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Long-term survival after hospitalization for acute heart failure — Differences in prognosis of acutely decompensated chronic and new-onset acute heart failure

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ABSTRACT

Aims: To analyze the five-year mortality after hospitalization for acute heart failure (AHF) and compare predictors of prognosis in patients with and without a previous history of heart failure.
Methods: Patients with AHF (n = 620) from the prospective multicenter FINN-AKVA study were classified as acutely decompensated chronic heart failure (ADCHF) or de-novo AHF if no previous history of heart failure was present. Both all-cause mortality during five years of follow-up and prognostic factors were determined.
Results: The overall mortality was 60.3% (n = 374) at five years. ADCHF was associated with significantly poorer outcome compared to de-novo AHF; five-year mortality rate 75.6% vs. 44.4% ($p<0.001$). Initially, mortality was high (33.5% in ADCHF and 21.7% in de-novo AHF after 12 months), but in de-novo AHF the annual mortality declined markedly already after the first year. Compared to de-novo AHF, patients with ADCHF had an increased risk of death for several years after the index hospitalization. A previous history of heart failure was an independent predictor of five-year mortality (adjusted hazard ratio 1.8 (95% CI 1.4–2.2; $p<0.001$). Older age and impaired renal function were associated with adverse long-term prognosis in both ADCHF and de-novo AHF, while higher systolic blood pressure on admission predicted better outcome.
Conclusion: The long-term prognosis after hospitalization for AHF is poor, with a significantly different survival observed in patients with de-novo AHF compared to ADCHF. A previous history of heart failure is an independent predictor of five-year mortality. Distinction between ADCHF and de-novo AHF may improve our understanding of patients with AHF.

1. Introduction

Acute heart failure (AHF) is characterized by rapid worsening of symptoms and signs of heart failure requiring urgent treatment, often with hospitalization. Recent guidelines recognize that patients presenting with AHF may not have a previous history of heart failure, and thus are new-onset (de-novo) cases [1,2]. The proportion of patients with de-novo AHF has been variable, between 12% and 63% [3–6]. Clinical presentation and management of AHF does not differ between acutely decompensated chronic heart failure (ADCHF) and de-novo AHF. Initial treatment is directed at relieving symptoms, stabilizing hemodynamic derangements and recognizing the precipitating factor(s). Initiation or adjustment of medical therapy for heart failure during the index hospitalization is also advocated.

The prognosis of patients with AHF remains poor. In-hospital mortality is as high as 5–10%, and around 25% of patients die within the first year after hospital admission [3,7–9]. Factors related to bad

Abbreviations: ACEI/ARB, angiotensin converting enzyme inhibitor/angiotensin receptor blocker; AHF, acute heart failure; ACS, acute coronary syndrome; ADCHF, acutely decompensated chronic heart failure; LVEF, left ventricular ejection fraction; eGFR, estimated glomerular filtration rate; MDRD, modified diet in renal disease; NT-proBNP, N-terminal pro B-type natriuretic peptide; HR, hazard ratio; SD, standard deviation; IQR, interquartile range; 95% CI, 95% confidence interval.

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short-term prognosis, such as older age, impaired renal function, low blood pressure, and higher levels of natriuretic peptide, are well known. Epidemiological studies have found little or no difference in mortality in patients with preserved compared to patients with impaired left ventricular ejection fraction (LVEF) [10–12]. An exacerbation of AHF has been suggested to cause deterioration in the prognosis of patients with chronic heart failure [13,14]. However, data on long-term survival after hospitalization for AHF are limited [11,15–18]. Even less is known about the long-term prognosis and factors related to outcome in patients with de-novo AHF.

The aim of this study was to investigate the five-year mortality and identify factors associated with long-term prognosis after hospitalization for AHF with special emphasis on possible differences between patients with ADCHF and de-novo heart failure.

2. Material and methods

FINN-AKVA is a prospective observational multicenter study on AHF [7]. During three months in 2004, consecutive patients from 14 hospitals in Finland hospitalized for AHF were enrolled. For inclusion in the study, the diagnosis of AHF had to be confirmed during the hospital stay. Clinical data on admission was recorded in detail and patients were systematically characterized with regard to demographics, co-morbidities and medication. Subjects with a previous history of heart failure were classified as acutely decompensated chronic heart failure (ADCHF), and the remaining were regarded as new onset (de-novo) AHF. Blood samples were obtained at presentation and at 48 h after admission. Blood hemoglobin, serum creatinine and serum sodium were analyzed from admission samples locally at each participating hospital. Estimated glomerular filtration rate (eGFR) was calculated using the abbreviated 4-variable MDRD equation [19]. Levels of N-terminal pro-B-type natriuretic peptide (NT-proBNP; Roche Diagnostics) were analyzed by the central laboratory from samples obtained at 48 h. In-hospital mortality was registered. Vital status at five years from the index hospitalization was ascertained for all patients through the national Population Register Centre and time of death was obtained. The end-point of interest was all-cause mortality.

All patients gave written informed consent. The FINN-AKVA study was approved by the local ethics committee and conducted in accordance with the declaration of Helsinki. The author(s) of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology.

2.1. Statistical analyses

Results are shown as numbers and percentages (%), means with standard deviation (SD) or median with interquartile range (IQR) for variables not normally distributed. Dichotomous variables were compared by chi-square test and continuous variables by Student's t-test or Mann–Whitney U test as appropriate. Cox proportional hazard analyses were performed to identify variables associated with five-year mortality. Hazard ratios (HR) are shown with 95% confidence intervals (CI). Independent predictors of long-term outcome were determined using a stepwise backward selection multivariable Cox regression model, and variables were removed at $p > 0.1$. Age, gender, clinical variables at presentation, and biochemistry on admission were included as baseline variables. Factors precipitating AHF were tested in a multivariable model, but were neither independently associated with outcome nor improving the model performance and were not retained in further analyses. Kaplan–Meier survival curves were plotted and groups compared using the log-rank test. p-values <0.05 were regarded statistically significant. SPSS statistical software (version 15.0.1) was used for statistical analyses.

3. Results

The study population consisted of 620 patients, of which 307 (49%) were women. Patients were on average 75 years old. Medical history and clinical presentation are shown in Table 1. A history of

Table 1
Study population and patients with ADCHF and de-novo AHF.

Characteristic	All n = 620	ADCHF n = 316	De-novo AHF n = 304	p-Value
Age, years; (mean[SD])	75.1 (10.4)	76.5 (9.8)	73.5 (10.8)	<0.001
Men; n = (%)	313 (51)	147 (47)	166 (55)	0.04
Medical history of (n = [%])				
Chronic heart failure	316 (51)	NA	NA	
Coronary artery disease	342 (55)	220 (70)	122 (40)	<0.001
Myocardial infarction	172 (28)	128 (41)	44 (15)	<0.001
Hypertension	339 (55)	180 (57)	159 (52)	0.24
Diabetes	200 (32)	120 (38)	80 (26)	0.002
Chronic atrial fibrillation	167 (27)	124 (39)	43 (14)	<0.001
Cerebrovascular disease	108 (17)	65 (21)	43 (14)	0.03
Obstructive pulmonary disease	78 (13)	48 (15)	30 (10)	0.05
Peripheral atherosclerotic disease	63 (10)	43 (14)	20 (7)	0.004
Smoker	68 (11)	27 (9)	43 (14)	0.05
Precipitating factors				
Acute coronary syndrome	198 (32)	77 (24)	121 (40)	<0.0001
Atrial fibrillation/flutter	182 (29)	78 (25)	104 (34)	0.009
Valvular disease	75 (12)	42 (13)	33 (11)	0.4
Infection	146 (24)	83 (26)	63 (21)	0.10
Clinical presentation (mean [SD])				
Blood pressure; mm Hg	147/82 (33/20)	144/78 (33/18)	151/86 (33/21)	0.01
Heart rate; bpm	92 (27)	87 (25)	96 (28)	<0.001
LVEF % (n = 410)	45 (16)	44 (17)	46 (15)	0.3
Biochemistry				
Hemoglobin (g/L)	127 (18)	124 (18)	131 (18)	<0.001
Sodium (mmol/L)	138 (5)	138 (5)	138 (5)	0.37
CRP (g/L)	10 (3–26)	10 (4–25)	9 (3–29)	0.35
Creatinine (μmol/L)	98 (81–125)	105 (86–135)	93 (76–116)	<0.001
eGFR (ml/min)	57 (22)	52 (21)	62 (23)	<0.001
NT-proBNP (n = 478)	3896 (1950–8497)	4882 (2267–9417)	3402 (1674–7393)	0.007
Medication at discharge (n = [%])				
Beta-blocker	493 (86)	253 (86)	240 (85)	0.75
ACEI/ARB	439 (76)	230 (78)	209 (74)	0.25
Loop diuretic	509 (89)	275 (94)	234 (83)	<0.001
Spironolactone	118 (20)	78 (27)	35 (13)	<0.001
Digoxin	187 (33)	117 (40)	70 (25)	<0.001
Mortality (n = [%])				
In-hospital deaths	44 (7.1)	22 (7.0)	22 (7.2)	0.9
Deaths at 5 years	374 (60.3)	239 (75.6)	135 (44.4)	<0.001

Results as numbers and percentages, mean and standard deviation (SD) or median with interquartile range. p-Value for difference between ADCHF and de-novo AHF. AHF = acute heart failure, ADCHF = acutely decompensated chronic heart failure, ACEI/ARB = angiotensin converting enzyme inhibitor/angiotensin receptor blocker, bpm = beats per minute, LVEF = left ventricular ejection fraction, CRP = c-reactive protein, and eGFR = estimated glomerular filtration rate.