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Predictors of In-Hospital Mortality in Patients Hospitalized for Heart Failure

Insights From the Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients With Heart Failure (OPTIMIZE-HF)

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Objectives The aim of this study was to develop a clinical model predictive of in-hospital mortality in a broad hospitalized heart failure (HF) patient population.

Background Heart failure patients experience high rates of hospital stays and poor outcomes. Although predictors of mortality have been identified in HF clinical trials, hospitalized patients might differ greatly from trial populations, and such predictors might underestimate mortality in a real-world population.

Methods The OPTIMIZE-HF (Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure) is a registry/performance improvement program for patients hospitalized with HF in 259 U.S. hospitals. Forty-five potential predictor variables were used in a stepwise logistic regression model for in-hospital mortality. Continuous variables that did not meet linearity assumptions were transformed. All significant variables ($p < 0.05$) were entered into multivariate analysis. Generalized estimating equations were used to account for the correlation of data within the same hospital in the adjusted models.

Results Of 48,612 patients enrolled, mean age was 73.1 years, 52% were women, 74% were Caucasian, and 46% had ischemic etiology. Mean left ventricular ejection fraction was 0.39 ± 0.18. In-hospital mortality occurred in 1,834 (3.8%). Multivariable predictors of mortality included age, heart rate, systolic blood pressure (SBP), sodium, creatinine, HF as primary cause of hospitalization, and presence/absence of left ventricular systolic dysfunction. A scoring system was developed to predict mortality.

Conclusions Risk of in-hospital mortality for patients hospitalized with HF remains high and is increased in patients who are older and have low SBP or sodium levels and elevated heart rate or creatinine at admission. Application of this risk-prediction algorithm might help identify patients at high risk for in-hospital mortality who might benefit from aggressive monitoring and intervention. (Organized Program to Initiate Lifesaving Treatment In Hospitalized Patients With Heart Failure [OPTIMIZE-HF]; NCT00344513) (J Am Coll Cardiol 2008;52:347–56) © 2008 by the American College of Cardiology Foundation

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Abbreviations and Acronyms

CART = classification and regression tree

HF = heart failure

LVEF = left ventricular ejection fraction

LVSD = left ventricular systolic dysfunction

SBP = systolic blood pressure

SCr = serum creatinine

Acute decompensated heart failure (HF) requiring hospitalization is common and has been steadily increasing: in 2004, there were more than 1 million HF discharges in the U.S., an increase of 175% since 1979 (1). Despite the prevalence of acute HF, research efforts over the last 15 years have focused primarily on chronic HF. As a result, few studies have been conducted specifically in the hospitalized HF population, and data describing clinical characteristics and outcomes for these patients have been lacking.

The increasing incidence and associated morbidity and mortality of acute HF create an urgent need to better understand this patient population. Because risk-prediction models are useful for focusing on factors influencing clinical outcomes, several analyses have been conducted to determine mortality risk after hospitalization for HF, with both clinical trial and administrative databases (2–7). Clinical trial datasets have contributed valuable information, but their general applicability is limited because these trials reflect a select patient group and the findings of risk-prediction models generated from these databases might or might not apply to a broader population (8). Whereas administrative datasets might not adequately capture clinical variables of prognostic importance, observational registries are a useful data source for evaluating event rates and developing risk-prediction models across a representative patient spectrum. With this in mind, an analysis of the OPTIMIZE-HF (Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure) registry database was conducted to identify predictors of in-hospital mortality in a large, unselected sample of observed patients hospitalized with HF and to develop a practical risk-prediction tool that could be applied in routine clinical practice.

Methods

The OPTIMIZE-HF registry is a national hospital-based registry and quality-improvement program conducted in 259 hospitals across the U.S. The rationale and design have been discussed in detail elsewhere and will be summarized here (9–11). The primary objective of the program was to improve medical care and education given to HF patients by accelerating the initiation of evidence-based, guideline-recommended HF therapies. The OPTIMIZE-HF registry combined a web-based registry data collection tool with a process-of-care intervention that included standing orders, algorithms, and care paths that encouraged the use of evidence-based therapies for all eligible patients (9). The web-based registry collected data on all Joint Commission on Accreditation of Healthcare Organizations performance measures, and these data were available for sites to review and analyze in real time. The registry data coordinating center was Outcome Sciences, Inc. (Cambridge, Massachusetts).

Patients were eligible for registry enrollment if they were ≥18 years of age and the primary reason for their hospital admission was new or worsening HF or if they developed significant HF symptoms during their hospitalization, even if HF was not the reason for their initial admission but was the primary discharge diagnosis (9). The registry enrolled consecutive patients and included patients with left ventricular systolic dysfunction (LVSD), defined as a left ventricular ejection fraction (LVEF) <40% or moderate/severe left ventricular dysfunction by qualitative report; those with preserved systolic function, defined as LVEF ≥40% or qualitatively normal left ventricular function; and those without ventricular function measured. Baseline characteristics, treatment patterns, and in-hospital outcomes were collected on all patients participating in the study. Admission staff, medical staff, or both recorded race/ethnicity, usually as the patient was registered. Prior studies in patients hospitalized with HF have suggested differences in characteristics and outcomes on the basis of race/ethnicity. Automated electronic data checks were used to prevent out-of-range entry or duplicate patients. A database audit was performed, on the basis of predetermined criteria, of a random sample of 5% of the first 10,000 patients verified against source documents (10,11). The protocol was approved by each participating center's institutional review board or through use of a central institutional review board.

Statistical methods. All statistical analyses were performed independently by the Duke Clinical Research Institute, Durham, North Carolina. Data are reported as mean ± SD for continuous variables or percentages of patients with nonmissing values for categorical variables. A logistic model was developed to identify significant predictors of in-hospital mortality. Deaths beyond the first 120 days of hospitalization were censured. There were 30 patients where vital status was missing. Forty-five candidate predictor variables were considered in the model (Table 1). The final model was derived in the population of patients without missing data for any variable retained in the model (Fig. 1). These baseline clinical and treatment factors were applied with both stepwise and backward variable selection techniques with a p value of 0.05 as criteria for both entering and remaining in the model. The restricted cubic spline transformation method was used to determine the functional form for continuous variables. The most common transformation applied for modeling was piecewise linear splines. The final model was repeated with generalized estimating equations to account for the correlation of data within the same hospital in the adjusted models. The final model presented is based on the model including the hospital effect. The SAS statistical software, version 8.2 (SAS Institute Inc., Cary, North Carolina) was used for all statistical analyses.