

Role of NT-proBNP and Troponin I in Assessing the Severity of Pulmonary Embolism

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Abstract

Introduction: Pulmonary embolism is a diagnostic and therapeutic emergency that can be life-threatening. Its mortality is largely attributable to severe forms classically defined by clinical and morphological criteria. The aim of this study is to establish the role of two cardiac biomarkers (NT-proBNP and troponin) in assessing the severity of pulmonary embolism. **Patients and Methods:** We conducted a descriptive and analytical cross-sectional study. Data collection was retrospective over the period from January 1, 2011 to December 31, 2021. All patients hospitalized for pulmonary embolism in two cardiology referral clinics in Cotonou (Atinkanmey Polyclinic and CICA Clinic) were included. **Results:** The hospital prevalence of pulmonary embolism was 9.08%. The mean age was 52.6 years, with extremes of 18 and 92 years. The sex ratio was 0.73. Pulmonary embolism was severe according to hemodynamic, morphological and sPESI criteria in 12%, 24% and 39% of cases respectively, and mortality was 61.53%. Mean NT-ProBNP and troponin I levels were significantly higher in patients with severe criteria than in those without. NT-proBNP and troponin had good specificity for predicting cardiovascular arrest (99% and 90%), shock (100% and 98%), and hypotension (99% and 96%). NT-proBNP has the best positive predictive values in relation to the occurrence of shock (100%) and right ventricular dilatation (93%). The best correlation coefficient was obtained between right ventricular dilatation and NT-proBNP (0.78). **Conclusion:** NT-proBNP and troponin I are good biomarkers for predicting the severity of pulmonary embolism and allowing therapeutic adaptation when they are elevated.

Keywords

Pulmonary Embolism, Mortality, NT-proBNP, Troponin I

1. Introduction

Pulmonary embolism is a diagnostic and therapeutic emergency that can be life-threatening [1]. In Benin, Houenanssi *et al.* noted in 2019 an increase in the hospital prevalence of pulmonary embolism from 5.9% to 12% in the space of 9 years [2]. High mortality is largely attributable to severe forms, defined by clinical and morphological criteria [3] [4] [5]. However, the risk of death is highest in cases of arterial hypotension [5]. In the context of Africa, even if recognition of hypotension is cheap and accessible whatever the level of the healthcare system, the weakness of technical facilities and inaccessibility to care leave little chance of a favorable outcome. The need was therefore to propose markers that would enable early identification of patients at risk of shock and death so that treatment could be adjusted at an early stage. Morphological criteria such as dilatation of the right heart cavities and visualization of thrombus in the right heart cavities correlate with the severity of pulmonary embolism [5], but access to cardiac ultrasound remains very limited in Africa and dependent on the availability of the cardiologist. Biomarkers of myocardial suffering such as NT-proBNP and troponin I, a powerful biochemical marker of cardiac function, could be good biomarkers for predicting the severity of pulmonary embolism.

Several studies have shown that elevated plasma NT-proBNP or troponin I levels are associated with pulmonary embolism severity and 1-month mortality [6] [7] [8].

The question is whether these biomarkers have sufficient sensitivity and specificity to be proposed as markers of the severity of pulmonary embolism in sub-Saharan African countries. The aim of the present study was to define the role of these two cardiac biomarkers in assessing the severity of pulmonary embolism by analyzing their diagnostic parameters and their correlation with conventional severity criteria.

2. Study Framework and Methods

It was a cross-sectional, descriptive and analytical study. Data collection was retrospective over a 10-year period, from January 1, 2011 to December 31, 2021.

The study population consisted of all patients hospitalized for pulmonary embolism in two cardiology referral clinics in Cotonou, the Atinkanmey Polyclinic and the Aupiais International Cardiology Clinic (CICA).

Patients with pulmonary embolism were selected on the basis of hospitalization records. Pulmonary embolism was selected on the basis of thoracic angiotatin findings of thrombus in the pulmonary artery or its branches. Records that could not be exploited or could not be found were excluded. Patients with acute left heart failure or recent myocardial infarction have been excluded.

The variables studied were informational indices such as sensitivity (Se), specificity (Sp), positive predictive value (PPV), negative predictive value (NPV) and correlation coefficient (r) of NT-proBNP and troponin I compared with clinical criteria of severity (hemodynamic instability, hypotension, cardiac arrest, shock,

sPESI) and morphology (right ventricular dilatation).

Hemodynamic instability and arterial hypotension are the parameters that classically define the severity of pulmonary embolism, as they are associated with high mortality [5]. Other parameters associated with severity are dilatation of the right cavities and sPESI [5]. As these criteria are already used in international recommendations, we have chosen to use them as comparators for the markers studied.

The threshold for NT-proBNP positivity was set at 1000 ng/mL and for troponin I at 0.1 ng/mL. Hemodynamic instability was characterized by the presence of one of the clinical features of hypotension, cardiac arrest or shock. Hypotension was defined as systolic blood pressure < 90 mmHg or a fall in systolic BP of more than 40 mmHg, lasting more than 15 min and not caused by arrhythmia, hypovolemia or recent-onset sepsis. Shock is defined as systolic blood pressure < 90 mmHg, unresponsive to vascular repletion or requiring catecholamine infusion to maintain adequate blood pressure. Cardiac arrest was defined as the need for cardiopulmonary resuscitation. The sPESI is the simplified version of the pulmonary embolism severity index. sPESI > 0 defines a high risk of death.

Socio-demographic (age, sex), clinical (history) and evolutionary (death) variables were also collected.

Data were collected using a survey form based on information contained in patients' medical records. Means were compared using the Student's t-test. A p-value of less than 0.05 was considered statistically significant. Biomarker performance was assessed by calculating various informational indices.

3. Results

3.1. Frequency, Socio-Demographic and Clinical Characteristics

217 patients with pulmonary embolism were included among the 2389 hospitalized, representing a hospital prevalence of 9.08%. The mean age was 52.6 years, with extremes of 18 and 92 years. Females were predominant, with a sex ratio of 0.73. The main antecedents found were arterial hypertension (47%), obesity (35%), diabetes (12%) and cancer (9%).

Pulmonary embolism was severe according to hemodynamic, morphological and sPESI criteria in 12.0%, 24.0% and 38.7% of cases respectively (**Table 1**).

3.2. Case-Fatality

The case-fatality rate of pulmonary embolism was highest in the presence of cardiac arrest (94.1%), hemodynamic instability (61.5%) or shock (44.4%). The lowest case fatality was observed in the presence of right ventricular dilatation (3.9%). **Table 2** shows the case-fatality rate according to the criteria studied.

3.3. Diagnostic Value of Troponin I and NT-ProBNP

Of all the patients included, 111 had performed the NT-proBNP test and 107 had

Table 1. Distribution of the population according to severity criteria.

	Numbers	Percentage (%)
Clinical criteria (hemodynamics and sPESI)		
Hemodynamic instability	26	12.0
Cardiac arrest	17	7.8
Hypotension	5	2.3
Shock	9	4.1
sPESI > 0	84	38.7
Morphological criteria		
Right ventricle dilatation	52	24.0

Table 2. Distribution of case-fatality rates according to severity criteria.

	Number of patients	Number of deaths	Percentage (%)
Hemodynamic instability	26	16	61.5
Cardiovascular arrest	17	16	94.1
Hypotension	05	01	20.0
Shock	09	04	44.4
Right ventricular dilatation	52	02	3.9
sPESI > 0	84	14	16.7

performed the troponin I test. The mean value of NT-proBNP or troponin I was significantly higher in the presence of the severity criteria studied than in the absence of these criteria (**Table 3**).

The best sensitivity of NT-proBNP was observed with right ventricular dilatation (84%). It has good specificity for cardiovascular arrest (99%), shock (100%), hypotension (99%), and right ventricular dilatation (93%). Its best positive predictive values are obtained for shock (100%) and right ventricular dilatation (93%). Its best negative predictive value was obtained for right ventricular dilatation (82%). The diagnostic value of NT-proBNP are shown in **Table 4**.

The sensitivity of troponin I was low whatever the severity criteria. However, it had good specificity for cardiovascular arrest (100%), shock (98%) and hypotension (96%), and an excellent positive predictive value only for cardiovascular arrest (100%) (**Table 5**).

Correlation coefficients between cardiac biomarkers (NT-proBNP and troponin) varied according to severity criteria. The highest correlation was obtained with right ventricular dilatation (0.78) for NT-proBNP and with PESI score (0.22) for troponin I. **Table 6** shows the correlation coefficients and their interpretations.

4. Discussion

Of the 2389 patients hospitalized during the study period, 217 presented with

Table 3. Comparison of NT-proBNP and troponin means according to the presence or absence of severity criteria.

	Mean NT-proBNP			Mean Troponin I		
	present	absent	p-value	present	absent	p-value
Shock	3621	1739.01	<0.05	20.00	1.94	0.0003411
Hypotension	7032.3	1514.23	<0.05	10.14	2.05	0.0003734
sPESI score	2592.6(>0)	1147.3(<0)	<0.05	3.54 (>0)	1.49(<0)	0.002408
Right ventricular dilatation	3664.4	582.4	<0.05	3.99	1.41	0.001848

Table 4. Diagnostic value of NT-proBNP.

	NT-proBNP		Diagnostic value			
	Low	Hight	Se	Sp	PPV	NPV
Cardiovascular arrest						
Absent	67	37	3%	99%	50%	64%
Present	1	1				
Shock						
Absent	68	36	5%	100%	100%	65%
Present	0	2				
Hypotension						
Absent	67	34	11%	99%	80%	66%
Present	1	4				
Right ventricle dilatation						
Absent	37	8	84%	93%	93%	82%
Present	3	42				
sPESI						
Score = 0	46	14	63%	68%	52%	77%
Score ≥ 1	22	24				

Table 5. Diagnostic value of troponin I.

	NT-proBNP		Diagnostic value			
	Low	Hight	Se	Sp	PPV	NPV
Cardiovascular arrest						
Absent	48	57	3%	100%	100%	46%
Present	0	2				
Shock						
Absent	48	59	2%	98%	50%	45%
Present	1	1				
Hypotension						
Absent	46	58	2%	96%	33%	44%
Present	2	1				

Continued

Right ventricle dilatation							
Absent	30	18	55%	71%	65%	63%	
Present	12	22					
sPESI							
Score = 0	33	33	44%	69%	63%	50%	
Score ≥ 1	15	26					

Table 6. Correlation between cardiac biomarkers NT-proBNP, troponin I and studied severity criteria.

Severity factor	NT-proBNP		Troponin I	
	r	Interpretation	r	Interpretation
Dilation of the right ventricle	0.78	Strong positive correlation	0.20	Very low positive correlation
Shock	0.18	Very low positive correlation	-0.01	Very low negative correlation
Cardiac arrest	0.01	Very low positive correlation	0.12	Very low positive correlation
Hypotension	0.24	Very low positive correlation	0.21	Very low positive correlation
sPESI	0.47	Low positive correlation	0.13	Very low positive correlation

pulmonary embolism, representing a in-hospital prevalence of 9.08%. This prevalence is close to the 11% reported by Houenansi *et al.* at the CNHU-HKM Cardiology Clinic in 2019 [9], but lower than that reported by Maiga *et al.* who found 55% in the Cardiology Department of the Mother and Child University Hospital Centre “le Luxembourg” in Bamako in 2019 [10]. This difference may be explained by the fact that our study was carried out in centers catering for a wide range of pathologies, whereas the population studied by Maiga *et al.* consisted mainly of women with multiple VTE risk factors.

Of the 217 cases of pulmonary embolism, around 12% were severe according to hemodynamic criteria. This rate is lower than the 27.5% found by Pessibaba *et al.* in Togo [11], and the 26% reported by Babaka Kana *et al.* in Dakar [12]. We can explain this difference by the fact that the above-mentioned studies were carried out in reference departments performing thrombolysis.

In terms of mortality, we recorded 16 in-hospital deaths among the 26 cases of severe pulmonary embolism, giving a case-fatality ratio of 61.53%. This number of deaths in relation to the total number of hospitalized patients gives an overall in-hospital mortality of 7.37%, which is close to those reported by Dossou [13] and Lagoye [14], who found 8.3% and 8.5% respectively in their series in the cardiology department of the CNHU-HKM. The case-fatality rate for severe forms is close to that reported by Babaka Kana *et al.*, who found a rate of 60% [12]. These statistics clearly illustrate the extreme severity of pulmonary embolism.

In our study, there was a significant increase in mean NT-proBNP in patients with severity criteria compared with those without ($p < 0.05$). Kuchert *et al.* have made the same observation [15]. Dores *et al.* made the same findings and further

reported that elevated NT-proBNP is associated with a higher risk of death [6]. Patients with a high NT-proBNP value would therefore be at greater risk of presenting elements of severity.

Analysis of the correlation coefficients between NT-proBNP values and the various severity criteria shows a significant link between high NT-proBNP values and the presence of morphological severity criteria. In our study, the strongest correlation ($R = 0.7821578$) was obtained between NT-proBNP values and right ventricular dilatation indicative of cardiac dysfunction. Indeed, NT-proBNP secretion is stimulated by ventricular distension [16]. Ventricular wall stretching found in right ventricular dilatation and ischemia are among the mechanisms leading to hypotension during pulmonary embolism [17]. Pruszczyk *et al.* also report a significant relationship between the RV/LV ratio and elevated NT-proBNP values ($r = 0.53$, $p < 0.001$) [18]. Early detection or prediction of such dilatation could enable a consequent therapeutic decision.

The sensitivity of NT-proBNP is low for the detection of the criteria studied, with the exception of right ventricular dilatation, for which it achieves 84% with the best specificity (93%) and positive predictive value (93%); its specificity is also high, varying between 99 and 100% when compared with other morphological and hemodynamic criteria. Zannou *et al.* found a specificity of 92.8% and a positive predictive value of 100% [19]. But the specificity and negative predictive value reported were low. It should be noted that Agbodande *et al.* [19] excluded patients with certain causes of NT-proBNP elevation, such as age more than 75 years and heart failure. They also worked with a smaller number of patients. Henzler *et al.* observed that serum levels of NT-proBNP or troponin I were correlated with right ventricular dysfunction [20]. These findings were reinforced in the systematic review by Cavallazi *et al.*, who concluded that NT-proBNP is associated with the diagnosis of right ventricular dysfunction in patients with acute pulmonary embolism and are significant predictors of short-term, all-cause in-hospital mortality [21].

Troponin I values are also significantly elevated in patients with severe criteria. This is because troponin is the most sensitive and specific biomarker of myocardial cell damage, reflecting microscopic myocardial necrosis [22]. Ischemia is part of the mechanism leading to hypotension in pulmonary embolism [17]. In our study, the correlation coefficient between elevated troponin I values and the presence of right-sided cavity dilatation was positive ($r = 0.205$). The correlation between troponin I elevation and hypotension is better ($r = 0.210$). AMORIM *et al.* reported that 81.3% of patients with right ventricular dilatation had elevated troponin I [23]. Troponin I would appear to be a good indicator of cardiac failure during pulmonary embolism.

The diagnostic values of troponin I for the detection of ventricular dilatation were 55% and 71% for sensitivity and specificity respectively. These values are lower than those calculated by FF LIU [24]. The high specificity values (100%, 98% and 96%) for cardiovascular arrest, shock and hypotension respectively,

should raise fears of an unfavorable outcome when troponin is elevated during pulmonary embolism, and indicate rapid adaptation of treatment. Wenmiao *et al.* observed in their study on the prognostic value of NT-proBNP, troponin I, D-dimers and neutrophil-lymphocyte ratio in pulmonary embolism that the sensitivity and specificity of these biomarkers are lower when they are taken in isolation than when they are combined [8].

In view of these results, biomarker tests should be performed systematically in patients with pulmonary embolism. Their elevation should lead to decisions to reduce the risk of death. However, because of the limitations of the present study, particularly its retrospective nature, a large-scale prospective study seems essential before generalization.

5. Conclusion

NT-proBNP and troponin seem to be good biomarkers for predicting the severity of pulmonary embolism, with good sensitivity and specificity for NT-proBNP. They also seem to be correlated with the status of the heart during pulmonary embolism. These results need to be further investigated in a multicenter study including a larger number of patients.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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