Can we predict the clinical scenario of acute heart failure based only on NT proBNP rate without using echocardiography?

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Abstract

Background: The acute heart failure (AHF) is a common pattern to seek care in the emergency department (ED). The objective of our study was to investigate the relationship between NT pro-BNP and acute heart failure (AHF) syndrome in the emergency department (ED).

Methods: We conducted a descriptive prospective study over eight months. Were included all patients who presented to the emergency department (ED) with dyspnea and in whom the diagnosis of acute heart failure (AHF) was made. All patients had an NT pro-BNP laboratory test and underwent echocardiography.

Results: One hundred seven patients were included. Mean age was 65 ± 12 years. Sex ratio was 2.34. A clinical scenario CS1 was noted in 28% of cases, CS2 in 36% of cases, CS4 in 16% of cases, CS3 in 12% of cases and CS5 in 8% of cases. Thirty percent of patients had preserved left ventricular ejection fraction (LVEF) with diastolic dysfunction and 70% had a reduced left ventricular ejection fraction (LVEF). Elevated left ventricular filling pressures were found in 95% of patients. Disorders of wall motion in 14% of cases and isolated right heart failure in 12% of cases. The median natriuretic brain peptides (NT pro-BNP) level was higher when left ventricular ejection fraction (LVEF) was preserved: 4073 [410 – 25 550] pg/ml vs2025 [409 – 25 200] pg/ml (p=0,043).

Conclusion: Natriuretic brain peptides level was a good predictor of the clinical scenario CS1 with a cut-off at 5565 pg/ml. Though, the potential clinical applications of B-type natriuretic peptide in AHFS should be more studied.

Keywords: Echocardiography; Emergency; Heart Failure; Natriuretic Peptides.

BACKGROUND

Acute heart failure (AHF) is increasingly common among emergency department (ED) patients. It is a major problem on several levels: for the individual patient, for the healthcare system due to the complexity of diagnosis and treatment, and for society because of its high costs.

The term acute heart failure includes a wide variety of clinical presentations ranging from AHF de novo, acute decompensated heart failure, isolated right heart failure, and cardiogenic shock.

The diagnosis of AHFS is sometimes difficult in emergency situations. Emergency physicians have often recourse to specific diagnostic methods: biochemical by NT pro-BNP dosage, or imaging: transthoracic Doppler echocardiography.

The dosage of NT pro-BNP is simple to realize but it does not completely dispense echocardiography. Echocardiography provides powerful assessment of cardiac function: systolic dysfunction, diastolic dysfunction or right heart failure.

The relationship between the rate of NT pro-BNP and AHFS is not well studied in the literature.

Some studies have shown that a very high rate of NT pro-BNP would orient towards left ventricle (LV) systolic dysfunction and lower rates would rather be related to diastolic dysfunction.

The objective of our study was to investigate the relationship between the rate of NT pro-BNP and the AHFS, referring to echocardiography data. In other words, can we predict the clinical scenario of acute heart failure based only on NT pro-BNP rate without using echocardiography?

METHODS

Design: A prospective observational study was conducted over a period of 8 months. The study was approved by the hospital's Research Ethics Committee.

Participants: The study was conducted in the ED of the military hospital of Tunis, the capital of Tunisia. The ED has an active teaching program. The ED had approximately 38,000 patient visits per year. We included all patients aged of 18 years and more, who presented to the ED with acute dyspnea and in whom the diagnosis of AHF was retained.

The AHF was defined based on the recommendations of the European Society of Cardiology [1].

Were not included all the patients aged below 18 years and those with known significant valve disease.

Were excluded the patients with negative rate of NT pro-BNP for AHF:

- NT pro-BNP below 300 pg / ml [2].
- NT pro-BNP in the gray area, and negative after adjusting according to age [3].
- NT pro-BNP in the gray area, and negative after adjusting according to creatinine clearance (<60 ml / min [3,4]). (figure 1)

- Patients in which echocardiography was not in favor of AHF.

- Patients lost or with incomplete data.

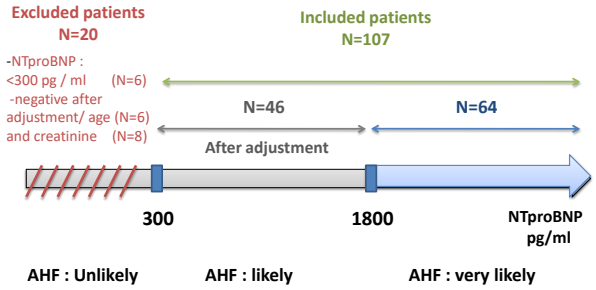

Figure 1: Distribution of patients according to NT proBNP rates

Study design: The study design is summarized in Figure 2.

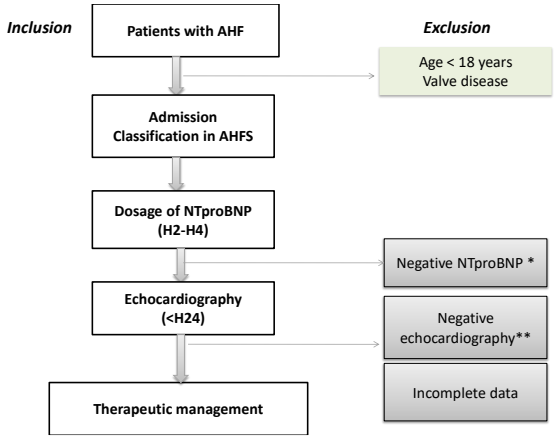

Figure 2: study design

Each patient was classified according to AHFS classification. We adopted for all patients; a classification proposed by an international, multidisciplinary group of experts [5].

This classification is based primarily on systolic blood pressure (SBP), the presence of peripheral signs of shock, the association with acute coronary syndrome (ACS), or an isolated right heart failure. These five clinical scenarios (CS) define the AHFS (Table 1).

Table 1: Clinical scenarios in acute heart failure syndrome, Critical Care 2008 [5]

Clinical scenario	Characteristics
CS1	SBP > 140mmHg Symptoms develop abruptly Predominantly diffuse pulmonary edema Minimal systemic edema (patient may be euvolemic or hypovolemic) Acute elevation of filling pressure often with preserved LVEF Vascular pathophysiology
CS2	SBP 100-140 mmHg Symptoms develop gradually, together with a gradual increase in body weight Predominantly systemic edema Minimal pulmonary edema Chronic elevation of filling pressure, including increased venous pressure and elevated pulmonary arterial pressure Manifestations of organ dysfunction (renal impairment, liver dysfunction, anemia, hypoalbuminemia)
CS3	SBP < 100 mmHg Rapid or gradual onset of symptoms Predominantly signs of hypoperfusion Minimal systemic and pulmonary edema Elevation of filling pressure Two subsets : Clear hypoperfusion or cardiogenic shock No hypoperfusion/cardiogenic shock
CS4	Symptoms and signs of acute heart failure Evidence of ACS Isolated elevation of cardiac troponin is inadequate for CS4 classification
CS5	Rapid or gradual onset No pulmonary edema Right ventricular dysfunction Signs of systemic venous congestion

Appropriate therapeutic management for all patients has been started by emergency physicians.

All patients had a dosage of NT proBNP within 2 to 4 hours, and an echocardiography, performed by the same operator, within a period not exceeding 24 hours.

The echocardiography was performed according to the American recommendations (ASE) [6, 7] by Vivid 7 Dimension Echocardiographic.

Were noted all the demographics, clinical, biological, echocardiographic, and outcomes criteria.

Statistical analysis: Statistics were calculated by SPSS (version 20.0).

Dichotomized data were analyzed by the Chi2-test. The level of significance was p =0.05.ROC (Receiver Operator Characteristics) analysis was performed to calculate sensitivity, specificity, negative and positive predictive values, and an optimal cut-point of NT proBNP to detect AHFS.

RESULTS

During the study period, the AHFS accounted for 6.8 % of consultants to the ED.

One hundred and seven patients were enrolled. The patient flow diagram is summarized in Figure 3.

The Mean age was 65 ± 12 years. The sex ratio was 2.34. Patient characteristics are summarized in Table 2.

Based on the clinic hypertensive heart failure (CS 1) was noted in 28% of cases, normotensive heart failure (CS2) in 36%, and heart failure associated with acute coronary syndrome (CS4) in 16 % of cases. Hypotensive heart failure (CS3) was noted in 12% of cases and isolated right heart failure (CS5) in 8% of cases.

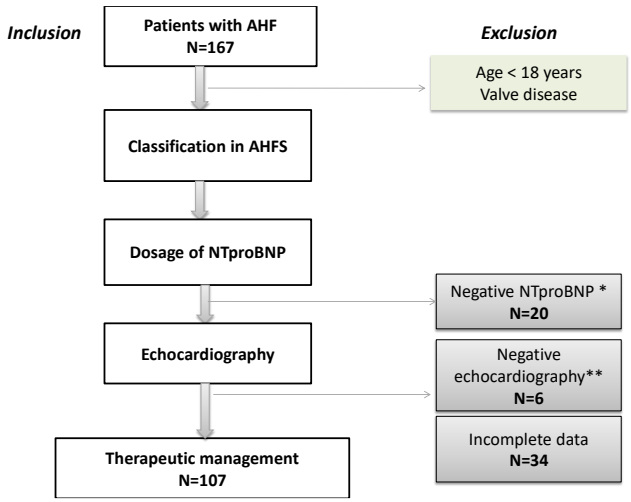

Figure 3: Patient flow diagram

** NT pro-BNP negative: NT pro-BNP<300 pg/ml (6 patients) or NT pro-BNP in the gray zone and still negative after adjustment according to age (6 patients) and to creatinine clearance (8 patients)*

*** Echocardiography not in favor of AHF*

NT pro-BNP median rates were 4576 [780 – 25 550] pg/ml for CS1 group, 2370 [410 – 25 500] pg/ml for CS2 group, 1324 [409 – 14 205] pg/ml for CS3 group, 1404 [457 – 19 889] pg/ml for CS4 group and 2394 [1150 – 15 291] pg/ml for group CS5.

Concerning the echocardiography data, 30% of patients had preserved left ventricular ejection fraction (LVEF) with diastolic dysfunction and 70% had a reduced LVEF.

Elevated LV filling pressures were found in 95% of patients. Disorders of wall motion in 14% of cases and isolated right heart failure in 12% of cases.

Table 2: Patients comorbidities

Comorbidities	N (%)
Hypertension	55 (51)
Diabetes	57 (53)
Cardiopathy	48 (50)
Heart failure	56 (52)
Dyslipidemia	29 (27)
Respiratory insufficiency	14 (13)
Chronic renal failure	11 (10)
Valvulopathy	7 (6)
Arrhythmia	23 (21)
Smoking	51 (48)

The most important level of NT pro-BNP was associated with a restrictive profile and an E / E'> 15 (Figures 4, 5).

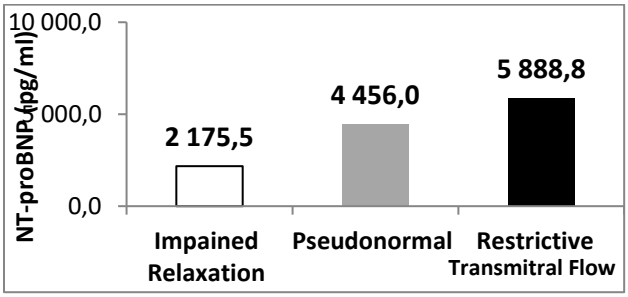

Figure 4: NT pro-BNP and transmitral flow

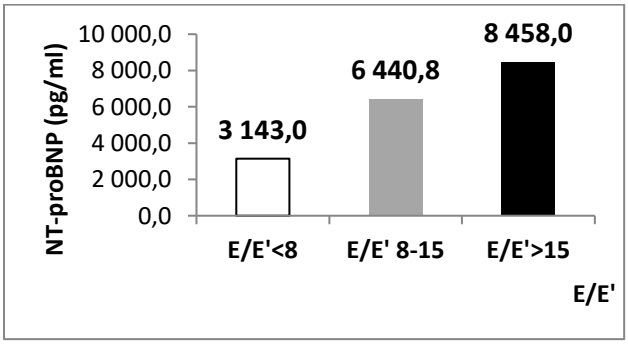

Figure 5: NT proBNP and E/E' ratio

The median NT pro-BNP level was higher when LVEF was preserved: 4073 [410 – 25 550] pg/ml vs2025 [409 – 25 200] pg/ml (p=0,043).

The median NT pro-BNP level significantly differs according to the clinical scenario and to the LVEF (figure 6).

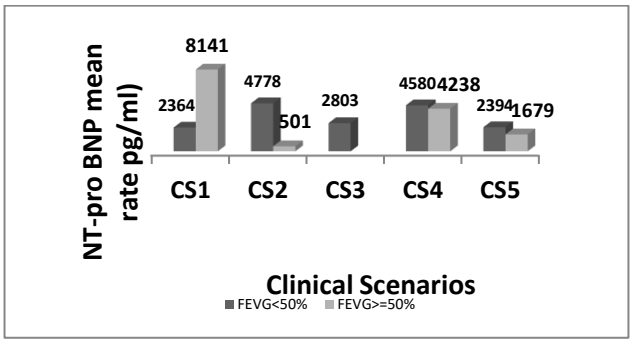

Figure 6: Distribution of the mean rates of NT proBNP according to clinical scenarios and echographic data

The NT pro-BNP is a good predictor of CS1with a cut-off of 5565 pg/ml, with an area under the curve (AUC) of 0.69; p = 0.002; confidence interval (CI) 95% [0.58 to 0.80]; 52% sensitivity; a specificity of 86%, a likelihood ratio (LR) Positive LR + 3.71 and a negative LR to 0.26.

Regarding the other clinical scenarios, the difference was not statistically significant.

DISCUSSION

This study showed that the mean NT pro-BNP was higher when LVEF was preserved. We found that the NT pro-BNP could predict the clinical scenario CS1 from a threshold of 5565 pg/ml.

Acute heart failure is a major healthcare problem. It represents more than 26 million visits to the ED worldwide [2] and more than 1 million hospitalizations annually in the United States and Europe [8,9].

In Tunisia, we do not have yet a heart failure registry. However, in a study conducted in the ED of Ben Arous Regional Hospital in Tunisia in 2009 [10], the prevalence of AHFS was 5.5 % of consultants. Our results were similar to previous findings.

Regarding the clinical distribution of AHFS, the majority of our patients had a clinical scenario CS2 (36%) which was in line with previous findings [11-13].

Concerning the mean rates of NT pro-BNP in each clinical scenario, unlike other studies [14-16], the highest levels of NT pro-BNP were found in hypertensive heart failure (CS1). Besides, the LV filling pressures in CSA were the highest. Indeed, according to Throughton [17], the rates of NT proBNP increase proportionally to the LV filling pressures. He demonstrated that E ' and the ratio E / E' were associated with high levels of NT-pro-BNP. In our study, the highest NT pro-BNP rate (8454 pg/ml) was found in patients who had an E / E '> 15 (Figure 3,4).

This difference could be explained by the fact that most similar studies were conducted in cardiology departments or Intensive care units (ICU) and only a few in the ED [14-16]. The acute phase has already been subdued and the LV filling pressures were no longer elevated.

Tshöpe [18] had also shown that the rate of NT pro-BNP increased with the severity of the diastolic dysfunction with a rate of 151.6 pg/ml for the patients who had the relaxation disorders vs 308.1 pg / mL for the pseudonormal profile and 2307.1 pg/ml for those with a restrictive profile. These rates were lower compared to those found in our study: 2175 pg/ml in case of relaxation disorders, 4456 pg/ml for pseudo-normal profile, and 5888 pg/ml for restrictive profile (Figure 4). The Tshöpe study was also conducted in the cardiology department, the dosage of NT pro-BNP was made after adequate treatment was introduced.

Another explanation suggested by Solomon [19]: Apart from acute decompensation, patients with hypertension have higher NT pro-BNP baseline rates than those with chronic heart failure. During Acute Decompensated heart failure, NT pro-BNP rates increase with the elevation of LV filling pressure. The LV filling pressures are more pronounced for CS1 compared to CS2. This could explain the higher rates of NT pro-BNP for hypertensive AHF in our study. However, in our population, the baseline NT pro-BNP rates were missed.

In our study, an NT pro-BNP cut-off of 5565 pg/ml was predictive of CS1. To our knowledge, the level of NT pro-BNP for each clinical scenario has not been studied yet.

Further studies are warranted to identify a cut-off of NT pro-BNP that could predict the clinical scenario of AHFS.

LIMITATIONS

Some limitations of our study should be addressed. In our study, the mean NT pro-BNP was higher when LVEF was preserved. The NT pro-BNP could predict the clinical scenario CS1 but it did not predict other clinical scenarios considering the small sample size.

Indeed, the number of patients included was low compared to other international studies. larger-scale studies, including multicenter, are needed.

Concerning the NT pro-BNP levels, it would have been interesting to have the basic rate of NT pro-BNP for all patients to calculate the delta NT pro-BNP.

CONCLUSION

In conclusion, the mean NT pro-BNP was higher when LVEF was preserved. The NT pro-BNP could predict the clinical scenario CS1 from a threshold of 5565 pg/ml.

Peptide measurements provide information complementary or incremental to echocardiography for assessment of cardiac function, clinical status, and outcome. Tough, the potential clinical applications of B-type natriuretic peptide in AHFS should be more studied.

What is known about this topic

- Acute heart failure (AHF) is a public health issue characterized by high mortality and a high rate of hospital admissions and re-hospitalizations.
- The diagnosis of AHF may not be straightforward and at times may be difficult in an undifferentiated patient with acute dyspnea, especially in patients with advanced age and comorbid disease.
- Some studies have shown that a very high rate of NT pro-BNP would orient towards left ventricle (LV) systolic dysfunction and lower rates would rather be related to diastolic dysfunction.

What this study adds

- The NT pro-BNP could predict the clinical scenario CS1 but it did not predict other clinical scenarios considering the small sample size.
- Peptide measurements provide information complementary or incremental to echocardiography for assessment of cardiac function, clinical status, and outcome

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