

Evaluation of the Short, Medium and Long-term Prognosis of Pulmonary Embolism

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Received date: April 13, 2018; Accepted date: November 02, 2018; Published date: November 09, 2018

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Abstract

Introduction: Pulmonary Embolism (PE) is the most severe form of venous thromboembolic disease. This is a serious condition not only because of its mortality but also its sequelae.

Methodology: The aim of this study is to evaluate the prognosis of patients who had an episode of PE, hospitalized in the cardiology department of the Aristide Le Dantec University Hospital in Dakar. We performed a cohort study that included all patients admitted for pulmonary embolism during the period of May 1, 2011 to February 29, 2016. Subjects were contacted for a re-evaluation during the period of August 1st to September 1st 2016. We evaluated the status of patients (death or alive), to look for signs of chronic pulmonary heart based on the electrocardiogram (right atrial and ventricular hypertrophies, aspect S1S2S3, right bundle branch) and especially on the echocardiogram (right cavitory and parietal dimensions, measurement of the PASP).

Results: A total of 77 pulmonary embolism cases were counted during the study period; 70 files were retained. It was a predominantly female population, with an average age of 51.2. Low risk forms (PESI I-II) accounted for 85.7% of the sample, versus 14.3% of PESI III-IV-V forms. At the re-evaluation, we counted 18 deaths (25.7%); twenty-two patients were lost to follow up. No recurrence was noted since hospitalization. Two patients had bilateral, non-inflammatory edema. Dyspnea was found in 3 patients. No patient had any sign of right heart failure. Doppler echocardiography showed dilatation of the right ventricle along parasternal long axis in 6 cases and along apical section in 5 cases respectively. Right ventricular wall hypertrophy was noted in 6 patients. The systolic function of the right ventricle was normal in all cases. The right atrium was dilated in 5 cases. Pulmonary hypertension and increased pulmonary vascular resistance were noted in 7 cases, respectively. The overall mortality factors were acute circular insufficiency, right ventricular systolic dysfunction, PESI score of at least 1, tachycardia, PASP value greater than 50 mmHg, right heart failure and dilatation of the right atrium.

Conclusion: Wall dilatation and hypertrophy of the right ventricle as well as pulmonary hypertension are frequent sequelae. The parameters of the hemodynamic impact of pulmonary embolism constitute the main prognostic factors.

Keywords: Pulmonary embolism; Mortality; Chronic pulmonary heart

Abbreviations: COPD: Chronic Obstructive Pulmonary Disease; PHT: Pulmonary Hypertension; LV: Left Ventricle; OTPE: Outpatient Treatment of Pulmonary Embolism; PASP: Pulmonary Artery Systolic Pressure; PE: Pulmonary Embolism; PESI: Pulmonary Embolism Severity Index; PVR: Pulmonary Vascular Resistances; RA: Right Atrium; RV: Right Ventricle; Sa T: Speed of the Systolic Wave to the Tricuspid Ring in Tissue Doppler; TAPSE: Tricuspid Annular Plane Systolic Excursion.

Introduction

Pulmonary Embolism (PE) is the most severe form of venous thromboembolism, and the third most common cardiovascular disease

worldwide [1]. It is responsible for 1-2% of hospitalizations in Cardiology in our region [2,3]. The diagnosis is sometimes difficult and the etiologies multiple. Prognosis remains poor despite advances in diagnosis and treatment. The associated usual co-morbidities aggravate the picture. Prognosis assessment is essential for management. PESI score is currently the most appropriate tool for assessing the risk of death within 30 days [1]. The international randomized study "Outpatient Treatment of Pulmonary Embolism" (OTPE) demonstrated in 2011 the possibility of outpatient and safe management of patients at low risk of early death; accounting for 30-50% of cases [4,5]. The treatment lasts at least 03 months and can be maintained for life. The resorption of the clot is expected from the third week in the majority of patients under effective treatment [6]. In the event of adverse progression, deaths occurs most often in a context of cardiogenic shock, or recurrence or post-embolic chronic obstructive pulmonary disease (COPD). Pulmonary embolism is

associated to an intra-hospital mortality of 7.9% and 12% in the year following the acute episode when there are signs of acute pulmonary heart disease [7]. The risk of death is increased by three times when pulmonary hypertension is greater than 50 mmHg and by five times when the age is greater than 70 years [6]. Acute pulmonary heart signs regress completely within 2 months of effective treatment. The progression to postembolic disease remains underestimated with a large divergence of current data [8]. Our work was aimed at assessing the prognosis of patients who had had an episode of PE, hospitalized in our department. The specific objectives were to evaluate the incidence of chronic pulmonary disease and determine the prognostic factors.

Methodology

We did a cohort study. The inclusion period was from May 1st, 2011 to February 29th, 2016. The re-evaluation period was August 1st to September 1st, 2016.

We used the files of patients admitted for pulmonary embolism during the defined period. They were contacted by telephone and informed of the study; then called for reassessment after a free and informed consent.

The inclusion criteria were: patients of all ages and sex, admitted to the department for pulmonary embolism proven by thoracic angio-CT. Patients with pre-existing left cardiopathy, those with high suspicion of PE unconfirmed and those who did not consent to participate were not included. The studied parameters were epidemiological (age, gender), clinical (risk factors for venous thromboembolic disease, functional and physical signs of pulmonary embolism), paraclinical data: biological (hemogram, creatinine), electrocardiographic and echocardiographic (signs of acute pulmonary heart), CT scans (topography of pulmonary embolism.) Therapeutic data were also evaluated including fibrinolysis, amines. During the reassessment, we looked for signs of pulmonary heart disease: (recurrence of venous thromboembolism, signs of heart failure, S1S2S3 on the electrocardiogram, right atrial hypertrophy, right ventricular hypertrophy, right bundle block and at Doppler echocardiography (7): RV diameters, RV/LV ratio, systolic and diastolic functions of the right ventricle, diameter of the pulmonary artery and its branches, and pulmonary pressures. The guidelines of American society of echocardiography were considered. The pulmonary vascular resistances were appreciated by the ratio of the maximum speed of tricuspid insufficiency on the integral subpulmonary velocity time. Data entry was done using Sphynx software. The analysis of the data was done using SPSS software version 18. The averages and percentages were compared using the Fischer exact test and the chi-square test according to their applicability conditions. Any difference below 0.05 was considered statistically significant.

Results

During the study period, 77 cases of pulmonary embolism were recorded, a proportion of 1.47% compared to all hospitalizations (5205) during the same period.

70 files out of the 77 were studied. The general characteristics of this population were showed on Table 1.

Trans-thoracic echocardiography showed right ventricular dysfunction in 30% of cases, intracavitary thrombus in 8.6% of cases and pulmonary hypertension in 62.7% of cases. In tomodensitometry,

proximal topography predominated (70% of cases) and bilateral involvement accounted for 78.6% of cases.

Characteristics	Number (n=77)	Percentage (%)
Sex Ratio Men/Women	0.79	-
Mean age (Years)	51.2 ± 15.2 (23 to 83)	-
Obesity	17	22
Long-duration bed rest	14	18.18
Sickle cell trait)	10	13
Surgery	8	10.4
Neoplasia	8	10.4
Dyspnea	63	81.4
Chest pain	51	65.7
Tachycardia	54	70
Right heart failure	30	38.6
Deep vein thrombosis	18	22.8
Increase in serum creatinine	10	-
Anteroseptal subepicardial ischemia	37	48.6
Right ventricular hypertrophy	20	25.7
S1Q3T3 aspect	40	51.4
Cardiac arrest with successful resuscitation	1	1

Table 1: General characteristics of the study population.

The low-risk forms of PESI I-II accounted for 85.7% of the sample, versus 14.3% of moderate-to-high risk PESI III-IV-V forms. In the therapeutic management, fibrinolysis was used in 9 patients. Dobutamine was administered to 4 patients. Acenocumarol was prescribed to 93.3% of patients. A patient with antivitamin K resistance was put on oral anti-XA. The average hospital stay was 12.1 ± 5.1 days with extremes of 2 and 26 days.

Patient assessment showed the following results: We counted 18 deaths or 25.7% of the total sample. In addition, 22 patients were lost from view. These were mainly patients living in the Sub-region. In total, 30 patients had been reassessed. Data collected were as follows: The duration of the anticoagulant treatment was between 3 and 12 months, except for 6 patients (20%). Of these, 4 had at least one previous episode of venous thromboembolic disease. No recurrence was noted during the study. 2 patients had bilateral, non-inflammatory edema. 3 patients presented a dyspnea. No patient showed signs of right heart failure.

On electrocardiogram, right atrial hypertrophy was the most common sign (5 cases), followed by right axial deviation and S1S2S3.

On echocardiography, the results obtained were as follows: the RV/LV ratio averaged 0.91 with extremes of 0.71-1.12. Five patients had an increased ratio. The average diameter of right ventricle in parasternal long axis view was 24.7 mm with extremes of 17 mm and

31 mm. It was increased in 6 patients. The median average diameter of 4 cavities was 30.8 mm with extremes of 19 mm and 42 mm. It was increased in 5 patients. The length of the RV in longitudinal 4 cavities was on average 65.4 mm with extremes of 53 mm and 89 mm. It was increased in 1 patient. Average thickness was 5.1 mm with extremes of 3.7 and 11 mm. Wall hypertrophy was noted in 6 patients (20%).

The SaT and Tricuspid annular plane systolic excursion (TAPSE) indices were normal in all patients with respective averages of 15.6 cm/s and 22 mm. The average value of PASP was 30 mmHg (15 mmHg to 49 mmHg). A PASP greater than 35 mmHg was noted in 7 cases (23.3%). Pulmonary vascular resistances (PVR) were high in 7 patients (23.3%). Average value was 0.17. The trunk of the PA was measured on average at 24 mm and extremes of 16 mm and 34 mm. It was dilated in 2 patients (6.7%). The left branch was dilated in 9 out of 30 patients (30%) and the right limb in 6 patients (20%). The right atrium (RA) was dilated in 5 patients, or 16.7% of cases. Table 2 illustrated summary of echocardiographic abnormalities.

In univariate analysis RV dilation (long-axis parasternal dimension) was significantly associated with circulatory insufficiency at admission (p=0.001), intravascular thrombus (p=0.03), and dilation of the inferior vena cava (p=0.003). The increase of median diameter in four apical cavity sections was associated with acute circulatory insufficiency (p=0.001), S1Q3T3 appearance (p=0.001), intracavitary thrombus (p=0.001) and RV dysfunction (p=0.004).

With regard to mortality, 18 deaths were recorded, 8 of which were intra-hospital. In 10 cases, death occurred, after the discharge from the hospital, in an average of 9.6 months (03months-17 months). The prognostic factors of death (overall) were acute circular insufficiency, RV systolic dysfunction, PESI score over 1, tachycardia, PASP value

greater than 50 mmHg, right heart failure, and dilation of the right atrium. The extra-hospital death factors were pre-existing chronic pulmonary heart and the right leg block. Table 3 summarizes the prognostic factors.

Echocardiographic parameters	Baseline N (%)	At reevaluation N (%)
Left atrial enlargement	33 (47)	5 (16.7)
Increased of Right ventricle in long-axis parasternal view	46 (65.7)	6 (20)
Ratio RV/LV>1	-	5 (16.7)
Increased median diameter of the right ventricle	-	5 (16.7)
Increased longitudinal diameter of the right ventricle	-	1 (3.3)
Right ventricle hypertrophy	-	8 (26.7)
Right ventricle systolic dysfunction	21 (30)	0
Main pulmonary artery dilation	-	2 (6.7)
Pulmonary pressures		
High PASP	42 (62.7)	7 (23.3)
High pulmonary vascular resistances	-	7 (23.3)

Table 2: Summary of echocardiographic abnormalities (RV: Right ventricle; LV: Left ventricle; PASP: Pulmonary artery systolic pressure).

Prognostic factors	Death N=18 (%)	Survivor N=52 (%)	p value
Right ventricle systolic dysfunction	11 (61)	11 (21)	0.002
PESI ≥ 1 score	14 (77)	25 (48)	0.029
Acute circulatory insufficiency	8 (44)	0 (0)	0.0001
Tachycardia	16 (88)	33 (63)	0.042
Right heart failure	13 (72)	14	0.001
PASP>50 mm Hg	12	19 (27)	0.02
Fibrinolysis	6 (33)	3 (5.7)	0.03
Pre-existing chronic pulmonary heart	7 (38)	8 (15)	0.036

Table 3: Prognostic factors of deaths.

Discussion

The severity of pulmonary embolism is related to the risk of early death in relation to the immediate hemodynamic repercussions of vascular obstruction and the neuro-hormonal reaction, but also to sequelae, namely the chronic pulmonary heart disease. These are related to the organization of the intra-arterial thrombus associated with fibrous stenosis or complete arterial obliteration. The incidence of post-embolic chronic pulmonary heart is very variable in the literature between 0.1%-8.8% [9-12]. The attack is often asymptomatic at first,

leading to a late diagnosis and explaining the undervaluation of this condition in previous studies.

Korkmaz et al. [13] emphasized the need for close follow-up of patients after an episode of pulmonary embolism. They reported a residual intra-luminal thrombus frequency of 48%, 27.4% and 18.2%, respectively, at 3, 6 and 12 months, and a post-embolic pulmonary heart incidence of 4.6% [13]. Klok and Co. tried to identify post-embolic pulmonary heart risk factors in a cohort of 772 patients followed for pulmonary embolism. After a follow-up of one and a half years, the incidence of cor pulmonale was 2.8%. Factors significantly

associated with this complication were idiopathic pulmonary embolism, hypothyroidism, onset of symptoms greater than two weeks (at the time of diagnosis), diabetes, fibrinolytic therapy, or embolectomy [14]. In this series the overall mortality factors were acute circular insufficiency, right ventricular systolic dysfunction, PESI score over 1, tachycardia, PASP value greater than 50 mmHg, right heart failure, and dilatation of the right atrium. At admission, 30% of our patients had a RV dysfunction. After reassessment, the systolic function of RV was normalized in all our patients on the basis of TAPSE and SaT parameters. In his work, Ribeiro [6] noted 64% of RV dysfunction at diagnosis. The reassessment at 1 year, then at 5 years, revealed a persistence of this dysfunction in 5.3% of cases. Normalization of ventricular function occurred in 96% of cases by day 8 and in 3% of cases between day 8 and day 30. There was no change in ventricular function beyond.

Factors associated with the persistence of pulmonary hypertension (PH) were chest pain ($p=0.025$) and hypercreatininemia ($p=0.009$). Those associated with high vascular resistance were prolonged bed rest ($p=0.016$) and concomitant deep venous thrombosis ($p=0.029$). In the literature [6] PASP greater than 50mmHg, age greater than 70 years, and congestive heart failure had been shown to be independent prognostic factors that increased the risk of persistent RV dysfunction by 3-fold and HTP at 5 years [6]. In addition, Riedel [9] found that recurrent PE and those with PASP greater than or equal to 30 mmHg were associated with a worse prognosis. In his series, 7% of patients had relapsed in the year.

We noted 8 in-hospital deaths, or 11.4% (8/70), including 7 patients who had pulmonary embolism with a high risk of early death. The average time was 8 days (2 to 17 days). Others authors reported similar intra-hospital mortality (13%) mainly between days 1 and 3 [15]. And another study [16] reported 10.5% intra-hospital mortality associated primarily with age and hemodynamic instability coupled with RV dysfunction. Combining the 04 series results, Allard [17] determined that the short-term mortality in patients with RV dysfunction at echocardiography was 9.3% versus 0.4% in patients whose echocardiograms were normal.

We had 14.3% of extra-hospital deaths. Prognostic factors were preexisting chronic lung heart ($p=0.02$) and the existence of a right bundle block ($p=0.017$). According to the literature, chronic respiratory failure, congestive heart failure, and cancer were the underlying conditions correlated with PE mortality [18]. Ribeiro found mortality at 1 year of 15.1%, and 16.4% at 5 years [6]. Kucher [19] reported a 3 months mortality of 52.4% for massive PEs and 14.7% for non-massive PEs. After a multivariate analysis of 1135 patients, Allard [17] observed a double risk of mortality at 3 months in subjects with RV dysfunction. Overall we emphasize for close follow-up of patients after an episode of pulmonary embolism, as it would be the best way to avoid most of these complications.

Conclusion

Pulmonary embolism is a condition whose severity is related to its mortality. That mortality is hospitable but also extra-hospital. The parameters of the hemodynamic impact of pulmonary embolism constitute the main prognostic factors. Comorbidities are to be taken into account in the outpatient prognosis. Wall dilatation and hypertrophy of the right ventricle as well as pulmonary hypertension are frequent sequela, contrary to the persistence of systolic dysfunction of the right ventricle.

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