CRITICAL CARE

COMMENTARY

In-hospital brain natriuretic peptide and N-terminal prohormone brain natriuretic peptide variations are predictors of short-term and long-term outcome in acute decompensated heart failure

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Abstract

Acute decompensated heart failure is one of the most important causes of hospitalisation worldwide. Natriuretic peptides have shown their usefulness in the diagnosis and management of heart failure. Their variations during hospitalisation also appear useful to predict outcomes. In particular, data from the literature demonstrate that reduction from admission to discharge of brain natriuretic peptide and N-terminal prohormone brain natriuretic peptide in these patients is a predictor of future cardiovascular events.

In the present issue of *Critical Care*, Noveanu and colleagues evaluated brain natriuretic peptide (BNP) and N-terminal prohormone brain natriuretic peptide (NT-proBNP) serial measurements as predictive of 30-day and 1-year mortality and readmission in patients admitted to the emergency department for acute decompensated heart failure (ADHF) [1].

The usefulness of measuring BNP and NT-proBNP in the diagnosis and management of congestive heart failure is well known [2,3]. Both BNP and NT-proBNP are useful for diagnosis in patients presenting with undifferentiated dyspnoea in the emergency department and have been shown to accurately reflect heart failure severity and prognosis [3-6]. Moreover, in some studies, serial BNP evaluations have been demonstrated to be useful in clinical management [7].

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Noveanu and colleagues showed during 1-year follow-up in a multivariate analysis that BNP at 24 hours (mean 95% confidence interval) (1.02 (1.01 to 1.04), P = 0.003), at 48 hours (1.04 (1.02 to 1.06), P <0.001) and at discharge (1.02 (1.01 to 1.03), P <0.001) independently predicted 1-year mortality, while only predischarge NT-proBNP was predictive (1.07 (1.01 to 1.13), P = 0.016). Comparable results could be obtained for the secondary endpoint of 30-day mortality but not for 1-year heart failure readmissions.

These results from Noveanu and colleagues' paper are in accordance with data reported by our group [8]. We demonstrated that a reduction of BNP >46% at hospital discharge coupled with a BNP absolute value <300 pg/ml resulted in a very powerful negative prognostic value for future cardiovascular outcomes in patients hospitalised with ADHF [8].

Other studies demonstrated the usefulness of repeated measurements of natriuretic peptides during hospitalisation in predicting survival of ADHF patients [8-11]. BNP variations during hospitalisation could give prognostic information, particularly at discharge, and could also suggest a qualitative variation of treatment (intensification or decrement of drugs) on the basis of natriuretic peptide levels.

Noveanu and colleagues have also demonstrated that the prognostic accuracy of BNP was comparable at 24 hours with 48 hours and with discharge [1]. The authors suggested that BNP at 24 hours could be suitable to assess prognosis and to vary treatment in order to decrease mortality in patients with constant elevated levels of BNP. This suggestion is in accordance again with data from our laboratory, where we showed that a drop of BNP >25% at 24 hours was a strong negative prognostic factor for future cardiovascular events [8], suggesting

intensified treatment in patients who did not decrease their BNP >25% at 24 hours.

Rapid change in BNP levels seems to reflect an adequate response to heart failure therapy, and could be considered very important for early risk stratification and therapy guidance. A lack of this response, assuming optimal medical treatment, implies a more complex and therapy-refractory disease, associated with an adverse long-term outcome. Accordingly, if this change in BNP level does not occur, treatment intensification should be the consequence. In patients with a comparable decrease in BNP levels (roughly 30% between admission and 24 hours), we would expect a favourable outcome; however, future prospective studies need to evaluate a distinct cut-off point to allow more precise recommendations [12].

Moreover, from the data of Noveanu and colleagues, BNP and NT-proBNP seem to show a different response to treatment due to their different kinetics. This difference is probably due to the slower decrease of NT-proBNP during treatment in ADHF patients in comparison with BNP [9-12]. Compared with NT-proBNP, BNP could be more useful to determine initial clinical stabilisation of ADHF patients, and to assess clinical improvement in hospitalisation as we also demonstrated [13]. NT-proBNP could be used to assess initial diagnosis but is of limited help for repeat measurements during hospitalisation because its variations are not as sensitive and rapid as those of BNP [9-12,14].

In conclusion, in patients admitted to the emergency department for ADHF, serial measurements of BNP and NT-proBNP are useful because they show a similar powerful predictive role for mortality in the short term and in the long term. Interestingly, patients' BNP and NT-proBNP variations could help the physician to vary the therapeutic approach during the initial hours of hospitalisation in order to obtain favourable outcomes.

Nevertheless, when considering hospital readmissions after discharge it seems that the variation of the two bio-markers during hospitalisation at various time points is of no utility. Logeart and colleagues showed that only predischarge BNP was a strong predictor of death, and also of readmissions for heart failure with a cut-off point of 350 ng/ml [10]. Previously published studies presuming this finding – including Cheng and colleagues using BNP [15] or Bettencourt and colleagues using NT-proBNP [16] – used combined endpoints consisting of all-cause mortality and readmission for heart failure.

Although the results of Noveanu and colleagues' study are to be considered of importance for the role of natriuretic peptides in prognostic stratification for patients with ADHF, multicentre studies on a larger number of patients should be carried out to better elucidate the real value of natriuretic peptides in avoiding readmission after hospital discharge in heart failure patients.

Abbreviations
ADHF, acute decompensated heart failure; BNP, brain natriuretic peptide; NT-proBNP, N-terminal prohormone brain natriuretic peptide.

Competing interests
The authors declare that they have no competing interests.

References
1. Noveanu M, Breidthardt T, Potocki M, Reichlin T, Socrates T, Arenja N, Reiter M, Twerenbold R, Meissner J, Heinisch C, Stalder S, Mueller C: **Direct comparison of serial B-type natriuretic peptide and NT-proBNP levels for prediction of short- and long-term outcome in acute decompensated heart failure.** *Crit Care* 2011, **15**:R1.
2. Mueller C, Scholer A, Laule-Kilian K, Martina B, Schindler C, Buser P, Pfisterer M, Perruchoud AP: **Use of B-type natriuretic peptide in the evaluation and management of acute dyspnea.** *N Engl J Med* 2004, **350**:647-654.
3. Daniels LB, Maisel AS: **Natriuretic peptides.** *J Am Coll Cardiol* 2007, **50**:2357-2368.
4. Maisel AS, Krishnaswamy P, Nowak RM, McCord J, Hollander JE, Duc P, Omland T, Storrow AB, Abraham WT, Wu A, Clopton P, Steg PG, Westheim A, Knudsen CW, Perez A, Kazanegra R, Herrmann HC, McCullough PA; Breathing Not Properly Multinational Study Investigators: **Rapid measurement of B-type natriuretic peptide in the emergency diagnosis of heart failure.** *N Engl J Med* 2002, **347**:161-167.
5. Krumholtz HM, Chen YT, Wan Y, Vaccarino V, Radford MJ, Horwitz RI: **Predictors of readmission among elderly survivors of admission with heart failure.** *Am Heart J* 2002, **139**:72-77.
6. Alibay Y, Beauchet A, El Mahmoud R, Schmitt C, Brun-Ney D, Benoit MO, Dubourg O, Boileau C, Jondeau G, Puy H: **Plasma N-terminal pro-brain natriuretic peptide and brain natriuretic peptide in assesmemt of acute dyspnea.** *Biomed Pharmacother* 2005, **59**:20-24.
7. Silver MA, Maisel A, Yancy CW, McCullough PA, Burnett JC Jr, Francis GS, Mehra MR, Peacock WF 4th, Fonarow G, Gibler WB, Morrow DA, Hollander J; BNP Consensus Panel: **BNP Consensus Panel 2004: a clinical approach for the diagnostic, prognostic, screening, treatment monitoring and therapeutic roles of natriuretic peptides in cardiovascular diseases.** *Congest Heart Fail* 2004, **10(5 Suppl 3):**1-30.
8. Di Somma S, Magrini L, Pittoni V, Marino R, Mastrantuono A, Ferri E, Ballarino P, Semplicini A, Bertazzoni G, Carpinteri G, Mulè P, Pazzaglia M, Shah K, Maisel A, Clopton P: **In-hospital percentage BNP reduction is highly predictive for adverse events in patients admitted for acute heart failure. The Italian RED study.** *Crit Care* 2010, **14**:R116.
9. Di Somma S, Magrini L, Mazzone M, de Leva R, Tabacco F, Marino R, Talucci V, Ferri E, Forte P, Cardelli P, P, Gentiloni N, Pittoni: **Decrease in NTproBNP plasma levels indicates clinical improvement of acute decompensated heart failure.** *Am J Emerg Med* 2007, **25**:335-339.
10. Logeart D, Thabut G, Jourdain P, Chavelas C, Beyne P, Beauvais F, Bouvier E, Solal AC: **Predischarge B-type natriuretic peptide assay for identifying patients at high risk of re-admission after decompensated heart failure.** *J Am Coll Cardiol* 2004, **43**:635-641.
11. Bayes-Genis A, Lopez L, Zapico E, Cotes C, Santalo M, Ordonez-Llanos J, Cinca J: **NT-proBNP reduction percentage during admission for acutely decompensated heart failure predicts long-term cardiovascular mortality.** *J Card Fail* 2005, **11(5 Suppl):**S3-S8.
12. Pfisterer M, Buser P, Rikli H, Gutmann M, Erne P, Rickenbacher P, Vuillomenet A, Jeker U, Dubach P, Beer H, Yoon SI, Suter T, Osterhues HH, Schieber MM, Hilti P, Schindler R, Brunner-La Rocca HP; TIME-CHF Investigators: **BNP-guided vs symptom-guided heart failure therapy: the Trial of Intensified vs Standard medical therapy in Elderly Patients with Congestive Heart Failure (TIME-CHF) randomized trial.** *JAMA* 2009, **301**:383-392.
13. Di Somma S, Magrini L, Pittoni V, Marino R, Peacock F, Maisel A: **Usefulness of serial assessment of natriuretic peptides in the emergency department for patients with acute decompensated heart failure.** *Congest Heart Fail* 2008, **14(4 Suppl 1):**21-24.
14. Di Somma S, Magrini L, Tabacco F, Marino R, Talucci V, Marrocco F, Cardelli P, Ferri E, Pittoni V: **Brain natriuretic peptide and N-terminal pro-B-type natriuretic peptide show a different profile in response to acute decompensated heart failure treatment.** *Congest Heart Fail* 2008, **14**:245-250.

15. Cheng V, Kazanegra R, Garcia A, Ienert L, Krishnaswamy P, Gardetto N, Clopton P, Maisel A: **A rapid bedside test for B-type peptide predicts treatment outcomes in patients admitted for decompensated heart failure: a pilot study.** *J Am Coll Cardiol* 2001, **37:**386-391.

16. Bettencourt P, Azevedo A, Pimenta J Frioes F, Ferreira S, Ferreira A: **N-terminal-pro-brain natriuretic peptide predicts outcome after hospital discharge in heart failure patients.** *Circulation* 2004, **110:**2168-2174.