Brief Report

N-Terminal Pro−B-Type Natriuretic Peptide (NT-proBNP) Measurements Until a 30% Reduction Is Attained During Acute Decompensated Heart Failure Admissions and Comparison With Discharge NT-proBNP Levels: Implications for In-Hospital Guidance of Treatment

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ABSTRACT

Background: A >30% N-terminal pro−B-type natriuretic peptide (NT-proBNP) reduction at discharge in acute decompensated heart failure (ADHF) predicts a favorable prognosis. To study the feasibility of guiding ADHF treatment by measuring NT-proBNP well before discharge, we assessed at which moment during hospitalization patients attain a NT-proBNP reduction of >30% (target) and whether this target is still attained at discharge.

Methods: Twenty-five consecutive ADHF patients with NT-proBNP >1,700 ng/L were included (original cohort). NT-proBNP was measured daily until the target was attained, at clinical stability, and at discharge and was analyzed as percentages of patients on target. For comparison purposes, the same analysis was performed in individual patient data from 2 other ADHF cohorts (42 and 111 patients, respectively), in which NT-proBNP was measured from admission to day 3 and at discharge.

Results: In the original cohort of 25 patients (median age 70 years, 40% male), the cumulative percentage of patients attaining the target increased gradually during admission to 22 patients (88%) in a median of 3 days (interquartile range 2−5). In the comparison cohorts, a similar course was observed in patients attaining the target before discharge. Compared with levels measured at days 2 and 3, rebound NT-proBNP increases to levels off-target at discharge were seen in up to 33% of patients in the original and comparison cohorts.

Conclusion: A target >30% NT-proBNP reduction is gradually attained before discharge, and rebound NT-proBNP increases to levels off-target occur in up to 33% of ADHF patients who initially attained target early during admission. (*J Cardiac Fail 2015;21:930−934*)

Key Words: NT-proBNP, relative reduction, serial, acute decompensated heart failure.

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Hospital admissions for acute decompensated heart failure (ADHF) are frequent and accompanied by high percentages of mortality and readmissions.[1] The best predictors of prognosis in ADHF patients appear to be plasma B-type natriuretic peptide (BNP) and the inactive N-terminal fragment of its precursor pro-BNP, NT-proBNP,[2–6] indicators of ventricular wall stretch.[7] Several studies have demonstrated that a relative NT-proBNP reduction of ≤30% at discharge for ADHF is a significant predictor of readmissions and mortality.[2,3,6,8] A role for NT-proBNP–guided ADHF treatment targeting a reduction of >30% is therefore suggested.[9] Whether an NT-proBNP target can be set at a time point well before discharge (at, eg, day 2 or 3) is unknown. The advantage of an early measurement would be to be able to adjust therapy within the usual time of admission. In contrast, an NT-proBNP measurement too early during admission may predate clinical circumstances that increase NT-proBNP levels again (such as worsening of heart failure [HF]). More NT-proBNP measurements are then warranted to ascertain that patients are discharged with a reduction of >30%.

To study the feasibility of performing an NT-proBNP measurement well before discharge with the future possibility to guide ADHF treatment targeting a >30% NT-proBNP reduction, we assessed the moment at which hospitalized patients attain this reduction and determined the percentage of patients who experienced rebound NT-proBNP increases to levels off-target at discharge.

Methods

Original Cohort

Daily NT-proBNP measurements were performed in 25 consecutive ADHF patients in a prospective substudy of the PRIMA II (hereafter named original cohort) enrolled from May 2012 to June 2013 in the Academic Medical Center in Amsterdam, The Netherlands. Rationale and design of the study have been previously reported.[9] This substudy was approved by the Medical Ethics Committee of the University of Amsterdam and Academic Medical Center, The Netherlands, and written informed consents were obtained from all patients.

From admission (day 0), daily NT-proBNP measurements were performed until a >30% reduction (target) was attained, at randomization, and at discharge. Patients were randomized on the day of clinical stability, a discharge criterion requiring the presence of 3 of 4 clinical variables.[9] No attempts were made to adjust therapy using these measurements before randomization. In patients subjected to conventional therapy, NT-proBNP measurements at randomization and discharge were blinded. In patients subjected to NT-proBNP–guided therapy, additional treatment options were reconsidered only after randomization and if applicable adjusted to attain target.

Analysis

In the original cohort, we evaluated—for each day of admission—the cumulative percentages of patients on target. Percentage of patients on target was also determined at the day of discharge. Percentages of patients that were on target at day 2 and 3 of admission but demonstrated a rebound NT-proBNP increase to levels off-target at discharge (hereafter named rebound NT-proBNP increase) were determined. Categoric variables are reported as frequencies and percentages; continuous variables are reported as mean ± SD or as median and interquartile range (IQR).

Comparison Cohorts

We analyzed individual data from 2 ADHF prospective registries for comparison of the results of the original cohort for the time-dependent course of patients attaining target during admission and rebound NT-proBNP increases between days 2 and 3 and discharge.[10,11] In the Rome cohort (n = 42), NT-proBNP was measured at admission, after 12, 24, 48, and 72 hours, and at discharge.[10] In the Brescia cohort (n = 121), NT-proBNP was measured at admission, after 6, 12, 24, and 48 hours, and at discharge.[11] We excluded 10 patients from the Brescia cohort for having a noncardiovascular cause of admission or for presence of multiple missing NT-proBNP values. Physicians in these cohorts were blinded for the NT-proBNP results.

Baseline characteristics and cumulative percentages of patients attaining target between cohorts were compared with the use of either Student *t* or Mann-Whitney *U* test where appropriate for continuous and chi-square test for categoric variables.

Results

Original Cohort

Baseline characteristics of the original cohort are listed in Table 1. None of the patients died during admission. The percentage of patients that attained the target during admission is depicted cumulatively in Figure 1. The target was gradually attained in 22 patients (88%) in a median of 3 days (IQR 2–5). Of the patients on target at days 2 and 3, 0% (0/9) and 8% (1/13), respectively, demonstrated a rebound NT-proBNP increase. In total, 4 of the patients that attained the target throughout the hospitalization demonstrated a rebound NT-proBNP increase. Clinical circumstances that could explain this NT-proBNP increase were development of a gastroenteritis (n = 1), atrial fibrillation (n = 1), cardiogenic shock after complete AV block (n = 1), and HF medication down-titration after experiencing lightheadedness (n = 1). Three patients did not attain the target during admission and discharge.

Thus, of 22 patients initially on target, 18 patients (72%) were discharged on target.

Comparison Cohorts

Baseline characteristics of the comparison cohorts are also listed in Table 1. The cohorts were heterogeneous, particularly regarding age, left ventricular ejection fraction, admission blood urea nitrogen and NT-proBNP levels, and intravenous furosemide starting doses.

Significant differences in percentages of patients attaining the target between the Rome and original cohort were observed at discharge (Fig. 2). The Brescia cohort showed significant differences in cumulative percentages of patients attaining the target at days 1 and 2 and discharge (Fig. 2). In patients that attained the target at day 2, a rebound