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**Original Article**

# Prediction of Outcome of In-Hospital Mortality for Acute Heart Failure

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**Background:** Prediction of in-hospital mortality in acute heart failure (AHF) is sought to evaluate the blood pressure and renal function. Acute heart failure with systolic pressure and impaired renal function is common but not well understood.
**Methods:** We reviewed 187 patients with acute heart failure from 2013-2014. Then we apply validation of a risk stratification tool to predict in-hospital mortality for acute HF group. The analysis of the in-hospital mortality with acute heart failure group will based on BUN level, systolic blood pressure, and serum creatinine level.
**Results:** There were 23 patients in the in-hospital mortality group and 164 patients in the survived group after hospitalization. The 3 physiological parameters were compared between in-hospital mortality and survival group from the validation of a risk stratification tool: systolic blood pressure (123.7 ± 30.1 vs. 143.7 ± 34.2 mmHg, $p$ value = 0.009), blood urea nitrogen (57.2 ± 27.7 vs. 38.7 ± 24.7 mg/dL, $p$ value = 0.001), serum creatinine (2.38 ± 1.91 vs. 2.06 ± 1.62 mg/dL, $p$ value = 0.390). Finding from NTUH compared with ADHERE was the group with blood urea nitrogen 43 mg/dL, systolic BP < 115 mmHg, and serum creatinine < 2.75 mg/dL will be high risk of in-hospital mortality (50% in NTUH vs. 12.42% in ADHERE). In our validation of a risk stratification tool, the accuracy was 77.8 % by receiver-operator characteristic curve analysis.
**Conclusion:** On the basis of these 3 variables- BUN level, systolic blood pressure, and serum creatinine level from the current analysis, the acute heart failure patient can be readily stratified into groups at high risk for in-hospital mortality.

**Key words:** *acute heart failure, risk stratification, systolic blood pressure, blood urea nitrogen, creatinine*

## Introduction

Acute Heart Failure Symptoms (AHFS) is defined as gradual or rapid change in heart failure (HF) signs and symptoms resulting in a need for urgent therapy.[1] It can cause high morbidity and mortality in emergency department and is responsible for men power burden after being admitted for hospitalization care. Under the health care system, it will spend much budget and resources for care of AHF. Models for the risk stratification of acute heart failure (AHF) is needed to decrease health burden of hospitalization care for heart failure.[2] Although several systems have been developed for risk stratification in emergency care,

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there is no clinically practical model of risk stratification for AHF patients in emergency department.[3,4] Clinical risk prediction tools is helpful in guiding decision for treatment and disposition for AHF patients. Lower risk patient can be managed in a hospital general ward, while higher risk patients need intensive treatment in an intensive care unit. Previous studies try to predict the risk of AHF by left ventricular ejection fraction,[5] serum sodium concentration,[6] and B-type natriuretic peptide concentration.[7] However, it is a challenge in the clinical assessment of AHF at the time of emergent department or hospitalization.

The objective of this analysis in emergency department was to develop a practical and friendly method of risk stratification for patients with AHF. The prediction of high in-hospital mortality with AHF could be applicable to routine clinical practice. Data used to model risk were taken from AHF patient in the emergency room in a tertiary medical center in the study. As an observational role, we tried to predict the in-hospital mortality of patients with AHF.

## Materials and Methods

For the purpose of the registry, AHF is defined as acute or chronic decompensated heart failure with symptoms sufficient to hospitalization. The medical records are reviewed by trained abstractors and data from patients aged 18 years or older at the time of hospitalization are entered into the registry using an electronic case report form incorporating real-time validity checking.[8] These data include demographic information, past medical history, baseline clinical characteristics, initial evaluation, treatment received, hospital course, patient disposition and in-hospital mortality.[9]

The classification and regression tree method involves the segregation of different values of classification variables through a decision tree composed of progressive binary splits. Each parent node in the decision tree produces 2 child nodes, which in turn can become parent nodes producing additional child nodes. As a result, validation of a risk stratification tool produces decision trees that are simple to interpret and may be applied at the bedside.[10]

The study enrolled patients with acute heart failure who being admitted in the tertiary medical center from January 2013 to December 2014. Patients were included if the first primary diagnosis was heart failure when discharge. The primary diagnosis with both text and code from the medical charting system was reviewed. The diagnosis is confirmed by the attending physician. For applying the model, the patients were excluded if the data of systolic blood pressure, blood urea nitrogen or creatinine was not available. These data were subjected to validation of a risk stratification tool to identify the best predictors of in-hospital mortality and survival groups. The analysis of the in-hospital mortality with acute heart failure group will based on blood urea nitrogen (BUN) level equals 43 mg/dL or higher, systolic blood pressure (BP) less than 115 mmHg, and serum creatinine level 2.75 mg/dL or higher. TRIPOD checklist was applied for the validation study (Table 1).

Continuous variables were presented as mean ± standard deviation and t-test was used to check statistical significance. Categorical variables were presented as number with percentage and chi-square test was applied. Values of $p < 0.05$ were considered significant. Statistics were performed using SPSS12.0 software (SPSS Inc., Chicago, USA).

## Results

We analyzed 187 patients with acute heart failure who being admitted in the tertiary medical center from January 2013 to December 2014. Baseline characteristics included age and gender were similar between the 23 patients of in-hospital mortality group and 164 patients in the survived group after hospitalization. The other values such as heart failure history; coronary artery disease; prior myocardial infarction; chronic renal failure (serum creatinine > 2.0 mg/dL); atrial fibrillation; diabetes mellitus; hyperlipidemia ; strokes; and chronic obstructive pulmonary diseases (COPD) do not have significant deviation. But hypertension has shown as significant deviation ($p$ value = 0.009) (Table 2).

In Table 3, the physiological parameters had shown significant difference between the in-hospital mortality and survival groups in systolic blood pressure (123.7 ± 30.1 vs. 143.7 ± 34.2 mmHg, $p$ value = 0.009) and BUN (57.2 ± 27.7 vs. 38.7 ± 24.7 mg/dL, $p$ value = 0.001). The diastolic BP (65.2 ± 19.7 vs. 77.4 ± 22.5 mmHg, $p$ value = 0.015) and serum creatinine (2.38 ± 1.91 vs. 2.06 ± 1.62 mg/dL, $p$ value = 0.390) was not significant different between the in-hospital mortality and survival groups. The duration of hospitalization (16.0 ± 19.2 vs. 13.9 ± 9.9 days, $p$ value = 0.606) and the duration from emergency

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**Table 1.** TRIPOD checklist: prediction model validation

| Section/Topic | Item | Checklist Item | Page |
|---|---|---|---|
| Title and abstract | | | |
| Title | 1 | Identify the study as developing and/or validating a multivariable prediction model, the target population, and the outcome to be predicted. | Title page |
| Abstract | 2 | Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions. | 1 |
| Introduction | | | |
| Background and objectives | 3a | Explain the medical context (including whether diagnostic or prognostic) and rationale for developing or validating the multivariable prediction model, including references to existing models. | 2 |
| | 3b | Specify the objectives, including whether the study describes the development or validation of the model or both. | 2 |
| Methods | | | |
| Source of data | 4a | Describe the study design or source of data (e.g., randomized trial, cohort, or registry data), separately for the development and validation data sets, if applicable. | 3 |
| | 4b | Specify the key study dates, including start of accrual; end of accrual; and, if applicable, end of follow-up. | 3 |
| Participants | 5a | Specify key elements of the study setting (e.g., primary care, secondary care, general population) including number and location of centres. | 3 |
| | 5b | Describe eligibility criteria for participants. | 3 |
| | 5c | Give details of treatments received, if relevant. | NA |
| Outcome | 6a | Clearly define the outcome that is predicted by the prediction model, including how and when assessed. | 3 |
| | 6b | Report any actions to blind assessment of the outcome to be predicted. | 3 |
| Predictors | 7a | Clearly define all predictors used in developing or validating the multivariable prediction model, including how and when they were measured. | 4 |
| | 7b | Report any actions to blind assessment of predictors for the outcome and other predictors. | 4 |
| Sample size | 8 | Explain how the study size was arrived at. | 3 |
| Missing data | 9 | Describe how missing data were handled (e.g., complete-case analysis, single imputation, multiple imputation) with details of any imputation method. | 3 |
| Statistical analysis methods | 10c | For validation, describe how the predictions were calculated. | 4 |
| | 10d | Specify all measures used to assess model performance and, if relevant, to compare multiple models. | 4 |
| | 10e | Describe any model updating (e.g., recalibration) arising from the validation, if done. | NA |
| Risk groups | 11 | Provide details on how risk groups were created, if done. | 3 |
| Development vs. validation | 12 | For validation, identify any differences from the development data in setting, eligibility criteria, outcome, and predictors. | 3 |

**Table 1.** TRIPOD checklist: prediction model validation (continued)

| Section/Topic | Item | Checklist Item | Page |
|---|---|---|---|
| Results | | | |
| Participants | 13a | Describe the flow of participants through the study, including the number of participants with and without the outcome and, if applicable, a summary of the follow-up time. A diagram may be helpful. | 4 |
| | 13b | Describe the characteristics of the participants (basic demographics, clinical features, available predictors), including the number of participants with missing data for predictors and outcome. | 4 |
| | 13c | For validation, show a comparison with the development data of the distribution of important variables (demographics, predictors and outcome). | 5 |
| Model performance | 16 | Report performance measures (with CIs) for the prediction model. | 5 |
| Model-updating | 17 | If done, report the results from any model updating (i.e., model specification, model performance). | 5 |
| Discussion | | | |
| Limitations | 18 | Discuss any limitations of the study (such as nonrepresentative sample, few events per predictor, missing data). | 8 |
| Interpretation | 19a | For validation, discuss the results with reference to performance in the development data, and any other validation data. | 6 |
| | 19b | Give an overall interpretation of the results, considering objectives, limitations, results from similar studies, and other relevant evidence. | 6 |
| Implications | 20 | Discuss the potential clinical use of the model and implications for future research. | 7 |
| Other information | | | |
| Supplementary information | 21 | Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets. | NA |
| Funding | 22 | Give the source of funding and the role of the funders for the present study. | NA |

We recommend using the TRIPOD Checklist in conjunction with the TRIPOD Explanation and Elaboration document.

**Table 2.** Clinical characteristics of acute heart failure patients

| | In-hospital mortality (n = 23) | Surviva (n = 164) | *p* value |
|---|---|---|---|
| Age (year) | 76.4 ± 11.5 | 72.9 ± 14.7 | 0.266 |
| Gender Men (%) | 16 (69.6) | 80 (48.8) | 0.076 |
| Concurrent diseases (%) | | | |
| Hear failure history | 8 (34.8) | 45 (27.4) | 0.307 |
| Coronary artery disease | 11 (47.8) | 71 (43.3) | 0.424 |
| Prior myocardial infarction | 5 (21.7) | 22 (13.4) | 0.22 |
| Chronic renal failure or creatinine > 2.0 md/dL | 6 (26.1) | 28 (23.2) | 0.467 |
| Atrial fibrillation | 7 (30.4) | 53 (32.3) | 0.532 |
| Diabetes mellitus | 10 (43.5) | 84 (51.2) | 0.319 |
| Hypertension | 9 (39.1) | 113 (68.9) | 0.009 |
| Hyperlipidemia | 2 (8.7) | 24 (14.6) | 0.747 |
| Stroke | 3 (13.0) | 14 (8.5) | 0.445 |
| Chronic obstructive pulmonary disease or asthma | 3 (13.0) | 26 (15.9) | 1.00 |

admission to hospitalization discharge (17.4 ± 19.5 days vs. 14.8 ± 9.7 days, $p$ value = 0.532) were both non-significant longer in in-hospital mortality group as shown in Table 4.

Final tree generated by the validation of a risk stratification tool along with the mortality data for each child node of this tree was shown in Fig. 1. The total in-hospital mortality patients from NTUH were 23 patients, which occupied 12.3% compared to 4.2% from ADHERE. The ratio of group with blood urea nitrogen (BUN) level < 43 mg/dL and systolic blood pressure (SBP) ≥ 115 mmHg was 2.3% from NTUH vs. 2.14 % from ADHERE. The ratio of group with blood urea nitrogen (BUN) level < 43 mg/dL and systolic blood pressure (SBP) < 115 mmHg was 17.9% from NTUH vs. 5.49 % from ADHERE. The ratio of group with blood urea nitrogen (BUN) level ≥ 43 mg/dL and systolic blood pressure (SBP) ≥ 115 mmHg was 17.9% from NTUH vs. 6.41% from ADHERE. The ratio of group with blood urea nitrogen (BUN) level ≥ 43 mg/dL ,systolic blood pressure (SBP) < 115 mmHg and serum creatinine level < 2.75 mg/dL was 50.0% from NTUH vs. 12.42% from ADHERE. The ratio of group with blood urea nitrogen (BUN) level ≥ 43 mg/dL ,systolic blood pressure (SBP) < 115 mmHg and serum creatinine level ≥ 2.75 mg/dL was 28.6% from NTUH vs. 21.94% from ADHERE. Based on the area under the receiver operating characteristic curves, the accuracy of the ADHERE study was 75.9% in derivation cohort by logistic regression model by receiver-operator characteristic (ROC) curve analysis. In our validation of a risk stratification tool, the accuracy was 77.8% by ROC curve analysis.

## Discussion

Several evaluations of patients hospitalized for acute heart failure have demonstrated an association between in-hospital mortality and indices of renal function and blood pressure.[11] In the current evaluation, we applied the model which identifies 3 of 39 potential variables as significant predictors of in-hospital mortality risk.[2] In a simple 2- to 3-step process, these variables permit identification of patients

**Table 3.** Physiological parameters in acute heart failure patients

| | In-hospital mortality (n = 23) | Survival (n = 164) | $p$ value |
|---|---|---|---|
| Physiological parameters | | | |
| Body temperature (°C) | 36.4 ± 0.9 | 36.6 ± 0.7 | 0.387 |
| Systolic BP (mmHg) | 123.7 ± 30.1 | 143.7 ± 34.2 | 0.009 |
| Diastolic BP (mmHg) | 65.2 ± 19.7 | 77.4 ± 22.5 | 0.015 |
| Heart rate (/min) | 92.7 ± 21.6 | 90.4 ± 24.5 | 0.673 |
| Respiratory rate (/min) | 23.8 ± 5.2 | 22.1 ± 5.8 | 0.531 |
| Laboratory test | | | |
| Sodium (mmol/l) | 136.1 ± 6.2 | 136.9 ± 5.3 | 0.530 |
| Potassium (mmol/l) | 5.1 ± 2.7 | 4.4 ± 1.0 | 0.289 |
| Creatinine (mg/dL) | 2.38 ± 1.91 | 2.06 ± 1.62 | 0.390 |
| Blood urea nitrogen (mg/dL) | 57.2 ± 27.7 | 38.7 ± 24.7 | 0.001 |
| Troponin I (ng/dL) | 5.1 ± 18.8 | 1.68 ± 9.5 | 0.442 |
| B-type natriuretic peptide (ng/dL) | 1,983.9 ± 2,194.6 | 1,592.7 ± 1,773.3 | 0.663 |

**Table 4.** Outcomes of acute heart failure patients

| | In-hospital mortality (n = 23) | Survival (n = 164) | $p$ value |
|---|---|---|---|
| Hospitalization duration | 16.0 ± 19.2 | 13.9 ± 9.9 | 0.606 |
| Duration from ED visit to discharge | 17.4 ± 19.5 | 14.8 ± 9.7 | 0.532 |

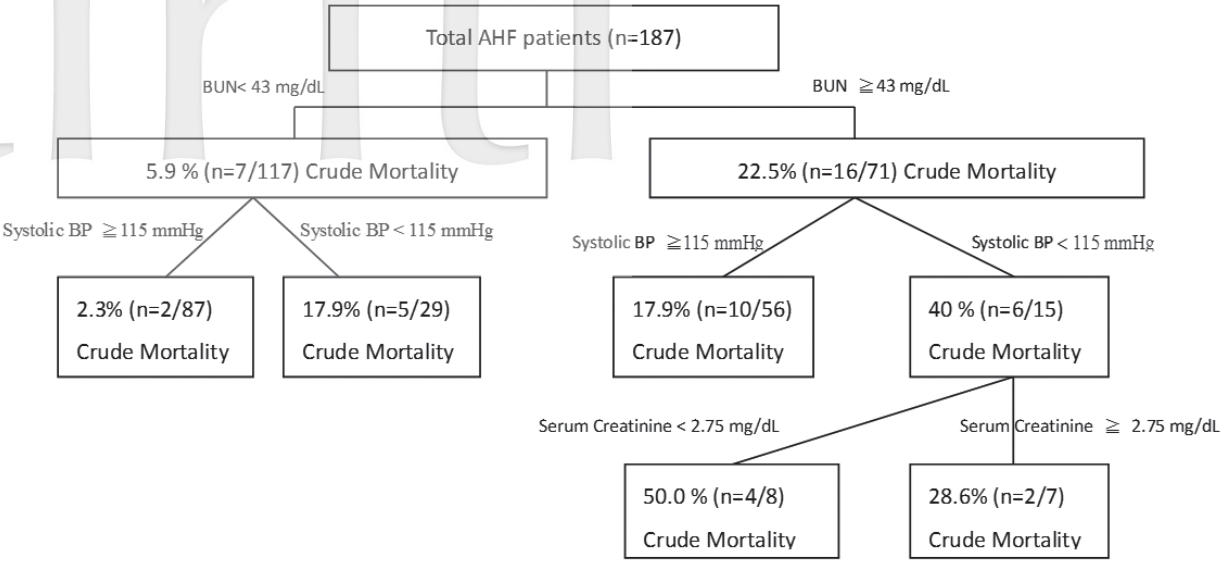


**Fig. 1.** Validation of a risk stratification tool for mortality of acute heart failure patients: classification and regression tree analysis

with in-hospital mortality. This model, which can be easily applied at the bedside, is helpful for risk stratification for AHF in emergency department. Because of multiple risk factors existing in the single patient, risk factor analysis is difficult to consider factors in isolation. It has been reported that parameters such as coronary artery disease, prior MI, chronic renal failure (serum creatinine > 2.0 mg/dL), atrial fibrillation, DM, hyperlipidemia, strokes, and chronic obstructive pulmonary diseases (COPD) do not have significant deviation in predicting the risk for AHF patient, while hypertension had been correlated with in-hospital mortality in patients hospitalized with heart failure. From the baseline characteristics in acute HF studies, the percentage of current diseases with hypertension in survive group had occupied more than in-hospital group.[12] It means loss of blood pressure control, it will be in high risk of in-hospital mortality with AHF. From the current Validation of a risk stratification tool for in-hospital mortality, we can quickly and accurately determine using admission clinical and laboratory variables. We applied to the independent predictors for risk stratification in previous CART analysis, including BUN level of 43 mg/dL or higher, serum creatinine level of 2.75 mg/dL or higher, and SBP of less than 115 mmHg.[2] On the basis of these 3 variables, AHF patients can be readily stratified into five groups with mortality risks ranging from 2.3% to 50.0%. The finding that indices of renal status is BUN level predictors providing the best mortality risk discrimination underscores the importance of renal function in AHF patients. Similarly, in a retrospective review of 1,004 consecutive patients hospitalized for heart failure at 11 geographically diverse hospitals, worsening renal function was associated with a 7.5-fold increase (95% CI, 2.9- to 19.3-fold increase) in the adjusted risk of in-hospital mortality.[11] In the Enhanced Feedback for Effective Cardiac Treatment study, increasing BUN levels and decreasing SBP were significant and independent predictors of both 30-day and 1-year mortality.[11] In our study, we find the SBP, BUN and serum creatinine level can stratify the risk of in-hospital mortality for acute heart failure patient. The association of in-hospital mortality and cardiorenal function has been demonstrated in acute heart failure studies.[6,11,13] Activation of neurohormonal system which exacerbates the cardiac function is noted in acute heart failure patients. Decreased systolic blood pressure was found to be an independent predictors for short term and long term mortality in acute heart failure patients. The association could be come from the poor perfusion for vital organs or a reflection of poor left ventricular function in patients with low systolic blood pressure.[8,12]

We show the feasibility of using the validation of a risk stratification tool for AHF patient in emergency department. It can aid medical decision making in patients hospitalized with AHF. Higher risk patients may receive earlier and higher-level of care and monitoring and more intensive treatment. Patients with

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lower risk may be reassured and managed with less intensive and avoid overusing of emergency resources. In addition, the application of predication models may be valuable in designing further clinical trials to evaluate heart failure treatment with appropriate selection of patients at high risk for in-hospital mortality. According to the validation of a risk stratification tool used for the study, we can identify high risk AHF patients in our study population. The validation of the result in study can be the basis for exploring new treatment strategies for patients with different risk in the future. Global hospitalized heart failure (HHF) registries show that the median length of stay (LOS) ranges from 4 to 20 days and in-hospital mortality from 4% to 30%.[13] In general, registries with a shorter LOS tend to have lower in-hospital mortality. But to our study in hospitalization, there is no difference between in-hospital mortality group and survive group. The wide variation of LOS in previous registry and also in our study may be due to lack of standardized protocols for hospital discharge in AHF. Different physicians may use different criteria for hospital discharge in clinical practice. Standard protocol or other evaluations by surrogate markers such as biomarkers could be helpful for evaluation LOS in future study.

There are limitations for the current analysis by the method. The study is retrospective study. There would be some bias in enrolling the study subjects although inclusion and exclusion were applied. The validation of a risk stratification tool favors variables available for analysis of patients with AHF. But study results can be influenced by differences in disease assessment, treatment, and many factors not measured or considered clinically. The additional variables such as B-type natriuretic peptide or ejection fraction that either were not considered or were considered and rejected could improve the risk discrimination if a sufficient number of patients were assessed. The difference of treatment could influence the in-hospital mortality in different cohorts. No data of treatment in other compared cohort was a limitation for the study. Because of the small sample size, updating model is not doable in the study.

In conclusion, acute heart failure has its epidemiologic characteristics. The prediction of in-hospital mortality in acute heart failure while patient admitted with BUN level of 43 mg/dL or higher, and SBP of less than 115 mmHg will have high in-hospital mortality. Even the current validation of a risk stratification tool analysis has created a simple tool to predict in-hospital mortality that is easy to use and has good discriminative ability, we need more effort to figure out the factors triggering the occurrence of acute heart failure.

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