Differences in clinical characteristics and mortality of de novo acute heart failure and acutely decompensated chronic heart failure: A prospective cohort study

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ABSTRACT

Background: Acute heart failure carries a high risk of mortality. Understanding the characteristics and outcomes of acute heart failure subgroups may have important implications for clinical risk stratification.

Objective: We examined the clinical characteristics and rates of the 12-month all-cause mortality in a cohort of patients hospitalized with acute heart failure according to heart failure duration new-onset or de novo acute heart failure and acutely decompensated chronic heart failure (ADCHF).

Methods and Materials: The cohort study, with a 12-month follow-up, was conducted at Nhan Dan Gia Dinh Hospital in Vietnam from February 2022 to October 2023.

Results: Among 316 patients with acute heart failure, 159 patients (50%) were admitted presenting de novo AHF, while the remaining 157 patients (50%) exhibited ADCHF. Patients with ADCHF were characterized by a higher proportion of elders, comorbidities including chronic kidney disease and atrial fibrillation, and a larger left atrial diameter than those with de novo acute heart failure. The rates of mortality in patients with ADCHF were 1.69 times more than in patients with de novo acute heart failure (the hazard ratio (HR): 1.69 (The 95% confidence interval (CI 95%): 1.10 - 2.60, p = 0.016). However, patients with ADCHF had not an independent predictor of 12-month mortality after adjusting factors in multivariable Cox regression models, including age, chronic pulmonary disease, diabetes mellitus, coronary heart disease, atrial fibrillation, sodium, hemoglobin, N-terminal prohormone BNP (NT-proBNP).

Conclusions: Among patients hospitalized with acute heart failure, acutely decompensated chronic heart failure was associated with poorer outcomes.

Keywords: Acute heart failure, de novo heart failure, acutely decompensated chronic heart failure, all-cause mortality.

INTRODUCTION

Acute heart failure (AHF) is the rapid onset of worsening of signs and symptoms of heart failure and usually requires emergency care¹. AHF is a
leading cause of hospitalization in patients aged > 65
years and is associated with high mortality. In-hospital
mortality ranges from 4% to 10%\(^2,3\), post-discharged
1-year mortality can be 25% - 30%\(^4,6\).

Based on the temporal progression of AHF, the
European Society of Cardiology (ESC) 2021 classifies
AHF into two categories: de novo AHF, which presents
in patients with initial AHF decompensation, and
acutely decompensated chronic heart failure, which
corresponds to an exacerbation of heart failure in
patients with at least one previous decompensation\(^1\).
However, there has been little investigation of how
these groups compare to their characteristics and
mortality. De novo acute heart failure may have
a higher in-hospital mortality\(^2\) but have lower
post-discharge mortality\(^7,8\). Understanding the
characteristics and outcomes of these two distinct
subpopulations may have important implications
for clinical risk stratification. We examined the clinical
characteristics and rates of all-cause mortality in a
cohort of patients hospitalized with heart failure,
stratifying as to whether the patients presented with
de novo or worsening of chronic heart failure.

**METHODS**

**Study population**

The study was designed as a cohort investigation.
The patients with AHF were hospitalized in Nhan Dan
Gia Dinh Hospital from February 2022 to October
2023. Diagnosis of acute heart failure followed 2021
ESC Guidelines\(^1\). Diagnosis of AHF was defined as
the rapid onset or worsening of symptoms and/or
signs of heart failure, such as pulmonary crackles,
peripheral edema, and cardiomegaly. Inclusion of
criteria in this study was: (1) Patients admitted with a
diagnosis of AHF; (2) Patients over 18 years of age;
(3) Patients in response to a diuretic drug, inotropic
drug or vasodilators; (4) NT-proBNP > 2000 pg/ml.
Exclusion ones were: end-stage renal or liver disease,
pregnancy, and malignancy.

Data on the demographic characteristics and
laboratory tests were collected from the medical record.
Venous blood sampling for bio-markers was obtained
48 hours after admission. Patients followed up for 12
months after discharge. The primary endpoint was all-
cause mortality. Survival or death status was confirmed
by reviewing the death certificates, telephone
interviews, and data from the eHospital software
of Nhan Dan Gia Dinh Hospital. The study protocol
adhered to the Declaration of Helsinki and received
approval from the Ethics Committee of Biomedical
Research at the University of Medicine and Pharmacy
at Ho Chi Minh City (21598-DHYD) before initial patient
recruitment. All patients gave informed consent.

**Statistical analysis**

Sample size: Based on the previous study, the
mortality rates of patients with acute decompensated
chronic heart failure had been 32.9%\(^9\) in 1 year. With
a statistical power of 0.9 for detecting a significant
difference (\(p = 0.05\), two-sided), 152 patients were
required to test the hypothesis of the difference in
mortality rate between both groups.

Continuous variables and categorical data are
expressed as means ± standard deviation (SD) and
percentages, respectively. The clinical characteristics
of the patients at baseline by the different categories
of AHF were compared with the use of the t-test
for continuous variables and the chi-square test for
categorical variables. Kaplan-Meier survival analysis
was used to graphically present survival estimates
according to the different categories of AHF and
the subsequent 1-year survival probability. The
difference in cumulative mortality rates of the two
AHF groups was compared using the log-rank test.
Multivariate Cox proportional hazard regression
modeling was used to assess the independent
effect of AHF type on the primary end point of all-
cause mortality. The covariates were independent
predictors in the mortality of AHF patients which
identified in literature, including age, chronic
pulmonary disease, chronic coronary disease, atrial
fibrillation, sodium, hemoglobin, and NT-proBNP\(^10\).
Statistical significance was accepted for a 2-sided \(p < 0.05\). The statistical analysis was performed with
R Statistical Software (R 4.3.1: R Foundation for
RESULTS

From February 2022 to October 2023, 316 patients were hospitalized with a diagnosis of either ADCHF or de novo AHF. Based on our classification of the different AHF groups, 157 (50%) patients were classified as ADCHF and 159 (50%) patients as de novo AHF. The median age of the study population was 67.4 ± 14.8 years, and 52% were women. Baseline characteristics of the 2 AHF groups are presented in Table 1.

The comparison between both groups showed that patients admitted for de novo AHF were younger 4 years (65.4 ± 6 years vs 69.4 ± 6 years, p = 0.018), hypertensive heart disease increased 1.6 times (11.3% vs 7.0%, p = 0.04), had a 6 beats/minute higher heart rate (99.4 ± 23.2 beats/minute vs 93.8 ± 23.1 beats/minute, p = 0.031), had a higher 11 mmHg systolic blood pressure (137.2 ± 27.5 mmHg vs 126 ± 26.1 mmHg, p < 0.001), had a higher 5 mmHg diastolic blood pressure (80.9 ± 14.1 mmHg vs 75.1 ± 14.6 mmHg, p < 0.001). There were significant differences in the etiology of heart failure; patients with ADCHF had increased 1.3 times chronic coronary disease (22.6% vs 29.3%, p = 0.04), increased 1.5 times valvular heart disease (12.6% vs 19.1%, p = 0.04), increased 1.3 times cardiomyopathy disease (15.1% vs 19.1%, p = 0.04). In addition, patients with ADCHF had increased 1.4 times atrial fibrillation (28.3% vs 39.5%, p = 0.036), increased 1.9 times chronic kidney disease (21.4% vs 41.4%, p = 0.04) and increased 2 mm left atrial diameter (38.8 ± 8.2 mm vs 41.9 ± 8.9 mm, p = 0.001)

Mortality

During 12 months, there were 87 died patients (27.5%) in follow-up 316 patients. The mortality rate was significantly lower in patients with de novo AHF than ADCHF (20.8% vs 34.4%; p = 0.007). Kaplan-Meier plot showed a higher mortality rate in ADCHF with a significant difference (p = 0.015) compared to that in de novo AHF (Figure 1).

Cox model analysis showed that patients with ADCHF had an increased mortality rate of 1.69 times de novo AHF (HR: 1.69 (CI 95%: 1.10 - 2.60, p = 0.016)). However, the mortality hazard ratio was insignificantly different after adjustment for age, chronic pulmonary disease, diabetes mellitus, coronary heart disease, atrial fibrillation, sodium, hemoglobin, and NT-proBNP (Table 2).

Table 1. Multivariate Cox Regression analysis to identify factors associated with 1 year all-cause mortality in acute heart failure patients

<table>
<thead>
<tr>
<th></th>
<th>Hazard ratio</th>
<th>95% confidence interval</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADCHF</td>
<td>1.35</td>
<td>0.85 - 2.13</td>
<td>0.19</td>
</tr>
<tr>
<td>Age</td>
<td>1.02</td>
<td>1.00 - 1.04</td>
<td>0.002</td>
</tr>
<tr>
<td>Chronic pulmonary disease</td>
<td>1.84</td>
<td>1.03 - 3.26</td>
<td>0.03</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>0.89</td>
<td>0.56 - 1.40</td>
<td>0.61</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>1.11</td>
<td>0.55 - 1.45</td>
<td>0.65</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>1.44</td>
<td>0.88 - 2.36</td>
<td>0.15</td>
</tr>
<tr>
<td>Sodium</td>
<td>0.96</td>
<td>0.94 - 0.99</td>
<td>0.01</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>0.98</td>
<td>0.98 - 0.99</td>
<td>0.02</td>
</tr>
<tr>
<td>NT-proBNP</td>
<td>1.00</td>
<td>1.00 - 1.00</td>
<td>0.08</td>
</tr>
</tbody>
</table>

ADCHF, acutely decompensated chronic heart failure; NT-proBNP, N-terminal prohormone BNP.
Table 2. Baseline characteristics of 316 patients with de novo acute heart failure versus acutely decompensated chronic heart failure

<table>
<thead>
<tr>
<th>Variable</th>
<th>De novo AHF n=159</th>
<th>ADCHF n=157</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>65.4 ± 6</td>
<td>69.4 ± 6</td>
<td>0.018</td>
</tr>
<tr>
<td>Women, n (%)</td>
<td>75 (47.2)</td>
<td>89 (56.7)</td>
<td>0.090</td>
</tr>
<tr>
<td>Aetiology of heart failure</td>
<td></td>
<td></td>
<td>0.04</td>
</tr>
<tr>
<td>Chronic coronary disease, n (%)</td>
<td>36 (22.6)</td>
<td>46 (29.3)</td>
<td></td>
</tr>
<tr>
<td>Hypertensive heart disease, n (%)</td>
<td>18 (11.3)</td>
<td>11 (7.0)</td>
<td></td>
</tr>
<tr>
<td>Valvular heart disease, n (%)</td>
<td>20 (12.6)</td>
<td>30 (19.1)</td>
<td></td>
</tr>
<tr>
<td>Cardiomyopathy, n (%)</td>
<td>24 (15.1)</td>
<td>30 (19.1)</td>
<td></td>
</tr>
<tr>
<td>Others, n (%)</td>
<td>61 (38.4)</td>
<td>40 (25.5)</td>
<td></td>
</tr>
<tr>
<td>Past medical history</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking, n (%)</td>
<td>55 (34.6)</td>
<td>51 (32.5)</td>
<td>0.692</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>112 (70.4)</td>
<td>118 (75.2)</td>
<td>0.346</td>
</tr>
<tr>
<td>Diabetes mellitus, n(%)</td>
<td>56 (35.2)</td>
<td>69 (43.9)</td>
<td>0.113</td>
</tr>
<tr>
<td>Coronary artery disease, n (%)</td>
<td>57 (35.8)</td>
<td>70 (44.6)</td>
<td>0.113</td>
</tr>
<tr>
<td>Valvular heart disease, n (%)</td>
<td>22 (13.8)</td>
<td>28 (17.8)</td>
<td>0.330</td>
</tr>
<tr>
<td>Atrial fibrillation, n (%)</td>
<td>45 (28.3)</td>
<td>62 (39.5)</td>
<td>0.036</td>
</tr>
<tr>
<td>Cerebrovascular accident/transient ischemic attack, n (%)</td>
<td>14 (8.8)</td>
<td>17 (10.8)</td>
<td>0.546</td>
</tr>
<tr>
<td>Chronic pulmonary disease, n (%)</td>
<td>21 (13.2)</td>
<td>17 (10.8)</td>
<td>0.516</td>
</tr>
<tr>
<td>Chronic kidney disease, n (%)</td>
<td>34 (21.4)</td>
<td>65 (41.4)</td>
<td>0.003</td>
</tr>
<tr>
<td>Clinical presentation</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Systolic blood pressure, mmHg</td>
<td>137.2 ± 27.6</td>
<td>126.9 ± 26.1</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Diastolic blood pressure, mmHg</td>
<td>80.9±14.2</td>
<td>75.1 ± 14.6</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>99.4 ± 23.2</td>
<td>93.8 ± 23.1</td>
<td>0.031</td>
</tr>
<tr>
<td>Laboratory findings</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemoglobin, g/dl</td>
<td>120.5 ± 23.9</td>
<td>118 ± 23.5</td>
<td>0.396</td>
</tr>
<tr>
<td>Serum creatinine, μg/l</td>
<td>132.2 ± 108.3</td>
<td>135.4 ± 56.1</td>
<td>0.745</td>
</tr>
<tr>
<td>Sodium, mmol/l</td>
<td>135.7 ± 6.8</td>
<td>135.2 ± 5.8</td>
<td>0.481</td>
</tr>
<tr>
<td>NT-proBNP, pg/ml</td>
<td>9637 ± 8528</td>
<td>10417 ± 9234</td>
<td>0.436</td>
</tr>
<tr>
<td>Echocardiography</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left ventricle end-diastolic diameter, mm</td>
<td>51.7 ± 9.9</td>
<td>53.4 ± 11.3</td>
<td>0.152</td>
</tr>
<tr>
<td>Left atrial diameter, mm</td>
<td>38.8 ± 8.2</td>
<td>41.9 ± 8.9</td>
<td>0.001</td>
</tr>
<tr>
<td>Left ventricular ejection fraction, %</td>
<td>43.2 ± 16.2</td>
<td>41.8 ± 16.6</td>
<td>0.428</td>
</tr>
<tr>
<td>All-cause mortality, %</td>
<td>33 (20.8)</td>
<td>54 (34.4)</td>
<td>0.007</td>
</tr>
</tbody>
</table>

Bold-faced values indicated statistical significance at P <0.05; AHF, acute heart failure; ADCHF, acutely decompensated chronic heart failure; NT-proBNP, N-terminal prohormone BNP.
DISCUSSIONS

In this cohort study of all acute heart failure patients admitted to Nhan Dan Gia Dinh Hospital, we found that approximately 50% of those presented de novo AHF. We compared clinical characteristics and outcomes of de novo AHF and ADCHF patients. Our study yielded four major findings. First, ACDHF patients were older and had comorbidities, which were similar to de novo AHF patients, except for chronic kidney disease and atrial fibrillation. Second, de novo AHF had a higher heart rate and blood pressure level upon arrival at an emergency department. Third, there was a larger left atrial remodeling in patients with ADCHF. Finally, there was a graded relationship between increasing heart failure duration of heart failure and the rate of all-cause mortality, with a longer duration of heart failure associated with higher mortality rates.

Patients with ADCHF often experience comorbidities\(^1\), and our investigation identified that chronic kidney disease and atrial fibrillation dominated the others. The former is one of the most common comorbidities in AHF patients, with a prevalence ranging from 30% to 67%\(^12,13\). It stands as an independent prognosis factor in the mortality of AHF patients. Our study disclosed a significant difference in the ratio of chronic kidney disease in ADCHF patients, resulting from impaired kidney function possibly arising from renal vein congestion during the AHF period, heart failure medications, and frequent fluid overload during the treatment of chronic heart failure. The impaired kidney function in ADCHF patients could be unrecoverable and culminate in the progression of chronic kidney disease. The latter is both a cause and consequence of heart failure and also plays a significant role in exacerbating the condition. Atrial fibrillation induces heart failure through the mechanism of diminished left atrial contractile function due to increased left ventricular filling pressure and reduced cardiac output, particularly in patients with diastolic heart failure.

failure. The presence of atrial fibrillation is associated with adverse outcomes in heart failure patients. It can be said that the occurrence of atrial fibrillation and chronic kidney disease are poor prognostic factors in ADCHF patients.

An intriguing finding in our study was the graded relationship between heart failure duration and all-cause mortality rates. Nevertheless, this is intuitive due to the older and larger left atrial diameter of patients with longstanding heart failure and the association between increasing heart failure duration and subsequent risk of outcomes. The results may be due to prolonged exposure to neurohormonal activation and greater maladaptive cardiac remodeling and may reflect the natural course of the disease. However, our findings contrast with those of the acute study of clinical effectiveness of nesiritide and decompensated heart failure (ASCEND-HF), where this graded relationship was not found. The reasons for this are unclear but may be attributed to essential differences in patient characteristics, including age, ethnicity, and prevalence of comorbidity. In addition, patients with de novo AHF had higher blood pressure and heart rate, possibly because they had not undergone drug therapy. Previous studies showed that preserved or high blood pressure during an AHF episode is associated with a better prognosis, which is consistent with the results observed in our study.

The limitations of our study were: (1) Because the study was conducted in one setting, the findings might not help to reflect the health care conditions of other health settings in Vietnam; (2) We did not control data on drug doses during hospitalization or at the time of discharge and follow-up, which might affect mortality; (3) The study did not investigate precipitating factor of the AHF. Despite these limitations, the present prospective cohort study provided new insights into differences in admission between variables de novo AHF and ADCHF as well as predictive of mortality.

CONCLUSIONS

In our cohort study, including the patients hospitalized with HF, acutely decompensated chronic heart failure had a tendency for poorer outcomes compared with de novo AHF. These findings may have important implications for risk stratification in acute heart failure.

REFERENCES


