Central Versus Peripheral Pulmonary Embolism: Analysis of the Impact on the Physiological Parameters and Long-term Survival

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Abstract

Background: Studies aimed at assessing whether the emboli lodged in the central pulmonary arteries carry a worse prognosis than more peripheral emboli have yielded controversial results. **Aims:** To explore the impact on survival and long-term prognosis of central pulmonary embolism. **Patients and Methods:** Consecutive patients diagnosed with acute symptomatic pulmonary embolism by means of computed tomography (CT) angiography were evaluated at episode index and traced through the computed system of clinical recording and following-up. Central pulmonary embolism was diagnosed when thrombi were seen in the trunk or in the main pulmonary arteries and peripheral pulmonary embolism when segmental or subsegmental arteries were affected. **Results:** A total of 530 consecutive patients diagnosed with pulmonary embolism were evaluated; 255 patients had central pulmonary embolism and 275 patients had segmental or subsegmental pulmonary embolism. Patients with central pulmonary embolism were older, had higher plasma levels of N-terminal of the prohormone brain natriuretic peptide (NT-ProBNP), troponin I, D-dimer, alveolar-arterial gradient, and shock index ($P < .001$ for each one). Patients with central pulmonary embolism had an all-cause mortality of 40% while patients with segmental or subsegmental pulmonary embolism (PE) had an overall mortality of 27% and odds ratio of 1.81 [confidence interval (CI) 95% 1.16-1.9]. Survival was lower in patients with central PE than in patients with segmental or subsegmental pulmonary embolism, even after avoiding confounders ($P = .018$). **Conclusions:** Apart from a greater impact on hemodynamics, gas exchange, and right ventricular dysfunction, central pulmonary embolism associates a shorter survival and an increased long-term mortality.

Keywords: Cardiac peptides, central pulmonary embolism, pulmonary embolism, survival

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Introduction

With the increasing use of the computed tomography (CT) angiography as the main diagnostic method in pulmonary thromboembolism, new approaches for categorizing the severity of pulmonary embolism have been conducted mainly based on thrombus burden and its impact on the right ventricle.[1-17] Data from radiographic studies, which used CT angiography

to evaluate the prognostic factors associated with pulmonary embolism (such as the relationship between the diameter of the right ventricle and the diameter of the left ventricle, the bowing of the interventricular septum,[1-4] the thrombus burden,[14-17] the reflux contrast to the cava,[18] and the diameter of the pulmonary

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artery regarding the azygos vein) have been studied as prognostic factors of morbidity and mortality in the context of acute pulmonary thromboembolism.

The impact of pulmonary embolism on the right ventricle measured by biomarkers and D-dimer has also been correlated with the thrombotic burden in several investigations,[19,20] and recently the European Society of Cardiology has included the right ventricular dysfunction in the risk assessment of pulmonary embolism[21] evaluated by echocardiography as well as measured by CT though in both cases the prediction of an adverse outcome has been difficult to standardize.

The location of the thrombi in the pulmonary arterial tree has received some attention as a prognostic factor. Prognosis is worse when the trunk or main pulmonary arteries are occupied by thrombi with either complete or incomplete occlusion[22-25] although this has not been shown consistently in all studies since several of them have been unable to demonstrate an association between image scores and mortality.[26-28]

Although many radiologists consider a pulmonary embolism to be massive when thrombi are visualized in the main pulmonary arteries, the current criterion is the state of the blood pressure, categorizing the patients as normotensive or hypotensive patients, with the latter needing fibrinolysis. However, a number of normotensive patients develop clinical deterioration requiring subsequent thrombolysis. Therefore, this has contributed to the conclusion that size does not matter.[29]

A recent meta-analysis assessing the localization of emboli visualized at CT angiography was useful for the stratification of patients[30] though there was no correlation between the obstruction index and prognosis. Another meta-analysis has concluded that the strongest radiological predictive value for adverse outcome in patients with pulmonary embolism is the right to left ventricular ratio measured on CT.[31]

However, the analysis of the adverse outcomes using as predictive tools the CT angiography and echocardiography both have been estimated at short-term [i.e., in-hospital and 30-days mortality or intensive care unit (ICU) admission].

To our knowledge, there are no studies approaching the long-term prognosis of pulmonary embolism affecting the main pulmonary arteries. Therefore, our aim was to study the prognostic significance of pulmonary embolism affecting pulmonary arteries of different sizes and to check the survival in the long term differentiating central pulmonary embolism and peripheral pulmonary embolism.

Patients and Methods

In the period 2004-2013, all consecutive outpatients hospitalized in the Internal Medicine Service Department with a diagnosis of acute symptomatic hemodynamically stable pulmonary embolism, diagnosed by helical chest CT, and were evaluated within 24 h of admission. This study was approved by the local ethics committee. Because the study was observational and did not interfere with diagnostic or therapeutic work-ups, informed consents were not obtained. Each patient approved and signed the informed consent for radiologic contrast administration.

Study design and methods

Systematically, we recorded on admission the blood pressure, shock index (the ratio of heart rate to systolic blood pressure), heart and respiratory rates, blood gases value before supplementary oxygen administration, electrocardiographic recording, days of symptoms up to diagnosis, and calculated alveolar-arterial difference of oxygen. Alveolar-arterial oxygen gradient was calculated as:

$$FiO2\,(Pb\text{-}47)\_PACO2/R\_F1O2/R\,(1\text{-}R)\,(PaCO2/R)\_PaO2$$

where FIO2 is the O_2 inspiratory fraction, Pb is the barometric pressure, and $PACO_2$ is alveolar CO_2 pressure, $PaCO_2$ is arterial CO_2 pressure, assumed to be equal to PCO_2, and PaO_2 is arterial oxygen pressure. R is the respiratory exchange ratio, set to be 0.8.

Single-slice helical CT was used for diagnosis in 23% of the patients and multidetector scanner of 64 rows was used for diagnosis in the rest; both were general electric devices (Medical Systems, Milwaukee, WI, USA). One mm slices and standard sequential acquisition were obtained in every patient. Breath-hold acquisition was employed. After the intravenous injection of contrast material, the scanning area comprised the chest and upper abdomen, acquiring images in the craniocaudal direction. Central PE was diagnosed when thrombi were visualized in the main trunk of the pulmonary artery and/or in the right or left main pulmonary arteries. Peripheral PE was diagnosed when thrombi were seen exclusively in segmental or subsegmental pulmonary arteries. Each scan was read by a radiologist as in usual clinical practice. Radiologists were blinded to the clinical, laboratory outcomes and survival. Subsequently, the scans were also reviewed by investigators belonging to the Internal Medicine Service Department.

Thrombotic burden was calculated with the formula for the CT obstruction index[32] applied to the initial CT angiography, which was diagnostic of pulmonary

embolism. Each lung is considered to have 10 arteries, 3 in the upper lobe, 2 in the middle lobe and *lingula*, and 5 in the lower lobe. The presence of embolus in a segmental artery was scored as 1 point, and emboli in the most proximal arterial level was scored as the value equal to the number of segmental arteries arising distally. A weight factor was assigned depending on the degree of vascular obstruction: 1 point when the thrombus was partially occlusive, and 2 points with total occlusion. Therefore, maximal CT obstruction index was 40 points. The percentage of vascular pulmonary obstruction was calculated as follows: $n \cdot d/40 \times 100$ where n is the value of the proximal thrombus in the pulmonary arterial tree equal to the number of segmental branches arising distally and d is the degree of obstruction.

The degree of pulmonary obstruction was calculated by the clinicians who were taking care of the patients and they were authors belonging to the Internal Medicine Department. We scored 2 points for the artery where the irrigated territory of a pulmonary infarction was seen and when contrast was not observed distal to the thrombus. The rest of the cases were scored 1 point.

In every patient, blood was drawn within 24 h of admission for pro-BNP and troponin I determination. Plasma D-dimer levels were measured previously in the emergency ward. Echocardiography was not routinely performed.

The coexistence of deep venous thrombosis was diagnosed when lower limb swelling was present and confirmed with venous Doppler ultrasound.

Standard therapy consisted of enoxaparin 1 mg/kg twice a day for 3-5 days, initiation of oral anticoagulants (coumarone) on the first day of hospitalization, overlap of enoxaparin and oral anticoagulants for a minimum of 3 days, and cessation of enoxaparin when international normalized ratio (INR) was greater than 2. During hospitalization fibrinolysis was subsequently indicated in three patients due to hemodynamic instability. After treatment with enoxaparin, secondary prophylaxis was made with direct action anticoagulants in seven patients: Apixaban-two patients, rivaroxaban-4 patients, and dabigatran-1 patient.

Death rate was defined as deaths by all causes during hospitalization and those occurring at follow-up. The cause of death by recurrent pulmonary embolism was considered when new thrombotic material in the pulmonary arterial tree was demonstrated either with angiography CT or lung scan and also when the patient had a sudden death with dyspnea.

Cardiovascular death included patients who died because of myocardial infarction, heart failure, or reported ventricular dysrrhytmias. Death by all causes was considered in the mortality rate. When the death occurred in the hospital, the cause was adjudicated by one of the researches involved in the study or taken from clinical reports by primary care physicians and death certificates.

Statistical analysis

All continuous variables were tested for normal distribution with the Kolmogorov-Smirnov test. Continuous variables are expressed as median and interquartile range (IQR) for variables without normal distribution and as mean ± standard deviation (SD) for variable with Gaussian distribution.

Comparison of the two means was performed with the *t*-test for normally distributed variables and with the Mann–Whitney *U* test for non-Gaussian variables. Fisher's exact test and χ^2 test were used for proportional comparisons.

Survival analysis was made by using the Mantel–Haenszel test. We tested survival at several times after the index episode in order to see the short-, mid-, and long-term survivals.

The independence of significant variables obtained from bivariant statistical analysis for central pulmonary embolism was tested with logistic regression by means of a step-by-step process, eliminating those variables without a level of significance <.05 up to reach of the last useful model. We used standardized coefficient due to the wide variability in measurement units.

All statistical tests were two-tailed, and a $P < 0.05$ was considered to be statistically significant. P values greater than 0.05 were considered to be nonsignificant.

Results

In the period from January 2004 to December 2013, 530 consecutively hospitalized patients because of acute pulmonary embolism were analyzed. Patients were traced during a total time period of 12 years.

The median time of follow-up was 34 (IQR 52) months. The median age was 76 (IQR 16) years, and 45% were male. Demographic and baseline data are depicted in Table 1.

Central pulmonary embolism was diagnosed in 255 (48.5%) patients and segmental or subsegmental (peripheral) thromboembolism in 275 (51.5%) patients. The median age of central pulmonary embolism was 78 (IQR: 13) years while the median age of

peripheral pulmonary embolism was 74 (IQR: 18) years (*P* < .001). The concordance between the readings of CT angiography by the radiologist and internist doctors was kappa 0.87.

Fifty-nine (23%) patients with central pulmonary embolism and 56 (20%) patients with peripheral pulmonary embolism had previous cardiac disease (*P* = .43). Twenty-five (10%) patients had central pulmonary embolism and 39 (14%) patients had chronic respiratory disease (*P* = .11).

Patients with central pulmonary embolism showed a smaller proportion of clinical deep venous thrombosis (28% versus 37% *P* < .05 CI 95% 0.019-0.17), higher burden of pulmonary thrombi and higher plasma levels of N-terminal of the prohormone brain natriuretic peptide (NT-ProBNP), troponin I, D-dimer, alveolar to arterial gradient of oxygen, shock index, and respiratory rate (*P* < .001 in each one of the above) while they showed lower arterial partial pressure of oxygen (*P* < .001), lower arterial partial pressure of carbon dioxide (*P* < .001), and systolic blood pressure (*P* < .05) than patients with peripheral pulmonary embolism [Table 1].

Bleeding occurred in 21 (4%) patients, brain hemorrhage in 10 patients (central pulmonary embolism in 6 and peripheral pulmonary embolism in 4 patients, *P* = .53), gastrointestinal hemorrhage in 6 patients (central pulmonary embolism in 1 patient and peripheral pulmonary embolism in 5 patients, *P* = .21), and one retroperitoneal hemorrhage, one muscle hemorrhage, and one hematuria requiring blood transfusion in central pulmonary embolism, and two hematurias in peripheral pulmonary embolism.

Continuous anticoagulant therapy was indicated in 217 (41%) patients with central pulmonary embolism and in 110 (43%) patients with peripheral pulmonary embolism (*P* = .32).

During follow-up, 102 (40%) patients with central pulmonary embolism at the index episode died while 74 (27%) patients who had a segmental or subsegmental pulmonary embolism died (*P* < .01 CI 95% 0.04-0.21); odds ratio was 1.81 (CI 95% 1.16–1.9).

The median time up to death of patients who had central pulmonary embolism was 19.5 (IQR 52) months after the episode of pulmonary embolism. The median time

Table 1: Demographic, baseline characteristics, and differential characteristics between central and peripheral pulmonary embolism

	All patients	Central PE*	Peripheral PE	*P*
Number of patients	530	255 (48.5%)	275 51.5%)	
Age (years)	76 (IQR‡ 16)	78 (IQR 13)	74 (IQR 18)	<.001
Gender male	238 (45%)	103 (43%)	134 (52%)	.057
Unprovoked pulmonary embolism	195 (37%)	92 (37%)	103 (37%)	0.92
Previous cancer	65 (12%)	38 (15%)	27 (10%)	0.08
Previous venous thromboembolism	90 (17%)	43 (16%)	47 (18%)	0.54
DVT* clinically evident	175 (33%)	71 (28%)	102 (37%	<.05
Death	176 (33%)	102 (40%)	74 (27%)	<.01
Calculated thrombi burden %	32.5 (IQR 27.5)	48.13±11.77	28.45±12.07	<.001
NT-ProBNP¥ ng/mL	866 (IQR 2971)	2496 (IQR 4581)	311.6 (IQR)1112	<.001
Troponin I ng/mL	0.04 (IQR 0,11)	0.07 (IQR 0.14)	0.02 (IQR) 0.05	<.001
D-dimer ng/mL	3841 (IQR 5354)	4462 (IQR 1124)	3508 (IQR 4450)	<.001
Days up to initial therapy	5 (IQR 8)	5 (IQR 11)	5 (IQR) 8	0.84
Months of anticoagulation	11 (IQR 20)	12 (IQR 25)	10 (IQR) 14	<.05
PaO$_2$ mmHg	60 (IQR 16)	58 (IQR 17)	63 (IQR) 25	<.001
PaCO$_2$ mmHg	35 (IQR 8)	33.2 (IQR 6)	36 (IQR)7	<.001
AaO$_2$ mmHg†	43.75 (IQR 18.2)	47.63 (IQR 18)	39.75 (IQR 17)	<.001
SBP# mmHg	129 (IQR 26)	126 (IQR 30)	130 (IQR 24)	<.05
Heart rate	86 (IQR 25)	89 (IQR 12)	83 (IQR 25)	<.05
Shock index	0.66 (IQR 0.25)	0.7 (IQR 0.30)	0.65 (IQR 0.24)	<.001
Respiratory rate	22 (IQR12)	24 (IQR 10)	20 (IQR 8)	<.001
% INR§ of prothrombin >2	75 (IQR 29)	75 (IQR 24)	75 (IQR 30)	0.44
Bleeding	21 (4%)	10 (4%)	11 (4%)	0.96
Cava filter	12 (2%)	6 (2%)	6 (2%)	0.91

*PE = Pulmonary embolism, *DVT = Deep venous thrombosis, †AaO$_2$ = Alveolar to arterial difference of oxygen, ‡IQR = Interquartile range, §INR = International normalized ratio, #SBP = Systolic blood pressure, ¥NT-ProBNP = N-terminal of the prohormone brain natriuretic peptide

up to death in patients with segmental or subsegmental pulmonary embolism was 11.62 (IQR 31.9) months (*P* = .14). We show in Table 2 mortality at different times from the initial episode.

The analysis of survival curves showed a longer survival in patients with segmental and subsegmental pulmonary thrombi than in patients with central pulmonary thrombi at 10 months (*P* = .03), 26 months (*P* = .03), and 96 months (*P* = .0005). When we adjusted the survival curves for patients without previous cardiac and respiratory diseases and cancer, we observed that the survival continued to be better in segmental or subsegmental pulmonary embolism than in central pulmonary embolism (*P* = .018) [Figure 1].

The thrombi burden of dead patients was 33.75% (IQR: 25) while the thrombi burden of survivors was 30% (IQR: 32.25) (*P* < .001).

Fifty-four patients died while they were on anticoagulant therapy, 34 (33%) belonging to the group of central pulmonary embolism and 21 (28%) belonging to the group of peripheral pulmonary embolism (*P* = .48). In 40 (39%) patients with central pulmonary embolism who died, anticoagulation had been withdrawn 7 ± 5 months after the initial episode and in 31 (42%) patients

Table 2: Mortality at different times in patients with central or peripheral pulmonary embolism

Time	Overall (%)	Central PE[†] (%)	Peripheral PE (%)	*P*
15 days	19 (3.5)	14 (5)	5 (2)	=.025
30 days	28 (5)	16 (6)	12 (4)	=0.30
3 months	50 (9.5)	31 (12)	19 (7)	=.03
2 years	105 (20)	61 (24)	44 (16)	=.02
3 years	120 (23)	67 (26)	53 (19)	=.05
5 years	143 (27)	82 (32)	61 (22)	=.009

[†]PE = Pulmonary embolism

Figure 1: The curves of survival shown have been adjusted for confounders: Patients with cardiac, respiratory disease, or cancer have not been included in the analysis

with peripheral pulmonary embolism (*P* = .72 and *P* = .21 respectively). Table 3 shows the causes of death, globally and separated by groups of central or peripheral pulmonary embolism.

At the follow-up, patients dead because of a recurrent pulmonary embolism were 18 (7%) belonging to the group of central pulmonary embolism and 9 (3%) belonging to the group of peripheral pulmonary embolism (*P* < .05 CI 95% 0.003–0.07).

When the initial episode was a central pulmonary embolism, the patients died because of a recurrent pulmonary embolism at a median time of 0.28 (IQR: 13) months while patients who had had peripheral pulmonary embolism died because of a recurrent pulmonary embolism 18 (IQR: 46) months later (*P* = .12).

Deaths caused by recurrent pulmonary embolism occurred in 12 (40%) patients with permanent anticoagulation, which had a median value of prothrombin in therapeutic range of between 2 and 3 of 61.5%, and in 15 (60%) patients in whom anticoagulation was withdrawn.
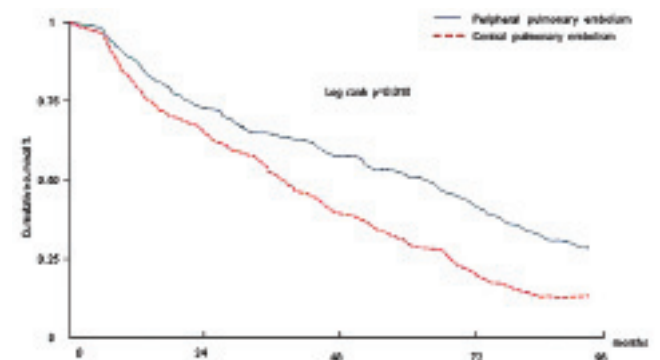
Twenty-nine patients (11%) with central pulmonary embolism and 10 (4%) patients with peripheral pulmonary embolism both at the index episode died because of different cancers (*P* < .001 CI 95% 0.02–0.12). Deaths by cancer in patients with central pulmonary embolism occurred 19 (IQR: 40) months after the initial episode and 6.6 (IQR: 33) months after the initial episode in those patients with peripheral pulmonary embolism (*P* nonsignificant).

In Table 4, we show the results of logistic regression analysis. Independent variables predicting death were the age of the patient at the index episode (OR 2.89 CI 95% 1.04-1.10), the development of cancer during the follow-up of the patient (OR 1.48 CI 95% 1.64-7.71), the central thrombi at the index episode (OR 1.31 CI 95% 1.007-3), and the plasma level of NT-ProBNP measured at the index episode (OR 1.61 CI 95% 1.0001-1.0002). Respiratory rate at the index episode was not an independent predictive variable of death.

Discussion

Although the localization of pulmonary emboli within the pulmonary arterial tree is not currently considered a matter of severity, there are several studies supporting the fact that the closer to the right ventricle the pulmonary emboli are, the earlier and higher the sort-term mortality is[24] while emboli affecting small pulmonary arteries carry a better prognosis. However,

Table 3: Causes of death classified by central or segmental and subsegmental (peripheral) pulmonary embolisms

	All patients (%)	Central PE* (%)	Peripheral PE (%)	P
Pulmonary embolism	27 (15)	18 (7)	9 (3)	<.05
Cancer	39 (22)	29 (11)	10 (4)	<.001
Cardiovascular death	32 (18)	18 (7)	14 (5)	.34
Bleeding	9 (5)	8 (3)	1 (0.4)	<.05*
Stroke	3 (2)	2 (1)	1 (0.4)	.61*
Pneumonia	28 (16)	17 (7)	11 (4)	.17
Sepsis	11 (6)	2 (1)	9 (9)	.06*
COPD†	7 (5)	1 (0.4)	6 (2)	.12*
IPD‡	3 (2)	0 (0)	3 (1)	.24*
Other causes	6 (3)	1 (0.4)	5 (2)	.21*
Unknown	11 (6)	6 (2)	5 (2)	.76*

*Two-tail Fisher's test, †COPD = Chronic obstructive pulmonary disease, ‡IPD = Interstitial pulmonary disease, *PE = Pulmonary embolism

Table 4: Logistic regression of variables predicting death

	β	P	Odds ratio	CI 95%
Age	1.06	.00001	2.89	1.04-1.10
Cancer diagnosed during follow-up	0.39	.001	1.48	1.64-7.71
Central thrombi	0.27	.04	1.31	1.007-3
NT-ProBNP†	0.48	.002	1.61	1.001-1.002
Respiratory rate	0.22	.09	1.23	0.99-1.07

†NT-ProBNP = N-terminal of the prohormone brain natriuretic peptide

not all studies have shown a direct relationship between the size of the occluded vessel and mortality, with several investigations including a moderate number of patients[26-28] unable to show a correlation between image and prognosis.

In the same way, the arterial obstruction index has shown to be useful in several investigations in order to predict right ventricular dysfunction and death although in a recent meta-analysis, despite the localization of pulmonary emboli assessed by CT angiography show usefulness for risk stratification, the obstruction index did not show a relation with prognosis.[30]

In our patients, the central localization of emboli with respect to segmental or subsegmental emboli was associated with more stress of the right ventricle measured with higher plasma levels of NT-ProBNP and troponin I and a more intense disorder in gas exchange and hemodynamic status.

The clot burden was also higher in central pulmonary embolism than in segmental and subsegmental pulmonary embolisms. However, this fact seems derived from the characteristic of the equation for calculating the clot burden since it could not demonstrate whether it is an independent factor in the prediction of death.

Patients with segmental and subsegmental pulmonary embolisms had more clinically overt signs of deep venous thrombosis than patients with central pulmonary embolism. This fact could be explained by migration of thrombi from the lower limbs to the pulmonary circulation in patients with central pulmonary embolism showing a higher thrombi burden. A defective fibrinolytic system joined to a higher degree of hypoxemia and activation of inflammatory pathways could also interact, favoring the greater size of emboli although in our patients a higher plasma level of D-dimer goes against quantitative defects in fibrinolysis.

On the other hand, our patients were mostly the elderly and the age of patients with central pulmonary embolism was higher than the age of patients with segmental and subsegmental pulmonary embolisms. In this way, defective fibrinolysis and endothelial function have been showed in the elderly, and so all these factors could contribute to the higher size of emboli,[33] which would cause the lodging of thrombi in the proximal pulmonary arteries.

In our study, patients with central lodged thrombi showed a higher overall mortality than patients with more peripheral pulmonary embolism, with more mortality rate specifically due to subsequent pulmonary embolism, cancer, and bleeding. However, neither the time of anticoagulant therapy of patients with central and more peripheral pulmonary embolism nor the proportion of patients dead while they were under anticoagulant therapy were different enough to explain the higher mortality of central pulmonary embolism. The number of patients with direct-action anticoagulants was too small to analyze and to draw valid conclusions.

Survival in patients with central pulmonary embolism was significantly lower than in patients with segmental or subsegmental thrombi. Subanalysis at different

times from the initial episode also demonstrated an increased mortality for central pulmonary embolism at short- (i.e. ,10 months), mid- (i.e., 26 months), and long terms (i.e., 96 months).

In our patients, the in-hospital mortality rate measured at 15 days and 30 days was lower than the mortality reported in the literature, which has been estimated to range 9-11% at 30 days and 8.6-17% at 3 months.[34-37] The high long-term mortality in our study (33%) may be explained in part by the advanced age of our patients.

Variables such as gas exchange data, hemodynamic values, the plasma level of troponin I, clot burden, and absence of overt signs of deep venous thrombosis disappeared from the model of logistic regression on losing significance.

In the final model, independent variables predicting death were the age of the patient and plasma level of NT-ProBNP, both measured at the index episode, and the development of cancer during the follow-up of the patients while the segmental or subsegmental pulmonary embolism was a protective factor. In the final model, the respiratory rate remained although it did not show any significance.

However, our study had several limitations. The patients were taken from a single center; therefore, our results should be tested in other studies or in meta-analysis. Although radiologists who interpreted the CT angiography were blinded for the study, different assessments of the localization of thrombi made by them could have been due to the fact that the radiologists on duty were not always specialized in thorax radiology. Thereafter, the review of the scans for the authors belonging to Internal Medicine Department produced a high level of concordance, playing down the potential bias. Another limitation of our study was that the death of a number of patients occurred because of unknown causes although the number was similar in both groups, minimizing the impact over the other causes of death.

Another potential limitation of our study could be due to an overestimation of deaths caused by recurrent pulmonary embolism since sudden deaths were included as recurrent pulmonary embolism and they might have occurred by other causes such as ventricular arrhythmia.

Patients of this study were mostly hemodynamically stable with a few patients needing subsequent fibrinolysis. Thereafter, our results cannot be extrapolated to patients with hemodynamic instability but only to patients who meet the criteria for submassive or nonmassive pulmonary embolism.

A potential strength of our study is the fact that it was conducted in a relatively closed community. This fact has allowed a close follow-up of the patients with no patient being lost.

Conclusions

Patients with hemodynamically stable acute pulmonary embolism, which show thrombi lodged in the main pulmonary arteries have a higher overall mortality and lower survival than patients with segmental or subsegmental pulmonary embolism.

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Conflicts of interest

There are no conflicts of interest.

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