Effect of precipitating factors and signs of acute heart failure on length of hospital stay

Jiří Dokoupil[1], Juraj Hrečko[1], Eva Čermáková[2], Radek Pudil[1]
[1]1st Department of Internal Medicine – Cardioangiology, Charles University, Faculty of Medicine and University Hospital in Hradec Králové
[2]Department of Medical Biophysics, Faculty of Medicine in Hradec Králové, Charles University

Aim: We aimed to assess the impact of precipitating factors and signs of acute heart failure on the length of hospital stay according to the ejection fraction (EF) subgroups.
Methods: We conducted a retrospective study among acute heart failure patients hospitalized at the Department of Cardioangiology in 2017. The most frequent precipitants and signs were included in the multivariate analysis to assess their association with the length of hospital stay.
Results: We included 376 patients with a median length of hospital stay 11 days. There were 198, 58, and 120 patients with reduced, mildly reduced, and preserved EF, respectively. In reduced EF, peripheral swelling (OR 1.97, CI 1.02–3.78) and pulmonary congestion (OR 2.72, CI 1.38–5.34) were associated with a longer hospital stay. Non-pulmonary infection (OR 50.57, CI 2.82–906.84) and heart failure progression (OR 15.33, CI 1.25–188.53) were associated with a longer hospital stay in mildly reduced EF, and acute pulmonary disease was associated with a longer hospital stay in patients with mildly reduced (OR 10.77, CI 1.07–108.81) and preserved (OR 3.96, CI 1.05–14.99) EF.
Conclusion: Precipitating factors and signs of acute heart failure have different impacts on the length of hospital stay among patients with reduced, mildly reduced or preserved EF.

Key words: acute heart failure, epidemiology, length of hospital stay, precipitating factors, signs of heart failure.

Vliv precipitujících faktorů a známek akutního srdečního selhání na délku hospitalizace

Cíl: Naším cílem bylo zhodnotit vliv precipitujících faktorů a známek akutního srdečního selhání na délku hospitalizace podle jednotlivých podskupin ejekční frakce (EF).
Metodika: Provedli jsme retrospektivní studii u pacientů s akutním srdečním selháním hospitalizovaných v roce 2017 na kardioangiologické klinice. Nejčastější precipitanty a známky byly zařazeny do multivariantní analýzy za účelem posouzení jejich souvislosti s délkou hospitalizace.
Výsledky: Do studie jsme zařadili 376 pacientů s mediánem délky hospitalizace 11 dní. Z těchto pacientů mělo 198 sníženou, 58 mírně sníženou a 120 zachovalou EF. V případě snížené EF byl s delší hospitalizací spojen periferní edém (OR 1,97, CI 1,02–3,78) a plicní kongesce (OR 2,72, CI 1,38–5,34). Naproti tomu mimoplicní infekce (OR 50,57, CI 2,82–906,84) a progrese srdečního selhání (OR 15,33, CI 1,25–188,53) byly spojené s delší hospitalizací v případě mírně snížené EF a akutní plicní onemocnění souviselo s delší hospitalizací u pacientů s mírně sníženou (OR 10,77, CI 1,07–108,81) a zachovalou (OR 3,96, CI 1,05–14,99) EF.
Závěr: Precipitující faktory a známky srdečního selhání mají u pacientů se sníženou, mírně sníženou nebo zachovalou EF rozdílný vliv na délku hospitalizace.

Klíčová slova: akutní srdeční selhání, epidemiologie, délka hospitalizace, precipitující faktory, známky srdečního selhání.

KORESPONDENČNÍ ADRESA AUTORA: Jiří Dokoupil, MD, jiri.dokoupil@fnhk.cz
1st Department of Internal Medicine – Cardioangiology, University Hospital Hradec Králové
Sokolská 581, 500 05 Hradec Králové

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Introduction

Acute heart failure is a severe medical condition with high mortality rates in the short-term and long-term follow-up (1). Along with pharmacological expenditures, investigation methods, and personal expenses, the length of hospital stay is the main contributor to the overall financial burden of acute heart failure care (2).

The recognition of precipitating factors according to the patient's history and laboratory or imaging methods is an integral part of the patient's initial evaluation in an emergency department setting. Moreover, physicians can evaluate many physical signs of heart failure, which aids in making a correct diagnosis. This approach is of great importance, as avoidable or adequately treated factors may lead to outpatient management or shorter hospital stay.

Multiple studies (3–12) have assessed the prevalence of precipitating factors or signs of heart failure in populations of patients with acute heart failure. The effect of precipitating factors on mortality or readmission rates has also been reported (1, 13). However, there are limited data on their impact on the length of hospital stay in different subgroups of ejection fraction (EF) (14).

The aim of our study was to compare the frequencies of precipitating factors and signs of acute heart failure among hospitalized patients according to the categories of ejection fraction as well as to assess their impact on the length of hospital stay.

Methods

We used a retrospective design in our single-centre study. To obtain valuable data on patient characteristics during a specific time frame, we collected information about patients hospitalized from January 2017 to December 2017 at the Department of Cardioangiology of a tertiary medical centre. We included patients hospitalized in both intensive and standard care units. Data were collected from the hospital information system and medical records. We identified 376 patients hospitalized with acute heart failure in whom EF was known. Every patient was included only once during the year, as many rehospitalizations occurred. For the present study, patients were categorized into three main groups according to the EF value: reduced (<40%), mildly reduced (40–49%), and preserved (≥50%) EF subgroup. The diagnosis of acute heart failure was based on the personal clinical judgement of a professional cardiologist together with a clinical examination, laboratory findings, and imaging methods (chest X-ray, echocardiography).

Precipitating factors and signs of heart failure were identified retrospectively according to the final reports, examinations, and personal medical history. More than one precipitant was allowed to characterize a patient's admission. Among all precipitating factors observed in our patients, we identified six as the most common ones: acute coronary syndrome, bradycardia, non-pulmonary infection, tachyarrhythmia, acute pulmonary disease (including pulmonary infection or exacerbation of chronic obstructive pulmonary disease), and gradual progression of heart failure prior to admission. Signs of heart failure were evaluated based on the physical examination (peripheral leg swelling, crackles, jugular vein distension) and findings on chest X-ray (signs of congestion and pleural effusion).

Categorical data are reported as numbers of patients and percentages, continuous data are presented as median (with interquartile range, IQR) because of non-normal distribution. Categorical data were compared using the Pearson's chi-square test; continuous variables were compared by the non-parametrical Kruskal-Wallis test with multiple comparisons (post hoc testing) using Dunn's test and Bonferroni adjustment of the level of significance.

Multivariate logistic regression was performed to identify independent predictors of longer hospital stay. We compared the length of stay <11 days against ≥11 days because 11 days was the median length of stay of the entire cohort. Results are presented as odds ratios with corresponding 95% confidence intervals. A P-value less than 0.05 is considered a statistically significant difference. Statistical analysis was performed using the statistical software NCSS 2019, version 19. 0. 6.

Tab. 1. *General characteristics of patients*

	EF <40%	EF 40-49%	EF ≥50%	P
Number of patients, n (%)	198 (52.7%)	58 (15.4%)	120 (31.9%)	
Age, median (IQR)	72 (66 - 78)	74 (70.5 - 81.5)	76 (69 - 83)	< 0.001
Females, n (%)	52 (26.3)	23 (39.7)	53 (44.2)	0.003
LOH, median (IQR)	11 (6 - 17)	11 (5 - 20.25)	10 (7 - 17.75)	0.92
SBP, median (IQR)	127 (112 - 145)	125 (108 - 144)	137 (120 - 159)	0.002
DBP, median (IQR)	75 (66 - 89)	72 (58 - 87)	76 (64 - 87)	0.19
Heart rate, median (IQR)	91 (78 - 110)	91 (79 - 114)	90 (72 - 115)	0.91
BMI, median (IQR)	29.4 (25.8 - 33.2)	29.7 (26.4 - 35.7)	29.2 (26.3 - 34.3)	0.57
BSA, median (IQR)	2 (1.9 - 2.2)	2 (1.9 - 2.2)	1.95 (1.8 - 2.2)	0.33
Ischaemic aetiology, n (%)	125 (63.1)	36 (62.1)	38 (31.7)	< 0.001
De novo heart failure, n (%)	101 (51)	35 (60.3)	78 (65)	0.04
Pulmonary oedema, n (%)	22 (11.1)	5 (8.6)	14 (11.7)	0.82
Smokers, n (%)	41 (20.7)	7 (12.1)	10 (8.3)	0.009
CAD, n (%)	141 (71.2)	40 (69)	58 (48.3)	< 0.001
Previous MI, n (%)	70 (35.4)	16 (27.6)	19 (15.8)	< 0.001
CKD, n (%)	111 (56)	29 (50)	76 (63.3)	0.21
Atrial fibrillation, n (%)	102 (51.5)	28 (48.3)	76 (63.3)	0.07
Atrial flutter, n (%)	11 (5.6)	4 (6.9)	7 (5.8)	0.93
COPD, n (%)	34 (17.2)	7 (12)	19 (15.8)	0.65
Dyslipidaemia, n (%)	140 (70.7)	40 (69)	76 (63.3)	0.39
Depression, n (%)	14 (7)	2 (3.5)	14 (11.7)	0.13
AH, n (%)	142 (71.7)	51 (87.9)	99 (82.5)	0.01
Diabetes mellitus, n (%)	94 (47.5)	30 (51.7)	52 (43.3)	0.55
Stroke, n (%)	21 (10.6)	3 (5.2)	12 (10)	0.46
CRP, median (IQR)	12.2 (4.6 - 44.8)	15.8 (4 - 59.3)	11.5 (4.4 - 45.2)	0.75
Anaemia, n (%)	94 (47.5)	27 (46.6)	69 (57.5)	0.18

AH – arterial hypertension, BMI – body mass index, BSA – body surface area, CAD – coronary artery disease, CKD – chronic kidney disease, COPD – chronic obstructive pulmonary disease, CRP – C-reactive protein, DBP – diastolic blood pressure, EF – ejection fraction, LOH – length of hospitalization, MI – myocardial infarction, SBP – systolic blood pressure

The study was based on retrospective data collection and no ethics committee approval or patient consent was required.

Results

Our study population consisted of 376 hospitalized patients diagnosed with acute heart failure. The median age was 73 years (IQR 67–79) and 34% of the patients were female. Of the entire population, 198 patients (52.7%) had reduced EF, 58 patients (15.4%) had mildly reduced EF, and 120 patients (31.9%) had preserved EF. The baseline characteristics of these subgroups are presented in Table 1. Compared to other groups, patients with reduced EF were younger and the proportion of females was lower. They presented less frequently with *de novo* heart failure and arterial hypertension. By contrast, patients with preserved EF had significantly less frequently coronary artery disease, previous myocardial infarction, and ischaemic aetiology of heart failure.

The rates of the most frequent precipitating factors and the initial clinical and radiological signs of heart failure are shown in Table 2. At least one of these precipitating factors was present in 324 patients (86%). Of all factors identified in our study, progression of heart failure (36.4%), acute coronary syndrome (17.3%), tachyarrhythmia (16%), acute pulmonary disease (14.1%), non-pulmonary infection (10.6%), and bradycardia (4.3%) were the most common in the entire cohort. In comparison to other subgroups, acute coronary syndrome was most frequently present in patients with mildly reduced EF. These patients had the lowest frequency of progression of heart failure. Other factors and signs of heart failure were equally distributed among the subgroups.

The median length of hospital stay in the overall population was 11 days. Factors independently associated with longer hospital stays are shown in Table 3. The presence of peripheral leg swelling (OR 1.97, 95% CI 1.02–3.78, P = 0.04) and signs of pulmonary congestion on chest X-ray (OR 2.72, 95% CI 1.38–5.34, P = 0.003) was associated with longer hospital stays (≥11 days) in patients with reduced EF. By contrast, among those with mildly reduced EF, non-pulmonary infection (OR 50.57, 95% CI 2.82–906.84, P < 0.001), progression of heart failure (OR 15.33, 95% CI 1.25–188.53, P = 0.02), and acute pulmonary disease (OR 10.77, 95% CI 1.07–108.81, P = 0.03) were associated with longer hospital stays. Acute pulmonary disease (OR 3.96, 95% CI 1.05–14.99, P = 0.03) was associated with longer hospital stays in patients with preserved EF.

Tab. 2. *Precipitating factors and signs of acute heart failure*

	EF <40%	EF 40-49%	EF ≥50%	P
Acute coronary syndrome, n (%)	36 (18.2)	17 (29.3)	12 (10)	0.005
Bradycardia, n (%)	9 (4.6)	4 (6.9)	3 (2.5)	0.38
Infection (non-pulmonary), n (%)	15 (7.6)	9 (15.5)	16 (13.3)	0.12
Progression of heart failure, n (%)	84 (42.4)	13 (22.4)	40 (33.3)	0.01
Tachyarrhythmia, n (%)	28 (14.1)	8 (13.8)	24 (20)	0.34
Acute pulmonary disease, n (%)	28 (14.1)	9 (15.5)	16 (13.3)	0.93
Crackles, n (%)	127 (64.1)	40 (69)	81 (67.5)	0.72
Peripheral swelling, n (%)	115 (58.1)	32 (55.2)	73 (60.8)	0.76
Jugular vein distension, n (%)	73 (36.9)	15 (25.9)	45 (37.5)	0.26
X-ray pulmonary congestion, n (%)	141 (71.2)	36 (62.1)	75 (62.5)	0.19
X-ray pleural effusion, n (%)	72 (36.4)	19 (32.8)	40 (33.3)	0.81

EF – ejection fraction

Tab. 3. *The multivariate analysis of predictors of longer hospital stays (≥ 11 days)*

EF <40% subgroup	Odds ratio	95% CI	P
Acute coronary syndrome	0.41	0.15 - 1.14	0.09
Bradycardia	1.12	0.24 - 5.26	0.88
Infection (non-pulmonary)	1.48	0.46 - 4.81	0.51
Progression of heart failure	1.24	0.55 - 2.8	0.6
Tachyarrhythmia	1	0.38 - 2.66	0.99
Acute pulmonary disease	1.58	0.61 - 4.11	0.35
Peripheral swelling	1.97	1.02 - 3.78	0.04
Crackles	1.46	0.76 - 2.82	0.25
Jugular vein distension	0.92	0.47 - 1.81	0.81
X-ray pulmonary congestion	2.72	1.38 - 5.34	0.003
X-ray pleural effusion	0.61	0.3 - 1.23	0.17
EF 40-49% subgroup	**Odds ratio**	**95% CI**	**P**
Acute coronary syndrome	2.92	0.26 - 32.75	0.36
Bradycardia	2.77	0.09 - 81.37	0.56
Infection (non-pulmonary)	50.57	2.82 - 906.84	< 0.001
Progression of heart failure	15.33	1.25 - 188.53	0.02
Tachyarrhythmia	5.68	0.47 - 68.89	0.17
Acute pulmonary disease	10.77	1.06 - 108.81	0.03
Peripheral swelling	2.87	0.57 - 14.5	0.2
Crackles	1.07	0.17 - 6.86	0.94
Jugular vein distension	3.33	0.45 - 24.44	0.22
X-ray pulmonary congestion	1.99	0.34 - 11.49	0.44
X-ray pleural effusion	1.97	0.38 - 10.39	0.42
EF ≥50% subgroup	**Odds ratio**	**95% CI**	**P**
Acute coronary syndrome	0.58	0.12 - 2.88	0.5
Bradycardia	4.1	0.32 - 51.95	0.26
Infection (non-pulmonary)	1.46	0.43 - 4.99	0.55
Progression of heart failure	2.17	0.79 - 5.95	0.13
Tachyarrhythmia	0.93	0.29 - 2.94	0.9
Acute pulmonary disease	3.96	1.05 - 14.96	0.03
Peripheral swelling	1.94	0.78 - 4.82	0.15
Crackles	1.74	0.74 - 4.1	0.2
Jugular vein distension	1.28	0.55 - 2.96	0.57
X-ray pulmonary congestion	1.12	0.49 - 2.53	0.79
X-ray pleural effusion	1.38	0.6 - 3.2	0.45

EF – ejection fraction, CI – confidence interval (upper and lower limit)

Discussion

The results of our study demonstrate that recognition of the precipitating factors and signs of heart failure during the initial investigation contributes to the characterization of

a patient's state and describes a possible trajectory of the patient's hospitalization with regard to the length of hospital stay. Therefore, the precipitating factors that contribute to the hospitalization of patients with acute heart failure should be at the forefront of the physicians' interest because they have a significant implication in the course of hospitalization. The value and main contribution of our study are in the characterization of a relatively consistent population during a consecutive 12-month period across a broad spectrum of EF values and specifically in each EF subgroup.

Many external factors are considered to be the precipitating factors for heart failure. Their contribution to the development of acute heart failure (*de novo* or decompensation of chronic heart failure) depends on the severity and characterization of heart failure in a patient, including age, frailty, comorbidities, and the underlying cause of heart failure. Many of these factors were identified in retrospective studies or were used to characterize and monitor patients in prospective observational registries (3-5). The most common precipitating factors identified in a prospective multicentre study (3) with 7,764 patients and a single precipitant included acute coronary syndrome (52%), atrial fibrillation (16%), infection (14%), uncontrolled hypertension (11%), and non-compliance (8%). In another prospective study with 755 patients with acute heart failure (4), the frequencies of acute coronary syndrome (6%), atrial fibrillation with a rapid ventricular response (17%), and acute pulmonary disease (20%) were reported. Similar precipitants were also identified in a study with 692 patients in a primary care setting, with a reported rate of respiratory infection (28.2%), another infection (7.1%), atrial fibrillation (14.5%), cardiac ischaemia (5.3%), or drug treatment and diet non-compliance (22.8% and 26.8%, respectively) (5). In an analysis of the CHARM (Candesartan in Heart Failure Assessment of Reduction in Mortality and morbidity) programme (6) with 1,668 patients hospitalized for heart failure, the investigators identified a cardiovascular precipitant in 54% of the patients, with arrhythmia (15%), non-compliance/decrease in heart failure therapy (10%), and myocardial ischaemia (8%) being the most common. In the same study and among non-cardiovascular reasons for hospitalization, respiratory infection (10%), worsening renal function (4%), or other infections (2%) were reported. According to these reported results, the cardiorespiratory causes predominate and potentially preventable causes (drug or diet non-compliance) are present at a significant rate.

The presence of signs of heart failure may vary across different studies, but they remain important characteristics of patients with acute heart failure and aid in assessing the congestion and perfusion status (10). The rates of heart failure signs in our study correspond to the prevalence of signs reported previously. The prevalence of jugular vein distension is reported to be between 14% and 63% (4, 6, 7) and its presence may be associated with increased short-term and long-term mortality (7). The frequency of peripheral oedema in acute heart failure patients is relatively high, accounting for 55-77% (10, 11). However, its sensitivity is low in detecting elevated pulmonary capillary wedge pressure in patients with advanced heart failure (15). It is also more frequently present in patients with decompensation of chronic heart failure than in those with *de novo* heart failure (67% vs. 49%) (8) and is more common in patients with preserved EF than in those with reduced EF (9). Similarly, pulmonary rales or crackles can be present in up to 75–90% of patients (8, 10, 12) with slightly higher rates in those with preserved EF than in those with reduced EF (9).

The characterization of patients according to the value of EF is essential for identifying patients with chronic heart failure and left ventricular systolic dysfunction, in whom specific pharmacotherapy has been shown to be clearly beneficial. In the setting of acute heart failure, the value of EF (along with other echocardiographic parameters such as valve function and morphology, diastolic function, or myocardial wall motion abnormalities) primarily has a diagnostic significance for patients with dyspnoea or haemodynamic alteration. However, patients with acute heart failure also exhibit distinct characteristics when categorized according to the value of EF. In the present study, patients with mildly reduced EF were more similar to the preserved EF subgroup in terms of age. By contrast, they were more similar to the reduced EF subgroup in terms of a higher rate of an ischaemic aetiology of heart failure and the presence of coronary artery disease. They had similarly lower systolic blood pressure on admission. However, the mildly reduced EF subgroup was intermediate in the prevalence of previous myocardial infarction and current smokers between the preserved and reduced EF subgroups. In terms of precipitating factors, compared to the other subgroups, patients with mildly reduced EF had a higher rate of acute coronary syndromes, but the lowest rate of progression of heart failure. These data underscore that patients with mildly reduced EF share many common characteristics with those with reduced or preserved EF, even in the setting of acute heart failure. As also shown in our study, coronary artery disease is generally one of the most common causes of heart failure. In addition, acute coronary syndromes are identified as one of the most common precipitating factors. But in patients with preserved EF, in whom the prevalence of coronary artery disease, history of myocardial infarction, and ischaemic aetiology of heart failure are significantly lower, other precipitants than acute coronary syndromes must be considered. As shown by our results, the prevalence of acute coronary syndrome in this subgroup is lower.

A comparison with other studies investigating precipitating factors, signs of heart failure, and the risk of a longer hospital stay is partially limited because of a different size of the study population and criteria for data collection. However, many parallel findings can be reported. Similarly to our results, in OPTIMIZE-HF (Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure) (16), pneumonia/respiratory processes as a precipitating factor identified patients with acute heart failure at a significantly increased risk of a longer hospital stay. But, comparable to other publications concerning the risk factors for the length of hospital stay (12, 17), these studies did not distinguish patients according to the value of EF.

In GWTG-HF (Get With The Guidelines – Heart Failure) (14), pulmonary disease and arrhythmia were similarly reported among the most frequent precipitating factors (be-

sides medication and diet non-compliance, worsening renal failure, and uncontrolled hypertension). In addition, pulmonary disease was associated with a longer hospital stay in each EF subgroup. Further precipitants associated with a longer hospital stay included worsening renal failure (in patients with reduced and preserved EF), arrhythmia (in those with reduced EF), and medication non-adherence (in the mildly reduced and preserved EF subgroups).

In our study, while acute pulmonary disease was a significant predictor of a longer hospital stay in patients with preserved and mildly reduced EF, signs of congestion (peripheral swelling and pulmonary congestion on chest X-ray) were related to a longer hospital stay in patients with reduced EF. Furthermore, two other precipitating factors for acute heart failure (non-pulmonary infection and progression of heart failure) were identified as predictors of a longer hospital stay in patients with mildly reduced EF. The effect of these precipitating factors in mildly reduced EF subgroup and signs of congestion in reduced EF subgroup on the length of hospital stay is a novel observation, and our data extend the evidence of the different influence of precipitating factors and signs of acute heart failure on the length of hospital stay in distinct EF subgroups.

Recent European heart failure guidelines (18) recommend the evaluation of precipitating factors during the first medical contact with acute heart failure patients. Moreover, the treatment of precipitating factors is a mandatory part of heart failure management.

Study Limitations

There were several limitations in our study. First, the study was a retrospective one in a single cardiology centre. The search for information was based on the accuracy and availability of different types of data. The retrospective design did not allow the recognition of possible precipitating factors according to the authors' intention, and only the most common factors were included in the analysis. Second, the analysis did not include potential risk factors for mortality because of a relatively small number of patients in each EF subgroup. Furthermore, only some variables (precipitating factors and signs of heart failure) were included in the multivariate analysis, although many other factors are known to influence the duration of hospitalization.

Conclusion

In conclusion, this retrospective single-centre study has shown that more than half of the patients hospitalized for acute heart failure had a reduced ejection fraction. Although these subgroups have many similarities in the rate of comorbidities or initial haemodynamic parameters, there are numerous differences in the precipitating factors for heart failure and, along with signs of heart failure, they have a significant implication for the length of hospital stay.

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