A Simple Risk Score to Predict In-Hospital Death of Elderly Patients With Acute Decompensated Heart Failure

—— Hypoalbuminemia as an Additional Prognostic Factor ——

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Background: Risk stratification for elderly patients with acute decompensated heart failure (ADHF) may help clinicians to select the appropriate therapy and raise the quality of care.

Methods and Results: The present study enrolled 349 patients aged over 65 years who were hospitalized with ADHF from January 2004 to October 2008. Five independent prognostic factors were identified by multivariate logistic regression analysis, and each factor was assigned a number of points proportional to its regression coefficient: prior heart failure hospitalization (2 points), sodium ≤138 mmol/L (2 points), BUN ≥35 mg/dl (2 points), albumin ≤3.2 g/dl (3 points), and BNP ≥980 pg/ml (2 points); in particular, hypoalbuminemia was identified as the strongest prognostic factor. The patients were stratified into 3 groups: low risk (0–4 points), moderate risk (5–7 points), and high risk (8–11 points). The respective in-hospital mortality rates were 1.6%, 15.8%, and 42.1% (P<0.05).

Conclusions: In addition to known prognostic factors, hypoalbuminemia may provide important information for elderly patients with ADHF. A simple risk score may help to stratify the risk of in-hospital mortality and contribute to better clinical management of these elderly patients.  (Circ J 2009; 73: 2276–2281)

Key Words: Acute decompensated heart failure; Elderly; Hypoalbuminemia; Risk stratification

People aged 65 years and older are the fastest growing segment of the population, and the prevalence of heart failure (HF) increases with advancing age. In recent years, HF has become the leading cause of hospitalization in adults over 65 years and is associated with high morbidity and mortality, which imposes a considerable burden on the healthcare system. Despite major advances in therapy, patients with advanced HF have poor prognosis. In a large population-based study, the 5-year survival following first admission for HF was worse than that for most common cancers. Recent guidelines support that patients with advanced HF whose symptoms and clinical status have progressed despite maximal medical therapy should be offered palliative care as the optimal treatment. However, advance planning of end-of-life care is less discussed at hospital admission of elderly patients with HF than with cancer patients. For one thing, there are few useful methods of assessing prognosis in these patients. Several prior studies have developed prognostic risk score models that predict in-hospital mortality in patients hospitalized with acute decompensated HF (ADHF); however, these models are not targeted at the very old patient population, and frequently require access to a computer or an electronic calculator to generate the score. Therefore, the purpose of this present study was to develop a simple risk score model for predicting in-hospital mortality in elderly patients with ADHF.

Methods Data Collection A detailed retrospective chart review was conducted for 349 patients aged 65 years and older who were hospitalized in Tottori University hospital with a primary diagnosis of ADHF from January 2004 to October 2008. ADHF is defined as new-onset decompensated HF or decompensation of chronic HF, and new-onset acute coronary syndrome was excluded. HF was defined according to the Framingham criteria, together with other clinical findings, including pulmonary congestion on X-ray or pulmonary hypertension evaluated by Doppler echocardiography. Patients with severe renal failure who receive dialysis were included.

Received July 8, 2009; accepted August 12, 2009; released online October 13, 2009
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Medical records were retrospectively reviewed with regard to demography, medical history, etiology of HF, comorbidities, laboratory data at the time of hospital admission, pre-hospital medication, and in-hospital outcome. The underlying cause of HF was classified as ischemic or non-ischemic heart disease. Ischemic heart disease was considered as the etiology of HF if the patients had 1 of the following: a history of myocardial infarction (MI), angina or prior coronary revascularization, pathologic Q waves on ECG, or >75% stenosis in 1 or more coronary arteries on coronary angiography.\textsuperscript{11} Left ventricular function was determined by echocardiography performed on hospital admission. Left ventricular systolic dysfunction was defined as a left ventricular ejection fraction (LVEF) <40\% or, if not quantified, visual assessment of moderate/severe left ventricular dysfunction as previously described.\textsuperscript{7} LVEF was calculated by using the M-mode Teichholz method or modified Simpson method. The cause of death was classified as cardiac, stroke/vascular, or non-cardiovascular based on the clinical information. Death from cardiac cause was defined as death from HF, sudden cardiac death or MI that occurred during hospitalization. Death from stroke/vascular cause was defined as death from stroke or other vascular diseases. Death from non-cardiovascular cause was defined as death from non-cardiovascular diseases such as infection, renal failure, lung disease, and cancer. The study was approved by the institutional Review Board for Human Investigation.

### Statistical Analysis

Continuous variables are expressed as mean±SD, whereas categorical variables are expressed as percentages. Comparisons of 2 groups were made using Student’s t-test for continuous variables and the $\chi^2$ test for categorical variables. We performed forward, stepwise multivariate logistic regression analyses to determine the independent predictors of in-hospital mortality. We entered age, sex, and all clinical variables associated with in-hospital mortality in the univariate analysis (P<0.05: a strict level was applied because of the relatively small samples of in-hospital mortality) into the multivariate model. Finally, a clinical risk score was created using identified independent predictors of in-hospital mortality that were dichotomized at cutoff points. The cutoff point for each variable was determined by receiver-operator characteristic (ROC) curves. Each predictor was assigned a number of points proportional to its regression coefficient, as previously described.\textsuperscript{12} A risk score was assigned to each subject by adding up the points for each risk factor present. Subjects were then divided into 3 groups according to their risk scores. The area under the ROC curves (AUC) was used to assess the performance of the model in predicting in-hospital mortality. A P value...
All analyses were performed using SPSS version 11.5 J (SPSS, Inc, Chicago, IL, USA).

**Results**

Baseline patients’ characteristics are shown in Table 1. The mean age of the overall cohort was 79±6 years, and 56% were male. The prevalence of ischemic heart disease was 28.4%. Systolic dysfunction was relatively less prevalent (34.4%), which suggested that HF with preserved systolic function was more common in this cohort. Hypertension (46.9%) was the most common comorbidity, followed by atrial fibrillation (43.0%). Angiotensin-receptor blockers (ARB) (37.5%) were more likely to be administered to this patient population than angiotensin-converting enzyme inhibitors (ACEI: 26.9%). The β-blockers and spironolactone were administered to 31.8% and 26.9% of patients, respectively. The in-hospital mortality rate was 9.7% (n=34); cardiac: 4.6% (n=16), stroke/vascular: 0.9% (n=3), and non-cardiovascular: 4.3% (n=15). The mean and median length of hospital stay was 34±32 days and 25 (interquartile range: 16–41) days, respectively.

The characteristics of the 2 groups (survivors and non-survivors) during hospital stay are also shown in Table 1.

Patients in the non-survival group (in-hospital mortality) more often had a history of prior HF hospitalization and received spironolactone before hospital admission. In the non-survival group, blood pressure, hemoglobin, serum sodium, and serum albumin were significantly lower, whereas blood urea nitrogen (BUN), serum creatinine, C-reactive protein (CRP), and BNP were significantly higher compared with the survival group. The mean length of hospital stay in the non-survival group was significantly longer compared with the survival group. Candidate variables associated with in-hospital mortality in the univariate analysis (P<0.05) are shown in Table 2. Multivariate logistic regression analysis identified previous hospitalization for HF, lower serum sodium and albumin concentrations, and elevated BUN and BNP concentrations as independent predictors of in-hospital mortality (Table 2). Lower systolic blood pressure tended to be associated with in-hospital mortality, but did not reach statistical significance (P=0.06). A risk score was developed by using these variables, which were dichotomized at cutoff points derived from the ROC curves. The optimal cutoff point of each prognostic factor and its predictive ability is shown in Table 3.

Other abbreviations see in Tables 1, 2.
Risk Stratification of Elderly Patients With ADHF

≤3.2 g/dl (3 points), BUN ≥35 mg/dl (2 points), and BNP ≥980 pg/ml (2 points) (Table 4). The regression coefficient of albumin was approximately 1.5, whereas for the other variables it was approximately 1. Thus we assigned 3 points to albumin, and 2 points to the other variables. The ROC curve for the risk score model is shown in Figure 1. The AUC for the risk score model was 0.86. We calculated a risk score for each patient by adding the points of each risk factor and stratified the patients into 3 groups: low risk (0–4 points; n=210), moderate risk (5–7 points; n=108), and high risk (8–11 points; n=31). The respective in hospital mortality rates were 1.6%, 15.8%, and 42.1% (P<0.05) (Figure 2).

Discussion

We have developed a simple risk score model based on 5 available clinical parameters measured on hospital admission, which can be readily applied at the bedside, and has excellent discriminative ability for identifying elderly patients with ADHF at low (1.6%), moderate (15.8%), and high risk (42.1%) for in-hospital mortality.

Several prior studies have developed risk score models for predicting in-hospital mortality or post-discharge outcomes in patients hospitalized with ADHF. However, there is no risk score model for the predicting in-hospital mortality in elderly patients with ADHF, which is significantly higher compared with middle-aged patients with ADHF, because not only cardiac conditions, but also non-cardiac factors such as comorbidities or cognitive function may affect the in-hospital clinical course, and may lead to difficulty with treatment. Therefore, it is necessary to establish specialized risk assessment and management of elderly patients with ADHF.

This study group comprised elderly patients aged 65 years and older (mean age 79 years), who account for the majority of the HF population and are more likely to need hospital admission. In addition, unlike most other prognostic models, our risk score model can be easily used at the bedside without access to a computer or electronic calculator to generate the score. Furthermore, the predictive ability of the model is reasonable, with a ROC area of 0.86. Thus our model is unique and likely to be applied in routine clinical practice.

Similar to recent registry data from ADHERE and OPTIMIZE-HF, prior HF hospitalization, serum sodium, BUN, and BNP concentrations were independently associated with in-hospital mortality in this model. The patient population of our study was older (mean age 79 years) than those of previous reports (mean age 73 years), so our data confirm that these traditional prognostic factors can be applied to assess mortality risk in very old patients with ADHF.

Our important finding is that in elderly patients with ADHF the serum albumin level is strongly associated with in-hospital mortality, even after adjustment for other known prognostic factors. Hypoalbuminemia is well known to predict poor prognosis in several comorbid conditions and the older patient population. Recent reports have also shown that hypoalbuminemia is an independent predictor of mortality in patients with advanced systolic HF.
very old patients with ADHF. There are several potential explanations for the relationship between the albumin level and survival of patients with HF. Hypoalbuminemia is associated with advanced age, malnutrition, and inflammation, which are known to predict worse HF outcomes. Hypoalbuminemia is a major cause of diuretic resistance that is refractory to HF treatment. In addition, decreased colloid osmotic pressure because of the low albumin level may lead to the development of pulmonary edema and exacerbation of acute HF. And more importantly, hypoalbuminemia predicts a worse prognosis in several comorbid conditions such as end-stage renal disease, infection, lung disease, and cancer, which are highly prevalent in elderly patients with HF, and may contribute to their increased mortality risk. In the present study, 4.3% of deaths were from non-cardiac cause (infection was the leading cause of death), which suggests that non-cardiac comorbidity is strongly associated with adverse clinical outcomes in elderly patients with ADHF. Given these findings, hypoalbuminemia may provide additional prognostic information about not only HF, but also non-cardiac comorbidities, which may explain its prognostic significance in elderly patients with ADHF.

A previous study has developed a risk score model for predicting shorter survival in elderly patients aged over 70 years after hospitalization for ADHF. That model consists of 7 prognostic factors including older age, systolic blood pressure, serum sodium, BUN, coronary artery disease, peripheral artery disease, and dementia. The patient population was very similar to that of our study (mean age 79 years), but it evaluated post-discharge mortality (all-cause mortality at 6 month, 1 year, and 5 years), not in-hospital mortality, which may lead to the difference in the identified prognostic factors.

Age was not a discriminatory factor in our analysis as it has been in past risk scores and a potential reason is that the age range in the present study was more limited than in the other studies. It is well known that spironolactone reduces the risk of mortality in patients with severe HF. However, its administration was not associated with in-hospital mortality in the present study, despite its significantly higher use in the non-survival group. Patients with repeated hospitalization who were at high risk of mortality more often received spironolactone in this patient population, which suggests that higher use of spironolactone may reflect HF severity as a result of intensive intervention.

ARB were more likely to be administered to this patient population compared with ACEI, which may reflect the better tolerability of ARB than that of ACEIs in elderly patients with HF.

Our risk score model may help clinicians to select appropriate therapy and to raise the quality of care. Patients at high risk of mortality may require a higher level of monitoring, and earlier and more intensive treatment. If patients have not received standard medications, such as ACEIs/ARBs, β-blockers, and aldosterone antagonists, maximal medication should be tried. Ultrafiltration may be helpful in some patients who are refractory to diuretics. If patients have respiratory distress, noninvasive positive pressure ventilation should be tried, which is not only an effective respiratory management but also easily used and less invasive. However, if patients do not respond to these maximal medical therapies, end-of-life care should be discussed with the patient and the family. Patients who are refractory to intensive treatment may be unlikely to benefit from invasive procedures such as intubation and mechanical ventilation, which may contribute to pain and suffering. On the other hand, patients estimated to have a favorable prognosis may be suitable candidates for aggressive treatment, although individual patient factors and preferences would still require careful consideration.

**Study Limitations**

This model reported in-hospital mortality, not post-discharge outcomes. Other factors might be of prognostic value for post-discharge mortality or re-hospitalization. This study was conducted at a single center study, and the sample size was relatively small. Further investigations are necessary to validate the model’s accuracy, and demonstrate its superior predictive ability vs prior risk score models in another cohort.

In conclusion, we have developed a simple risk score model for predicting in-hospital mortality in elderly patients with ADHF. In addition to known prognostic factors, hypoalbuminemia is strongly associated with in-hospital mortality in this patient population. Hypoalbuminemia may provide additional prognostic information about not only HF, but also non-cardiac comorbidities, which may explain its clinical significance in our risk score that is focused on elderly patients with ADHF. Our simple risk score may help to stratify the risk of in-hospital mortality and contribute to better clinical management of elderly patients with ADHF.

**References**

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