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The Journal of Heart and Lung Transplantation

http://www.jhltonline.org

Prognostic utility of the Seattle Heart Failure Score and amino terminal pro B-type natriuretic peptide in varying stages of systolic heart failure

Christopher Adlbrecht, MD,[a] Martin Hülsmann, MD,[a] Stephanie Neuhold, MD,[b] Guido Strunk, PhD,[c] and Richard Pacher, MD[a]

From the Departments of [a]Internal Medicine II, Division of Cardiology; [b]Anesthesia, Division of Cardio-Thoracic-Vascular Anesthesia and Intensive Care Medicine, Medical University of Vienna; and the [c]Complexity-Research, Research Institute for Complex Systems, Vienna, Austria.

KEYWORDS:
heart failure;
cardiac transplantation;
natriuretic peptide;
Seattle Heart Failure Score

BACKGROUND: Cardiac transplantation represents the best procedure to improve long-term clinical outcome in advanced chronic heart failure (CHF), if pre-selection criteria are sufficient to outweigh the risk of the failing heart over the risk of transplantation. Although the cornerstone of success, risk assessment in heart transplant candidates is still under-investigated. Amino terminal pro B-type natriuretic peptide (NT-proBNP) is regarded as the best predictor of outcome in CHF, and the Seattle Heart Failure Score (SHFS), including clinical markers, is widely used if NT-proBNP is unavailable.

METHODS: The present study assessed the predictive value for all-cause death of the SHFS in CHF patients and compared it with NT-proBNP in a multivariate model including established baseline parameters known to predict survival.

RESULTS: A total of 429 patients receiving stable HF-specific pharmacotherapy were included and monitored for 53.4 ± 20.6 months. Of these, 133 patients (31%) died during follow-up. Several established predictors of death on univariate analysis proved significant for the total study cohort. Systolic pulmonary arterial pressure (hazard ratio [HR], 1.03; 95% confidence interval [CI], 1.02–1.05); $p < 0.001$, Wald 15.1), logNT-proBNP (HR, 1.51; 95% CI, 1.22–1.86; $p < 0.001$, Wald 14.9), and the SHFS (HR, 0.99; 95% CI, 0.99–1.00; $p < 0.001$, Wald 12.6) remained within the stepwise multivariate Cox regression model as independent predictors of all-cause death. Receiver operating characteristic curve analysis revealed an area under the curve of 0.802 for logNT-proBNP and 0.762 for the SHFS.

CONCLUSIONS: NT-proBNP is a more potent marker to identify patients at the highest risk. If the NT-proBNP measurement is unavailable, the SHFS may serve as an adequate clinical surrogate to predict all-cause death.

J Heart Lung Transplant 2013;32:533–538

On the one hand, chronic heart failure (CHF) therapy consists of lifestyle modification and medical therapy for all patients.[1] On the other hand, specific forms of therapy exist where patient selection is of the uttermost importance.[2–4] One of these options is heart transplantation (HTX), an established treatment for end-stage HF.[5,6] The success of HTX is markedly influenced by 3 components: death on the waiting list, perioperative risk, and long-term risk mainly caused by immunosuppressive therapy. HTX is indicated

Reprint requests: Martin Hülsmann, MD, Department of Internal Medicine II, Division of Cardiology, Medical University of Vienna, Waehringer Guertel 18-20, 1090 Vienna, Austria. Telephone: +43-1-40400-4614. Fax: +43-1-40400-4216.

E-mail address: martin.huelsmann@meduniwien.ac.at

1053-2498/$ - see front matter
http://dx.doi.org/10.1016/j.healun.2013.01.1048

only if these risks are outweighed against the risk of the natural course of the disease.

Although the cornerstone of success, risk assessment in HTX candidates is still under-investigated. Peak oxygen consumption is the only objective parameter in the guidelines for HTX indication, although for years other markers have been proven to be superior.[7] This is a serious cause of concern, because the scarcity of available donor organs should mandate optimal host selection. Patient selection for ventricular assist device implantation may represent a similar challenge.[8]

The Seattle Heart Failure Score (SHFS) includes several variables to estimate risk in HF patients[9] and has been shown to have excellent predictive value of event-free survival under contemporary HF-specific medical treatment in a heterogenous population of HF patients.[10] The SHFS is already widely used, and its components are easily available in the special setting of HTX in clinical routine.[11–13] Within a broad collective of severity of disease, combining the SHFS with biomarkers improved its predictive value.[14] Unfortunately, the SHFS overestimated life expectancy in distinct populations with CHF.[15]

The aim of the present study was to assess the predictive value of the SHFS for all-cause death in HF patients and compare it with amino terminal pro B-type natriuretic peptide (NT-proBNP). We focused on severely symptomatic patients because the decision for surgical intervention is most critical in this population.

Methods

This study was approved by the Medical University of Vienna Ethics Board (EK-No. 1454/2012). Owing to the retrospective nature of this study in severely ill HF patients, the study-authorizing entity did not require informed consent.

Patients

This retrospective study included consecutive patients with a broad spectrum of severity of CHF under stable HF-specific medical therapy who were treated at the HF specialist outpatient clinic of the Medical University of Vienna between May 2006 and July 2008. Patients included had a documented abnormal left ventricular (LV) function, defined as an LV ejection fraction (LVEF) $\leq 40\%$ within the last 6 months.[16] The variables included in this analysis were obtained at the baseline assessment of each patient.

The SHFS was calculated using an online tool available at http://depts.washington.edu/shfm/app.php.

Patient baseline characteristics (Table 1), results of echocardiographic examinations, including systolic pulmonary arterial pressure (sPAP) and LVEF, and laboratory test results were entered into a database. NT-proBNP was determined by the Elecsys Test (Roche Diagnostics, Mannheim, Germany). Comorbidities of HF patients were defined according to current guidelines: Anemia was defined as a hemoglobin concentration <13 g/dl in men and 12 g/dl in women, and chronic obstructive pulmonary disease was assessed as described elsewhere.[17] History of chronic kidney disease was derived from patient records. Central Office of Civil Registration (Zentrales Melderegister Oesterreich) data were used to confirm survival status of the patients.

Statistical methods

Categoric variables are described by frequency and percentage. Continuous variables with symmetric distributions are described by means $\pm$ standard deviations. For continuous variables with skewed distributions, we used medians and interquartile range (25th, 75th percentiles) to describe their distribution.

Baseline variables with known predictive value were analyzed within our patient population by univariate Cox regression analyses. Variables demonstrating significance in univariate analysis were entered into the stepwise multivariate Cox regression model if they were not already part of the SHFS. Risk is expressed as hazard ratio (HR), 95% confidence interval (CI), and p-value. Parameters were plotted as receiver operating characteristic (ROC) curves to illustrate their performance as binary classifier system and the individual discrimination threshold. This was a retrospective data analysis of a prospectively maintained database, and no sample size calculation was performed. A post hoc power analysis was not performed because the HR for the end point all-cause death confirmed the adequacy of the sample size. SPSS 16.0 software (SPSS, Chicago, IL) was used for all statistical analyses. Two-sided p-values < 0.05 were considered significant.

Results

Patient outcome

The study included 429 patients, and only 1 was lost to follow-up. Patients had received HF-specific pharmacotherapy according to current guidelines for at least 3 months before inclusion.[16] Patient baseline characteristics are presented in Table 1. Right ventricular dysfunction, defined as any reduction in systolic right ventricular function, was detected in 77 patients (18%). The sPAP could not be determined in 212 patients (49%). The assessment of sPAP was more often feasible in patients with New York Heart Association (NHYA) class III to IV (58%) than in patients with NYHA class I or II (44%, $p = 0.004$). Patients initially included had a documented reduced LVEF of $\leq 40\%$ in their history for the diagnosis of systolic HF. At the index evaluation, 49 patients had recovered to an LVEF $> 55\%$, having improved under stable HF-specific medical therapy. LVEFs of patients with mild to moderate HF compared with those with severe HF symptoms are reported in Table 1. During the observation period of 53.4 $\pm$ 20.6 months, 133 patients (31%) died, 11 (3%) underwent HTX, and 9 (2%) received a ventricular assist device.

Predictors for the total study cohort

Univariate Cox regression analyses and the multivariate model for predicting all-cause death in all study patients are presented in Table S2 (available on the JHLTonline.org Web site) and Table 2, respectively. sPAP (HR, 1.03; 95% CI, 1.02–1.05; $p < 0.001$, Wald 15.1), logNT-proBNP (HR, 1.51; 95% CI, 1.22–1.86; $p < 0.001$, Wald 14.9), and the SHFS (HR, 0.99; 95% CI, 0.99–1.00; $p < 0.001$, Wald 12.6) remained within the stepwise Cox regression model as independent predictors of all-cause death. Because sPAP is often unavailable in clinical research and even more so in