

Natriuretic Peptides as Prognosticators in Congestive Heart Failure

Susan Isakson BA and Alan Maisel MD FACC

Divisão de Cardiologia e Departamento de Medicina do Sistema de Saúde para Veteranos e Universidade da Califórnia, San Diego - San Diego, CA - USA

Decompensated congestive heart failure (CHF) is a clinical syndrome often characterized by elevated left ventricular filling pressures (LVEDP). Therapy for decompensated CHF aims at normalizing filling pressures and thereby improves both symptoms and outcomes. However, therapy guided by direct measurements of filling pressure is not practical in most patients, focusing attention on non-invasive surrogate measures of LVEDP for tailoring of heart failure therapy.

Natriuretic peptide levels (NP) are closely correlated with LVEDP, which is consistently elevated in decompensated heart failure. In the absence of acute mitral regurgitation and flash pulmonary edema, and in the presence of volume overload, NP levels are a useful indication of pulmonary capillary wedge pressure (PCWP). In a study by Kazenegra et al, patients admitted for decompensated CHF had BNP levels and hemodynamic measurements taken every 2 hours for the first 24 hours and every four hours for the next 24-48 hours. PCWP showed a decrease from 33 to 25 mmHg over the first 24 hours, while BNP levels decreased from 1472 to 670 pg/ml. However, no change in BNP was noted in patients with end-stage heart failure, even as wedge pressures dropped¹.

In the study by Pereira-Barretto et al², in this issue (*Serum NT-proBNP levels are a prognostic predictor in patients with advanced heart failure*), 105 subjects with poor LV function and significant symptoms were evaluated in terms of baseline NP levels and subsequent mortality. Natriuretic peptide levels, in this case, NT-proBNP, were strong predictors of 90 day survival. Despite the limitations of the study design (patient heterogeneity, paucity of events, and absence of serial sampling), the paper adds to a growing body of evidence that natriuretic peptides, measured in the decompensated period, provide significant risk stratification.

NP levels are useful tools in the assessment of patients even prior to hospitalization. The Rapid Emergency Department Heart Failure Outpatient Trial (REDHOT) examined the relationship between perceived severity of disease by physicians and severity as indicated by BNP levels. Patients who were discharged from the hospital had higher BNP levels than those admitted for treatment.

The median BNP level for discharged patients was 976 pg/ml, compared with a mean BNP of 766 pg/ml for patients who were admitted to the hospital. Patients with BNP levels less than 200 pg/ml had an excellent prognosis, with a mortality of 0% at 30 days and only 2% at 90 days³.

The inclusion of NPs in clinical decision-making has been shown to be cost effective and to improve quality of care in the emergency and hospital settings. The BASEL study in Switzerland explored the cost effectiveness of using the BNP test as an adjunct to the standard clinical tools. Patients enrolled in the study were randomized to one of two groups- utilize BNP blood testing upon arrival in the ED and throughout hospitalization and standard care group without using BNP levels. Patients who received a BNP test upon presentation were shown to have 10% fewer admissions, decreased length of hospital stay by a mean of 3 days, and lower mean total cost of treatment of 26%. This suggests that use of BNP in evaluating acute dyspnea improves both the cost and quality of care⁴.

Changes in NP levels during hospitalizations are important prognostic indicators of a patient's health during the months following a heart failure admission. In one study, only 16% of patients with a fall in BNP levels during hospitalization had a subsequent cardiac event, while 52% of those with rising BNP levels during treatment had either readmission or cardiac death. Patients whose discharge BNP levels fell below 430 pg/mL had a reasonable likelihood of not being readmitted within the following 30 days⁵. This data was supported by a study by Bettencourt et al who found that failure of BNP levels to fall over the hospitalization predicts death/rehospitalization and that discharge levels < 250 pg/ml predicted event free survival⁶.

NP measurements during hospitalization should probably be obtained at the very least on admission and discharge. NP levels taken 24 hours after the initiation of treatment have proven to be useful in determining whether the patient is in need of more aggressive treatment. Heart failure patients in the euvolemic state have an elevated, but moderately stable, "dry" NP level. A significant increase in NP levels is seen in these patients

Correspondência: Alan Maisel MD • VAMC Cardiology 111-A - 3350 La Jolla Village Drive - San Diego, CA 92161 - USA
E-mail: eliasj@terra.com.br, jeneto@cardiol.br

in the setting of acute volume overload. With regard to BNP, levels <200-300 pg/ml are likely representative of a true euvolemic state. It is important to establish a patient's dry BNP level at discharge for the purpose of tailoring treatment to reach an optimal condition and for subsequent outpatient monitoring of volume status.

In patients whose NP levels fail to fall with treatment, several possible causes should be considered. Patients with NYHA functional class IV heart failure may have very high "dry" BNP levels, and therefore high BNP levels may not necessarily reflect acute volume overload. Patients with significant peripheral edema and/or severe ascites may not show an immediate decrease in NP levels. A NP decrease may only be seen in these patients after of several liters of urine output. This effect is due to mobilization and excretion of third space volume prior to any direct reduction in wedge pressure. When a NP level does not fall with treatment, it is also possible that the primary cause of symptoms is not acute decompensated heart failure, and further differential diagnoses should be considered. Worsening renal function during diuresis can

also cause paradoxically increased NP levels.

Tailoring treatment and post-discharge clinic visits based on discharge BNP levels is now a common practice. Logeart et al found that patients discharged with BNP levels above 350 pg/ml were at much higher risk of adverse events than those with lower BNPs. Additionally, patients with discharge BNP levels greater than 700 pg/ml had a 31% prevalence of death or heart failure readmission after one month. This prevalence increased to 93% after six months⁷.

CONCLUSION

As illustrated in this issue by Barretto et al natriuretic peptides have become increasingly important tools for the evaluation and management of patients with decompensated heart failure, NPs are not stand-alone tests and there is a learning curve associated with their use. Further research is likely to help elucidate and refine our understanding and clinical use of the natriuretic peptide levels.

REFERENCES

1. Kazanegra R, Cheng V, Garcia A, et al. A rapid test for B-type natriuretic peptide correlates with falling wedge pressures in patients treated for decompensated heart failure: a pilot study. *J Card Fail.* 2001;7:21-9.
2. Pereira-Barretto ACP, Oliveira Jr MT, Strunz CC, Del Carlo CH, Scipioni AR, Ramires JAF. O nível sérico de NT-proBNP é um excelente preditor prognóstico em pacientes com insuficiência cardíaca avançada. *Arq Bras Cardiol.* 2006; 87:174-77.
3. Maisel A, Hollander JE, Guss D, et al. Primary results of the Rapid Emergency Department Heart Failure Outpatient Trial (REDHOT). A multicenter study of B-type natriuretic peptide levels, emergency department decision making, and outcomes in patients presenting with shortness of breath. *J Am Coll Cardiol.* 2004;44:1328-33.
4. Mueller C, Scholer A, Laule-Kilian K, et al. Use of B-type natriuretic peptide in the evaluation and management of acute dyspnea. *N Engl J Med.* 2004;350:647-54.
5. Cheng V, Kazanegra R, Garcia A, et al. 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;37:386-91.
6. Bettencourt P, Ferreira S, Azevedo A, et al. Preliminary data on the potential usefulness of B-type natriuretic peptide levels in predicting outcome after hospital discharge in patients with heart failure. *Am J Med.* 2002;113:215-19.
7. Logeart D, Thabut G, Jourdain P, et al. Predischarge B-type natriuretic peptide assay for identifying patients at high risk of re-admission after decompensated heart failure. *J Am Coll Cardiol.* 2004;43:635-41.