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Prognostic Impact of BNP Variations in Patients Admitted for Acute Decompensated Heart Failure with In-Hospital Worsening Renal Function

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Background

The significance of worsening renal function (WRF) in patients admitted for acute decompensated heart failure (ADHF) is still controversial. We hypothesised that changes in brain natriuretic peptide (BNP) might identify patients with optimal diuretic responsiveness resulting in transient WRF, not negatively affecting the prognosis. Our aim was to verify if in-hospital trends of BNP might be helpful in the stratification of patients with WRF after treatment for ADHF.

Methods

122 consecutive patients admitted for ADHF were enrolled. Brain natriuretic peptide and eGFR were evaluated at admission and discharge. A 20% relative decrease in eGFR defined WRF, whereas a BNP reduction $\geq 40\%$ was considered significant. The primary combined endpoint was death/urgent heart transplantation and re-hospitalisation for ADHF.

Results

Worsening renal function occurred in 23% of patients without differences in outcome between patients with and without WRF (43% vs. 45%, $p=0.597$). A significant reduction in BNP levels over the hospitalisation occurred in 59% of the overall population and in 71% of patients with WRF. At a median follow-up of 13.0 (IQR 6–36) months, WRF patients with $\geq 40\%$ BNP reduction had a lower rate of death/urgent heart transplantation/re-hospitalisation compared to WRF patients without BNP reduction (30% and 75%, respectively; $p=0.007$). Favourable BNP trend was the strongest variable in predicting the outcome in WRF patients (HR 0.222, 95% CI 0.066–0.753, $p=0.016$).

Conclusions

Worsening renal function does not affect the prognosis of ADHF and, when associated with a significant BNP reduction, identifies patients with adequate decongestion at discharge and favourable outcome.

Keywords

Diuretics • Heart failure • Natriuretic peptides • Worsening renal function

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Introduction

Heart failure (HF) is a major public health problem with an increasing prevalence, high morbidity and mortality[1]. Despite therapeutic advances, hospitalisations for acute decompensated heart failure (ADHF) have grown and the prognosis remains poor[2].

The most responsible factor for ADHF symptoms is the severity of congestion, highlighting the importance of volume status optimisation with therapies[1,3,4]. However, diuretics dosage for adequate decongestion still remains uncertain and patients frequently present signs of congestion at discharge, which is associated with increased risk of re-hospitalisation and mortality[5].

Conversely, higher diuretic doses are associated with worsening renal function (WRF) during hospitalisation[6]. The effect of WRF on survival in ADHF patients is controversial. While recent studies confirmed the association between WRF and a worse outcome[7], other data showed that transient WRF favourably affected survival in patients with ADHF[8,9,10,11,12].

Natriuretic peptides (NPs) are powerful markers of cardiovascular risk in patients with HF and are strongly related to prognosis in patients admitted for ADHF; they reflect the congestion grade and can be helpful in guiding therapy [13,14]. One of the most important limits of NPs in the HF management is the influence of impaired renal function on their values[15]. This issue is of particular importance, because patients with ADHF often present with acute cardio-renal syndrome and significant variations in glomerular filtration rate (eGFR) frequently occur during in-hospital stay.

The prognostic value of NPs in patients with WRF during hospitalisation, such as the correlation between changes in eGFR and NPs trend have not been extensively evaluated.

Therefore, considering the possible different prognostic significance of WRF depending on the reason of its occurrence, we sought to verify if the in-hospital trends of brain natriuretic peptide (BNP) might be helpful in the stratification of patients with WRF after ADHF treatment.

Methods

Study Design

We prospectively enrolled 122 patients admitted to our Cardiovascular Department (CD) for ADHF, between December 2010 and November 2012. Brain natriuretic peptide determination and eGFR estimation within 24 hours from admission and before discharge were essential to be eligible for this study. Patients with age <18 years, volume overload for other causes (eg, cirrhosis, nephrotic syndrome), stage V chronic kidney disease (CKD) or ongoing renal replacement therapy and length of index admission <2 days were excluded.

Acute decompensated heart failure was diagnosed by the attending physicians of our CD, who were aware of BNP

values, according to current international guidelines and based on the need of intravenous furosemide administration[16].

The primary aetiology of the cardiac disease was determined and a known coronary artery disease was recorded. We further defined as new-onset HF patients admitted for a first clinical presentation with acute or slow onset (within the previous month) of symptoms, and as worsening HF the patients admitted for acute worsening of previously diagnosed chronic HF.

The patients' clinical status was assessed by clinical examination, laboratory, chest X-ray, electrocardiogram and echocardiography at baseline. Left ventricular systolic dysfunction was defined as an ejection fraction (EF) <50%. Blood samples for measurements were taken at the time of enrolment and discharge.

A complete transthoracic echocardiography was performed at baseline. Systolic and diastolic function were evaluated according to international guidelines[17].

Initial medical therapy was based on intravenous loop diuretics, vasodilators and/or inotropic agents infusion as needed. After stabilisation, oral therapies were administered according to current guidelines[16].

Patients were discharged according to the CD physicians' judgment when the treatment goals (i.e. congestion resolution with haemodynamic stability) were obtained.

The study fulfilled the conditions of the Declaration of Helsinki and was approved by the Hospital Institutional Review Board of the "Ospedali Riuniti" Hospital of Trieste (Italy). Informed consent was obtained from each patient under the institutional review board policies of hospital administration.

Endpoint

The primary endpoint was defined by the composite of death from any causes and re-hospitalisation for ADHF. Urgent heart transplantation (status 1) (HT) was considered as equivalent to death. Re-hospitalisation was defined as any unplanned admission to hospital caused by worsening symptoms of HF with signs of fluid overload, requiring an overnight stay. For patients with multiple admissions, only the first hospitalisation occurring during the period under review was considered.

Information regarding the endpoints was obtained from the patients, from their physician or from the registers of death of the municipalities of residence.

Measurements

Renal failure was defined as eGFR < 60 (ml/min/1.73m²), determined by the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation[18].

Relative changes in eGFR and BNP from admission to discharge were calculated by the formula [(pre-discharge value - admission value)/ admission value]*100.

Worsening renal function (WRF) was defined as a 20% relative decrease in eGFR (Δ eGFR) from admission to discharge[10].

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