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Original Article

# Factors Influencing Hospital Stay for Pulmonary Embolism. A Cohort Study☆

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A B S T R A C T

*Introduction:* The aim of this study was to identify factors influencing hospital stay due to pulmonary embolism.
*Methods:* We performed a retrospective cohort study of patients hospitalized between 2010 and 2015. Patients were identified using information recorded in hospital discharge reports (ICD-9-CM codes 415.11 and 415.19).
*Results:* We included 965 patients with a median stay of 8 days (IQR 6–13 days). Higher scores on the simplified Pulmonary Embolism Severity Index (sPESI) were associated with increased probability of longer hospital stay. The probability of a hospital stay longer than the median was 8.65 (95% CI 5.42–13.79) for patients referred to the Internal Medicine Department and 1.54 (95% CI 1.07–2.24) for patients hospitalized in other departments, compared to those referred to the Pneumology Department. Patients with grade 3 on the modified Medical Research Council dyspnea scale had an odds ratio of 1.63 (95% CI: 1.07–2.49). The likelihood of a longer than median hospital stay was 1.72 (95% CI: 0.85–3.48) when oral anticoagulation (OAC) was initiated 2–3 days after admission, and 2.43 (95% CI: 1.16–5.07) when initiated at 4–5 days, compared to OAC initiation at 0–1 days.
*Conclusions:* sPESI grade, the department of referral from the Emergency Department, the grade of dyspnea and the time of initiating OAC were associated with a longer hospital stay.


## Factores que influyen en la estancia hospitalaria por embolia pulmonar. Un estudio de cohortes

*Palabras clave:*
Embolia pulmonar
Estancia hospitalaria
Pulmonary Embolism Severity Index simplificado (sPESI)
Inicio de anticoagulación oral
Disnea

R E S U M E N

*Introducción:* El objetivo de este estudio fue analizar qué factores influyen en la estancia hospitalaria tras una embolia pulmonar.
*Métodos:* Se diseñó un estudio retrospectivo de cohortes en pacientes ingresados entre 2010 y 2015 por embolia pulmonar. Los enfermos se identificaron utilizando los códigos de información registrados en los informes de alta hospitalaria (códigos CIE-9-CM 415.11 y 415.19).
*Resultados:* Se incluyó a 965 pacientes. La mediana de la estancia fue 8 días (rango intercuartílico 6-13 días). Las puntuaciones más altas en el *Pulmonary Embolism Severity Index* simplificado (sPESI) se asociaron

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con mayor probabilidad de aumento de la estancia hospitalaria. En comparación con la derivación al Servicio de Neumología, la *odds ratio* (OR) de una estancia hospitalaria superior a la mediana fue de 8.65 (IC 95%: 5,42-13,79) para los pacientes derivados al Servicio de Medicina Interna y de 1,54 (95%CI: 1,07-2,24) para los pacientes hospitalizados en otros servicios. Los pacientes con grado 3 en la escala de disnea modificada de la *Medical Research Council* tenían una OR de 1,63 (IC 95%: 1,07-2,49). La probabilidad de una estancia hospitalaria más larga que la mediana fue de 1,72 (IC 95%: 0,85-3,48) cuando la anticoagulación oral se inició 2-3 días después del ingreso y 2,43 (IC 95%: 1,16-5,07) cuando se inició los días 4-5, en comparación con la iniciada los días 0-1 desde el ingreso.

*Conclusiones:* El grado de sPESI, el servicio de derivación desde Urgencias, el grado de disnea y el momento de inicio de la anticoagulación oral se asociaron con una estancia hospitalaria más larga.



## Introduction

Pulmonary embolism (PE) is a public health problem of the first magnitude,[1] and is associated with a high economic burden.[6,7] It occurs at an incidence of 1–1.4 cases/1000 inhabitants/year,[2,3] and normally requires hospitalization.[4] Three-month mortality is estimated at 17%.[5]

Admissions due to PE in Spain and in other developed countries have increased in recent years,[8–15] although length of hospital stay has been steadily reducing.[14,16] This reduction in mean hospital stay in Spain suggests that the management of a patient with acute PE has improved. Several studies have shown that most of the costs derived from PE stem from hospitalization, the number of diagnostic procedures that need to be performed, and the comorbidities of these patients.[7,14,17–19]

The prognosis of PE can be estimated using the Pulmonary Embolism Severity Index (PESI) and the simplified PESI (sPESI), both of which measure 30-day mortality.[20] It is generally accepted that when the risk class is low (PESI) or zero (sPESI), patients can be treated as outpatients, or at least receive early discharge.[21] However, despite the wide variations in hospital stays, no predictive models are available to estimate length of hospital stay in PE.

The aim of this study was to identify factors that might affect length of stay in patients admitted due to PE. Identification of patients who may need short stays will help optimize hospital management.

## Materials and Methods

### *Study Design*

This was a retrospective cohort study that included patients admitted to the Complejo Hospitalario Universitario de Santiago de Compostela (Spain) for PE between 1 January 2010 and 31 December 2015. This is a 1145-bed tertiary level hospital with a Department of Respiratory Medicine that admits 2500 patients every year.

### *Inclusion and Exclusion Criteria*

Individuals were included if they had a confirmed diagnosis of PE using ventilation/perfusion scintigraphy with high clinical probability (according to the Prospective Investigation of the Pulmonary Embolism Diagnosis criteria),[22] proximal lower-extremity deep vein thrombosis, demonstrated on compression ultrasonography in patients with inconclusive findings on ventilation/perfusion scintigraphy,[23] or acute PE diagnosed by chest spiral computed tomography with contrast medium.[24] Cases in which PE was not the reason for admission but rather a complication occurring during the hospital stay were excluded.

Our study was approved by the Research Ethics Committee of the hospital (registry 2016/007).

### *Data Collection*

The International Classification of Disease, 9th revision (ICD-9-CM codes 415.11 y 415.19) hospital discharge codes were used to identify patients in the hospital database. The hospital stay of each patient was retrieved from the discharge report archived in the electronic clinical records.

### *Statistical Analysis*

A multivariate logistic regression was used to predict the influence of different variables on the possibility of a longer- or shorter-than-average hospital stay for patients with PE. The dependent variable was a hospital stay of 8 days or more, or less than 8 days (median length of stay), and independent variables taken into account were: sPESI score (calculated according to Jiménez et al.),[20] sex, Charlson index (in 4 categories),[25] hospital department to which the patient was transferred from the emergency room (Respiratory Medicine, Internal Medicine, or other departments), temperature (higher or lower than 36 °C on admission), respiratory rate (higher or lower than 30 breaths/min), altered mental state (yes/no), and dyspnea grade (5 categories).[26] Odds ratios (OR) and corresponding 95% confidence intervals (CI) were calculated.

A subanalysis was performed to clarify the possible effect of starting an oral anticoagulant as soon as possible. For this analysis, patients in whom start of oral anticoagulation (OAC) was unknown and participants who started OAC after day 5 of hospitalization were excluded, our reasoning being that patients who started OAC on day 6 or later would have a much higher probability of a hospital stay lasting more than 8 days (the median). Covariates included in this analysis were the same as those of the overall analysis. Results are expressed as OR with corresponding 95% CIs. The analysis was performed using the IBM SPSS Statistics v20 software.

## Results

The study included 965 patients with PE diagnosed between 2010 and 2015. Median age was 75 years (range 19–97), interquartile range was 63–83, 584 were women, and 381 (39.5%) were men. A Charlson index of 3 or more was observed in 20.4% of the patients. In total, 61.1% of the patients were transferred from the emergency room to the Department of Respiratory Medicine, 19.1% to Internal Medicine, and the others to other hospital departments. Median length of stay was 8 days (interquartile range 6–13). Table 1 shows a detailed description of patient characteristics.

Table 2 shows the results of the multivariate model analyzing the effect of the different variables on length of stay. A significant relationship was found between the sPESI score and the probability of a prolonged stay. It seems that the higher the sPESI, the greater the probability of a longer-than-average hospital stay. The

**Table 1**
Study Population.

| Variable | n (%) | Stay ≤8 Days | Stay >8 Days |
|---|---|---|---|
| *Sex* | | | |
| Male | 381 (39.5) | 195 (51.2) | 186 (48.8) |
| Female | 584 (60.5) | 291 (49.8) | 293 (50.2) |
| *Age* | | | |
| ≤80 years | 649 (67.3) | 361 (55.6) | 288 (44.4) |
| >80 years | 316 (32.7) | 125 (39.6) | 191 (60.4) |
| *Department* | | | |
| Respiratory medicine | 590 (61.1) | 369 (62.5) | 221 (37.5) |
| Internal medicine | 184 (19.1) | 26 (14.1) | 158 (85.9) |
| Other departments | 191 (19.8) | 91 (47.6) | 100 (52.4) |
| *Charlson* | | | |
| 0 | 389 (40.3) | 224 (57.6) | 165 (42.4) |
| 1 | 235 (24.4) | 105 (44.7) | 130 (55.3) |
| 2 | 144 (14.9) | 66 (45.8) | 78 (54.2) |
| 3 or more | 197 (20.4) | 91 (46.2) | 106 (53.8) |
| *mMRC* | | | |
| 0 | 241 (25) | 137 (56.8) | 104 (43.2) |
| 1 | 113 (11.7) | 81 (71.7) | 32 (28.3) |
| 2 | 124 (12.8) | 61 (49.2) | 63 (50.8) |
| 3 | 215 (22.3) | 103 (47.9) | 112 (52.1) |
| 4 | 267 (27.7) | 101 (37.8) | 166 (62.2) |
| *Altered mental state* | | | |
| No | 939 (97.3) | 477 (50.8) | 462 (49.2) |
| Yes | 26 (2.7) | 9 (34.6) | 17 (65.4) |
| *Oxygen saturation* | | | |
| <90% | 366 (37.9) | 139 (38) | 227 (62) |
| ≥90% | 599 (62.1) | 347 (57.9) | 252 (42.1) |
| *Active malignancy* | | | |
| No | 802 (83.1) | 391 (48.8) | 411 (51.2) |
| Yes | 163 (16.9) | 95 (58.3) | 68 (41.7) |
| *sPESI*[a] | | | |
| 0 | 269 (27.9) | 180 (66.9) | 89 (33.1) |
| 1 | 331 (34.3) | 167 (50.5) | 164 (49.5) |
| 2 | 223 (23.1) | 91 (40.8) | 132 (59.2) |
| 3 | 112 (11.6) | 34 (30.4) | 78 (69.6) |
| 4 | 29 (3) | 13 (44.8) | 16 (55.2) |

mMRC: modified Medical Research Council dyspnea scale; sPESI: simplified Pulmonary Embolism Severity Index.
[a] The 2 last sPESI categories were pooled due to the low number of patients.

effect was not statistically significant for the last sPESI category, but only 29 individuals were classified in this category. Sex, Charlson index, temperature, respiratory rate, or altered mental state at admission had no observable effect of length of stay. In contrast, the department to which the patient was referred from the Emergency Department had a significant effect on length of stay. In comparison with hospitalization in the Respiratory Medicine department, patients referred to the Internal Medicine department had a higher probability of a longer-than-average stay, OR 8.65 (95% CI: 5.42–13.79). This probability was 1.54 (95% CI: 1.07–2.24) for patients hospitalized in other departments. Dyspnea on admission also affected length of stay. Patients with grade 3 on the Medical Research Council modified scale (mMRC) had an OR of a prolonged hospital stay of 1.63 (95% CI: 1.07–2.49). These results were practically identical when patients who died in hospital were excluded.

In a subanalysis of 421 individuals, time to start of OAC had a significant effect on length of stay (Table 3). Taking individuals who began OAC on days 0 and 1 as a reference, we found that the probability of a longer-than-average hospital stay in those who began on days 2 or 3 (intermediate initiators) was 1.72 (95% CI: 0.85–3.48), while for those who began OAC on days 4 or 5 (late initiators), this probability was 2.43 (95% CI: 1.16–5.07).

## Discussion

This study shows that certain factors, including sPESI score, department to which the patient was referred after the emergency room, and dyspnea grade, have a significant impact on length of stay after hospitalization for PE, and that these could be used to predict length of stay. Other factors such as sex, Charlson index, temperature, respiratory rate, and altered mental state had no significant impact. We also observed that the sooner OACs are started, the shorter the hospital stay. These results might represent an important change in the management of patients after PE.

No studies have been published analyzing the factors that might affect hospital stay in patients admitted with PE, although it seems that the new direct-acting anticoagulants might help reduce length of stay,[27] and that women have longer stays than men.[28] Several studies have found a relationship between length of hospital stay and all-cause mortality in PE patients,[11,13] but it is unclear whether some factors might affect one more than the other. Clinical variables used in this study (demographic data, comorbidities, and clinical characteristics) are those routinely collected when patients present in an emergency department, and have been shown to be associated with mortality, both in PE and other acute diseases.[29–31] Hospital stay for PE varies widely among countries, ranging from 4.6–6.6 days in France to 21.4–23.6 days in Germany.[32]

Dyspnea is a symptom that is usually observed in acute cardiopulmonary diseases, and PE is no exception. The mMRC scale, while designed to measure dyspnea in COPD patients, was the tool used in this study because it is recorded in the emergency department, regardless of the patient's underlying disease. Dyspnea grade in these cases refers to the patient's respiratory deficit since onset of the acute episode. Our results indicate that the greater the dyspnea grade, the greater the likelihood of a longer hospital stay. Both PESI and sPESI are prognostic models that predict 30-day mortality in PE patients. The utility of sPESI, the scale we used, lies in the fact that it includes domains that quantify patient age, capture comorbidities (cancer and chronic cardiopulmonary disease), and express the cardiopulmonary consequences of PE (systolic blood pressure, heart rate and $SaO_2$). Some of these variables are also predictors of the cost of hospitalization for PE, which, in turn, depends on the severity of the disease.[7] Evidence suggests that the higher the sPESI, the greater the probability of a longer-than-average hospital stay. Although the effect for the highest sPESI category is not statistically significant, this category only included 29 patients and was therefore pooled with the preceding category. Hospital stay was significantly shorter in patients referred to the Respiratory Medicine Department than to Internal Medicine and other departments. One might assume that this is due to the greater comorbidity burden of patients admitted to those departments. However, if the analysis is restricted to patients with a Charlson index of less than 2 (data not shown), the stay is still half the length of those treated in the Respiratory Medicine Department. Moreover, patients admitted to other departments had shorter stays than those in the Internal Medicine Department, despite more comorbidities. In our opinion, this difference may be due to better compliance with management guidelines for these patients[33–35]; for example, in the Respiratory Medicine Department, OAC with vitamin K antagonists is started significantly earlier than in the other departments, a factor that, in itself, was found to result in a significantly shorter hospital stay. A subanalysis of patients with a sPESI score of 0 and a longer-than-average stay (data not shown) shows them to be somewhat younger than the overall patient population, with fewer comorbidities, but almost 50% of this group were referred to departments other than Respiratory Medicine. The length of stay of many of these patients could probably have been reduced, and some could have been treated on an outpatient basis.

**Table 2**
Factors Influencing Mean Hospital Stay.

| Variable | *n* (%) | Unadjusted OR (95% CI) | Adjusted OR (95% CI) |
|---|---|---|---|
| *sPESI*[a] | | | |
| 0 | 269 (27.9) | 1 | 1 |
| 1 | 331 (34.3) | 1.99 (1.42–2.77) | 1.57 (1.07–2.30) |
| 2 | 223 (23.1) | 2.93 (2.03–4.24) | 2.09 (1.35–3.24) |
| 3 | 112 (11.6) | 4.64 (2.88–7.47) | 2.49 (1.42–4.38) |
| 4 | 29 (3) | 2.49 (1.15–5.40) | 0.98 (0.38–2.49) |
| *Sex* | | | |
| Female | 584 (60.5) | 1 | 1 |
| Male | 381 (39.5) | 1.06 (0.82–1.37) | 0.94 (0.70–1.27) |
| *Charlson* | | | |
| 0 | 389 (40.3) | 1 | 1 |
| 1 | 235 (24.4) | 1.68 (1.21–2.33) | 1.20 (0.82–1.73) |
| 2 | 144 (14.9) | 1.60 (1.09–2.36) | 1.03 (0.66–1.61) |
| 3 | 197 (20.4) | 1.58 (1.12–2.23) | 0.88 (0.57–1.35) |
| *Department* | | | |
| Respiratory medicine | 590 (61.1) | 1 | 1 |
| Internal medicine | 184 (19.1) | 10.15 (6.49–15.87) | 8.65 (5.42–13.79) |
| Other departments | 191 (19.8) | 1.84 (1.32–2.55) | 1.54 (1.07–2.24) |
| *Temperature* | | | |
| <36 °C | 198 (20.5) | 0.92 (0.68–1.26) | 0.78 (0.55–1.12) |
| *Respiratory rate* | | | |
| ≥30 | 133 (13.8) | 2.04 (1.39–2.98) | 1.01 (0.63–1.58) |
| *Altered mental state* | | | |
| No | 939 (97.3) | 1 | 1 |
| Yes | 26 (2.7) | 1.95 (0.86–4.42) | 1.60 (0.63–4.10) |
| *mMRC* | | | |
| 0 | 241 (25) | 1 | 1 |
| 1 | 113 (11.7) | 0.52 (0.32–0.84) | 0.71 (0.42–1.21) |
| 2 | 124 (12.8) | 1.36 (0.88–2.10) | 1.51 (0.94–2.42) |
| 3 | 215 (22.3) | 1.43 (0.99–2.07) | 1.26 (0.83–1.92) |
| 4 | 267 (27.7) | 2.17 (1.52–3.09) | 1.63 (1.07–2.49) |

mMRC: modified Medical Research Council dyspnea scale; sPESI: simplified Pulmonary Embolism Severity Index.
[a] The 2 last sPESI categories were pooled due to the low number of patients.

**Table 3**
Start of Oral Anticoagulation and Length of Hospital Stay.

| Start of OAC | *n*/*N* (%)[a] | Stay ≤8 Days | Stay >8 Days | Adjusted OR (95% CI) |
|---|---|---|---|---|
| Rapid (0–1 days) | 77/423 (8) | 61 (21.6) | 16 (11.4) | 1 |
| Intermediate (2–3 days) | 214/423 (22.2) | 148 (52.3) | 66 (47.1) | 1.72 (0.85–3.48) |
| Late (4–5 days) | 132/423 (13.7) | 74 (26.1) | 58 (41.4) | 2.43 (1.16–5.07) |

[a] Percentage calculated from total number of patients included in the cohort.
OAC: oral anticoagulation.

The time of starting OAC with vitamin K antagonists is only documented in less than half of the cohort, as this data point was not registered in the electronic clinical records of a large number of patients. This meant that we had to conduct a subanalysis exclusively with patients for whom these data were available. Patients who started OAC with vitamin K antagonists after day 5 of admission were also excluded, since it was highly likely that these patients would have had a longer-than-average stay, and this would introduce a bias into the analysis. The time of starting OAC impacts on length of hospital stay, independently of other variables that remain significant in the multivariate model. Starting OAC on the same day as admission, simultaneously with parenteral OAC, is recommended in current management guidelines for this disease,[33–35] and our results underline the importance of this intervention in reducing hospital stay. This finding coincides with a metaanalysis of 5 randomized trials in which hospital stay was approximately 4 days shorter in patients in whom OAC with vitamin K antagonists was started early.[36] Similarly, a recent study in subjects over the age of 65 years with acute venous thromboembolism showed that starting OAC with vitamin K antagonists on the first day of treatment is associated with a shorter hospital stay.[37] It is unlikely that the reason for timing differences in starting OAC is that these departments treat a greater number of patients with contraindications for using these drugs, because in general, very few patients present this limitation. The median age of patients with data on the start of OAC is almost the same as that of the overall cohort (72 vs 75 years, respectively). Distribution by sex is also very similar (36.9% vs 39.5%, respectively), suggesting that this subgroup of patients was similar to the overall population of patients included in the study.

The main limitations of this study are its retrospective and single-center design, and the small number of patients included in some categories. Our results still need to be validated with multicenter studies in larger numbers of patients.

The advantages of this study are that all data were recorded in electronic clinical records, diagnosis is confirmed in all cases, and the large number of covariates examined enabled us to obtain robust results. Moreover, the study population represents a systematic sample of PE patients seen between 2010 and 2015, thus ruling out any possible bias.

In conclusion, factors such as sPESI, the department to which the patient was transferred from the emergency room, the dyspnea grade, and time of starting OACs have a significant impact on the length of hospital stay. The implications of this study are that patients must be referred to departments in which the recommendations of the current clinical guideline are followed, and OACs must be introduced as soon as possible. However, more studies are needed to determine the exact influence of the timing of start of OACs on length of hospital stay.

## Authorship/Contributors

*Rodríguez-Núñez N*, author. Concept and design. Data analysis and interpretation. Preparation of the article. Approval of the final version.

*Ruano-Raviña A*, author. Concept and design. Data analysis and interpretation. Preparation of the article. Approval of the final version.

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## Conflict of Interests

The authors state that they have no conflict of interests.

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