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Clinical research

NT-proBNP testing for diagnosis and short-term prognosis in acute destabilized heart failure: an international pooled analysis of 1256 patients

The International Collaborative of NT-proBNP Study

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Methods

Component studies

The study population consisted of patients from three previously reported prospective clinical trials of NT-proBNP testing from Christchurch, New Zealand, Barcelona, Spain, and Boston, MA, USA, each performed to explore the use of NT-proBNP testing in dyspnoeic Emergency Department (ED) patients.[1,7,8] All three prospective trials had compatible inclusion/exclusion criteria and obtained similar clinical information. In addition, prospectively gathered data from 367 patients in a previously unpublished registry of patients with acute HF enrolled at the University Hospital of Maastricht, The Netherlands were included to complete the International Collaborative of NT-proBNP (ICON) data set.

The Christchurch study[8] comprised 205 patients presenting with dyspnoea to the ED. In this trial, the results of blinded NT-proBNP concentration were compared with a final adjudicated diagnosis, rendered utilizing the European Society of Cardiology Guidelines.[6] For the purposes of the present study, 195 subjects had complete data and were included for analysis. The Barcelona study[7] comprised 100 dyspnoeic patients presenting to the ED, and blinded NT-proBNP results were subsequently compared with the final diagnosis, which was assigned by a panel of physicians utilizing all available clinical data pertaining to each subject. Of the original 100 patients, 95 had complete data and were included in this study. Similar to the earlier trials, the ProBNP Investigation of Dyspnoea in the Emergency Department (PRIDE) study[1] was a prospective, blinded

NT-proBNP testing

For each trial, blood was collected into EDTA tubes and NT-proBNP was measured using a validated, commercially available immunoassay (Elecsys® ProBNP, Roche Diagnostics, Indianapolis, IN, USA), using established methodology. This assay has been reported to have $<0.001\%$ cross-reactivity with bioactive BNP, and in the constituent studies in this report, this assay had inter-run coefficients of variation ranging from 0.9 to 5.5%. For the purposes of this report, NT-proBNP levels are expressed in pg/mL (to convert pg/mL to pmol/L, multiply by 0.118).

Measurement of troponin T (cTnT, Troponin T Stat®, Roche Diagnostics) was performed at each institution using standard methodology.

Statistical analysis

Comparisons of clinical characteristics between patients across all four studies were performed utilizing χ^2 tests for categorical data and the Wilcoxon rank sum test for continuous data. Similar methods were subsequently used to compare clinical characteristics between patients with and without acute HF in the final pooled analysis. Correlations between left ventricular ejection fraction and log-transformed NT-proBNP concentrations were performed using Spearman correlation. Comparisons of NT-proBNP levels between groups categorized by NYHA symptom severity and by final diagnostic categories were performed using the Kruskal–Wallis test. For these analyses, SPSS software (SPSS Inc., Chicago, IL, USA) was used.