

# Characteristics and outcomes of patients admitted for acute heart failure in a single-centre study

Jiří Dokoupil<sup>1</sup>, Juraj Hrečko<sup>1</sup>, Eva Čermáková<sup>2</sup>, Michaela Adamcová<sup>3</sup> and Radek Pudil<sup>1\*</sup>

<sup>1</sup>1st Department of Medicine—Cardioangiology, Charles University, Faculty of Medicine and University Hospital in Hradec Králové, Sokolská 581, Hradec Králové, Czech Republic; <sup>2</sup>Department of Medical Biophysics, Faculty of Medicine in Hradec Kralove, Charles University, Prague, Czech Republic; and <sup>3</sup>Department of Physiology, Faculty of Medicine in Hradec Kralove, Charles University, Prague, Czech Republic

## Abstract

**Aims** Acute heart failure represents a medical condition with very high mortality. Accurate risk stratification can help physicians to improve the health care about these patients. The aim of our study was to characterize real-life patients admitted for acute heart failure in a specific region with one tertiary medical centre and to describe risk factors of short-term and long-term mortality.

**Methods and results** We performed a retrospective analysis of patients admitted from January 2017 to December 2017 to Department of cardiology of the tertiary medical centre University Hospital in Hradec Kralove. We identified 385 patients admitted for acute heart failure to the standard care and intensive care unit. The median of age was 74 years (IQR 67.5–80) and 34% of patients were female. Hospital admission was due to *de novo* heart failure in 222 (57.7%) patients. The most common comorbidities were arterial hypertension (77.7%), dyslipidaemia (67.3%) and coronary artery disease (63.1%). Coronary artery disease (52.7% of cases) and valve disease (28.1% of cases) were the most common aetiologies of heart failure. The all-cause in-hospital mortality was 12.7%, 30-day mortality was 14.6% and 1 year mortality was 34%. Among risk factors of in-hospital mortality, the most significant factors were haemodialysis during the hospitalization [odds ratio (OR) 15.82, 95% confidence interval (CI) 2.96–84.57,  $P = 0.0008$ ], chronic heart failure (OR 4.27, 95% CI 1.66–11.03,  $P = 0.001$ ) and STEMI as a precipitating factor of heart failure (OR 4.19, 95% CI 1.23–14.25,  $P = 0.023$ ). Haemodialysis during the hospitalization (OR 4.28, 95% CI 1.17–15.61,  $P = 0.025$ ) and the comorbidity depression and anxiety (OR 3.49, 95% CI 1.45–8.39,  $P = 0.005$ ) were the most significant risk factors of long-term mortality.

**Conclusions** Our study confirms very high mortality rates among patients with acute heart failure underlying poor prognosis of these patients. Comorbidities (peripheral artery disease, atrial fibrillation, chronic heart failure and depression and anxiety), precipitating factors of heart failure (myocardial infarction with ST segment elevation), complications occurring during the hospitalization (acute kidney injury, pulmonary ventilation for respiratory failure and haemodialysis) and the age of patients should be included in the risk stratification of in-hospital, 30 day and 1 year mortality.

**Keywords** Heart failure; Risk factors; Mortality; Epidemiology

Received: 30 May 2021; Revised: 7 November 2021; Accepted: 1 December 2021

\*Correspondence to: Radek Pudil, 1st Department of Medicine—Cardioangiology, Faculty of Medicine in Hradec Kralove, Charles University and University Hospital in Hradec Kralove, Hradec Králové, Czech Republic. Tel: +420 495 834 786; Fax: +420 495 832 006. Email: radek.pudil@fnhk.cz

## Introduction

Acute heart failure (AHF) represents one of the most common causes of hospital admissions. Despite successful progress in the therapy of chronic heart failure during last years, the morbidity and mortality of patients admitted with AHF remain still high.<sup>1</sup> Moreover, heart failure care's overall cost continues to rise as the incidence and prevalence of heart

failure have increased during last years,<sup>2</sup> with hospitalization for heart failure representing a significant part of the resource burden.<sup>3</sup>

Hospitalization for AHF (*de novo* or decompensation of chronic heart failure) itself means a negative prognostic factor in the natural history of the disease. Thus, the management of these events warrants careful attention to properly evaluate patients, identify underlying aetiologies and precip-

itating factors and consider treatment options with respect to the patient's prognosis and quality of life. The knowledge of risk factors of adverse events may potentially contribute to correct risk stratification, help to guide the treatment and finally improve a clinical outcome. To date, many predictive models with different variables have been proposed to estimate the risk of adverse events in patients with AHF. Their application in standard clinical practice is largely underused, primarily because of the elusive applicability in evaluating an individual patient's risk.<sup>4</sup>

To provide recent data about AHF patients' characteristics and prognosis, we present results of a retrospective study from the University Hospital in Hradec Kralove. We collected data about patients admitted to the Department of Cardiology during 12 consecutive months. Our hospital represents the only hospital in the city of Hradec Kralove (92 929 inhabitants in 2017) and it also serves as the only tertiary medical centre for Hradec Kralove Region (550 804 inhabitants in 2017) with the opportunity of an urgent cardiac surgery procedure, coronary catheterization or cardiac stimulation procedure. In our study, we focused on patients' profile on admission and differences between mortality groups, and we clarified their contribution to patient's prognosis.

## Study design and methods

The aim of this study was to provide a characterization of hospitalized patients with AHF in a single-centre study and determine risk factors for short-term (in-hospital and 30-day mortality) and long-term mortality (1-year mortality). We performed a retrospective analysis of patients hospitalized for AHF at the Department of Cardiology at the University Hospital in Hradec Kralove during 12 consecutive months from January 2017 to December 2017. Using data collected from Hospital information system and health records of patients we reviewed 3413 hospitalizations and subsequently identified in total 385 patients hospitalized for an AHF during 12 months in the standard care and intensive care unit. It accounted for 422 hospitalizations, but patients were included only once during the year.

We collected data regarding demographic characteristics, comorbidities, medications and basic clinical and imaging methods. The mortality of patients was assessed either directly by the information about the patient's death in his medical record or by the information about health insurance termination during 12 months after the index hospitalization.

Qualified cardiologists performed the diagnosis of clinical conditions and treatment of patients according to the personal clinical judgement and cardiology guidelines concerning heart failure from 2016.<sup>5</sup>

## Statistical analysis

Categorical data are presented as numbers of patients and percentages, continuous data are presented as median and interquartile range (IQR) because of non-normal distribution. Categorical data were compared by the Pearson's  $\chi^2$  test or Fisher's exact test if at least one cell had an expected value less than 5. Continuous data were compared by non-parametrical Mann-Whitney  $U$  test or Kolmogorov-Smirnov test. Multivariate logistic regression was performed to assess the effect of several variables on the all-cause in-hospital, 30 day and 1 year mortality, results are presented as odds ratios (ORs) with corresponding 95% confidence intervals (CIs). Variables with between-group significant differences and with relevant clinical interest were included in multivariate analysis. Variables with a significant association with death are characterized as independent predictors of mortality. A  $P$  value less than 0.05 is considered as a statistically significant difference.

Statistical analysis was performed using statistical software NCSS 2019 version 19.0.6.

## Results

### General characterization

During 12 months from January 2017 to December 2017 totally 385 patients with AHF were admitted to our department, from which 131 (34%) were females and the median age at the time of hospitalization was 74 years with 77 years (IQR 72–83) in women and 72 years (IQR 65–77) in men ( $P < 0.0001$ ). In total 247 (64.2%) patients were older than 70 years. The vast majority of patients (369, 95.8%) were from Hradec Kralove Region and 156 (40.5%) patients were from the city of Hradec Kralove. With respect to the size of the population, with an AHF, we thus hospitalized 0.07% of the population of Hradec Kralove Region and 0.17% of inhabitants of the city of Hradec Kralove. The median length of hospitalization was 10 days and 183 (47.5%) patients spent at least 1 day in the intensive care unit. Most of the patients (241, 71.7%) were discharged home and 75 (22.3%) patients required further hospitalization at another department or hospital. During 12 months, 67 (19.9%) patients surviving the index hospitalization required rehospitalization for an AHF at our hospital. Detailed characteristics are summarized in *Table 1*.

Of 385 patients, 49 (12.7%) died during the hospitalization with the median day of death 5. Following 30 days after admission, the death occurred in 56 (14.6%) patients and 131 (34%) patients died in 12 months following the hospitalization (*Table 2*). 71.4% of patients (35 of 49) died in the first 10 days of hospitalization. The cardiogenic shock (developed

**Table 1** General characteristics of patients at admission

General characteristics	
Demographic and clinical characteristics	
Age, median (IQR)	All (N = 385) 74 (67.5–80)
Female, n (%)	131 (34)
Heart rate, median (IQR)	90 (75–110)
Systolic blood pressure, median (IQR)	130 (112–150)
Diastolic blood pressure, median (IQR)	75 (64–88)
BMI, median (IQR), N = 376	29.3 (26–33.8)
BSA, median (IQR), N = 376	2 (1.85–2.21)
EF, median (IQR), N = 376	37.5 (25–50)
Peripheral swelling, n (%)	225 (58.4)
Crackles, n (%)	255 (66.2)
Jugular veins distension, n (%)	135 (35.1)
X-ray pulmonary congestion, n (%)	255 (66.9)
X-ray pleural effusion, n (%)	132 (34.7)
Cardiogenic shock, n (%)	28 (7.3)
Cardiopulmonary resuscitation before admission, n (%)	12 (3.1)
Comorbidities	
Chronic heart failure, n (%)	163 (42.3)
Coronary artery disease, n (%)	243 (63.1)
Diabetes mellitus, n (%)	181 (47)
Arterial hypertension, n (%)	299 (77.7)
Atrial fibrillation, n (%)	210 (54.6)
Atrial flutter, n (%)	23 (6)
Chronic kidney disease, n (%)	220 (57.1)
Valve disease (at least moderate), n (%)	283 (73.5)
Malignancy, n (%)	59 (15.3)
Peripheral artery disease, n (%)	77 (20)
Chronic obstructive pulmonary disease, n (%)	62 (16.1)
Depression, anxiety, n (%)	31 (8)
Dyslipidaemia, n (%)	259 (67.3)
Stroke, n (%)	38 (9.9)
ICD, n (%)	34 (8.8)
Pacemaker, n (%)	16 (4.2)
CRT, n (%)	21 (5.5)
Pharmacotherapy on admission	
Acetylsalicylic acid, n (%)	162 (42.1)
P2Y12 inhibitor, n (%)	28 (7.3)
Anticoagulation therapy, n (%)	131 (34)
Beta-blocker, n (%)	229 (59.5)
ACE inhibitor, n (%)	153 (39.7)
Angiotensin receptor blocker, n (%)	57 (14.8)
Spirolactone, n (%)	93 (24.2)
Furosemide, n (%)	195 (50.7)
Hydrochlorothiazide, n (%)	67 (17.4)
Amiodarone, n (%)	54 (14)
Statin, n (%)	146 (37.9)
Amiloride, n (%)	44 (11.4)
Digoxin, n (%)	18 (4.7)
Ivabradine, n (%)	2 (0.5)

BMI, body mass index; BSA, body surface area; CRT, cardiac resynchronization therapy; EF, ejection fraction; ICD, implantable cardioverter-defibrillator.

**Table 2** Mortality rates

Overall mortality	
All (N = 385)	
In-hospital mortality, n (%)	49 (12.7)
30 day mortality, n (%)	56 (14.6)
1 year mortality, n (%)	131 (34)

during 24 h after admission) was present in 28 (7.3%) patients with the in-hospital mortality accounting for 60.7% (17 patients).

The AHF was classified as *de novo* in 222 (57.7%) patients (without a previous diagnosis of heart failure), the rest of the patients had a recognized chronic heart failure before admission and presented as a decompensation of chronic heart failure (163, 42.3%).

The most common aetiologies of heart failure and precipitating factors are listed in *Table 3*. More than one causative and precipitating factor can participate in the development and sudden decompensation of heart failure in many patients. In our cohort of patients, totally 26 aetiologies and 30 triggers were recognized. Coronary artery disease was assessed as a causative factor in more than half of patients. STEMI as an aggravating factor was considered in 42 (10.9%) patients, but an acute coronary syndrome (composed of STEMI, non-STEMI, myocardial infarction in a subacute phase, global ischaemia and myocardial infarction with LBBB) was present in 79 (20.5%) patients.

Pharmacological, diagnostic and other therapeutic interventions during the patient’s hospitalization are reported in *Table 4*. Among complications associated with the hospitalization, at least a mild hepatic injury (defined as the elevation of both ALT and AST or GMT and ALP above the URL) occurred in 164 (42.6%) patients. Acute respiratory insufficiency (defined as resting saturation of O<sub>2</sub> below 90%) at admission or occurring during the hospitalization because of heart failure occurred in 156 (40.5%) patients. Electrolyte disturbances (at least two of hyponatraemia <135 mmol/L, hypokalaemia <3.5 mmol/L, hyperkalaemia >5.2 mmol/L or hypochloreaemia <97 mmol/L) occurred in 102 (26.5%) pa-

**Table 3** The most common aetiologies and precipitating factors of heart failure

Aetiologies (the most common)	All (N = 385)
Coronary artery disease, n (%)	203 (52.7)
Valve disease, n (%)	108 (28.1)
Tachyarrhythmia, n (%)	59 (15.3)
Dilated cardiomyopathy, n (%)	28 (7.3)
Unknown, n (%)	26 (6.8)
Diastolic dysfunction, n (%)	14 (3.6)
Cor pulmonale, n (%)	10 (2.6)
Arterial hypertension, n (%)	10 (2.6)
Precipitating factors (the most common)	All (N = 385)
Progression of heart failure, n (%)	134 (34.8)
Infection, n (%)	84 (21.8)
Supraventricular tachyarrhythmia, n (%)	60 (15.6)
STEMI, n (%)	42 (10.9)
Bradycardia, n (%)	17 (4.4)
Exacerbation of COPD, n (%)	17 (4.4)
non-STEMI, n (%)	14 (3.6)
Subacute myocardial infarction, n (%)	14 (3.6)
Non-adherence, n (%)	13 (3.4)
Hyperhydration, n (%)	12 (3.1)
Uncontrolled arterial hypertension, n (%)	9 (2.3)

COPD, chronic obstructive pulmonary disease; non-STEMI, myocardial infarction without elevations of ST segment; STEMI, myocardial infarction with elevations of ST segment

**Table 4** Treatment and diagnostic procedures during the hospitalization

Treatment and diagnostic procedures	All (N = 385)
Artificial pulmonary ventilation, n (%)	73 (19)
Invasive, n (%), N = 73	36 (49.3)
Non-invasive, n (%), N = 73	40 (54.8)
ECMO, n (%)	4 (1)
Coronarography, n (%)	159 (41.3)
Intervention, n (%), N = 159	73 (45.9)
Intravenous furosemide, n (%)	331 (86)
Intravenous nitrate, n (%)	56 (14.6)
Dobutamine, n (%)	38 (9.9)
Noradrenaline, n (%)	69 (17.9)
Intravenous amiodarone, n (%)	46 (12)
Haemodialysis, n (%)	15 (3.9)
continuous renal replacement therapy, n (%), N = 15	7 (46.7)
intermittent renal replacement therapy, n (%), N = 15	8 (53.3)

ECMO, extracorporeal membrane oxygenation.

tients. Acute kidney injury<sup>6</sup> in patients without a previous chronic kidney disease occurred in 63 (16.4%) patients with Stages I, II and III in 46 (11.9%), 12 (3.1%) and 5 (1.3%) patients, respectively, and deterioration of previously known chronic kidney disease at least by one category occurred in 90 (23.4%) patients.

Echocardiographic examination was done in 376 (97.7%) patients with 315 examinations during the hospitalization. The median of EF was 37.5% (IQR 25–50). Most of the patients (198, 52.7%) had the EF < 40% and 120 (31.9%) patients had the EF ≥ 50%. The median of TAPSE was 18 mm (IQR 13–21).

### Comparison of in-hospital, 30 day and 1 year mortality groups

Differences between mortality groups in specific characteristics are shown in *Table 5*. There are many significant differences in demographic and clinical characteristics between survivors and non-survivors. Those, who died in the hospital, compared with those, who survived, had a significantly higher rate of atherosclerotic diseases such as coronary artery disease and peripheral artery disease. This difference persisted after 1 year (but not in the 30 day mortality group for peripheral artery disease). The median of the length of hospitalization was 11 days and 5 days for survivors and non-survivors, respectively, for both in-hospital and 30 day mortality with a statistically significant difference. Patients who presented with a decompensation of chronic heart failure had significantly higher mortality during the hospital stay, after 30 days and even after 1 year. The deceased also had significantly lower systolic and diastolic blood pressure compared with survivors in all three groups. Although there is not any difference in BMI or BSA in patients who survived or died in the hospital or after 30 days, the difference is statistically significant in 1-year mortality group.

### Predictors of mortality

Results of multivariate logistic regression with clinically relevant variables are performed in *Table 6*. This analysis revealed that a longer hospital stay and higher systolic blood pressure were related to a better in-hospital outcome. In contrast, patients with an acute kidney injury or patients requiring haemodialysis had a worse prognosis. These factors also persisted in a 30 day mortality model. For 1 year mortality, only a higher BMI and higher systolic blood pressure at admission were associated with a better outcome.

### Discussions

In this single-centre retrospective study, we analysed real-life AHF patients admitted to the tertiary medical centre and we yield new and recent information about their demographic characteristics, comorbidities and outcomes. The value and main contribution of our study are in the enrolment of a consecutive and well-defined population of patients in a specific period. We further considered these characteristics for reporting prognostic factors of short-term (in-hospital and 30 day) and long-term (1 year) mortality. Considering the retrospective design, we provide results without large treatment modifications during the relatively short period of data collection.

Most of the data that we know today about the epidemiology of AHF are derived from large-scale registries mainly from the first decade of this century,<sup>1,7–17</sup> selected data are presented in *Table 7*. More recent registries from Europe or Asia regions<sup>18,19</sup> follow the trends in outcomes and demographic characteristics observed in those pivotal studies, but differences in local clinical practice or different clinical thresholds for hospital admission may vary among registries and they may also change over a period of time. Comparison of these results with our study is partially limited because of different sizes of the population, multicentre setting and prospective design. However, many similar or distinct findings from our study can be reported.

The median age of 74 years in our study was slightly higher than that observed in most registries. Markedly higher age was reported only in the prospective registry in Japan.<sup>18</sup> We also observed significantly older patients among the deceased compared to survivors in 30 day and 1 year mortality groups. The age (as a continuous variable) was subsequently a mild but significant predictor of 30 day and 1 year mortality.

With the ageing of the population, there is an increase in the prevalence of chronic conditions such as coronary artery disease, diabetes mellitus, arterial hypertension or chronic kid-

**Table 5** Comparison between mortality groups

In-hospital mortality			
Variable	Survivors (N = 336)	Deceased (N = 49)	P
Days of hospitalization, median (IQR)	11 (7–17.75)	5 (2–15)	<0.0001
Coronary artery disease, n (%)	205 (61)	38 (77.6)	0.025
Peripheral artery disease, n (%)	61 (18.2)	16 (32.7)	0.018
Chronic heart failure, n (%)	133 (39.6)	30 (61.2)	0.004
Acute kidney injury, n (%) <sup>a</sup>	121 (36)	32 (65.3)	<0.0001
Haemodialysis, n (%) (during hospitalization)	6 (1.8)	9 (18.4)	<0.0001
Artificial pulmonary ventilation, n (%)	52 (15.5)	21 (42.9)	<0.0001
Systolic blood pressure, median (IQR) <sup>b</sup>	131 (115–151)	116 (92–132)	<0.0001
Diastolic blood pressure, median (IQR) <sup>b</sup>	77 (66–89.75)	65 (52–75)	<0.0001
EF, median (IQR)	37.5 (25–50)	30 (18.125–50)	0.047
30 day mortality			
Variable	Survivors (N = 329)	Deceased (N = 56)	P
Days of hospitalization, median (IQR)	11 (7–18.5)	5 (2–8.75)	<0.0001
Age, median (IQR)	73 (67–79)	77 (71–85)	0.003
Coronary artery disease, n (%)	201 (61.1)	41 (75)	0.046
Atrial fibrillation, n (%)	172 (52.3)	38 (67.9)	0.03
Depression, anxiety, n (%)	22 (6.7)	9 (16.1)	0.029
Chronic heart failure, n (%)	132 (40.1)	31 (55.4)	0.033
Acute kidney injury, n (%) <sup>a</sup>	119 (36.2)	34 (60.7)	0.0005
Haemodialysis, n (%) (during hospitalization)	9 (2.7)	6 (10.7)	0.013
Artificial pulmonary ventilation, n (%)	52 (15.8)	21 (37.5)	0.0001
Systolic blood pressure, median (IQR) <sup>b</sup>	132 (116.5–152.5)	115.5 (99.25–130.5)	<0.0001
Diastolic blood pressure, median (IQR) <sup>b</sup>	77 (65.5–89)	67 (58–80)	0.0005
Pulse pressure, median (IQR) <sup>b</sup>	52 (41–70)	45 (30–60.75)	0.002
EF, median (IQR)	37.5 (25–51.875)	30 (20–46.87)	0.021
1 year mortality			
Variable	Survivors (N = 254)	Deceased (N = 131)	P
Age, median (IQR)	72 (65–78)	76 (71–84)	<0.0001
Coronary artery disease, n (%)	149 (58.7)	94 (71.8)	0.012
Atrial fibrillation, n (%)	129 (50.8)	81 (61.8)	0.039
Peripheral artery disease, n (%)	41 (16.1)	36 (27.5)	0.008
Depression, anxiety, n (%)	15 (5.9)	16 (12.2)	0.031
Chronic heart failure, n (%)	90 (35.4)	73 (55.7)	0.0001
Acute kidney injury, n (%) <sup>a</sup>	89 (35)	64 (48.9)	0.009
Haemodialysis, n (%) (during hospitalization)	5 (2)	10 (7.6)	0.007
Artificial pulmonary ventilation, n (%)	40 (15.8)	33 (25.2)	0.025
Spironolactone, n (%) <sup>b</sup>	52 (20.5)	41 (31.3)	0.019
Furosemide, n (%) <sup>b</sup>	113 (44.5)	82 (62.6)	0.0008
Systolic blood pressure, median (IQR) <sup>b</sup>	134 (117–153)	122 (110–140.75)	0.001
Diastolic blood pressure, median (IQR) <sup>b</sup>	77 (66–90)	73 (62.25–83.75)	0.009
BMI, median (IQR) <sup>b</sup>	29.6 (26.5–34.8)	27.6 (24.4–32.2)	0.003
BSA, median (IQR) <sup>b</sup>	2.02 (1.87–2.23)	1.97 (1.76–2.16)	0.028

BMI, body mass index; BSA, body surface area; EF, ejection fraction.

<sup>a</sup>Complication during the hospitalization

<sup>b</sup>At admission

ney disease, when all of them are important risk factors<sup>20</sup> for the development of heart failure. Compared with previous registries, we also report higher rates of comorbidities such as arterial hypertension (77.7% vs. 53–73.1%), diabetes mellitus (47% vs. 27–45.3%), atrial fibrillation (54.6% vs. 24.4–44%) or chronic kidney disease (57.1% vs. 9.4–32.5%). Similarly, the prevalence of coronary artery disease was higher than in most of these registries. Higher age and comorbidities are generally considered negative prognostic factors in patients with AHF or other critically ill cardiac patients.<sup>21</sup> Thus, they are important variables in many mortality prediction risk scores, including short-term and long-term outcomes.<sup>22,23</sup>

In the multivariate analysis (*Table 6*), many comorbidities were significantly associated with all-cause mortality. Notably, the presence of chronic heart failure is reported with an odds ratio higher than 4 in the analysis of in-hospital and 30-day mortality. This observation is in contrast with previous reports where patients with *de novo* heart failure may have higher in-hospital mortality.<sup>10</sup> Another cardiovascular comorbidity, peripheral artery disease (PAD), which occurred in one third of patients who died during the hospitalization, was significantly associated with in-hospital mortality. The presence of PAD is often described as a marker of generalized atherosclerosis<sup>24</sup> together with coronary artery disease and



**Table 6** Risk factors of short-term and long-term mortality

In-hospital mortality			
Variable	Odds ratio	Lower and upper 95% confidence limit	P value
Haemodialysis <sup>a</sup>	15.817	2.958–84.571	0.0008
Chronic heart failure	4.271	1.655–11.026	0.001
STEMI <sup>b</sup>	4.186	1.23–14.247	0.023
Peripheral artery disease	3.694	1.513–9.02	0.004
Artificial pulmonary ventilation	2.974	1.256–7.04	0.015
Acute kidney injury <sup>a</sup>	2.277	1.011–5.125	0.045
Depression, anxiety	1.574	0.462–5.358	0.48
EF	1.015	0.989–1.041	0.257
Systolic blood pressure <sup>c</sup>	0.968	0.952–0.985	<0.0001
Days of hospitalization	0.963	0.934–0.994	0.008
Supraventricular tachyarrhythmia <sup>b</sup>	0.343	0.071–1.662	0.14
30 day mortality			
Variable	Odds ratio	Lower and upper 95% confidence limit	P value
Haemodialysis <sup>a</sup>	13.706	1.267–148.284	0.031
Chronic heart failure	4.291	1.531–12.027	0.003
Depression, anxiety	4.097	1.161–14.457	0.035
Atrial fibrillation <sup>d</sup>	3.627	1.401–9.389	0.005
Acute kidney injury <sup>a</sup>	3.357	1.374–8.2	0.007
STEMI <sup>b</sup>	3.312	0.942–11.639	0.061
Artificial pulmonary ventilation	2.483	0.905–6.813	0.082
Age	1.051	1.000–1.105	0.045
EF	0.989	0.962–1.017	0.451
Systolic blood pressure <sup>c</sup>	0.975	0.959–0.992	0.002
Days of hospitalization	0.887	0.834–0.945	<0.0001
Crackles at admission	0.395	0.171–0.91	0.028
BSA <sup>c</sup>	0.21	0.033–1.334	0.088
1 year mortality			
Variable	Odds ratio	Lower and upper 95% confidence limit	P value
Haemodialysis <sup>a</sup>	4.281	1.174–15.611	0.025
Depression, anxiety	3.486	1.449–8.385	0.005
Furosemide <sup>c</sup>	2.012	1.176–3.441	0.01
Artificial pulmonary ventilation	1.702	0.873–3.18	0.12
Progression of heart failure <sup>b</sup>	1.7	0.968–2.986	0.065
Atrial fibrillation <sup>d</sup>	1.635	0.941–2.841	0.08
Peripheral swelling <sup>c</sup>	1.57	0.881–2.799	0.124
Peripheral artery disease	1.494	0.799–2.792	0.211
Coronary artery disease	1.298	0.721–2.335	0.383
Valve disease <sup>d</sup>	1.283	0.665–2.477	0.455
Acute kidney injury <sup>a</sup>	1.276	0.747–2.179	0.373
Age	1.053	1.022–1.085	0.0004
Systolic blood pressure <sup>c</sup>	0.985	0.976–0.995	0.002
BMI <sup>c</sup>	0.954	0.912–0.999	0.039
Supraventricular tachyarrhythmia <sup>b</sup>	0.524	0.232–1.182	0.113

BMI, body mass index; BSA, body surface area; EF, ejection fraction; STEMI, myocardial infarction with elevations of ST segment.

<sup>a</sup>Complication during the hospitalization.

<sup>b</sup>Precipitating factor.

<sup>c</sup>At admission.

<sup>d</sup>Comorbidity.

cerebrovascular disease. In a state of acute hemodynamic decompensation, which occurs in AHF, limited blood flow to target organs may enhance an adverse course of the disease. On the other hand, the optimal modern pharmacotherapy of PAD with the use of antithrombotics, statins or invasive treatment may result in the non-significant impact on 1-year mortality.

Although presented in relatively low numbers of patients, depression or anxiety as a comorbidity in patients with AHF represents another independent predictor of 30 day or 1 year mortality. The prevalence of depression and anxiety disorders

in patients with heart failure is significantly higher than in the general population,<sup>25,26</sup> accounting for approximately one fifth in heart failure patients. According to the previous reports, depression not only represents a predictor of mortality but is also associated with an increased risk of hospitalization and emergency department visits.<sup>27</sup> Once heart failure develops, a correct treatment of these comorbidities together with proper adherence to guideline-directed medical therapy, especially for patients with heart failure with reduced ejection fraction, represents a crucial factor affecting the quality

Table 7 Acute heart failure registries

	Dokoupil et al.		ESC-HF										KCHF
	ADHERE	OPTIMISE-HF	EHFS I	EHFS II	Long-term	ATTEND	ALARM-HF	IN-HF	AHEAD	FINN-AKVA	KorAHF		
Time period	2017	2001–2004	2003–2004	2000–2001	2004–2005	2011–2013	2007–2011	2006–2007	2007–2009	2006–2009	2004	2011–2014	2014–2016
number of patients	385	105 388	48 612	11 327	3580	5039	4842	4953	1855	4153	620	5625	4056
Age (mean, SD)	74	72 (14)	73.2 (14)	71	69.9	71	73	66–70	72 (12)	71.5 (12.4)	75.1 (10.4)	68.5 (14.5)	80
	(median)				(12.5)	(median)	(13.8)	(median)					(median)
Female (%)	34	52	52	47	39	37.3	42	38	39.8	42.4	49.6	46.8	45
Arterial hypertension (%)	77.7	73	71	53	62.5	64.5	69.4	70.2	57.8	73.1	54.7	62.2	72
Diabetes mellitus (%)	47	44	42	27	32.8	38.9	33.8	45.3	40.4	42.6	32.3	40	37
Coronary artery disease (%)	63.1	57	50	68	53.6	54	31.1	70.2	—	64.9	55.2	42.9	33
Atrial fibrillation (%)	54.6	31	31	43	38.7	44	39.6	24.4	37.7	26.5	27	28.5	41
Chronic kidney disease (%)	57.1	30	30	17	16.8	26.4	—	21.4	32.5	—	9.4	14.3	45
COPD (%)	16.1	31	28	—	19.3	20.2	9.5	24.8	30.1	16.2	12.6	11.3	8.2
History of heart failure (%)	57.7	75	87	65	63	54.5	36.2	64	57	41.7	51	47.8	36
Cardiogenic shock (%)	7.3	2	—	<1	3.9	—	—	11.7	2.3	14.7	2.3	—	—
ICU/CCU care (%)	47.5	19	—	7	51	—	—	75	51.9	—	11.9/39.5	—	—
Length of hospital stay (median)	10	4	4	11	9	—	21	6	10	7.1	7	9	16
In-hospital mortality (%)	12.7	4	3.8	6.9	6.7	4.9	6.4	11	6.4	12.7	7.1	4.8	6.7

COPD, chronic obstructive pulmonary disease; ICU, intensive care unit; CCU, cardiac care unit.

of life, a number of rehospitalizations and long-term survival in patients admitted for AHF.<sup>5</sup>

Above all, haemodialysis during the hospitalization represents a significant predictor of mortality in all three subgroups with the highest odds ratio among all risk factors. In our study, we assessed the factor of haemodialysis, which included patients who required chronic haemodialysis as well as a continuous or intermittent renal replacement therapy as a consequence of acute kidney injury during the hospitalization. The acute kidney injury was also observed as a negative prognostic factor for a short-term prognosis (in-hospital and 30 day mortality). New renal function decline in patients admitted for AHF develops in 18–40% of patients.<sup>28</sup> The impact of elevated creatinine at admission or worsening of renal function during hospitalization is a well-defined prognostic factor associated with a poor outcome.<sup>17,29</sup> According to the recent meta-analysis, in patients who achieved decongestion before hospital discharge, this decongestion was associated with mitigating the harmful effects of kidney injury in patients with AHF.<sup>30</sup> The current evidence also does not support the routine use of ultrafiltration in patients with AHF<sup>31</sup> because of no improvement in mortality compared with standard diuretic treatment. It may be explained by a multiorgan involvement and injury in chronic kidney disease or a chronic volume overload limiting a proper decongestion.

In the multivariate analysis, we also identified several variables associated with reduced mortality in both short and long terms: systolic blood pressure, body mass index and length of hospitalization. Higher systolic blood pressure (SBP) at admission was associated with a better outcome, as confirmed in previous studies.<sup>32,33</sup> Its significance was higher when considering the in-hospital mortality. Patients with heart failure and elevated SBP at admission might have a greater myocardial reserve and lower mortality risk.<sup>34</sup> A longer follow-up would be beneficial because of the well-known unfavourable outcomes of patients with uncontrolled arterial hypertension with further progression of heart failure.<sup>35</sup> On the other hand, lower SBP prevents the administration of heart failure treatment at discharge, leading to a worse long-term outcome.<sup>36</sup> Furthermore, low SBP may be associated with signs of low cardiac output or peripheral hypoperfusion. Management of these patients often requires the use of inotropes or vasopressors. Their use is commonly associated with a worse prognosis<sup>37</sup> because of the administration in patients in a more severe condition. The percentage of use of inotropes or vasopressors in different heart failure registries can vary according to the availability of these agents, the number of patients with cardiogenic shock or the rate of complications other than cardiogenic shock (e.g. haemorrhagic shock, sepsis or hypovolemia). Compared with our study, the use of inotropic agent (dobutamine) was higher in ALARM-HF<sup>14</sup> (22.3%) or ATTEND<sup>13</sup> (11.3%) but lower in IN-HF<sup>15</sup> (7.7%). The use of vasopressor agent (noradrenaline) was markedly lower in ALARM-HF<sup>14</sup> (4.2%) or ATTEND<sup>13</sup> (4.7%). The use of both was comparable with the

AHEAD<sup>16</sup> registry (19% and 10% for noradrenaline and dobutamine).

Obesity is a well-known risk factor for cardiovascular morbidity, including coronary artery disease, stroke or heart failure.<sup>38</sup> On the other hand, among patients with heart failure and obesity, a significant reduction in all-cause and cardiovascular mortality was reported.<sup>39,40</sup> This obesity paradox was also shown in patients with AHF regarding in-hospital<sup>41</sup> or long-term mortality.<sup>42,43</sup> Our study confirmed that a higher BMI is associated with a better outcome in 1 year following the hospitalization.

Regarding the all-cause mortality rates (in-hospital, 30 day and 1 year) (*Table 2*) observed in our study, all of them were markedly high. Although the short-term and long-term mortality of patients with AHF remains high, with approximately one-quarter of AHF patients dying in the following year, a recent meta-analysis of 285 AHF studies between 1980 and 2017 reported a decline in 30 day all-cause death that persisted at 1 year.<sup>44</sup> The authors reported that the 30 day and 1 year all-cause deaths were 7% and 24%. According to the published outcomes from registries (*Table 7*), the in-hospital mortality varies from 4 to 7.1%, with a higher rate (up to 11–12.7%) in registries with a higher proportion of cardiogenic shock.<sup>14,16</sup> The trend in lower short- and long-term mortality in patients with AHF was also observed in the United Kingdom National heart failure audit.<sup>45</sup> Despite this, the in-hospital all-cause mortality was similar to the results observed only in the AHEAD registry.<sup>16</sup> The in-hospital mortality typically reflects the quality of in-patient care with respect to the severity and stage of the disease, together with proper management of complications during the hospital stay. As mentioned above, the character of our hospital (university hospital and tertiary centre) involves the care about patients with a more severe or complicated course of the disease with a potentially higher risk of adverse outcomes or requiring a higher level of medical cardiology care.

## Limitations

There were several limitations in our study. First, this registry was designed in a retrospective setting. Therefore, the management and follow-up were not standardized and decisions about the treatment, which could further influence the patient's prognosis, were made individually based on the patient's clinical state. Second, we assessed the all-cause mortality as the final endpoint without considering other detailed causes (such as heart failure, sudden death or non-cardiac causes). Third, we included patients admitted only to our Department of cardiology and we did not analyse patients admitted to other internal wards during the year. With respect to this, our cohort of patients might not represent the general population in our region.

## Conclusion

Acute heart failure represents a severe medical condition with significant public consequences. Patients, who present with AHF, are at a very high risk of adverse in-hospital and out-of-hospital outcomes. In our single-centre retrospective study with 385 patients admitted to Department of cardiology of the tertiary medical centre, we observed a very high rate of comorbidities, simultaneous complications and causative and precipitating factors with further influence on patient's prognosis. With regard to the short-time prognosis (in-hospital or 30 day mortality), beside traditional laboratory or clinical markers of unfavourable outcome, our results emphasize further consideration of comorbidities (peripheral artery disease, atrial fibrillation and chronic heart failure), precipitating factors of heart failure (myocardial infarction with ST segment elevation) and complications occurring during the hospitalization (acute kidney injury, pulmonary ventilation for respiratory failure and haemodialysis) in the risk stratification of hospitalized patients with AHF. In the stratification of long-term mortality, higher age, haemodialysis during the hospitalization and a frequently omitted comorbidity depression and anxiety represent a negative prognostic factor. Although there is a global trend in the improvement of care about patients during the hospitalization and follow-up, a proper risk evaluation of patients at the time of admission is necessary. It represents a crucial point in a physician's approach. Our study provides recent real-life data about patients' characteristics and outcomes and may contribute to the planning of further clinical trials.

## Acknowledgements

The authors are grateful to the administrative staff of the Cardiology Department of University Hospital in Hradec Kralove for their contribution in data collection.

## Conflict of interest

None declared.

## Funding

This work was supported by the financial grant Ministry of Health Czech Republic, NV19-02-00297 and by the research project of Charles University Prague Progres Q40/03.



## References

- Crespo-Leiro MG, Anker SD, Maggioni AP, Coats AJ, Filippatos G, Ruschitzka F, Ferrari R, Piepoli MF, Delgado Jimenez JF, Metra M, Fonseca C, Hradec J, Amir O, Logeart D, Dahlström U, Merkely B, Drozd J, Goncalvesova E, Hassanein M, Chioncel O, Lainscak M, Seferovic PM, Tousoulis D, Kavaliuniene A, Fruhwald F, Fazlibegovic E, Temizhan A, Gatzov P, Erglis A, Laroche C, Mebazaa A, Heart Failure Association (HFA) of the European Society of Cardiology (ESC). European Society of Cardiology Heart Failure Long-Term Registry (ESC-HF-LT): 1-year follow-up outcomes and differences across regions. *Eur J Heart Fail* 2016; **18**: 613–625.
- Virani SS, Alonso A, Aparicio HJ, Benjamin EJ, Bittencourt MS, Callaway CW, Carson AP, Chamberlain AM, Cheng S, Delling FN, Elkind MSV, Evenson KR, Ferguson JF, Gupta DK, Khan SS, Kissela BM, Knutson KL, Lee CD, Lewis TT, Liu J, Loop MS, Lutsey PL, Ma J, Mackey J, Martin SS, Matchar DB, Mussolino ME, Navaneethan SD, Perak AM, Roth GA, Samad Z, Satou GM, Schroeder EB, Shah SH, Shay CM, Stokes A, VanWagner L, Wang NY, Tsao CW, American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics Subcommittee. American Heart Association Council on Epidemiology and Prevention Statistics Subcommittee and Stroke Statistics Subcommittee. Heart disease and stroke statistics-2021 update: a report from the American Heart Association. *Circulation* 2021; **143**: e254–e743.
- Kanaoka K, Okayama S, Nakai M, Sumita Y, Nishimura K, Kawakami R, Okura H, Miyamoto Y, Yasuda S, Tsutsui H, Komuro I, Ogawa H, Saito Y. Hospitalization costs for patients with acute congestive heart failure in Japan. *Circ J* 2019; **83**: 1025–1031.
- Passantino A. Predicting mortality in patients with acute heart failure: role of risk scores. *World J Cardiol* 2015; **7**: 902–911.
- Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JGF, Coats AJS, Falk V, González-Juanatey JR, Harjola VP, Jankowska EA, Jessup M, Linde C, Nihoyannopoulos P, Parissis JT, Pieske B, Riley JP, Rosano GMC, Ruilope LM, Ruschitzka F, Rutten FH, van der Meer P, ESC Scientific Document Group. 2016 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure: the task force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) developed with the special contribution of the heart failure association (HFA) of the ESC. *Eur Heart J* 2016; **37**: 2129–2200.
- Mehta RL, Kellum JA, Shah SV, Molitoris BA, Ronco C, Warnock DG, Levin A, Acute Kidney Injury Network. Acute kidney injury network: report of an initiative to improve outcomes in acute kidney injury. *Crit Care* 2007; **11**: R31.
- Kociol RD, Hammill BG, Fonarow GC, Klaskala W, Mills RM, Hernandez AF, Curtis LH. Generalizability and longitudinal outcomes of a national heart failure clinical registry: comparison of acute decompensated heart failure National Registry (ADHERE) and non-ADHERE Medicare beneficiaries. *Am Heart J* 2010; **160**: 885–892.
- Adams KF Jr, Fonarow GC, Emerman CL, LeJemtel TH, Costanzo MR, Abraham WT, Berkowitz RL, Galvao M, Horton DP, ADHERE Scientific Advisory Committee and Investigators. Characteristics and outcomes of patients hospitalized for heart failure in the United States: rationale, design, and preliminary observations from the first 100,000 cases in the acute decompensated heart failure National Registry (ADHERE). *Am Heart J* 2005; **149**: 209–216.
- Abraham WT, Fonarow GC, Albert NM, Stough WG, Gheorghiade M, Greenberg BH, O'Connor CM, Sun JL, Yancy CW, Young JB. Predictors of in-hospital mortality in patients hospitalized for heart failure. *J Am Coll Cardiol* 2008; **52**: 347–356.
- Nieminen MS, Brutsaert D, Dickstein K, Drexler H, Follath F, Harjola V-P, Hochadel M, Komajda M, Lassus J, Lopez-Sendon JL, Ponikowski P, Tavazzi L, EuroHeart Survey Investigators, Heart Failure Association, European Society of Cardiology. EuroHeart Failure Survey II (EHFS II): a survey on hospitalized acute heart failure patients: description of population. *Eur Heart J* 2006; **27**: 2725–2736.
- Cleland J, Swedberg K, Follath F, Komajda M, Cohen-Solal A, Aguilar JC, Dietz R, Gavazzi A, Hobbs R, Korewicki J, Madeira HC, Moiseyev VS, Preda I, van Gilst W, Widimsky J, Freemantle N, Eastaugh J, Mason J, Study Group on Diagnosis of the Working Group on Heart Failure of the European Society of Cardiology. The EuroHeart Failure survey programme—a survey on the quality of care among patients with heart failure in Europe part 1: patient characteristics and diagnosis. *Eur Heart J* 2003; **24**: 442–463.
- Komajda M, Follath F, Swedberg K, Cleland J, Aguilar JC, Cohen-Solal A, Dietz R, Gavazzi A, van Gilst W, Hobbs R, Korewicki J, Madeira HC, Moiseyev VS, Preda I, Widimsky J, Freemantle N, Eastaugh J, Mason J, Study Group on Diagnosis of the Working Group on Heart Failure of the European Society of Cardiology. The EuroHeart Failure survey programme—a survey on the quality of care among patients with heart failure in Europe part 2: treatment. *Eur Heart J* 2003; **24**: 464–474.
- Sato N, Kajimoto K, Keida T, Mizuno M, Minami Y, Yumino D, Asai K, Murai K, Muanakata R, Aokage T, Sakata Y, Mizuno K, Takano T, TEND Investigators. Clinical features and outcome in hospitalized heart failure in Japan (from the ATTEND registry). *Circ J* 2013; **77**: 944–951.
- Follath F, Yilmaz MB, Delgado JF, Parissis JT, Porcher R, Gayat E, Burrows N, Mclean A, Vilas-Boas F, Mebazaa A. Clinical presentation, management and outcomes in the acute heart failure global survey of standard treatment (ALARM-HF). *Intensive Care Med* 2011; **37**: 619–626.
- Oliva F, Mortara A, Cacciatore G, Chinaglia A, di Lenarda A, Gorini M, Metra M, Senni M, Maggioni AP, Tavazzi L, IN-HF Outcome Investigators. Acute heart failure patient profiles, management and in-hospital outcome: results of the Italian registry on heart failure outcome. *Eur J Heart Fail* 2012; **14**: 1208–1217.
- Spinar J, Parenica J, Vitovec J, Widimsky P, Linhart A, Fedorco M, Malek F, Cihalik C, Spinarová L, Miklik R, Felsoci M, Bambuch M, Dusek L, Jarkovsky J. Baseline characteristics and hospital mortality in the acute heart failure database (AHEAD) Main registry. *Crit Care* 2011; **15**: R291.
- Siirila-Waris K, Lassus J, Melin J, Peuhkurinen K, Nieminen MS, Harjola V-P, FINN-AKVA study group. Characteristics, outcomes, and predictors of 1-year mortality in patients hospitalized for acute heart failure. *Eur Heart J* 2006; **27**: 3011–3017.
- Yaku H, Ozasa N, Morimoto T, Inuzuka Y, Tamaki Y, Yamamoto E, Yoshikawa Y, Kitai T, Taniguchi R, Iguchi M, Kato M, Takahashi M, Jinnai T, Ikeda T, Nagao K, Kawai T, Komasa A, Nishikawa R, Kawase Y, Morinaga T, Su K, Kawato M, Sasaki K, Toyofuku M, Furukawa Y, Nakagawa Y, Ando K, Kadota K, Shizuta S, Ono K, Sato Y, Kuwahara K, Kato T, Kimura T, KCHF Study Investigators. Demographics, management, and in-hospital outcome of hospitalized acute heart failure syndrome patients in contemporary real clinical practice in Japan — observations from the prospective, multicenter Kyoto Congestive Heart Failure (KCHF) registry. *Circ J* 2018; **82**: 2811–2819.
- Lee SE, Lee H-Y, Cho H-J, Choe W-S, Kim H, Choi JO, Jeon ES, Kim MS, Kim JJ, Hwang KK, Chae SC, Baek SH, Kang SM, Choi DJ, Yoo BS, Kim KH, Park HY, Cho MC, Oh BH. Clinical characteristics and outcome of acute heart failure in Korea: results from the Korean acute heart failure registry (KorAHF). *Korean Circ J* 2017; **47**: 341–353.

20. Schocken DD, Benjamin EJ, Fonarow GC, Krumholz HM, Levy D, Mensah GA, Narula J, Shor ES, Young JB, Hong Y, American Heart Association Council on Epidemiology and Prevention, American Heart Association Council on Clinical Cardiology, American Heart Association Council on Cardiovascular Nursing, American Heart Association Council on High Blood Pressure Research, Quality of Care and Outcomes Research Interdisciplinary Working Group, Functional Genomics and Translational Biology Interdisciplinary Working Group. Prevention of heart failure: a scientific statement from the American Heart Association Councils on Epidemiology and Prevention, Clinical Cardiology, Cardiovascular Nursing, and High Blood Pressure Research; Quality of Care and Outcomes Research Interdisciplinary Working Group; and Functional Genomics and Translational Biology Interdisciplinary Working Group. *Circulation* 2008; **117**: 2544–2565.
21. Padkins M, Breen T, Anavekar N, Diepen S, Henry TD, Baran DA, Barsness GW, Kashani K, Holmes DR Jr, Jentzer JC. Age and shock severity predict mortality in cardiac intensive care unit patients with and without heart failure. *ESC Heart Fail* 2020; **7**: 3971–3982.
22. Cohen-Solal A, Laribi S, Ishihara S, Vergaro G, Baudet M, Logeart D, Mebazaa A, Gayat E, Vodovar N, Pascual-Figal DA, Seronde MF. Prognostic markers of acute decompensated heart failure: the emerging roles of cardiac biomarkers and prognostic scores. *Arch Cardiovasc Dis* 2015; **108**: 64–74.
23. Lee DS, Ezekowitz JA. Risk stratification in acute heart failure. *Can J Cardiol* 2014; **30**: 312–319.
24. Criqui MH, Aboyans V. Epidemiology of peripheral artery disease. *Circ Res* 2015; **116**: 1509–1526.
25. Celano CM, Villegas AC, Albanese AM, Gaggin HK, Huffman JC. Depression and anxiety in heart failure: a review. *Harv Rev Psychiatry* 2018; **26**: 175–184.
26. Rutledge T, Reis VA, Linke SE, Greenberg BH, Mills PJ. Depression in heart failure. *J Am Coll Cardiol* 2006; **48**: 1527–1537.
27. Moraska AR, Chamberlain AM, Shah ND, Vickers KS, Rummans TA, Dunlay SM, Spertus JA, Weston SA, McNallan SM, Redfield MM, Roger VL. Depression, healthcare utilization, and death in heart failure: a community study. *Circ Heart Fail* 2013; **6**: 387–394.
28. Gudsoorkar PS, Thakar CV. Acute kidney injury, heart failure, and health outcomes. *Cardiol Clin* 2019; **37**: 297–305.
29. Damman K, Valente MAE, Voors AA, O'Connor CM, van Veldhuisen DJ, Hillege HL. Renal impairment, worsening renal function, and outcome in patients with heart failure: an updated meta-analysis. *Eur Heart J* 2014; **35**: 455–469.
30. Yamada T, Ueyama H, Chopra N, Yamaji T, Azushima K, Kobayashi R, Kinguchi S, Urata S, Suzuki T, Abe E, Saigusa Y, Wakui H, Partridge P, Burger A, Bravo CA, Rodriguez MA, Ivey-Miranda J, Tamura K, Testani J, Coca S. Systematic review of the association between worsening renal function and mortality in patients with acute decompensated heart failure. *Kidney Int Rep* 2020; **5**: 1486–1494.
31. Kwok CS, Wong CW, Rushton CA, Ahmed F, Cunningham C, Davies SJ, Patwala A, Mamas MA, Satchithananda D. Ultrafiltration for acute decompensated cardiac failure: a systematic review and meta-analysis. *Int J Cardiol* 2017; **228**: 122–128.
32. Chioncel O, Mebazaa A, Harjola V-P, Coats AJ, Piepoli MF, Crespo-Leiro MG, Laroche C, Seferovic PM, Anker SD, Ferrari R, Ruschitzka F, Lopez-Fernandez S, Miani D, Filippatos G, Maggioni AP, ESC Heart Failure Long-Term Registry Investigators. Clinical phenotypes and outcome of patients hospitalized for acute heart failure: the ESC Heart Failure Long-Term Registry: outcome of patients hospitalized for acute heart failure. *Eur J Heart Fail* 2017; **19**: 1242–1254.
33. Fonarow GC, Adams KF Jr, Abraham WT, Yancy CW, Boscardin WJ, ADHERE Scientific Advisory Committee, Study Group, and Investigators. Risk stratification for in-hospital mortality in acutely decompensated heart failure: classification and regression tree analysis. *JAMA* 2005; **293**: 572–580.
34. Vidán MT, Bueno H, Wang Y, Schreiner G, Ross JS, Chen J, Krumholz HM. The relationship between systolic blood pressure on admission and mortality in older patients with heart failure. *Eur J Heart Fail* 2010; **12**: 148–155.
35. Oh GC, Cho H-J. Blood pressure and heart failure. *Clin Hypertens* 2020; **26**: 1.
36. Lombardi C, Peveri G, Cani D, Latta F, Bonelli A, Tomasoni D, Sbolli M, Ravera A, Carubelli V, Saccani N, Specchia C, Metra M. In-hospital and long-term mortality for acute heart failure: analysis at the time of admission to the emergency department. *ESC Heart Fail* 2020; **7**: 2650–2661.
37. Mebazaa A, Motiejunaite J, Gayat E, Crespo-Leiro MG, Lund LH, Maggioni AP, Chioncel O, Akiyama E, Harjola VP, Seferovic P, Laroche C, Julve MS, Roig E, Ruschitzka F, Filippatos G, ESC Heart Failure Long-Term Registry Investigators. Long-term safety of intravenous cardiovascular agents in acute heart failure: results from the European Society of Cardiology Heart Failure Long-Term Registry: safety of intravenous cardiovascular agents in acute heart failure. *Eur J Heart Fail* 2018; **20**: 332–341.
38. Hubert HB, Feinleib M, McNamara PM, Castelli WP. Obesity as an independent risk factor for cardiovascular disease: a 26-year follow-up of participants in the Framingham Heart Study. *Circulation* 1983; **67**: 968–977.
39. Nagarajan V, Kohan L, Holland E, Keeley EC, Mazimba S. Obesity paradox in heart failure: a heavy matter. *ESC Heart Fail* 2016; **3**: 227–234.
40. Oreopoulos A, Padwal R, Kalantar-Zadeh K, Fonarow GC, Norris CM, McAlister FA. Body mass index and mortality in heart failure: a meta-analysis. *Am Heart J* 2008; **156**: 13–22.
41. Fonarow GC, Srikanthan P, Costanzo MR, Cintron GB, Lopatin M. An obesity paradox in acute heart failure: analysis of body mass index and in-hospital mortality for 108927 patients in the Acute Decompensated Heart Failure National Registry. *Am Heart J* 2007; **153**: 74–81.
42. Seko Y, Kato T, Morimoto T, Yaku H, Inuzuka Y, Tamaki Y, Ozasa N, Shiba M, Yamamoto E, Yoshikawa Y, Yamashita Y, Kitai T, Taniguchi R, Iguchi M, Nagao K, Kawai T, Komasa A, Nishikawa R, Kawase Y, Morinaga T, Toyofuku M, Furukawa Y, Ando K, Kadota K, Sato Y, Kuwahara K, Kimura T. Association between body mass index and prognosis of patients hospitalized with heart failure. *Sci Rep* 2020; **10**: 16663.
43. Shah R, Gayat E, Januzzi JL Jr, Sato N, Cohen-Solal A, diSomma S, Fairman E, Harjola VP, Ishihara S, Lassus J, Maggioni A, Metra M, Mueller C, Mueller T, Parenica J, Pascual-Figal D, Peacock WF, Spinar J, van Kimmenade R, Mebazaa A, GREAT (Global Research on Acute Conditions Team) Network. Body mass index and mortality in acutely decompensated heart failure across the world. *J Am Coll Cardiol* 2014; **63**: 778–785.
44. Kimmoun A, Takagi K, Gall E, Ishihara S, Hammoum P, el Bèze N, Bourgeois A, Chassard G, Pegorer-Sfes H, Gayat E, Solal AC, Hollinger A, Merklings T, Mebazaa A, METAHF Team. Temporal trends in mortality and readmission after acute heart failure: a systematic review and meta-regression in the past four decades. *Eur J Heart Fail* 2021; **23**: 420–431.
45. National Heart Failure Audit 2020 summary report (2018/19 data). Available at: <https://www.nicor.org.uk/wp-content/uploads/2020/12/National-Heart-Failure-Audit-2020-FINAL.pdf> (Accessed May 22, 2021).