Risk profile, management, and outcomes of patients with venous thromboembolism attended in Spanish Emergency Departments
The ESPHERIA registry

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Abstract
The objective of this study was to determine the clinical profile of and diagnostic and therapeutic approach to patients with venous thromboembolism (VTE) in Spanish Emergency Departments (EDs). Risk factors, adherence to clinical practice guidelines, and outcomes were also evaluated.

Patients with VTE diagnosed in 53 Spanish EDs were prospectively and consecutively included. Demographic data, comorbidities, risk factors for VTE, index event characteristics, hemorrhagic risk, and mortality were evaluated. Adherence to clinical practice guidelines was assessed based on clinical probability scales, requests for determination of D-dimer, use of anticoagulant treatment before confirmation of diagnosis, and assessment of bleeding and prognostic risk. Recurrence, bleeding, and death during admission and at 30, 90, and 180 days after diagnosis in the EDs were recorded.

From 549,840 ED visits made over a mean period of 40 days, 905 patients were diagnosed with VTE (incidence 1.6 diagnoses per 1000 visits). The final analysis included 801 patients, of whom 49.8% had pulmonary embolism. The most frequent risk factors for VTE were age (≥70 years), obesity, and new immobility. Clinical probability, prognosis, and bleeding risk scales were recorded in only 7.6%, 7.5%, and 1% of cases, respectively. D-dimer was determined in 87.2% of patients with a high clinical probability of VTE, and treatment was initiated before confirmation in only 35.9% of these patients. In patients with pulmonary embolism, 31.3% had a low risk of VTE. Overall, 98.7% of patients with pulmonary embolism and 50.2% of patients with deep venous thrombosis were admitted. During follow-up, total bleeding was more frequent than recurrences: the rates of any bleeding event were 4.4%, 3.9%, 5.3%, and 3.5% at admission and at 30 and 90, and 180 days, respectively; the rates of VTE recurrence were 2.3%, 1.3%, 1.7%, and 0.6%, respectively. Mortality rates were 3.4%, 3.1%, 4.1%, and 2.6% during hospitalization and at 30, 90, and 180 days, respectively.

VTE had a substantial impact on Spanish EDs. The clinical presentation and risk profile for the development of VTE in patients diagnosed in the EDs was similar to that recorded in previous studies. During follow-up, bleeding (overall) was more frequent than recurrences. Adherence to clinical practice guidelines could improve significantly.

Abbreviations: CPG = clinical practice guideline, DVT = deep vein thrombosis, ED = emergency department, ESC = European Society of Cardiology, ICU = intensive care unit, LMWH = low-molecular-weight heparin, PE = pulmonary embolism, PESI = Pulmonary Embolism Severity Index, sPESI = simplified PESI, VTE = venous thromboembolism.

Keywords: emergency department, healthcare quality, venous thromboembolism

1. Introduction

Patients with venous thromboembolism (VTE) may show many nonspecific signs and symptoms. Management of VTE is complex and may last months or even years, and recurrence and bleeding complications can be observed during follow-up.[1] Most cases of VTE are diagnosed in the emergency department (ED), yet few studies have analyzed the characteristics and outcomes of patients with VTE from the perspective of the ED. Little is known about the epidemiology of VTE in the ED, whether patients are managed according to clinical practice guidelines (CPGs), and whether this has any impact on outcomes. The Multicenter Emergency Medicine Pulmonary Embolism in the Real World Registry (EMPEROR) registry,[2] which provided data on patients with pulmonary embolism (PE) from 22 ED in the United States, showed that patients diagnosed with PE in the ED had few comorbid conditions, and that the mortality rate and adherence to CPG recommendations were low. Therefore, it was hypothesized that the clinical presentation, risk factors, and care of patients with VTE diagnosed in the ED differ from those traditionally reflected in large VTE registries. In this context, it is of paramount importance to assess the risk profile of VTE in patients diagnosed in the ED, management of these patients, and adherence to CPG recommendations.

The primary aim of this study was to determine the clinical profile of and the diagnostic and therapeutic approach to patients diagnosed with VTE (deep vein thrombosis [DVT] and PE) in the ED. In addition, adherence to CPG recommendations by ED physicians and rates of recurrence of VTE, bleeding, and death during admission and at 30, 90, and 180 days of follow-up were analyzed.

2. Methods

A prospective and multicenter cohort study of patients from the ESPHERIA registry (perfil de riESgo de los Pacientes con ETV en Hospitales Españoles atendidos en los seRvicios de urgencias e Impacto Asistencial [Risk Profile of Patients With VTE Attended in Spanish Emergency Departments]) was performed in 53 EDs from throughout Spain. The study population included all patients aged ≥18 years who were consecutively attended in the EDs and diagnosed with VTE, and who signed the informed consent form. Each center needed to recruit a maximum of 15 to 20 consecutive patients. Patients were recruited from October 13 to December 14, 2014, with a median recruitment period of 40 days.

Data were collected using e-Clinical methodology that required data to be entered on an electronic form through a secure web site. Each patient was evaluated for data collection in the ED before and during hospitalization. Data were collected at 30, 90, and 180 days by telephone interview and from reports sent by the participating centers (appointments or admissions during follow-up). Otherwise, the patient was considered lost to follow-up. The evaluation was performed by the principal investigator of each center, who was not responsible for the treatment or management of the patient.

The study was approved by the local ethics committees of each participating center.

The index event was symptomatic DVT or PE (with or without DVT) diagnosed in the ED and confirmed by objective tests (compression ultrasonography or contrast venography for DVT; helical computed tomography scan or ventilation–perfusion lung scintigraphy for PE). VTE was classified as provoked or unprovoked based on whether the patient presented risk factors for VTE (previous VTE, obesity, admission for medical care or surgery in the previous 3 months, previous trauma requiring admission, active cancer, known thrombophilia, any journey lasting >6 hours in the previous 3 weeks, hormone treatment, pregnancy, childbirth, central venous catheter, and new immobility).[3]

Additional variables recorded included demographic data, comorbidities (Charlson comorbidity index), functional status (Barthel index at baseline and at admission), risk factors for VTE, number of hospital admissions, visits to the ED during the previous year, number and type of medications, and thrombo-prophylaxis administered in previous nonsurgical trauma. Severe comorbidity was defined as a Charlson comorbidity index of 3 or more points.[4] Severe functional status was defined as a Barthel index less than 60 points.[5]

The variables recorded during the index event included symptoms, vital signs, analytical and electrocardiographic parameters, and chest x-ray findings. Scores on the pretest scales of clinical probability for DVT (Wells) and PE (Wells and revised Geneva) were calculated by the research team. Time in hours from arrival at the ED to confirmation of diagnosis, treatment for VTE administered in the ED, data on the patient's destination, and referral at discharge were analyzed.

The modified Caprini score was used to assess the risk of VTE during previous admissions for surgery, and the Padua scale was used to assess risk in previous medical admissions.[6] The risk of bleeding was calculated according to the Wells and Registro Informatizado de Pacientes con Enfermedad TromboEmbólica (RIETE) scores.[7,8] The Pulmonary Embolism Severity Index (PESI) and simplified PESI (sPESI) prognostic risk scales were also determined. Based on these scales and data on right ventricular dysfunction and myocardial damage, patients were classified according to the risk groups described in the European Society of Cardiology (ESC) guidelines,[9] as follows: high-risk—patients who presented with shock or hypotension; intermediate-high-risk —patients with PESI class III to V or sPESI ≥1, signs of right ventricular dysfunction on an imaging test, and elevated cardiac laboratory parameters; intermediate-low-risk—patients with PESI class III to V or sPESI ≥1 and signs of right ventricular dysfunction on an imaging test or elevated cardiac laboratory parameters or no signs; and low-risk—patients for whom all of the above were negative.[9]

The indicators used to evaluate the quality of health care provided to VTE patients in the EDs were based on the recommendations of the main CPGs, as follows[9–11]:

1. Recording in the ED report of any score on a clinical probability scale for DVT or PE during the diagnostic work-up in the ED. Adherence of 90% to 100% was defined as standard.
2. Determination of D-dimer concentrations according to the clinical probability of DVT or PE. Percentage of patients with a high probability of PE or DVT according to clinical probability scales with D-dimer determination. Adherence of 0% to 10% was defined as standard.
3. Administration of treatment before confirmation of diagnosis according to clinical probability for PE or DVT. Percentage of patients with an intermediate or high probability in whom treatment was administered before confirmation of diagnosis. Adherence of 90% to 100% was defined as standard.
4. Recording risk of bleeding in the ED report. Adherence of 90% to 100% was defined as standard.
5. Recording any prognostic risk score for patients with PE (PESI or sPESI) in the ED report. Adherence of 100% was defined as standard.

6. Therapeutic management based on the prognostic risk group recommended by the ESC. Percentage of high-risk patients receiving fibrinolysis and admitted to the intensive care unit (ICU). Percentage of low-risk patients managed as outpatients. Adherence of 90% to 100% was defined as standard.

The time and cause of death were recorded. Major bleeding was defined as follows: hemorrhage leading to death; bleeding in a critical area or organ (eg, intracranial, intraspinal, intraocular, retroperitoneal, pericardial), or bleeding in a nonoperated joint, or intramuscular bleeding with compartment syndrome; and bleeding causing a fall in hemoglobin level of ≥2 g/dL or leading to transfusion of ≥2 units of whole blood or red cells. Clinically relevant nonmajor bleeding was defined as any sign or symptom of hemorrhage that did not fit the criteria for the definition of major bleeding, but required medical intervention or led to hospitalization. Bleeding that was not considered clinically relevant was defined as bleeding that did not fit with any of the previous criteria.[12]

Recurrence, bleeding, and death during admission and at 30, 90, and 180 days after diagnosis in the EDs were recorded, as were mean hospital stay and referral after hospital discharge. Nonfatal thromboembolic events or recurrence of VTE were defined as the presence of a new intraluminal defect or the extension of a previous defect in a multidetector computed tomography image, the detection of a new noncompressible venous segment, or an increase of ≥4 mm in the diameter of a thrombus in ultrasonography of the lower limb.[6]

2.1. Statistical analysis

2.1.1. Sample size.
The sample size was estimated at a minimum of 750 patients, taking into account an incidence of VTE in Spain of 160/100,000 person-years,[13] the prospective design of the study, a 3-month period for inclusion, a precision of 3.6%, a confidence interval (CI) of 95%, and a 6% loss to follow-up.

Qualitative variables were expressed as absolute and relative frequencies. Quantitative variables were expressed as mean and standard deviation, or median and interquartile range, when appropriate. The statistical analyses were performed using IBM SPSS Statistics for Windows, Version 19.0 (IBM Corp, Armonk, NY).

3. Results

From a total of 549,840 visits to the 53 participating EDs during the inclusion period, 905 patients were diagnosed with a VTE event (1.6 patients per 1000 ED visits). Of these, 801 fulfilled the criteria for inclusion in the analysis (Fig. 1). In all, 399 (49.8%) had PE and 95 (23.8%) had concomitant DVT.

The baseline clinical characteristics of patients are shown in Table 1. The most frequent risk factors for VTE were age ≥70 years (n = 408, 50.9%) and obesity (n = 252, 31.5%). In 201
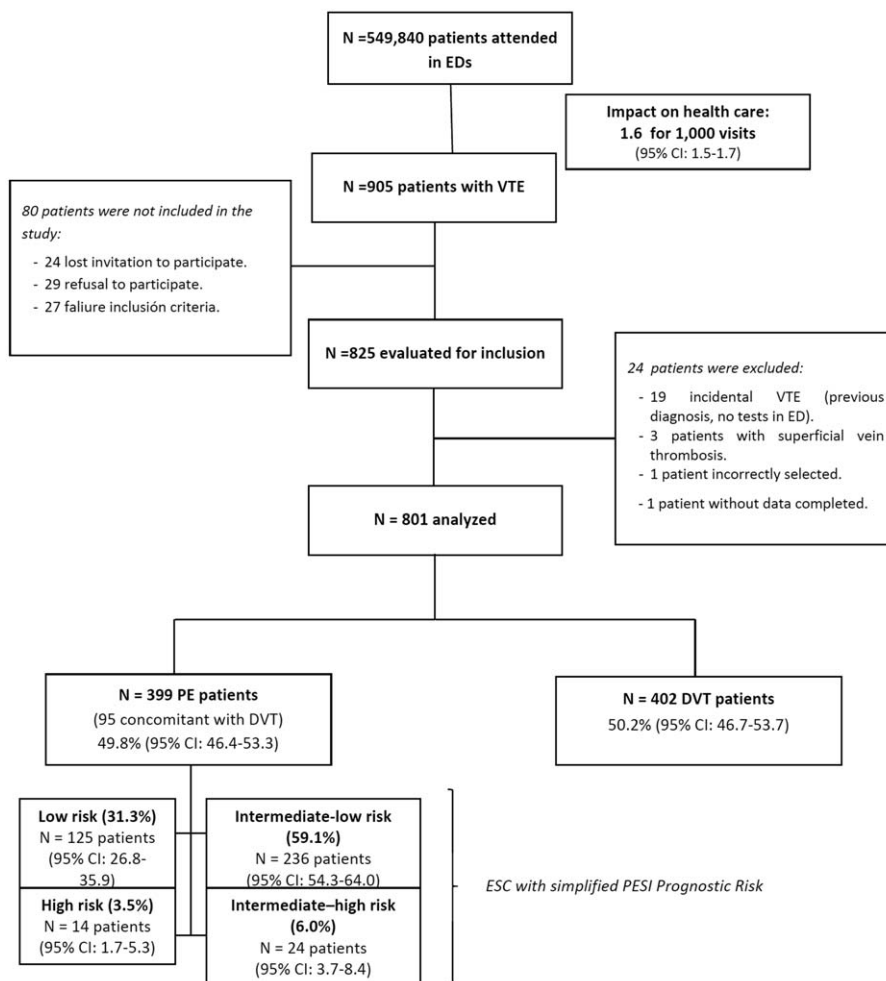

Figure 1. Patient flowchart.

Table 1

Clinical characteristics of patients and risk factors for VTE.

Variables, n (%)	Global (n = 801)	PE (n = 399)	DVT (n = 402)
Patient characteristics and comorbidities			
Age (mean ± SD, y)	66.2 ± 17.4	68.6 ± 16.5	63.9 ± 17.9
Sex (female)	414 (51.7)	202 (50.6)	212 (52.7)
Barthel index (≥60)	727 (90.8)	361 (90.5)	366 (91.0)
Charlson index			
0	357 (44.6)	158 (39.6)	199 (49.5)
1	167 (20.8)	93 (23.3)	74 (18.4)
2	116 (14.5)	58 (14.4)	58 (14.4)
≥3	161 (20.1)	90 (22.6)	71 (17.7)
Polymedication (≥5 drugs)	352 (43.9)	194 (48.6)	158 (39.3)
>3 comorbidities	172 (21.5)	110 (27.6)	62 (15.4)
Comorbidity	686 (85.6)	352 (88.2)	334 (83.1)
Hypertension	420 (52.4)	231 (57.9)	189 (47.0)
Dyslipidemia	276 (34.5)	147 (36.8)	129 (32.1)
Smoking (active and ex-smoker)	238 (29.7)	134 (33.6)	104 (25.9)
Active smoker	109 (13.6)	48 (12.0)	61 (15.2)
History of cancer	172 (21.5)	83 (20.8)	89 (22.1)
Diabetes	93 (11.6)	49 (12.3)	44 (10.9)
Ischemic heart disease	73 (9.11)	44 (11.0)	29 (7.2)
COPD	71 (8.9)	55 (13.8)	16 (4.0)
Rheumatologic disease	61 (7.6)	32 (8.0)	29 (7.2)
Stroke	59 (7.4)	31 (7.8)	28 (7.0)
Dementia	53 (6.6)	30 (7.5)	23 (5.7)
Alcohol abuse	47 (5.9)	18 (4.5)	29 (7.2)
Moderate to severe chronic renal insufficiency	45 (5.6)	26 (6.5)	19 (4.7)
Other	195 (24.3)	115 (28.8)	80 (19.9)
Risk factors for VTE, n (%)			
Unprovoked VTE[*]	201 (25.1)	98 (24.6)	103 (25.6)
Age ≥70 y	408 (50.9)	231 (57.9)	177 (44.0)
BMI ≥30 kg/m^2	252 (31.5)	138 (34.6)	114 (28.4)
New immobility	166 (20.7)	81 (20.3)	85 (21.1)
Previous VTE	139 (17.4)	63 (15.8)	76 (18.9)
Active cancer	124 (15.5)	63 (15.8)	61 (15.2)
Medical admission in previous 3 mos[*]	91 (11.4)	53 (13.3)	38 (9.5)
Low risk	32 (37.6)	20 (39.2)	12 (35.3)
Thromboprophylaxis	10 (31.2)	9 (45.0)	1 (8.3)
High risk	53 (62.4)	31 (60.8)	22 (64.7)
Thromboprophylaxis	20 (37.7)	11 (35.5)	9 (40.9)
Surgery in previous 3 mos[‡]	83 (10.4)	41 (10.3)	42 (10.4)
Low risk	3 (3.7)	1 (2.4)	2 (5.0)
Thromboprophylaxis	1 (33.3)	1 (100.0)	–
Intermediate risk	14 (17.3)	6 (14.6)	8 (20.0)
Thromboprophylaxis	7 (50.0)	3 (50.0)	4 (50.0)
High risk	30 (37.0)	12 (29.3)	18 (45.0)
Thromboprophylaxis	18 (60.0)	6 (50.0)	12 (66.7)
Very high risk	34 (42.0)	22 (53.7)	12 (30.0)
Thromboprophylaxis	29 (85.3)	19 (86.4)	10 (83.3)
Hormone therapy	47 (5.9)	27 (6.8)	20 (5.0)
Known thrombophilia	21 (2.6)	4 (1.0)	17 (4.2)
Journey lasting ≥6 h in previous 3 wks	15 (1.9)	7 (1.8)	8 (2.0)
Pregnancy	3 (0.4)	–	3 (0.7)
Childbirth in previous 3 mos	3 (0.4)	1 (0.3)	2 (0.5)
Central venous catheter	26 (3.2)	13 (3.3)	13 (3.2)
Concomitant treatment	325 (40.6)	181 (45.4)	144 (35.8)
Antidepressants	52 (19.0)	85 (21.3)	67 (16.7)
Antipsychotics	64 (18.0)	34 (8.5)	30 (7.5)
Corticosteroids	84 (10.5)	54 (13.5)	30 (7.5)
Chemotherapy	67 (8.4)	35 (8.8)	32 (8.0)
Hormonal contraceptives	37 (4.6)	18 (4.5)	19 (4.7)
Tamoxifen/raloxifene	11 (1.4)	6 (1.5)	5 (1.2)
Erythropoietin	4 (0.5)	3 (0.8)	1 (0.2)

BMI = body mass index, CHF = chronic heart failure, COPD = chronic obstructive pulmonary disease, DVT = deep vein thrombosis, PE = pulmonary embolism, SD = standard deviation, VTE = venous thromboembolism.

[*] Defined as patients without the following VTE risk factors: previous VTE, obesity (BMI ≥30 kg/m^2), admission for medical care or surgery in the previous 3 months, previous trauma requiring admission, active cancer, known thrombophilia, journey lasting ≥6 hours in the previous 3 weeks, hormone treatment, pregnancy, childbirth, central venous catheter, or new immobility.

[†] According to the Padua score.

[‡] According to the Caprini score.

(25.1%) patients, VTE was unprovoked. In all, 91 patients (11.4%) had been admitted for medical reasons, and 83 (10.4%) had been admitted for surgery within the previous 3 months (45 [54.2%] during the previous month).

The characteristics of the index event are shown in Table 2. The most frequent symptoms of PE were dyspnea (n = 304, 76.2%) and chest pain (n = 174, 43.6%), whereas in DVT, the most common symptoms were an increase in limb diameter (n = 335, 83.3%) and pain in the affected limb (n = 318, 79.1%).

The distribution of patients with PE and DVT according to findings obtained on using various clinical probability scales is shown in Table 3. Based on the Wells and revised Geneva scales, only 14 patients (35.9%) and 15 patients (29.4%), respectively, with a high clinical probability of PE, received treatment before diagnostic confirmation, with a median time to diagnosis of 4.4 and 4 hours, respectively, and an in-hospital mortality of 5.1% (n = 2) and 7.8% (n = 4). In the case of DVT, 7 high-risk patients (26.9%) received treatment before diagnostic confirmation. Clinical probability scores were recorded in the ED reports in 61 patients (7.6%; 8.7% of patients with DVT and 6.5% of those with PE). Prognosis was recorded in 30 (7.5%) patients with PE. The risk of bleeding was reported in 1% (n = 8) of medical reports.

Among patients with PE, 125 (31.3%) were low-risk, and 4 of these (3.2%) were discharged from the ED. Of the 14 high-risk patients (3.5%), 4 (28.6%) received fibrinolysis, and 5 (41.7%) were admitted to the ICU. Two intermediate-high-risk patients (8.3%) received fibrinolysis, 1 (4.2%) underwent catheter-guided thrombectomy, and 7 (30.4%) were admitted to the ICU. Of the

Table 2

Characteristics of the index event.

	Global 801	PE 399	DVT 402
Symptoms, n (%)			
Dyspnea	318 (39.7)	304 (76.2)	14 (3.5)
Chest pain	181 (22.6)	174 (43.6)	7 (1.7)
Cough	95 (11.9)	88 (22.1)	7 (1.7)
Increase in limb diameter	413 (51.6)	78 (19.5)	335 (83.3)
Limb pain	393 (49.1)	75 (18.8)	318 (79.1)
Limb induration	321 (40.1)	62 (15.5)	259 (64.4)
Rise in skin temperature	180 (22.5)	34 (8.5)	146 (36.3)
Cutaneous erythema	163 (20.3)	23 (5.8)	140 (34.8)
Vital signs (mean ± SD)			
SBP, mm Hg	134.4 ± 22.8	133.9 ± 24.1	135 ± 21.2
DBP, mm Hg	77.1 ± 14	77.4 ± 14.7	76.7 ± 13.2
HR, bpm	87.8 ± 19.3	93.1 ± 20.5	82 ± 16.1
RR, bpm	18.5 ± 5.8	20.6 ± 6.5	16 ± 3.6
Oxygen saturation, %	95.2 ± 4.4	93.7 ± 5.1	97.1 ± 2.1
Laboratory parameters (mean ± SD)			
Hemoglobin, g/dL	13.3 ± 2	13.4 ± 1.9	13.2 ± 2.1
Leukocytes, ×10^9/L	9.6 ± 3.8	10.3 ± 4.0	8.9 ± 3.3
Platelets, ×10^9/L	227.9 ± 92	225.3 ± 91.4	230.7 ± 92.7
INR	1.08 ± 0.2	1.10 ± 0.2	1.06 ± 0.2
Glucose, mg/dL	128.1 ± 53.8	135.5 ± 57.4	119.5 ± 47.9
Glomerular filtration rate,[*] mL/min	82.3 ± 40.6	79.4 ± 37.9	85.5 ± 43.2
Diagnostic tests, n (%)[†]			
Computed tomography angiography		385 (96.5)	
Echocardiogram		71 (17.8)	
Lung scintigraphy		6 (1.5)	
Doppler ultrasound	496 (61.9)	102 (25.5)	394 (98.0)
Upper	61 (12.3)	16 (15.6)	45 (11.2)
Lower	436 (87.9)	87 (85.3)	349 (86.8)
Proximal	306 (61.7)	54 (52.9)	252 (62.7)
Distal to the popliteal fossa	127 (25.6)	27 (26.4)	100 (24.9)

DBP = diastolic blood pressure, DVT = deep vein thrombosis, HR = heart rate, INR = international normalized ratio, PE = pulmonary embolism, RR = respiratory rate, SBP = systolic blood pressure.

[*] CKD-EPI.

[†] Some patients underwent more than one diagnostic test.

Table 3

D-dimer requests and mortality according to clinical probability.

	Low probability	Intermediate probability	High probability
Wells PE scale, n (%)	94 (25.7)	233 (63.6)	39 (10.7)
D-dimer determination	84 (89.4)	209 (89.7)	34 (87.2)
Positive D-dimer	80 (95.2)	208 (99.5)	34 (100.0)
Time to diagnosis in hours (median/IQR)	5.5 (3.1–9.1)	4.8 (2.7–6.7)	4.4 (2.8–6.7)
Initiation of treatment before confirmation	18 (19.1)	60 (25.8)	14 (35.9)
In-hospital mortality	2 (2.1)	9 (3.9)	2 (5.1)
Revised Geneva PE scale, n (%)	63 (16.6)	266 (70)	51 (13.4)
D-dimer determination	55 (87.3)	241 (90.6)	45 (88.2)
Positive D-dimer	54 (98.2)	236 (97.9)	45 (100.00)
Time to diagnosis in hours (median/IQR)	5 (3.1–6.8)	4.8 (2.9–7.3)	4 (2.5–6.4)
Initiation of treatment nefore confirmation	13 (20.6)	69 (25.9)	15 (29.4)
In-hospital mortality	1 (1.6)	8 (3.0)	4 (7.8)
Wells DVT scale, n (%)	21 (5,6)	196 (52,1)	159 (42,3)
D-dimer determination	18 (85.7)	166 (84.7)	135 (84.9)
Positive D-dimer	17 (94.4)	163 (98.2)	134 (99.3)
Time to diagnosis in hours (median/IQR)	3.5 (1.9–5.6)	3.6 (2.2–5.6)	3.8 (2.3–5.4)
Initiation of treatment before confirmation	4 (14.3)	17 (30.4)	7 (26.9)
In-hospital mortality	—	1 (1.9)	3 (12.0)

DVT = deep vein thrombosis, IQR = interquartile range, PE = pulmonary embolism.

Table 4

Management of patients with PE and DVT according to risk after diagnosis in the ED.

	PE				DVT (n = 402)
	Low (n = 125)	Intermediate-low (n = 236)	Intermediate-high (n = 24)	High (n = 14)	
Therapeutic management					
LMWH	119 (95.2)	222 (94.1)	23 (95.8)	12 (85.7)	377 (93.8)
Heparin sodium	1 (0.8)	4 (1.7)	1 (4.2)	1 (7.1)	1 (0.2)
Acenocoumarol	5 (4.0)	10 (4.2)	—	—	24 (6.0)
Rivaroxaban	–	3 (1.3)	1 (4.2)	—	3 (0.7)
Fibrinolysis	1 (0.8)	1 (0.4)	2 (8.3)	4 (28.6)	—
Catheter thrombectomy	1 (0.8)	1 (0.4)	1 (4.2)	—	2 (0.5)
Vena cava filter	1 (0.8)	3 (1.3)	—	—	1 (0.2)
Destination from ED,* n/N (%)					
Discharge home	2 (1.6)	—	—	—	186 (46.3)
Discharge with home care	2 (1.6)	1 (0.4)	—	—	14 (3.5)
Admission	121 (96.8)	235 (99.6)	24 (100.0)	14 (100.0)	202 (50.2)
Destination on admission,* n/N (%)					
SSU	—	4/215 (1.9)	—	—	23/191 (12.0)
Ward	108/112 (96.4)	195/215 (90.7)	16/23 (69.6)	7/12 (58.3)	168/191 (88.0)
ICU	4/112 (3.6)	16/215 (7.4)	7/23 (30.4)	5/12 (41.7)	—
Length of stay, d (median/IQR)	8 (6–9)	8 (6–12)	9 (7–14.5)	8 (5–13)	4 (2–7)
In-hospital mortality	2 (1.7)	12 (5.1)	1 (4.2)	—	5 (2.5)

Patients may have received more than 1 treatment.
DVT = deep venous thrombosis, ED = emergency department, ICU = intensive care unit, LMWH = low-molecular-weight heparin, PE = pulmonary embolism, SSU = short stay unit.
* Data regarding destination from ED or destination on admission were not available for some patients.

intermediate-low-risk patients, 222 (94.1%) received treatment with low-molecular-weight heparin (LMWH) and 3 (1.3%) with rivaroxaban. All except 1 were hospitalized (Table 4).

Outcomes during follow-up are shown in Table 5. In-hospital mortality was 3.8% (n = 15) for PE and 2.5% (n = 5) for DVT. During the follow-up, bleeding (overall) was more frequent than recurrences. The highest frequency of recurrence was recorded during admission.

4. Discussion

To the best of our knowledge, this is the first study to describe the clinical profile and management of patients diagnosed with VTE and adherence to CPGs in Spanish EDs.[9–11] Although several VTE registries have been published, data on the VTE event in EDs were reported retrospectively in most of them. Elsewhere, patients were diagnosed either in the outpatient setting or while they were in hospital.[14,15] Other registries have included VTE outpatients only, although these studies had a retrospective design and did not include detailed data on presentation and management in the ED. The only previously published prospective registry of VTE was limited to PE.[2] It is noteworthy that the ESPHERIA registry analyzed both DVT and PE.

Our study provided relevant data about the epidemiology and impact of VTE in the ED. The incidence of VTE was 1.6 per 1000 ED visits (approximately half of these events corresponded

Table 5

Outcomes during admission and follow-up, n (%).

	Overall	PE	DVT
Any bleeding*			
Admission (n = 596)	26 (4.4)	22 (5.6)	4 (2.0)
Follow-up 30 d (n = 743)	27 (3.9)	9 (3.0)	18 (4.8)
Follow-up 90 d (n = 723)	31 (5.3)	21 (7.0)	10 (3.6)
Follow-up 180 d (n = 682)	18 (3.5)	10 (3.6)	8 (3.5)
VTE recurrence			
Admission (n = 596)	14 (2.3)	10 (2.5)	4 (2.0)
Follow-up 30 d (n = 743)	10 (1.3)	3 (0.8)	7 (1.9)
Follow-up 90 d (n = 723)	12 (1.7)	3 (0.8)	9 (2.5)
Follow-up 180 d (n = 682)	4 (0.6)	1 (0.3)	3 (0.9)
Mortality (for any cause)			
Admission (n = 596)	20 (3.4)	15 (3.8)	5 (2.5)
Follow-up 30 d (n = 743)	23 (3.1)	11 (3.0)	12 (3.2)
Follow-up 90 d (n = 723)	30 (4.1)	14 (3.9)	16 (4.4)
Follow-up 180 d (n = 682)	18 (2.6)	11 (3.3)	7 (2.0)

DVT = deep venous thrombosis, PE = pulmonary embolism, VTE = venous thromboembolism.

* Any bleeding included major bleeding, clinically relevant nonmajor bleeding, and no clinically relevant bleeding.

to PE). These data are consistent with recently published findings.[1,15]

Only one-third of the patients with a history of previous high-risk medical admissions had received thromboprophylaxis. This was similar to the percentages reported in previous studies in Spanish EDs,[16,17] and in other clinical settings, such as acutely ill hospitalized medical patients[18] and patients admitted to Spanish hospitals,[19] thus indicating the need to improve thromboprophylaxis in medical patients at risk of developing VTE. A similar percentage of patients had been hospitalized for surgery, and a quarter did not receive thromboprophylaxis, despite presenting a high or very high risk of VTE. Although these results were better than those reported for hospitalized medical patients, there remain a large number of patients in whom the development of VTE could potentially have been avoided with appropriate thromboprophylaxis.

Approximately a quarter of patients presented unprovoked or idiopathic VTE, as reported in the RIETE registry,[20] although this figure was lower than that reported in other studies,[2] thus demonstrating the considerable difficulty in providing a homogeneous definition of this type of VTE.

Quality of health care is assessed mainly by analyzing adherence to CPG recommendations.[9–11] In this respect, the present study showed that the use of clinical probability scales was not recorded in the medical reports, leading to doubts about their use by ED physicians. In addition, determination of D-dimer during the diagnostic work-up did not follow CPG recommendations and was requested in most patients with a high clinical probability of VTE.[7–9] Similar findings have been reported in other studies.[21]

Interestingly, a high proportion of patients did not receive early anticoagulant treatment (before confirmation of diagnosis), despite having a high or intermediate clinical probability of VTE (Table 3). This finding, which was similar to that reported in the EMPEROR study,[2] is important, because several studies have suggested that a delay in the initiation of anticoagulant treatment could have a negative impact on prognosis.[22]

The use of prognostic scales to assess risk of bleeding is controversial, because these include different variables and definitions[7,8]; nevertheless, the risk of bleeding must be determined in clinical practice to reduce it. Unfortunately, the medical report did not contain any information about the use of prognostic scales or scales to assess the risk of bleeding. This is especially relevant, since the therapeutic approach to patients with PE depends on the assessment of prognosis.[9,10]

Almost a third of patients diagnosed with PE in the ED were low-risk and were therefore more likely to benefit from outpatient treatment or early discharge.[23] However, most of the patients with PE (96.8%) were hospitalized, with a median stay of 8 days. As a result, our data suggest missed opportunities for outpatient management of low-risk VTE.

By contrast, less than half of the intermediate-high and high-risk patients were admitted to the ICU for intensive monitoring and reperfusion. As mortality is high in this population, intensive monitoring and reperfusion are recommended for high-risk PE patients. For intermediate-high-risk PE, rescue reperfusion is only recommended when the patient's condition deteriorates after starting anticoagulant therapy.[10,11]

The initial treatment of patients with VTE in the ED basically involved monotherapy with LMWH. Only a small proportion of patients received vitamin K antagonists or direct oral anticoagulants in EDs, even though they can be used according to CPGs.[9–11,23]

The in-hospital mortality of patients with PE was 3.8%, which was lower than that reported in other studies. However, it should be taken into account that this study involved outpatient VTE, and that the mortality and severity of PE in hospitalized patients were higher and were not included in the registry.[24] On the contrary, this mortality rate was very similar to that reported in other outpatient studies such as the EMPEROR registry.[2] In addition, only 3% of PE patients were hypotensive at presentation, as in EMPEROR.

The main limitation of the study was its observational design. However, it provides a clear picture of the clinical profile and management of patients in clinical practice. Other strengths include the fact that inclusion was consecutive and prospective and a high number of hospitals participated. The results may also be limited by a potential Hawthorne effect, because of the prospective design. However, the evaluation was performed by an ED physician who was not responsible for the treatment and management of the patient.

5. Conclusions

In conclusion, VTE had an appreciable impact on Spanish EDs. Patients diagnosed with VTE in the EDs presented a VTE risk profile similar to that described in other studies. Adherence to CPGs should be intensified to improve the quality of the healthcare process and the outcomes of patients with VTE attended in Spanish EDs.

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