Rate and duration of hospitalisation for acute pulmonary embolism in the real-world clinical practice of different countries: analysis from the RIETE registry

To the Editor:

The latest guidelines suggest considering home treatment or early hospital discharge in low-risk mortality pulmonary embolism (PE) patients, identified through widely validated clinical prediction rules [1, 2]. Nevertheless, it is still not clear if these patients are really treated on an outpatient basis in clinical practice.

Thus, we used the RIETE registry (ClinicalTrials.gov identifier: NCT02832245) to assess the proportion of outpatients with acute PE initially treated in-hospital, the mean duration of hospitalisation and to identify predictors for home treatment or for early discharge. We included data from 11 473 patients registered in 25 countries participating in the RIETE study from January 2010 to December 2016. Both local and academic hospitals were involved. Rate and duration of hospitalisation for acute PE in the four countries with highest enrolment and in other participating countries, grouped together as a unique group, were compared. Namely, patients enrolled in Spain (n=8270) were compared with those included in France (n=964), Italy (n=593), Israel (n=429) and in "other countries" (n=1217).

All the variables potentially associated with outpatient treatment and with early discharge (length of in-hospital stay (LOS) ⩽5 days) were evaluated at the univariate analysis using the Mann–Whitney test (for continuous variables) and the Chi-squared or Fisher's exact tests (for dichotomous variables). Statistically or marginally significant variables ($p<0.10$) were introduced in a multivariate model (backward binary logistic regression model). The role of different scores, such as the Pulmonary Embolism Severity Index (PESI) [3], the RIETE score [4] and the scheme suggested by the American College of Chest Physicians guidelines (ACCP scheme) for the bleeding risk [2], was assessed performing three different sensitivity analyses, excluding all the variables already included in each score. SPSS software (version 15; SPSS Inc., Chicago, IL, USA) was used for statistical analysis. A two-sided p-value of 0.01 was considered to be statistically significant.

A significantly lower proportion of complete outpatient treatment was found among PE subjects treated in Spain (2.5%), France (1.2%) and Israel (0.99%) than among those treated in Italy and the other countries (16% and 21%, respectively, $p<0.001$ for both). By contrast, the number of patients discharged within 5 days was significantly lower in Italy (23%), Spain (26%) and France (28%) than in Israel and the other countries examined (48% and 32%, respectively, $p<0.001$ for both). The mean LOS was substantially shorter in Israel (median (interquartile range) 6 (4–9) days, $p<0.001$) than in other countries. Only 5% of the overall population and ∼7% of the low-risk group were fully treated at home. The median duration of hospitalisation was 4 days for patients discharged early and 9 days for those with a longer hospitalisation.

On multivariate analysis, initial therapy with direct oral anticoagulants (DOACs) and cancer strongly predicted both home treatment and early discharge. Admission to university hospitals was significantly

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Real-life data from the RIETE study suggest only a few patients with pulmonary embolism at low risk of complications were treated at home or hospitalised for ⩽5 days. Management of PE appeared quite variable in different countries. http://ow.ly/o2b230mD8EY

Cite this article as: Mastroiacovo D, Dentali F, di Micco P, *et al.* Rate and duration of hospitalisation for acute pulmonary embolism in the real-world clinical practice of different countries: analysis from the RIETE registry. *Eur Respir J* 2019; 53: 1801677 [https://doi.org/10.1183/13993003.01677-2018].

TABLE 1 Multivariate analysis using complete home treatment and early discharge as the dependent variable[#]

Variables (number of patients)	Home *versus* in hospital therapy OR (CI)	Early discharge (⩽5 days) or home treatment *versus* admission >5 days OR (CI)
Clinical characteristics		
Age >65 years	0.59 (0.46–0.76)***	0.77 (0.69–0.86)***
Male sex (n=5413)		1.19 (1.08–1.32)***
Body weight <75 kg		1.12 (1.02–1.24)*
Initial presentation		
Pulse >110 beats per min (n=2214)	0.33 (0.23–0.48)***	0.62 (0.55–0.71)***
Systolic BP levels <100 mmHg (n=888)	0.50 (0.26–0.93)*	
Temperature <36°C (n=756)		0.82 (0.68–0.99)*
Risk factors		
Cancer (n=2550)	2.55 (2.00–3.27)***	1.30 (1.16–1.45)***
Immobility ⩾4 days (n=1663)		0.82 (0.71–0.95)**
Oestrogen therapy (n=630)		1.68 (1.37–2.07)***
Underlying conditions		
Chronic heart failure (n=931)		0.74 (0.61–0.89)**
Chronic lung disease (n=1598)		0.80 (0.70–0.92)**
Creatinine clearance levels <60 mL·min^{-1} (n=3963)		0.81 (0.72–0.91)***
Countries		
Spain (n=8270)	Ref.***	Ref.***
Italy (n=593)	5.17 (3.11–8.58)***	
France (n=964)	0.48 (0.25–0.90)*	
Israel (n=429)	0.36 (0.13–0.97)*	2.12 (1.68–2.67)***
Other countries (n=1217)	11.50 (9.02–14.66)***	2.25 (1.93–2.62)***
Initial therapy		
LMWH (n=9935)	Ref.***	Ref.***
Unfractionated heparin (n=647)	0.16 (0.07–0.35)***	0.36 (0.28–0.46)***
Thrombolytics (n=328)		0.35 (0.24–0.50)***
DOACs (n=196)	5.26 (3.36–8.24)***	2.92 (2.08–4.09)***
Fondaparinux (n=297)	0.41 (0.25–0.67)***	
Type of hospital		
University hospital (n=7025)	2.29 (1.74–3.01)***	1.11 (1.01–1.23)*
Scores		
PESI <85 points (n=4792)	1.20 (0.98–1.47)	1.33 (1.21–1.46)***
RIETE <1 point (n=3347)	1.29 (1.04–1.60)*	1.57 (1.42–1.74)***
ACCP scheme ⩽1 point (n=1759)[¶]	1.29 (0.98–1.69)	1.46 (1.28–1.66)***

BP: blood pressure; LMWH: low-molecular-weight heparin; Ref.: reference; DOACs: direct oral anticoagulants; PESI: Pulmonary Embolism Severity Index; ACCP: American College of Chest Physicians. [#]: patients dying ⩽24 h after the index event were excluded from this analysis; [¶]: modified version (information on control of anticoagulation was unavailable in the RIETE registry). Scores included one by one excluding all the variables already counted in each score. *: p<0.05; **: p<0.01; ***: p<0.001.

associated with home treatment and showed a tendency towards a shorter hospital stay. Use of oestrogenic therapy was solely a predictor of early discharge.

When scores were entered one by one in the model, results concerning all previous variables were comparable except for the weight of a number of comorbidities and initial presentation parameters (data not shown). Low PESI or low ACCP scores were not associated with home treatment, both resulting uniquely as weak predictors of a shorter LOS. Low RIETE score weakly predicted both home treatment and early discharge (table 1).

Considering this real-life data collected from several countries, overall, only one in every 13 patients eligible for home treatment was treated at home and less than half of the low-risk population was hospitalised for ⩽5 days.

These results are not surprising since, until now, the level of evidence on outpatient treatment remains limited by the lack of high-quality research [5]. The variable approaches observed among countries may reflect different healthcare systems and facilities across European and world countries. Various scores, classifying dissimilar low-risk patients, were tested in our cohort, but none of them appeared clearly related to outpatient treatment. It remains to be verified if, in the near future, further validations of well performing clinical prediction rules, such as the Hestia clinical criteria, may help to increase the rate of

outpatient-treated patients in real-life settings, reducing barriers concerning this practice [6]. The ongoing HOME-PE trial might clarify if a strategy based on the Hestia rule, compared with a strategy based on the simplified-PESI score, is at least as safe with regards to the 30-day rate of adverse events and more effective with regards to the rate of patients eligible for outpatient treatment [7].

Interestingly, in our study, cancer patients were more frequently treated at home or promptly discharged despite evident higher haemorrhagic and thrombotic risk [8]. Notably, incidentally detected asymptomatic cancer-related PE were not included in the population analysed. Commonly, cancer patients may be monitored by oncologists with close follow-up visits and such well-defined assistance programmes may facilitate either an outpatient strategy or a post-discharge management. At the same time, this category of patients may achieve more benefits from home treatment, since a new hospitalisation usually deteriorates their quality of life [9].

As expected, initial treatment with DOACs appeared correlated with outpatient treatment and a shorter LOS. At the time of data collection, only 196 patients in the initial phase of therapy and 996 in the long-term period were treated with DOACs. These drugs, especially those permitting the "single drug approach", may broadly facilitate a quick discharge from emergency wards after a comprehensive risk assessment of PE patients [10–13]. The ongoing Mercury-PE trial, designed to test the hypothesis that management with rivaroxaban, if compared with standard care, reduces the number of initial and subsequent hospitalisation days of low-risk PE, will probably confirm these findings [14]. However, in this observational analysis we are not able to exclude that, in daily clinical practice, DOACs were mainly preferred in the acute phase of treatment for less complex subgroups of patients.

Finally, additional considerations should be taken into account. Up until the end of 2013, the previous guidelines only suggested early discharge for low-risk PE [15] and use of DOACs was not allowed in most countries. From 2014, for the first time, the European Society of Cardiology guidelines suggested both use of DOACs and home treatment for low-risk PE patients [1]. In analysing data from 2010 to 2016, we are probably observing a period of great change with regards to managing PE. Our results relating to academic institutions may suggest that, in these centres, guideline recommendations could potentially be implemented more easily and quickly than in other institutions since a paradigm shift requires more time to be adopted in all clinical settings.

Our study has some limitations. Principally, RIETE is an ongoing observational registry. Therefore, our findings should be treated with caution considering the limitations of observational studies. Moreover, the data collected from multiple centres in different countries participating in the RIETE registry may not be representative of the general treatment in those countries and only patients evaluated in a specific setting may be included. Thus, our data can not be fully generalisable nor used as proof for implementing our results into daily clinical practice.

In the near future, diagnostic and therapeutic advances may be able to optimise low-risk PE patient selection and at the same time improve the management of this disease, providing an approach as safe as and more cost-effective than the current one.

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Received: Jan 14 2018 | Accepted after revision: Oct 30 2018

Acknowledgements: We express our gratitude to Sanofi Spain for supporting this Registry with an unrestricted educational grant. We also express our gratitude to Bayer Pharma AG for supporting this Registry. Bayer Pharma AG's support was limited to the part of RIETE outside Spain, which accounts for a 24.01% of the total patients included in the RIETE Registry. We also thank the RIETE Registry Coordinating Centre, S & H Medical Science Service, for their quality control data, logistic and administrative support.

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Conflict of interest: None declared.

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