Acute Pulmonary Embolism in Argentina. XX Conarec Registry

Tromboembolismo pulmonar agudo en la Argentina. Registro Conarec XX

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ABSTRACT

Background: Acute pulmonary embolism (PE) represents the third cause of cardiovascular mortality. However, there is lack of information about this entity in our country. Our aim was to describe baseline characteristics, clinical evolution and treatment of patients with acute PE in Argentina.

Methods: This was a prospective multicenter registry including patients with acute PE hospitalized in centers with cardiology residency from October 2016 to November 2017. Conventional analysis was performed for descriptive and comparative statistics. A value of p<0.05 was considered significant. Cross audit was performed to 20% of participating centers.

Results: We included 684 consecutive patients from 75 centers with an average age of 63.8 years and 388 (57%) women. Hospital admission was due to PE in 484 (71%) cases. The most frequent predisposing factors were obesity, recent hospitalization, transient rest and active cancer. Anticoagulation was indicated in 661 patients (97%) and reperfusion therapy was performed in 91 (13%). However, only 50 of the 102 patients who presented with hemodynamic instability received reperfusion therapy (49%). Global in-hospital mortality was 12%, mainly associated with acute PE (51%).

Conclusions: Acute pulmonary embolism presents with high in-hospital mortality in our setting, mainly related with the embolic event. We observed a low use of reperfusion therapies in patients with hemodynamic instability.

Key words: Registry - Pulmonary Embolism – Argentina – Reperfusion - Anticoagulants

RESUMEN

Introducción: El tromboembolismo de pulmón agudo (TEP) representa la tercera causa de mortalidad cardiovascular. Sin embargo, existen pocos datos de esta patología en nuestro país. Nuestro objetivo fue describir las características basales, evolución y tratamiento implementado en pacientes con tromboembolismo de pulmón agudo en Argentina.

Material y métodos: Se trata de un registro multicéntrico prospectivo que incorporó pacientes con diagnóstico de tromboembolismo de pulmón agudo internados en centros con residencia de cardiología desde octubre de 2016 a noviembre de 2017. Se realizó un análisis convencional para establecer una estadística descriptiva y comparativa. Se consideró significativo un valor de p < 0,05. Se realizó una auditoría cruzada al 20% de los centros participantes.

Resultados: Se incluyeron 684 pacientes consecutivos de 75 centros, con un promedio de edad de 63,8 años; 388 (57%) eran de sexo femenino. El TEP fue el motivo de internación en 484 (71%) de los casos. Los factores predisponentes más frecuentes fueron obesidad, hospitalización reciente, reposo transitorio y cáncer activo. Se indicó anticoagulación durante la internación en 661 (97%) pacientes y terapia de reperfusión en 91 (13%). Sin embargo, solo 50 de los 102 pacientes que se presentaron con inestabilidad hemodinámica recibieron alguna terapia de reperfusión (49%). La mortalidad hospitalaria fue del 12%, principalmente relacionada con el tromboembolismo de pulmón agudo (51%).

Conclusiones: El tromboembolismo de pulmón agudo en nuestro medio constituye una patología con elevada mortalidad en la internación atribuible principalmente al evento embólico. Se observó una baja utilización de terapias de reperfusión en pacientes con inestabilidad hemodinámica.

Palabras clave: Registro - Tromboembolismo de pulmón - Argentina - Reperfusión - Anticoagulantes

Abbreviations

DOAC	Direct oral anticoagulants	**PASP**	Pulmonary artery systolic pressure
DVT	Deep vein thrombosis	**RV**	Right ventricular
IQR	Interquartile range	**VKA**	Vitamin K antagonists
LMWH	Low molecular weight heparins	**VTD**	Venous thromboembolic disease
PE	Pulmonary embolism		

INTRODUCTION

Pulmonary embolism (PE) represents the third cause of cardiovascular death (1) and is responsible for at least 100,000 deaths per year in the United States (2) and 300,000 in Europe. (3) Its variable and frequently nonspecific clinical presentation is a diagnostic challenge with the risk of underestimating its real incidence (4) and delaying the initiation of specific treatment that will result in a worse prognosis. This situation indicates that PE is the main cause of preventable in-hospital mortality. (5)

Although there are numerous international registries that have collaborated in defining risk factors and their natural history, (6-9) there is scarce information in our setting about the management of PE. (10)

Yet, despite the advances and growing interest in this disease, there are still large "gray areas" and controversies, especially with regard to treatment in its acute phase. In addition, there is no information regarding the impact generated by the introduction of direct oral anticoagulants (COAD) in routine clinical practice.

These factors prompted the Argentine Council of Cardiology Residents to initiate a new national registry to help understand the reality of PE in our country.

METHODS

An observational, cross-sectional study was performed that prospectively included patients with acute PE admitted to centers with cardiology residency affiliated to CONAREC, regardless of whether this was the cause of hospitalization or arose as a complication of hospitalization for another cause.

Patients hospitalized in the coronary care unit, the intensive care unit, or the general ward were included during thirteen consecutive months (October 2016 to November 2017), with follow-up limited to the hospitalization period. Diagnostic algorithms or guidelines for patient management were not issued.

Data was loaded online in an electronic case report form with exclusive access for each center through an individual password. The research committee members, collaborating experts and participating centers, along with their leaders, are detailed in the supplementary material.

An independent committee also conducted a cross-audit to 20% of the centers, comparing random variables of the information submitted with the clinical records of the corresponding institutions.

The classification suggested by the European Society of Cardiology (ESC), (11) the Pulmonary Embolism Severity Index (PESI) (12, 13) and the simplified PESI (s-PESI) were used to stratify PE risk of death. (14) Also, the RIETE (15) and HAS-BLED (16) scores were used to determine the risk of bleeding. The analysis of the risk scores was performed independently and blindly by the principal investigator based on their constitutive variables.

The classification of the Bleeding Academic Research Consortium (BARC) (17) was considered to define the type of bleeding.

Statistical analysis

Continuous variables were expressed as mean and standard deviation or median and interquartile range (IQR), according to their distribution. Categorical variables were expressed as numbers and percentages.

Groups were compared using Student's test or the Wilcoxon rank sum test, as appropriate. Comparisons between proportions were performed using the chi square test or Fisher's exact test, according to the frequency of expected values. In all cases, an alpha error of 5% was assumed to establish statistical significance.

Epi Info 7.2 and STATA 13 were used for the statistical analysis.

Ethical considerations

The study protocol and informed consent form were sent to each center ethics committee for approval. The study protocol, together with the definitions used, have been previously published. (18)

RESULTS

Baseline characteristics

The study included 684 consecutive patients from 75 centers, distributed in 16 provinces across the country. Cross-audit was carried out to 15 centers (20%) chosen at random, with 97% accuracy in the randomly evaluated variables. All patients were included in the final analysis based on the audit results.

Mean age was 64 ±17 years, 57% were women, 86% had medical coverage and the maximum level of educational attainment was secondary school or higher in 79% of cases.

The predisposing factors for PE were classified according to the recommendations of the ESC (11) in those related to the patient (usually permanent) and those related to the context (usually temporary). Among the former, obesity (34%), active cancer (22%), and venous thromboembolic disease (VTD) were the most prevalent (18%), while recent hospitalization (34%), transient rest greater than 72 h (30%), and recent surgery (24%) were the most frequent context-related factors. The rest of the baseline characteristics are detailed in Table 1. Only 2% of the patients did not have predisposing factors for VTD.

In 9% of cases the patients had indication of anticoagulation. However, the degree of anticoagulation was inadequate in more than half of the cases.

Current illness

Pulmonary embolism was the cause for hospitalization in 71% of cases, while the rest developed PE during hospitalization due to another cause.

In patients admitted for PE, the time from onset of symptoms to admission was 48 h (IQR 8-168) and a retrospective diagnosis of PE was made in 10% of the cases after ruling out another diagnostic suspicion. On the other hand, only 68% of the subjects who presented with PE during hospitalization for another cause had adequate antithrombotic prophylaxis.

The main findings at admission and complementary studies are described in Table 2. Dyspnea (85%) was the most frequent manifestation, followed by tachypnea (47%) and tachycardia (37%). Sinus tachycardia

Table 1. Baseline patient characteristics

	N (%)
Age #	63.80 (±16.78)
Male sex	296 (43.27%)
Weight (kg) #	82.55 (±19.84)
Height (m) #	1.67 (±0.09)
Educational attainment *	
- Incomplete primary school	12 (2.65%)
- Primary school	83 (18.36%)
- Secondary school	267 (59.07%)
- University	90 (19.91%)
Medical coverage	
- Social work	307 (44.88%)
- Private/prepaid	196 (28.65%)
- PAMI	82 (11.99%)
Main predisposing factors related with the patient	
Previous VTD	120 (17.54%)
Deep vein thrombosis	106/120 (88.33%)
PE	32/120 (26.67%)
- Heart failure	78 (11.4%)
- COPD	61 (8.92%)
- Hormone therapy	51 (7.46%)
- Malignant neoplasm	
In progress	150 (21.93%)
In remission	40 (5.85%)
- Stroke	41 (5.99%)
- Pregnancy/puerperium<21 days	3 (1.29%)
- Procoagulant syndrome	27 (3.95%)
- Obesity	232 (33.92%)
- Varicose syndrome	93 (13.6%)
Main predisposing factors related with the context	
- Recent surgery (3 months)	164 (23.98%)
Lower limbs	61/164 (37.2%)
Neurosurgery	11/164 (6.71%)
Abdominal	34/164 (20.73%)
Cardiovascular	11/164 (6.71%)
Thoracic	5/164 (3.05%)
Other	46/164 (28.05%)
Recent hospitalization (3 months)	230 (33.63%)
Heart failure	16/230 (6.96%)
Atrial fibrillation	6/230 (2.61%)
Other cause	214/230 (93.04%)
- Major trauma	19 (2.78%)
- Central venous access	58 (8.48%)
- Infection	111 (16.23%)
Pneumonia	41/111 (36.94%)
Urinary tract infection	23/111 (20.72%)
HIV	3/111 (2.7%)
Chagas disease	3/111 (2.7%)
Other	50/111 (45.05%)
- Chemotherapy	79 (11.55%)
- Transient rest >72 h	186 (29.62%)
- Prolonged trip	42 (6.14%)
Arterial hypertension	383 (55.99%)
Diabetes	98 (14.33%)
Ex-smoker	188 (27.49%)
Current smoker	76 (11.11%)
Dyslipidemia	203 (29.68%)
Atrial fibrillation	48 (7.02%)
Previous ischemic heart disease	57 (8.33%)
Ambulation	
- Without help	517 (75.58%)
- Assisted	111 (16.23%)
- Bedridden	56 (8.19%)
Major hemorrhage	29 (4.26%)
Autoimmune disease	35 (5.12%)
Chronic renal failure	
- Conservative management	44 (6.43%)
- Dyalisis	10 (1.46%)
Previous anticoagulation	64 (9.36%)
- Reason for anticoagulation	
Atrial fibrillation /atrial flutter	15/64 (23.44%)
VTD	38/64 (59.38%)
Mechanical valve replacement	1/64 (1.56%)
Others	12/64 (18.75%)
- Adequate ‡	31/64 (48.44%)
- Type of anticoagulant used	
Acenocoumarol	41/64 (64.06%)
Warfarin	3/64 (4.69%)
Enoxaparin	11/64 (17.19%)
Apixaban	1/64 (1.56%)
Dabigatran	6/64 (9.38%)
Rivaroxaban	2/64 (3.13%)

VTD: Venous thromboembolic disease. PE: Pulmonary embolism. COPD: Chronic obstructive pulmonary disease. HIV: Human immunodeficiency virus infection-
Occasionally, for a factor or prior history, the sum of the different categories considered is greater than 100% because there are patients with more than one of them.
Value expressed as mean and standard deviation.
* The fully attained maximum level is considered. Missing data in 232 patients (33.92%).
‡ RIN 2-3 at admission for VKA or with correct doses of direct oral anticoagulants and low molecular weight heparins.

	N (%)
Signs and symptoms	
- Dyspnea	582 (85.09%)
- Palpitations	77 (11.26%)
- Angina	61 (8.92%)
- Pleuritic pain	100 (14.62%)
- Syncope	49 (7.16%)
- Hemoptysis	21 (3.07%)
- Sensory alteration	34 (4.97%)
- Pain / unilateral edema of lower limbs	135 (19.74%)
Heart rate (bpm)	95,9 (±22,4)
- Tachycardia (>100 bpm)	254 (37.35%)
Systolic blood pressure (mmHg)	122.2 (±23.4)
- Hypotension	79 (11.55%)
Respiratory frequency (bpm)	21.8 (±5.4)
- Tachypnea (> 20 bpm)	309 (46.96%)
Temperature (°C)	36.2 (±0.5)
- Temperature >37°	35 (5.3%)
Arterial O2 saturation (%)	94 (89.97)
- Desaturation (O2sat < 90%)	167/667 (25.04%)
Wells Score	4 (2.5-6)
Electrocardiogram	
- Sinus tachycardia	354 (51.75%)
- Pulmonary P	16 (2.34%)
- Q wave in LII-aVF	41 (5.99%)
- Negative T from V1 to V4	110 (16.08%)
- Fibrillation/atrial flutter	59 (8.63%)
- Complete right bundle branch block	68 (9.94%)
- ST-segment depression	32 (4.68%)
- S1Q3T3 pattern	138 (20.18%)
- QR in V1	19 (2.78%)
Laboratory tests	
- Hematocrit (%)	37.4 (±6.6)
- White blood cell count (mm3)	10,100 (7,600-13,000)
- Creatinine (mg/dL)	0.91 (0.72-1.2)
- Platelet count (mm3)	204.5 (158-273)
- pH	7.42 (7.39-7.46)
- Bicarbonate	21.75 (19-24)
- Arterial oxygen saturation	95 (91-97)
- PaO2/FiO2	299.05 (233.33-366.67)
- Troponin measurement	477 (69.74%)
Positive value‡	312/477 (65.41%)
- D dimer	215 (31.43%)
Positive value‡	207/215 (96.28%)
- BNP	56 (8.19%)
Positive value‡	41/56 (73.21%)
- NT-proBNP	152 (22.22%)
Positive value‡	126/152 (82.89%)
Transthoracic echocardiogram	625 (91.37%)
- Left ventricular systolic function	
Preserved	532/620 (85.81%)
Mild dysfunction	42/620 (6.77%)
Moderate dysfunction	19/620 (3.06%)
Severe dysfunction	27/620 (4.35%)
- Right ventricular systolic dysfunction	206/595 (34.62%)
- Tricuspid annular plane systolic excursion	18 (14-22)
- Pulmonary artery systolic pressure	43 (35-55)
- Right ventricular dilatation	250/610 (40.98%)
- Right ventricular motility disorder	128/580 (22.07%)
- Interventricular septum flattening	118/569 (20.74%)
Ventilation/perfusion scintigraphy	92 (13.45%)
- High probability	74/92 (80.43%)
- Intermediate probability	4/92 (4.35%)
- Normal/low probability	14/92 (15.22%)
Lower limb Doppler study	534 (78.07%)
- Positive for VTD	310/534 (58.05%)
Multislice computed tomography angiography	557 (81.43%)
- Positive result	546/557 (98.03%)
- Right ventricular dilatation	112/457 (24.51%)
- Pulmonary artery diameter greater than aortic diameter	67/429 (15.62%)
Pulmonary arteriography	54 (7.89%)
Thrombus location *	
- Main pulmonary artery	23/590 (3.9%)
- Both branches of the pulmonary artery	216/590 (36.61%)
- One pulmonary branch	112/590 (18.98%)
- Single subsegmental	69/590 (11.69%)
- Multiple subsegmental	170/590 (28.81%)

Table 2. Findings on admission and complementary studies

bpm: beats per minute (for heart rate) or breaths per minute (respiratory frequency.
PaO2/FiO2: Partial pressure of arterial oxygen to fraction of inspired oxygen ratio. VTD: Venous thrombo-embolic disease.
‡ Positive value according to the parameters of the local laboratory.
* By arteriography or computed tomography angiography

(52%) and S1Q3T3 pattern (20%) were the electrocardiographic signs most frequently found. An echocardiogram performed in 625 patients (91%) showed right ventricular (RV) dilatation or dysfunction in 41% and 35% of cases, respectively. Median pulmonary artery systolic pressure (PASP) was 43 mmHg (IQR 35-55). A venous echo-Doppler of the lower limbs in 534 patients showed deep vein thrombosis (DVT) in 310 patients.

The most used diagnostic method was multislice computed tomography angiography (81%) followed by ventilation/perfusion scintigraphy (14%) and pulmonary arteriography (8%). Only 52 patients (8%) required two or more specific diagnostic studies.
On admission, 42% of patients presented with anemia and baseline creatinine was 0.91 mg/dL (IQR 0.72-1.2). Biomarkers of myocardial injury were evaluated in 83% of cases, especially troponin (70%), which was positive in 65% of the cases.

Risk stratification
Median PESI score was 83 (IQR 47-112), with 41% of patients at low/very low risk, 26% at intermediate risk and the remaining 33% at high/very high risk (Table 3). Conversely, when assessing risk according to the simplified PESI scale, only 26% of patients were classified as low risk (PESI=0).

Considering clinical, echocardiographic and laboratory parameters according to the ESC classification, patients were stratified as low risk (24%), intermediate-low risk (34%), intermediate-high risk (26%) and high risk (15%).

On the other hand, bleeding according to the RIETE score yielded a median of 2.5 points (IQR 1-3.5), with 12% of patients at high risk. Likewise, a HAS-BLED median of 1 point (IQR 0-2) was recorded, with 9% of patients presenting a value ≥3 points.

Treatment during hospitalization
In our registry, 75% of the patients were under the care of the cardiology service, and 78% required admission to a closed unit during the acute episode. Ninety-seven percent of patients received anticoagulation during hospitalization, and low-molecular-weight heparins (LMWH) (56%) or unfractionated heparins (22%) were used more frequently as the first therapeutic scheme. The remaining 3% did not receive anticoagulation, mainly due to absolute (30%) or relative (22%) contraindications.

A vena cava filter was implanted in 43 patients, mainly in the context of anticoagulation contraindication (47%) or recurrent PE under anticoagulation therapy (21%).

Pharmacological, endovascular or surgical reperfusion therapy was performed in 91 patients (13%), with time to reperfusion of 2 days (IQR 1-5). The cases under cardiologic care received more reperfusion compared to other medical specialties (16% vs. 7%, p <0.01). When evaluating use of reperfusion according to risk stratification, we observed that it was performed in 16% of patients at high-intermediate risk and only in 49% of high-risk patients. In 77% of high-risk non-reperfused patients, there was no formal contraindication for its performance and this conduct

Table 3. Risk stratification and its association with events (in-hospital mortality and bleeding)

	N (%)	In-hospital mortality	p
PESI			
- Class I	107 (15.64%)	3 (2.8%)	p <0.001
- Class II	173 (25.29%)	9 (5.2%)	
- Class III	178 (26.02%)	23 (12.92%)	p <0.001
- Class IV	106 (15.5%)	10 (9.43%)	
- Class V	120 (17.54%)	38 (31.67%)	p <0.001
s-PESI			
- PESI 0	179 (26.17%)	3 (1.68%)	
- PESI ≥1	505 (73.83%)	80 (15.84%)	
Risk stratification according to ESC			
- Low risk	164 (24.26%)	3 (1.83%)	
- Low-intermediate risk	232 (34.32%)	20 (8.62%)	
- High-intermediate risk	178 (26.33%)	22 (12.36%)	
- High risk	102 (15.09%)	38 (37.25%)	
	N (%)	In-hospital mortality	p
RIETE			
- Intermediate risk (1-4 points)	594 (88.26%)	23 (3.87%)	p=0.6
- High risk (> 4 points)	79 (11.74%)	3 (3.8%)	
HAS-BLED			
- <3 points	607 (91.28%)	23 (3.79%)	p=0.4
- ≥3 points	58 (8.72%)	3 (5.17%)	

was strictly the decision of the attending physician.

Systemic lytic agents, mainly streptokinase (62%), was the most used reperfusion strategy (86%). Endovascular revascularization was performed in 14 patients, using aspiration (57%), fragmentation (50%) and local lytic administration (36%) techniques. Surgical revascularization was performed in only one patient.

In-hospital outcome
Median hospital stay was 8 days (IQR 5-14). The main complications recorded are described in Table 4. These were: renal dysfunction (15%) concomitant infection (12%) and bleeding (7%).

There were no differences in the RIETE or HAS-BLED scores between those who presented major bleeding and those who did not [RIETE 2.5 (IQR 1-3.5) vs. 2.5 (IQR 1-3.5), p=ns; HAS-BLED 1 (IQR 1-2) vs. 1 (IQR 0-2), p=ns].

Overall mortality was 12%, with a significant difference according to risk stratification (Table 3). The cause of death was mostly related with PE (51%), followed by other non-cardiovascular causes (30%), cardiovascular causes (16%) and bleeding (4%).

Treatment at discharge
Anticoagulation was indicated at discharge in 96% of patients: vitamin K antagonists (VKA) to 60%, LMWH to 21%, and DOAC to 19% of patients (Figure 1). One in four patients who were discharged with dicumarinic agents was not in the range of anticoagulation at discharge.

Patients who received DOAC at discharge were more frequently those in charge of the cardiology service (21% vs. other services 12%, p=0.012), with better educational attainment (20% with secondary school/university level vs. 9% with primary school/minimum level; p=0.013), private/social work coverage (22% vs. 8% state/PAMI, p <0.001) and lower severity condition (PESI 84.4±26.4 vs. 93.7±31.3; p=0.004). No DOAC was indicated in patients who presented major bleeding during hospitalization (0% vs. 19% in those without bleeding, p=0.035).

DISCUSSION
We present the data of the largest PE registry in Argentina and one of the largest in the region, a project that was central to an improvement program that included training and dissemination activities for residents of cardiology and the community in general.

Baseline patient characteristics are consistent with bibliographic findings, confirming the heterogeneity of this disease which comprises a population with a wide age range (16-97 years) and with a variable occurrence of predisposing factors.

Although we found a similar presentation in terms of average age, tendency to greater involvement in females and prevalence of the most relevant predisposing factors such as active neoplasia, the low number of patients with idiopathic or unprovoked presentation

Table 4. Complications during hospitalization

|	N (%)
Hemodynamic support	
- Inotropics	73 (10.67%)
- Vasopressors	58 (8.48%)
- Ventricular assistance	17 (2.49%)
Respiratory assistance	
- Non-invasive ventilation	42 (6.46%)
- Mechanical respiratory assistance	75 (11.54%)
PE recurrence	14 (2.05%)
Heart failure	51 (7.46%)
Atrial fibrillation	24 (3.51%)
Infection	79 (11.55%)
Bleeding *	
- Type I-II	22 (3.22%)
- Type III	25 (3.65%)
- Type IV	1 (0.15%)
- T Type V	1 (0.15%)
Renal failure #	
- Grade I	60 (8.77%)
- Grade II	26 (3.8%)
- Grade III	15 (2.19%)
Death	83 (12.13%)
- Related to PE	42/83 (50.6%)
- Other non-cardiovascular causes	25/83 (30.12%)
- Cardiovascular cause	13/83 (15.66%)
- Bleeding	3/83 (3.62%)

* * The BARC classification was used to define and stratify bleeding
Graded according to the AKIN classification.

is remarkable (2 %) with respect to other series: 9% in the SAC registry, (10) 19% in the ICOPER study, (8) and up to 43% in the MASTER registry. (19) Perhaps, the better understanding of the pathophysiology and detection of predisposing factors over the years has allowed their better identification in our population. However, an inadequate indication of prophylaxis in patients developing PE for other causes during hospitalization shows that there are still key aspects to improve in order to prevent this condition in our daily clinical practice.

Computed tomography angiography has been established as the most used diagnostic method and its use has increased in successive registries (37%, 55%, 86% and 81% in EMEPCO, (20) Brazilian, (21) SAC (10) and CONAREC XX, registries, respectively) replacing the ventilation/perfusion scan. Its greater sensitivity and specificity are probably responsible for a lower need of additional complementary studies: 8% of patients required two or more specific studies compared to 31% evidenced in the MASTER registry. (19) An increase in the use of arteriography as a diagnostic method (8%) compared to the SAC registry (1%) was also observed. (18)

Echocardiography in PE has become a fundamen-

Fig. 1. Anticoagulation at discharge
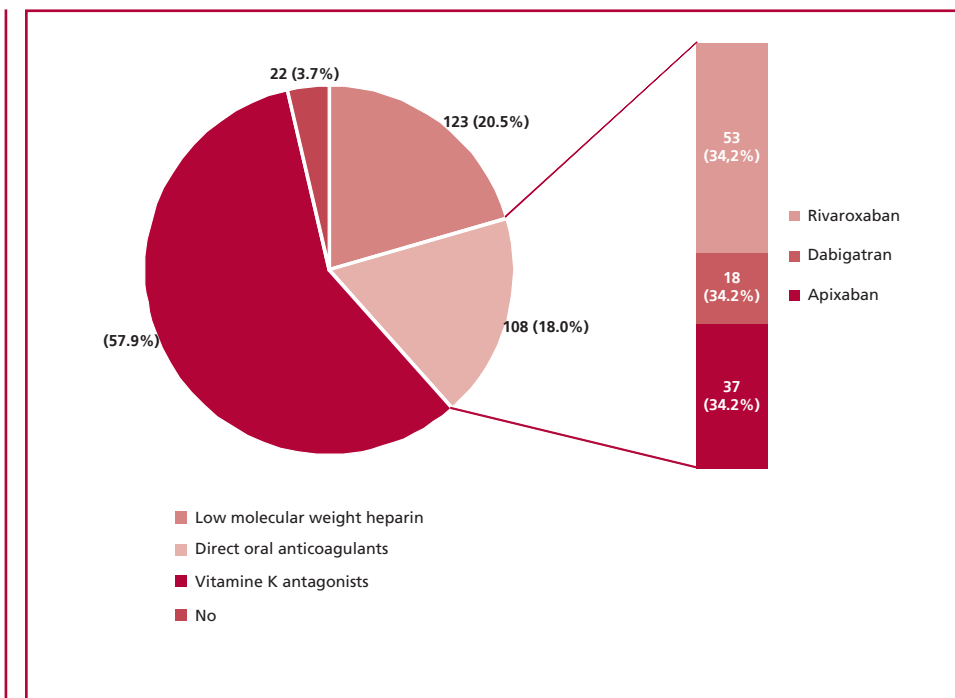
tal tool due to its wide availability and its ability to stratify risk (11, 22); dilatation and especially RV dysfunction were independent predictors of mortality. (23) In our registry, the mortality of patients with dilatation or RV dysfunction was 17%, and 7%, respectively, in those who did not evidence RV involvement (p <0.001).

Risk stratification suggested by the ESC, which combines clinical parameters with the evaluation of injury or ventricular dysfunction was used for the first time in a Latin American registry, (11) and a good correlation was observed with in-hospital mortality according to the different strata. Similar findings were observed with the PESI and s-PESI scores, although these deductions should be confirmed with specific analyses that exceed the objectives of this study.

Regarding treatment, the high rate of anticoagulation during hospitalization mainly with LMWH corresponds to the transition observed in different publications, relegating the use of unfractionated heparins. (24)

This is one of the only registries that describe reperfusion rate according to risk stratification, allowing the identification of low reperfusion rate in high-risk patients despite no strict contraindication for its use. The indication of reperfusion therapy is supported by different societies (11, 22) due to its demonstrated decrease in mortality. (25, 26) The increased risk of bleeding inherent to this practice could be the reason for its underutilization by treating physicians. (26)

In this sense, our study reflects the lack of tools to predict bleeding in patients with PE, since neither the RIETE nor the HAS-BLED scores could identify patients with a higher risk of bleeding during hospitalization. Although the HAS-BLED score was devel-

oped to evaluate the risk of bleeding in patients with atrial fibrillation under anticoagulant treatment, its widespread use in daily practice and recent evidence of its potential application in patients with VTD were the reasons for its inclusion in this registry. (16)

The recorded 12% mortality is comparable to that observed in other Latin American registries (20, 21) although remarkably greater than the 7% reported by the SAC registry. (10) The different classification used to stratify risk for PE and the smaller number of cases incorporated in the aforementioned registry make a direct comparison impossible. It is noteworthy, however, that the decrease in mortality in patients with PE observed in some series (24) is not reflected in our setting.

Vitamin K antagonists continue to be the most indicated anticoagulant at discharge, however, one out of every four patients was not in the therapeutic range upon discharge. The demonstrated safety and efficacy of DOAC in clinical trials (27-29) and subsequent meta-analyses (30) make them an attractive alternative in selected patients. In this regard, as it is the first report of DOAC use for PE in our setting, it is expected that these drugs will be used more frequently to replace VKA in the coming years. For the moment, their use was associated with the management by the cardiology service and a better social status of the patient, probably related to the higher cost of DOAC therapy.

Study limitations
The inclusion of patients admitted to centers with cardiology residency affiliated to CONAREC may not be representative of the general Argentine population due to the restricted participation to moderate-high

complexity academic centers. In addition, data from patients with low-risk PE with outpatient treatment are not provided. Similarly, since only patients with confirmed PE were enrolled, there is also the possibility of underreporting patients with more severe PE, in whom diagnostic confirmation prior to death was not achieved.

Finally, there was no confirmation of PE diagnosis, accepting the interpretations of the complementary studies carried out by the participating institutions. Nevertheless, a cross-audit to 20% of the participating centers based on an independent committee supports the data provided.

Despite the limitations described, the strength of this work lies on the prospective collection of real practice data of a large number of patients with PE based on diagnostic tests and clinical practices in a large sample of institutions of our country.

CONCLUSIONS

In our setting, PE presents as a disease that affects a heterogeneous group of patients, with high in-hospital mortality directly related with PE in more than half of the cases.

Although anticoagulant treatment during hospitalization is high, we highlight the low use of reperfusion therapies in high-risk patients without contraindications for its use. It is also the first report in our country on the use of DOAC for PE.

Conflicts of interest
None declared.

(See authors' conflicts of interest forms on the website/ Supplementary material)

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