The Munich Score: A Clinical Index to Predict Survival in Ambulatory Patients With Chronic Heart Failure in the Era of New Medical Therapies

Hans-Ulrich Stempfle, MD, PhD,[a,b] Andrea Alt, MD,[b] Jutta Stief, MD,[b] and Uwe Siebert, MD, PhD[c,d]

Background: Risk stratification in patients with congestive heart failure (CHF) is an obligatory part of the heart transplantation (HTx) selection process. New medical therapies and the predictive value of hemodynamic changes over time have not been adequately taken into account in previous stratification models. In this study we assessed the prognostic value of 55 variables at baseline and 9 variables representing changes of hemodynamic parameters over time.

Methods: A total of 178 patients with CHF were examined on 3.4 ± 2.6 occasions (mean follow-up 19 ± 19 months). Using the Cox proportional hazards model, univariate and multivariate relative risks (RRs) with 95% confidence intervals (CI) were determined for predicting event-free survival. A prognostic score (Munich score) was derived from the multivariate Cox model and three risk groups were derived.

Results: During follow-up, 23 patients (13%) died and 63 (35%) underwent HTx. The univariate analysis yielded 21 statistically significant ($p < 0.05$) predictors of event-free survival. However, only four baseline variables (etiology of ischemic cardiomyopathy, systolic blood pressure, left ventricular [LV] end-diastolic diameter, maximal workload) and the change over 12 months in fractional shortening remained statistically significant ($p < 0.05$) in the multivariate Cox model and were used for the prognostic score. Within 12 months, no event occurred in the low-risk group, 8.1% in the intermediate, and 30.1% in the high-risk group.

Conclusions: The incorporation of changes over time in hemodynamic parameters allowed for an improved baseline risk stratification model for the HTx selection process, especially in the era of new medical therapies such as β-blocker therapy. All significant variables of the Munich score can be obtained in routinely performed non-invasive tests. J Heart Lung Transplant 2008;27:222–8. Copyright © 2008 by the International Society for Heart and Lung Transplantation.

Careful pre-transplant risk stratification should be an obligatory part of the transplant candidate selection process due to the increasing number of patients with advanced congestive heart failure (CHF) and the limited number of organs.[1]

The heart failure survival score (HFSS), a prospectively validated clinical index, is still a widely used instrument to assess risk stratification in patients with advanced heart failure.[2] However, two factors—the changes in medical treatment of CHF since 1995 and the predictive value of hemodynamic changes over time—are not adequately taken into account in the HFSS stratification model.[3] For example, only 10% of the original cohorts from which the HFSS was derived were receiving β-blocking drugs.

A re-evaluation of the HFSS in patients on β-blocker therapy showed that the previous statistically different event-free survival between low-, medium- and high-risk patients is only valid between a low- and high-risk group.[4] Therefore, the threshold values of the risk groups need redefinition, or a β-blocker therapy should be included as parameter of the HFSS. Furthermore, there are varying results on the predictive values of peak Vo_2—a parameter that has served alone or in combination with other variables as a marker for the optimal timing of heart transplantation (HTx)—in patients receiving β-blocker therapy.[5–8] The Seattle Heart Failure Model, which provides survival rates based on 24 clinical, pharmacologic, device and laboratory characteristics, attempted to overcome the aforementioned

From the [a]Department of Internal Medicine, Asklepios Stadtklinik Bad Tölz; [b]Department of Cardiology Med. Poliklinik-Innenstadt Munich, Germany; [c]Institute for Technology Assessment, Massachusetts General Hospital, Harvard Medical School, Boston, MA, and [d]Department of Public Health, Medical Decision Making and Health Technology Assessment, UMIT-University of Health Sciences, Medical Informatics and Technology, Tyrol, Austria.

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Reprint requests: Hans-Ulrich Stempfle, MD, Department of Cardiology, Medizinische Poliklinik-Innenstadt, Ludwig-Maximilians University Munich, Ziemssenstrasse 1, 80336 Munich, Germany. Telephone: +49-89-5160-2497. Fax: +49-89-5160-4483. E-mail: u.stempfle@asklepios.com

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limitations.[9] Developed retrospectively among clinical trial patients, the value of the Seattle model still needs to be validated among general CHF patients. Therefore, a clinically practical model combining independent baseline characteristics with serial changes of hemodynamic parameters over time is needed in the current CHF treatment era.[10–13]

The aim of our study was to evaluate the prognostic value of clinical characteristics at baseline and variables representing changes of hemodynamic parameters over time in ambulatory patients with CHF. Furthermore, we sought to develop a multivariate prognostic score (Munich score) to guide the decision on HTx.

METHODS

Study Population

We conducted a cohort study with 178 consecutively enrolled patients with CHF (New York Heart Association [NYHA] Functional Classes I to IV, age <70 years) and left ventricular ejection fraction (LVEF) <45%. At baseline, all patients were referred to the Department of Cardiology, Medical Policlinic-Innenstadt, Ludwig Maximilians University, Munich, for assessment of heart failure status and/or evaluation of potential candidacy for heart transplantation between January 1999 and March 2004. All patients had to be in a stable condition for at least 4 weeks, with the medication individually optimized before assessment of the variables outlined subsequently. The study was conducted according to the principles of the Declaration of Helsinki and was approved by the ethics review board of the University of Munich. Written informed consent for participation was obtained from all subjects.

Clinical Measurements

Clinical parameters included history, physical examination, blood chemistry and electrocardiographic data.

Hemodynamic Measurements

Echocardiography. Transthoracic echocardiograms were obtained using a commercially available sector scanner (Sonos 5500, Philips GmbH, Böblingen, Germany) with a 2.5-MHz transducer. Left atrial size, left ventricular end-diastolic diameter (LVEDD) and left ventricular end-systolic dimension (LVESD) were measured from M-mode tracings of parasternal long- and short-axis views. Fractional shortening (FS) was calculated as the percentage of systolic fall in left ventricular dimension with respect to end-diastolic diameter. LVEF was derived from apical 2- and 4-chamber views according to the modified Simpson rule.

Radionuclide ventriculography. Radionuclide ventriculography studies were performed at rest by in vivo red blood cell labeling. Sn-Agens was injected intravenously. After 20 minutes, patients were placed upright in front of a multi-crystal camera (Picker SIM 400) that was equipped with a low-energy, high-sensitivity, parallel-hole collimator in approximately 30° right anterior oblique projection. Next, 740 MBq of 99m-technetium-pertechnetate was injected. First-pass right ventricular ejection fraction (RVEF) was calculated using a single region of interest (ROI), and first-pass left ventricular ejection fraction (LVEF) by a dual-ROI method. After first pass acquisition, patients were positioned supine on a scanning couch for a planar multiple-gated acquisition (MUGA) scan (Picker Prism 2000, low-energy, high-resolution collimator, 40° LAO projection). MUGA LVEF was calculated by the dual-ROI method.

Cardiopulmonary exercise test. All patients underwent an incremental cardiopulmonary exercise test (CPX) on a bicycle ergometer. Heart rate, blood pressure and a 12-lead electrocardiogram were obtained at rest, at each exercise stage, and during the 5-minute post-exercise phase. Oxygen consumption (V_{O_2}), carbon dioxide production (V_{CO_2}), minute ventilation (V_E), breathing rate, respiratory rate exchange ratio and ventilatory equivalents for O_2 (V_E/V_{E_2}) and CO_2 (V_E/V_{CO_2}) were measured continuously using a moving average for eight breaths (Oxycon-alpha; Jaeger, Würzburg, Germany). Peak V_{O_2} was defined as the highest V_{O_2} observed during the exercise test. Age-, gender- and weight-adjusted predicted V_{O_2} values were determined using the Wasserman formulas. The anaerobic threshold was calculated using the V-slope method. Respiratory effort was evaluated by the Borg scale.

Serial Measurements, Predictors, Clinical Follow-up and End-point

Patients received a prospective follow-up every 6 months to repeat the clinical and hemodynamic measurements. Variables representing changes over time were created by calculating the difference between the baseline and the 12-month values. For potential predictors of event-free survival the baseline variables and variables representing changes over time were selected. Outcome events were defined as UNOS 1 transplant (i.e., receiving mechanical or inotropic support before transplantation) or death without transplant. All patients who received a cardiac transplant (UNOS 2) were considered survivors until the date of their transplantation. For patients who remained alive and non-transplanted, follow-up was discontinued (censored) on March 31, 2006.

Statistical Analysis

The prognostic score was developed in three steps. First, we performed a series of univariate Cox regres-