESI prognostic model. The most frequent reasons for admission of these 37 low risk patients were: extensive PE (22.0%) such as saddle PE, hypoxia (22.0%) and severe comorbidities (22.0%) such as pneumonia, transaminitis, advanced cancer, stroke and coronary artery disease. Other reasons for admission were pain management, renal dysfunction, syncope and hypotension. Eight of these patients were treated with intravenous unfractionated heparin and 1 patient received thrombolysis. None of these 37 patients suffered from any adverse event during the first 14 days. There is 1 (2.7%; 95%CI, 0.1 – 14.2) recurrent event and 1 (2.7%; 95% CI, 0.1 – 14.2) major bleeding during the 3 months follow-up.

Discussion

The results of our study suggest that both PESI prognostic models accurately identify patients with acute PE who are at low risk for short-term adverse events, including death, recurrent venous thromboembolism and major hemorrhage. None of the low risk patients died or had any adverse event within the first 14 days. Both PESI prognostic models also seem to identify patients with acute PE at low risk of adverse outcome who can be safely managed as outpatients.

Our results are consistent with previously published studies validating the original and simplified PESI. [14,15,20–22]. The 3 months overall mortality in the low risk groups according to the original PESI model has been reported to be between 0% and 1.2% [14,20,21]. The overall mortality in the low risk group of our study was 0% (95% CI, 0.0 – 3.1). The overall mortality in our high risk group was 25.6% (95% CI, 18.2 – 34.2). Although this is consistent with two large validation studies [14,20], a recent cohort reported an overall mortality of 9% in the risk classes IV and V in the first 3 months. This discrepancy might be explained by the exclusion of patients with terminal illness, such as metastatic cancer, in that particular study [21]. There is only one derivation and one validation study using the simplified PESI [15,23]. Their 30-day overall mortality of approximately 1% in the low risk groups correspond to our 30-day overall mortality of 0% (95% CI 0 – 4.5). To our knowledge, our study is the first external validation study reporting a shorter term follow-up of 14 days. Besides overall and PE-related mortality we also report recurrent VTE and major bleeding episodes. In order to select patients for outpatient treatment, clinicians require risk estimates of any adverse event in a short-term follow-up.

The overall proportion of patients classified into the low-risk category according to both PESI-scores and our own criteria for outpatient treatment was similar. However, in the current study 53% of patients were hospitalized following the diagnosis of the acute PE. Sixteen to 29% of these patients had a low risk PESI score. None of these admitted patients developed an adverse event during the first 14 days. However, some of these patients needed to be admitted to the hospital because of large PE (one patient with a saddle PE, tachycardia and tachypnea underwent thrombolysis), hypoxia or other severe comorbidities (e.g. advanced cancer). These features likely influenced the clinical judgment of the treating physician to hospitalize these patients. This emphasizes that the clinical judgment of the treating physician may overrule a suggested decision by the PESI. On the contrary, 30 to 47% of patients with acute PE and a high risk PESI score were safely treated as outpatients. An underlying

malignancy contributed to the high PESI scores in 75% of these cases. This suggests that a proportion of patients with high risk PESI scores might be safely treated as outpatients. Although, cancer patients have a high risk of death, it does not seem to be associated with worse short term adverse events in these patients with acute PE who were treated out of the hospital ($P = 0.339$ for any adverse event during 14 and 30-days follow-up). Future research is needed to identify patients with a low risk of short term adverse events who do not need hospitalization especially in those with significant other comorbidities.

Our study is limited by the small number of patients. The confidence intervals are large as a consequence of the small sample size and therefore our results and conclusions should be further investigated in larger studies. Secondary, the study is also limited by its retrospective design. However, we tried to minimize bias by reviewing patients' paper charts completed at the emergency department and all other patient data in our hospital database in duplicates. Furthermore, it is important to acknowledge possible selection bias by the exclusion of patients not followed at the Ottawa Hospital ($n = 21$). None of the included patients were lost to follow-up and no patients with PE were missed since we reviewed all VQs and CTPAs during the study period.

In conclusion, the original PESI as well as the simplified PESI prognostic models accurately identify patients with acute PE who are at low risk for short-term adverse events, such as death, fatal PE, recurrent VTE and major bleeding episodes. However, many high risk patients according to the PESI prognostic model were safely treated as outpatients. Further research using different prognostic models is required to better stratify patients according to their risk of short term adverse event and optimize outpatient management of patients with acute PE.

Statement of conflict of interest

None declared.

References

[1] British Thoracic Society guidelines for the management of suspected acute pulmonary embolism. Thorax Jun 2003;58(6):470–83.
[2] Torbicki A, Perrier A, Stavros K, Giancarlo A, Nazzareno G, Pruszczyk P, et al. Guidelines on the diagnosis and management of acute pulmonary embolism. G Ital Cardiol (Rome) May 2009;10(5):303–47.
[3] Agterof MJ, Schutgens RE, Snijder RJ, Epping G, Peltenburg HG, Posthuma EF, et al. Out of hospital treatment of acute pulmonary embolism in patients with a low NT-proBNP level. J Thromb Haemost Mar 2010;3(8):1235–41.
[4] Erkens PM, Gandara E, Wells P, Shen AY, Bose G, Le Gal G, et al. Safety of outpatient treatment in acute pulmonary embolism. J Thromb Haemost Nov 2010;8(11):2412–7.
[5] Janjua M, Badshah A, Matta F, Danescu LG, Yaekoub AY, Stein PD. Treatment of acute pulmonary embolism as outpatients or following early discharge. A systematic review. Thromb Haemost Nov 2008;100(5):756–61.
[6] Kovacs MJ, Hawel JD, Rekman JF, Lazo-Langner A. Ambulatory management of pulmonary embolism: a pragmatic evaluation. J Thromb Haemost Nov 2010;8(11):2406–11.
[7] Squizzato A, Galli M, Dentali F, Ageno W. Outpatient treatment and early discharge of symptomatic pulmonary embolism: a systematic review. Eur Respir J May 2009;33(5):1148–55.
[8] Aujesky D, Mazzolai L, Hugli O, Perrier A. Outpatient treatment of pulmonary embolism. Swiss Med Wkly Nov 28 2009;139(47–48):685–90.
[9] Aujesky D, Stone RA, Kim S, Crick EJ, Fine MJ. Length of hospital stay and postdischarge mortality in patients with pulmonary embolism: a statewide perspective. Arch Intern Med Apr 14 2008;168(7):706–12.
[10] Park B, Messina L, Dargon P, Huang W, Ciocca R, Anderson FA. Recent trends in clinical outcomes and resource utilization for pulmonary embolism in the United States: findings from the nationwide inpatient sample. Chest Oct 2009;136(4):983–90.
[11] Shepperd S, Doll H, Angus RM, Clarke MJ, Iliffe S, Kalra L, et al. Admission avoidance hospital at home. Cochrane Database Syst Rev 2010(4):CD007491.
[12] Jimenez D, Yusen RD. Prognostic models for selecting patients with acute pulmonary embolism for initial outpatient therapy. Curr Opin Pulm Med Sep 2008;14(5):414–21.
[13] Jimenez D, Yusen RD, Otero R, Uresandi F, Nauffal D, Laserna E, et al. Prognostic models for selecting patients with acute pulmonary embolism for initial outpatient therapy. Chest Jul 2007;132(1):24–30.
[14] Aujesky D, Roy PM, Le Manach CP, Verschuren F, Meyer G, Obrosky DS, et al. Validation of a model to predict adverse outcomes in patients with pulmonary embolism. Eur Heart J 2006;27:476–81.
[15] Jimenez D, Aujesky D, Moores L, Gomez V, Lobo JL, Uresandi F, et al. Simplification of the pulmonary embolism severity index for prognostication in patients with acute symptomatic pulmonary embolism. Arch Intern Med Aug 9 2010;170(15):1383–9.
[16] Jaff MR, McMurtry MS, Archer SL, Cushman M, Goldenberg N, Goldhaber SZ, et al. Management of massive and submassive pulmonary embolism, iliofemoral deep vein thrombosis, and chronic thromboembolic pulmonary hypertension: a scientific statement from the American Heart Association. Circulation Apr 26 2011;123(16):1788–830.
[17] Torbicki A, Perrier A, Konstantinides S, Agnelli G, Galie N, Pruszczyk P, et al. Guidelines on the diagnosis and management of acute pulmonary embolism: the Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC). Eur Heart J Sep 2008;29(18):2276–315.
[18] Aujesky D, Obrosky DS, Stone RA, Auble TE, Perrier A, Cornuz J, et al. Derivation and validation of a prognostic model for pulmonary embolism. Am J Respir Crit Care Med Oct 15 2005;172(8):1041–6.
[19] Schulman S, Kearon C. Definition of major bleeding in clinical investigations of antihemostatic medicinal products in non-surgical patients. J Thromb Haemost Apr 2005;3(4):692–4.
[20] Aujesky D, Perrier A, Roy PM, Stone RA, Cornuz J, Meyer G, et al. Validation of a clinical prognostic model to identify low-risk patients with pulmonary embolism. J Intern Med 2007;261:597–604.
[21] Chan CM, Woods C, Shorr AF. The validation and reproducibility of the pulmonary embolism severity index. J Thromb Haemost Jul 2010;8(7):1509–14.
[22] Hariharan P, Takayesu JK, Kabrhel C. Association between the Pulmonary Embolism Severity Index (PESI) and short-term clinical deterioration. Thromb Haemost Jan 12 2011;105(4).
[23] Sam A, Sanchez D, Gomez V, Wagner C, Kopecna D, Zamarro C, et al. The shock index and the simplified PESI for identification of low-risk patients with acute pulmonary embolism. Eur Respir J Apr 2011;37(4):762–6.