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Contribution of the Dosage of Nt-ProBNP in the Assessment of Pulmonary Embolism Severity in Black African Community

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Abstract

Objective: To determine the role of NT-$_{pro}$BNP in the assessment of the severity of pulmonary embolism.

Patients and methods: The study was performed at Atinkanmey, a private hospital of Cotonou. It is a retrospective, analytical and transversal study, over a period of 3 years (1 January 2009 to 31 December 2011). The study included 35 patients ≤75 years followed for pulmonary embolism with whom the NT-$_{pro}$BNP dosage was performed. NT-proBNP was compared to other severity criteria such as low blood pressure, tachycardia, Pulmonary Embolism Severity Index, the right ventricular trombosis and dilatation of the right cavities associated with PAH.

Results: NT-$_{pro}$BNP is lower than 1000ng /L in 27 patients (77.1%) and higher than 1000ng/L in 8 patients. The sensitivity of NT-$_{pro}$BNP is low compared to severity criteria studied. It varies from 33% to 50%. The specificity is improved and reached 100% when the NT-$_{pro}$BNP is compared to dilation of the right cavities. The best negative predictive value is obtained with low blood pressure (92.6%). The best positive predictive value (PPV) was found by comparing the NT-$_{pro}$BNP to dilatation of the right cavities.

Conclusion: The rise of NT-$_{pro}$BNP is not always associated with the presence of gravity criteria studied. Normality seems more associated with lack of dilation of the right cavities.

Keywords: NT-$_{pro}$BNP; Pulmonary embolism; Gravity

Introduction

Pulmonary embolism is a diagnostic and therapeutic emergency increasingly reported in black Africa's growing prevalence is partly due to better availability of diagnostic means. Rapid assessment of its severity can encode therapeutic attitude. Several European studies have examined the criteria that define a severe pulmonary embolism. The two main determinants of mortality are hemodynamic tolerance and underlying terrain [1]. However, several other parameters such as NT-$_{pro}$BNP (amino-terminal pro-brain natriuretic peptide) troponin I, the severity score pseudo rabies the existence of a thrombus intra cavitary right, right cavitary dilation and PAH (Pulmonary Arterial Hypertension) were also studied. These parameters, only a state of shock or hypotension fall within the definition of a severe pulmonary embolism because associated with higher mortality [2,3]. NT-$_{pro}$BNP is a marker of myocardial distention, is it correlated to different criteria of severity of pulmonary embolism? Literature data does not exist on this topic in Africa.

In this study our goal is to compare the NT$_{pro}$BNP in blood pressure, the severity score of Aujesky and intraluminal of the right thrombosis and echocardiographic parameters of the right cavitary distension.

Materials and Methods

Nature and duration of the study

This is an analytical, transversal and retrospective study over a period of 3 years that is from 1 January 2009 to 31 December 2011.

Study population

It is made by both sexes hospitalized in the Polyclinic of Atinkanmey (a private hospital in Cotonou, cardiology service) during the study period and meeting the conditions below.

Inclusion criteria

Were included

- Patients in whom the diagnosis of pulmonary embolism was detected based on the results of the chest CT.
- These patients should be under the age of 75 (when the age is less than 75 years, NT-$_{pro}$BNP provides better sensitivity and better specificity for a positivity threshold of 900ng/L). [4]

Exclusion criteria

- Were excluded
- Patients older than 75 years
- Patients with congestive heart failure

- Patients with renal impairment
- Patients whose NT-proBNP is not realized at admission

Variables studied

The variables studied were:

- The general characteristics (age, gender).
- The clinical severity score of Aujesky or PESI (Pulmonary Embolism Severity Index) [5].
- Blood pressure and pulse rate values at admission. Hypotension was defined as systolic blood pressure less than 90 mmHg and tachycardia is defined as a heart rate greater than 100 beats per minute.
- Echocardiographic abnormalities: right cavitary dilation or PAH; existence of intraluminal thrombus (because of the retrospective nature of the study, the results of ultrasonography were only available in 26 patients. Because the exams are paid directly by the patient, ultrasound was not systematic when the diagnosis of pulmonary embolism is already confirmed by angio-Computed tomography and then realized when resources of the patient permitted).
- The value of NT-proBNP; the threshold value was set at 1000ng/L. A threshold NPV=100% to eliminate fatal pulmonary embolism [6].
- The sensitivity (Se), specificity (Sp), positive predictive value (PPV) and negative predictive value (NPV) of the NT-proBNP in the diagnosis of severity of pulmonary embolism; the severity factors being compared: the shock, tachycardia, severity score pseudo rabies and abnormal echocardiogram.
- The correlation coefficient between the NT-proBNP and each of these factors.

Statistical Analysis

For normally distributed variables, values are expressed as mean (SD). All statistical analyses were done using statistical analysis software (SPSS version 18.0 software and EPI Info 7.1.4.).

Differences in proportions were compared with a $\chi 2$ test. The relationship between NT-proBNP and other pulmonary embolism severity criteria was investigated by Fisher's exact test and by calculating the sensitivity, specificity, positive predictive value and negative predictive value. The coefficients of correlation between NT-proBNP and criteria were calculated and tested.

Probability values of $p<0.05$ were considered significant.

Results

35 patients were enrolled including 22 women and 13 men (sex ratio 0.59). The average age of patients was 47.1 ± 12.2 years, ranging from 27 to 73 years. Clinical probability of embolism by Wells score was intermediate or high in 94.3% of patients.

27 patients (77.10%) have NT-proBNP lower than 1000ng/L and 8 (22.9%) patients had a proBNP than or equal to 1000ng/L; the average value of NT- proBNP was 772ng/L with extremes of 3 and 8171ng/L.

Regarding the clinical severity of the pulmonary embolism, 28.6% of patients were superior or equal to class III (Table1). No deaths were recorded in the study population.

The sensitivity of NT-proBNP is low regardless of the assessed severity factor; varies from 33 to 50% ; its specificity reached 100% when used to determine the existence of a distended right heart chambers or the existence of PAH ; NPV varies from 36.8 to 92.6% and the PPV is 100 for the diagnosis of PAH (Table 2). The correlation between the NT-proBNP and the other criteria of gravity ranges from -0.113 to 0.267 (Table 3).

	Number	Percentage
class I	14	40.0
class II	11	31.4
class III	7	20.0
class IV	2	5.7
class V	1	2.9
Total	35	100.0

Table 1: distributions of cases of pulmonary embolism according to clinical severity score of Aujesky.

	NT-proBNP						
	< 1000,00	≥ 1000,00	p	Se (%)	Sp (%)	NPV (%)	PPV (%)
Hypotension N=35							
Absent	25	7	0.55	33	78	92.6	12.5
Present	2	1					
Tachycardy N=35							
Absent	17	2	0.105	37.5	89.5	63.0	75
Present	10	6					
Score of Aujesky N=35							
classes I et II	21	4	0.186	40	84	77.8	50

Classes III, IV, V	6	4					
Thrombusis of RV 26							
Absent	16	4	0.293	50	80	84.2	42.9
Present	3	3					
Dilatation of right cavities or PAH N=26							
Absent	7	0	0.133	36.8	100	36.8	100
Present	12	7					
RV= Right Ventricle; PAH=Pulmonary Arterial Hypertension							

Table 2: Relationship between NT–pro BNP and a few evaluation parameters of the severity of the pulmonary embolism.

	NT-proBNP	SBP	pulse	PAH	Thrombosis of RV	Score of Aujesky
NT-proBNP	1	0.113	0.182	0.267	0.049	0.191
P		0.518	0.294	0.187	0.814	0.271
N	35	35	35	26	26	35
SBP= Systolic Blood Pressure; RV= Right Ventricle; PAH=Pulmonary Arterial Hypertension						

Table 3: Correlation coefficient in NT-proBNP and the other severity scores.

Discussion

We conducted a retrospective study. This type of study does not allow a comprehensive collection of information. Thus, echocardiography was performed in only 26 patients out of 35. Besides, the threshold value of NT-proBNP determined to define its positivity is higher and the inclusion criteria excluded other clinical situations in which the elevation of NT–proBNP was observed. These criteria then clarify about the few patients included in the study and thus the lack of power.

However, in the absence of available data that evaluated the interest of the assay of NT-proBNP in pulmonary embolism in black Africa, the results could form the basis for another important prospective study.

Given the results of our study, NT-proBNP is elevated beyond the verge set at 22.9% of patients. This rate is lower than the results reported by Pruszczyk [7]. In his study, 83.5% of patients have a rate of NT-proBNP above the normal range. This difference is linked to lower positivity threshold in this study but also in its study population, massive pulmonary embolism or sub- massive predominate, whereas in our case, patients with high severity score represents only 28.6% of the study population (Table1). Consequently, the proportion of patients with high levels of NT-proBNP is superimposable with the one having a high severity score.

Regarding the relationship between NT-proBNP and the other severity criteria, we did not observe significant differences whatever the factor of interest. NT-proBNP does not seem to specifically identify or discriminate patients with clinically impaired hemodynamic, or the existence of echocardiographic abnormalities (PAH, intra cavitary thrombosis). These statistical tests are related to a lack of sensitivity (Table 2).

The study of the sensitivity, specificity, PPV and NPV of the NT-proBNP compared with different severity factors reveals in all cases a better specificity but poor sensitivity.

The hemodynamic study reveals that the VPN is the highest when the NT-proBNP is compared with the blood pressure (92.6%). This result is similar to that of WOLDE M. who reported that the positive predictive value of a BNP level of greater than 21.7 p mol/L was 17% for the deaths, while its negative predictive value was 99% [8]. Hypotension is the independent risk factor for mortality in pulmonary embolism [9]. In shock, the plasma concentrations of natriuretic peptides are high regardless of etiology [6]; it is a reflection of the myocardial dysfunction during these states of shock. The coefficient of correlation between blood pressure and ProBNP though different from zero is low (-0.113). Blinder reported a higher coefficient (-0.320). In our study, the correlation coefficient of the heart frequency with the rate of NT-proBNP is 0.294 and seam similar to the 0.26 reported by Blinder [6]. Tachycardia is often the first clinical sign announcing the shock, it may warrant a higher correlation to low blood pressure.

Accordingly, hemodynamic instability is the main predictive factor in pulmonary embolism. However, 85% of deaths occur in patients with stable hemodynamic admission [9]. From this, it seems appropriate to identify other criteria to be considered in the stratification of the severity of the EP. The clinical severity score of Aujesky is the one that stratifies patients into 5 classes increasing mortality. Its correlation with the levels of NT-proBNP is 0.191 which is low compared to other studied factors but remains above the intra cavitary thrombosis. This score incorporates in both heart rate and blood pressure and other clinical parameters, comorbidities and age. The inclusion of such dissimilar criteria may explain its low correlation with more specific NT-proBNP myocardial distension.

Definitely, in our study, regarding the detection of the right cavitary stretching, the NT-proBNP showed excellent specificity (100%). Its negativity is so strongly associated with the absence of right cavitary stretching. WOLDE made the same observation. Dilation of the right cavities is truly the only factor with which the NT-proBNP has the best correlation coefficient (0.267). NT-proBNP is also secreted by the right ventricle, distension thereof may explain its secretion and thus raising its plasma; these various results show that the plasma concentrations

of BNP and NT-proBNP correlate with the importance of the right ventricular dysfunction as it has been reported by several authors [7,8,10]. It is considered that greater than 30% obstruction is required for the development of a dilated right ventricle [11,12]. However, the majority of patients with right ventricular dysfunction show no clinical signs of heart disease. Therefore, the current management is based in part on the detection of the right ventricular dysfunction in usually asymptomatic patients. Mortality at 3 months in case of the right ventricular dysfunction is estimated to 21% and is an independent risk factor ICOPER [9,13]. Therefore in our context where access to echocardiography is limited to large cities, the dosage of the NT-proBNP may be a useful alternative for assessing myocardial effect; the blood sample could then be transported to the laboratories hence limiting the risks of moving a potentially precarious ill; the financial cost of ultrasound can be overcome.

Conclusion

NT-proBNP is a symbol showing the myocardial injury in pulmonary embolism. Its elevation of NT-proBNP is somewhat correlated with the presence of conventional gravity criteria while normality appears correlated with the absence of dilation of the right cavities. This dosage may be in our context an interesting alternative for assessing myocardial repercussion when access to ultrasound is limited. However, due to lack of some valid elements in this study, it is important to carry out a large prospective one on the role of NT-proBNP in pulmonary embolism in black African environment.

References

1. Meyer G, Sanchez O (2006) Risk stratification in acute pulmonary embolism. Cardiological realities pp: 219.
2. Planquette B, Belmont L, Meyer G , Sanchez O (2011) Getting diagnosis and treatment of severe pulmonary embolism. Journal of Respiratory Diseases 28: 778-789.
3. Sanchez O, Planquette B, Roux A, Gosset- WoimantM, Meyer G (2011) Prognostic Factors of pulmonary embolism. Resuscitation; March, Volume 20: 112-117.
4. Peynet J, Dehoux M, Lefèvre G, Philip I (2011) Cardiac dysfunction markers. In: Beaudeux JL, Durand G (eds) Medical Biochemistry current markers and perspectives. Paris: Lavoisier pp: 183-210.
5. Aujesky D, Obrosky DS, Stone RA, Auble TE, Perrier A, et al. (2005) Derivation and validation of a prognostic model for pulmonary embolism. Am J Respir Crit Care Med 172: 1041-1046.
6. Binder L, Pieske B, Olschewski M, Geibel A, Klostermann B, et al. (2005) N-terminal pro-brain natriuretic peptide or troponin testing followed by echocardiography for risk stratification of acute pulmonary embolism. Circulation 112: 1573-1579.
7. Pruszczyk P, Kostrubiec M, Bochowicz A, StyczyÅ„ski G, Szulc M, et al. (2003) N-terminal pro-brain natriuretic peptide in patients with acute pulmonary embolism. Eur Respir J 22: 649-653.
8. ten Wolde M, Tulevski II, Mulder JW, Söhne M, Boomsma F, et al. (2003) Brain natriuretic peptide as a predictor of adverse outcome in patients with pulmonary embolism. Circulation 107: 2082-2084.
9. Goldhaber SZ, Visani L, De Rosa M (1999) Acute pulmonary embolism: clinical outcomes in the International Cooperative Pulmonary Embolism Registry (ICOPER) Lancet 353: 1386-1389.
10. Tulevski II, Hirsch A, Sanson BJ, Romkes H, van der Wall EE, et al. (2001) Increased brain natriuretic peptide as a marker for right ventricular dysfunction in acute pulmonary embolism. Thromb Haemost 86: 1193-1196.
11. Wolfe MW, Lee RT, Feldstein ML, Parker JA, Come PC, et al. (1994) Prognostic significance of right ventricular hypokinesis and perfusion lung scan defects in pulmonary embolism. Am Heart J 127: 1371-1375.
12. Ribeiro A, Lindmarker P, Juhlin-Dannfelt A, Johnsson H, Jorfeldt L (1997) Echocardiography Doppler in pulmonary embolism: right ventricular dysfunction as a predictor of mortality rate. Am Heart J 134: 479-487.
13. Konstantinides S, Geibel A, Olschewski M (1997) Association between thrombolytic treatment and the prognosis of haemodynamically stable patients with major pulmonary embolism: results of a multicenter registry.96:882-8. 27.