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CLINICAL RESEARCH

Targeting N-Terminal Pro-Brain Natriuretic Peptide in Older Versus Younger Acute Decompensated Heart Failure Patients

Susan Stienen, MD,[a] Khibar Salah, MD,[a] Luc W. Eurlings, MD,[b] Paulo Bettencourt, MD, PhD,[c] Joana M. Pimenta, MD, PhD,[c] Marco Metra, MD, PhD,[d] Antoni Bayes-Genis, MD, PhD,[e] Valerio Verdiani, MD, PhD,[f] Luca Bettari, MD,[g] Valentina Lazzarini, MD,[h] Jan P. Tijssen, PhD,[a] Yigal M. Pinto, MD, PhD,[a] Wouter E. Kok, MD, PhD[a]

ABSTRACT

OBJECTIVES The aim of this study was to analyze the prognostic value and attainability of N-terminal pro-brain natriuretic peptide (NT-proBNP) levels in young and elderly acute decompensated heart failure (ADHF) patients.

BACKGROUND Less-effective NT-proBNP-guided therapy in chronic heart failure (HF) has been reported in elderly patients. Whether this can be attributed to differences in prognostic value of NT-proBNP or to differences in attaining a prognostic value is unclear. The authors studied this question in ADHF patients.

METHODS Our study population comprised 7 ADHF cohorts. We defined absolute (<1,500 ng/l, <3,000 ng/l, <5,000 ng/l, and <15,000 ng/l) and relative NT-proBNP discharge cut-off levels (>30%, >50%, and >70%). Six-month all-cause mortality after discharge was studied for each level in Cox regression analyses, and compared between elderly (age >75 years) and young patients (age ≤75 years). Thereafter, we compared percentages of elderly and young patients attaining NT-proBNP levels (= attainability).

RESULTS A total of 1,235 patients (59% male, 45% >75 years of age) was studied. Admission levels of NT-proBNP were significantly higher in elderly versus younger patients. The prognostic value of absolute and relative NT-proBNP levels was similar in elderly and young patients. Attainability was significantly lower in elderly patients for all absolute levels and a >50% relative reduction, but not for >30% and >70%. For absolute levels, attainability differences between age groups were decreased to a large extent after correction for admission NT-proBNP and anemia at discharge. For relative levels, attainability differences disappeared after correction for HF etiology and anemia at discharge.

CONCLUSIONS In young and elderly ADHF patients, it is not the prognostic value of absolute and relative NT-proBNP levels that is different, but the attainability of these levels that is lower in the elderly. This can largely be attributed to factors other than age. (J Am Coll Cardiol HF 2016;4:736–45) © 2016 by the American College of Cardiology Foundation.

From the [a]Department of Cardiology, Academic Medical Center, Amsterdam, the Netherlands; [b]Department of Cardiology, VieCuri Medical Center, Venlo, the Netherlands; [c]Department of Internal Medicine, Hospital S. João, University of Porto Medical School, Porto, Portugal; [d]Department of Medical and Surgical Specialties, Radiological Sciences and Public Health, University of Brescia, Brescia, Italy; [e]Department of Cardiology, Hospital Universitari Germans Trias i Pujol, Barcelona, Spain; [f]Department of Internal Medicine and Emergency, Careggi University Hospital, Florence, Italy; [g]Department of Cardiology, Azienda Istituti Ospitalieri di Cremona, Cremona, Italy; and the [h]Department of Cardiology, Ospedale San Pellegrino, Castiglione delle Stiviere, MN, Italy.
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After hospital admissions for acute decompensated heart failure (ADHF) there are high percentages of mortality and readmissions (1). Both a lack in reduction in N-terminal pro-brain natriuretic peptide (NT-proBNP) levels during hospitalization and higher absolute discharge NT-proBNP levels predict a worse prognosis after discharge for ADHF (2,3). A role for NT-proBNP-guided ADHF treatment is therefore suggested (4).

Pivotal studies investigating the effect of NT-proBNP-guided treatment in chronic heart failure (HF) patients stratified by age raised the suggestion that guided therapy is less effective in elderly (>75 years of age) than in younger patients (≤75 years of age) (5,6). In contrast, another study observed no interaction between age and treatment allocation for outcome (7). Nonetheless, 2 meta-analyses demonstrated that the beneficial effect of NT-proBNP guidance on reduction of all-cause mortality was only seen in patients ≤75 years of age (8,9). Subsequently, the use of age-adjusted natriuretic peptide targets in future HF trials has been proposed (10). At present, it is not clear whether this lesser effectivity can be attributed to age itself, with different comorbidities (11,12), to a difference in prognostic value of an NT-proBNP target (13), or to a difference in attaining a prognostic value (14).

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In ADHF patients, it is currently not known whether NT-proBNP–guided treatment is effective, and whether differences in effect of guiding should be expected for young and elderly patients. In ADHF patients, age >75 years predicts short-term prognosis after discharge (3,15), and—although there is a clear association between age and NT-proBNP suggestive of an interaction (16)—any interaction between age and NT-proBNP levels has not been reported thus far.

To define possible age-dependent differences in NT-proBNP–related outcomes in an ADHF population, we addressed the following questions. First, does attaining a certain NT-proBNP level or percentage NT-proBNP reduction at discharge provide the same prognostic information for young and elderly ADHF patients? Second, does attainability of discharge NT-proBNP cut-off levels differ between young and elderly patients, even without the effect of guiding therapy?

We studied these questions in 2 predefined age groups (≤75 years and >75 years) in a large database of 7 prospective European registries of ADHF patients.

METHODS

DATA SOURCES. The study cohort was assembled from individual patient data from 7 ADHF cohorts (N = 1,301). Details of the source gathering and development of the final database have been reported previously (3). For the present study, unique patients were included with NT-proBNP measurements available at admission and discharge (N = 1,235). Data on all-cause mortality and cardiovascular readmissions within 6 months after discharge was present for all patients. All studies were approved by the ethical commission in their respective centers. Demographic characteristics are presented as frequencies and percentages for categorical data, and compared using Fisher exact test. Normally distributed, continuous variables are reported as mean ± SD, and were compared using the Student *t* test. Not normally distributed continuous variables, expressed as median with interquartile ratio (IQR), were compared using the Mann-Whitney U test.

DATA ANALYSIS. All patients were categorized as being discharged with absolute discharge NT-proBNP levels of <1,500 ng/l, <3,000 ng/l, <5,000 ng/l, and <15,000 ng/l, and with relative NT-proBNP reductions of >30%, >50%, and >70% from admission to discharge (17).

The endpoint was all-cause mortality within 6 months after discharge. The distribution of the endpoint among the above-mentioned categories of absolute discharge and relative reduction levels was studied for young (age ≤75 years) and elderly (age >75 years) patients using Fisher exact test. A cut-off level of 75 years for age was used in this study as this was the cut-off in previous studies indicating a difference in effect of NT-proBNP–guided therapy in chronic HF patients (5,6,8,9), as well as having significance to prognosis in studies on ADHF-related outcome (3,15).

To compare the risk of 6-month all-cause mortality in young and elderly ADHF patients associated with several NT-proBNP cut-off levels, we calculated adjusted hazard ratios (HRs), and 95% confidence intervals using Cox proportional hazards regression models for each absolute and relative NT-proBNP level. Our aim was to construct models to study the potential effect of guidance on prognosis using a single NT-proBNP cut-off level, and not to determine independent predictors for prognosis. Therefore, only 1 NT-proBNP level was added per model. This in contrast to the European collaboration on acute

ABBREVIATIONS AND ACRONYMS

ACEI = angiotensin-converting enzyme inhibitor

ARB = angiotensin II receptor blocker

ADHF = acute decompensated heart failure

eGFR = estimated glomerular filtration rate

Hb = hemoglobin

HF = heart failure

HR = hazard ratio

IQR = interquartile range

LVEF = left ventricular ejection fraction

NYHA = New York Heart Association functional class

SBP = systolic blood pressure