

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 decompensation¹. 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 mortality² 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 Guidelines¹. 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 \pm 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-proBNP¹⁰. 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 Statistical Computing, Vietnam).

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

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

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

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

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.

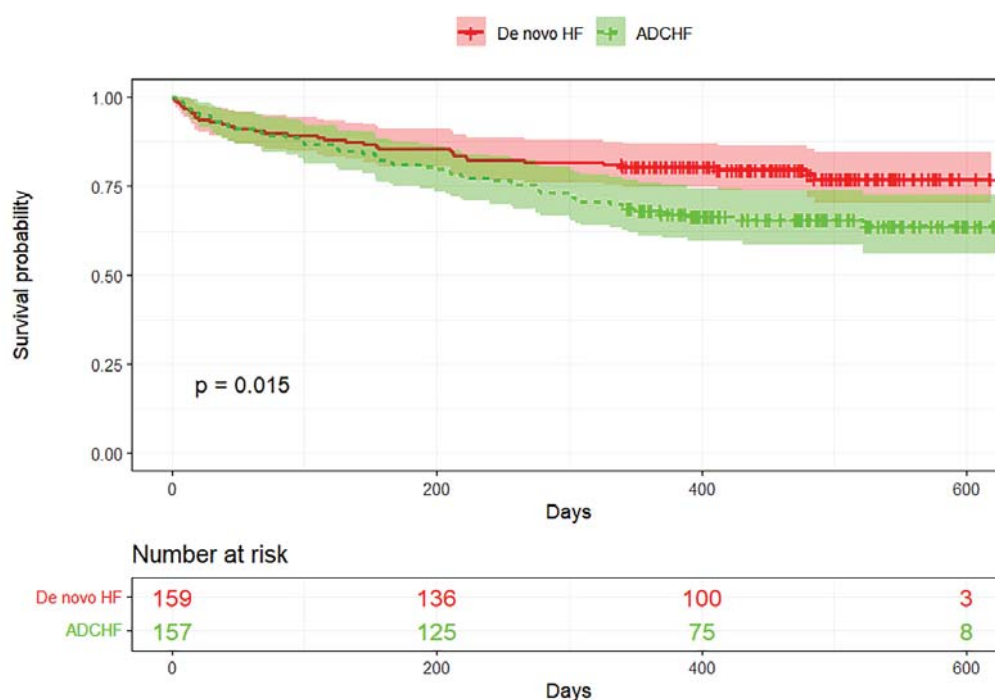


Figure 1. Kaplan-Meier curves in patients with acutely decompensated chronic heart failure (green line) versus de novo acute heart failure (red line) for death within 1 year. Acutely decompensated chronic heart failure (ADCHF), heart failure (HF)

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 comorbidities¹¹, 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. The presence of atrial fibrillation is associated with adverse outcomes in heart failure patients^{14,15}. 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)¹⁶, 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 therapy¹⁷. Previous studies showed that preserved or high blood pressure during an AHF episode is associated with a better prognosis¹⁰, 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.

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