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Original Article

Short-term prognostic factors in the patients after acute heart failure

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Abstract: To explore risk factors of short-term prognosis of acute heart failure (AHF) patients and compare the difference between acute heart failure with reduced ejection fraction (AHFREF) and acute heart failure with preserved ejection fraction (AHFPEF). A retrospective analysis of medical records of AHF patients was performed. Eligible patients were at the age of more than 18 years old, excluding malignancy, acute pulmonary embolism, heart valve diseases (such as mild valvular regurgitation), severe renal insufficiency, and N-terminal pro-brain natriuretic peptide (NT-proBNP) < 300 pg/ml. AHFREF group (LVEF < 0.5) and AHFPEF group (LVEF ≥ 0.5) were classified depending on the left ventricular ejection fraction (LVEF). The involved patients were followed up *via* telephone contact and consult of medical recording. Unfavorable prognosis was defined upon the cardiac death and re-hospitalization within 6 months; otherwise they had a favorable prognosis. We analyzed the impact factors of short-term prognosis, including patient's age, gender, systolic blood pressure, diastolic blood pressure, heart rate, NT-proBNP, blood glucose, heart ultrasound LVEF, cardiothoracic ration in chest radiograph, history of hypertension, coronary heart disease and diabetes mellitus, for multivariate logistic regression analysis. A total of 130 AHF patients were included in the analysis, including 79 male (60.8%) and 51 female (39.2%). The average age of all involved patients was 74.0 years [M (P_{25}, P_{75}) = 64.0, 80.0]. Fifteen cases (11.5%) had unfavorable prognosis and 35 cases (27.0%) had favorable prognosis in the AHFREF group, while the cases in the AHFPEF group were respectively 31 (23.8%) and 49 (37.7%). There was no significant difference in the short-term prognosis between the two groups (χ^2 = 1.030, P = 0.310). The short-term prognosis in AHF patients was mainly influenced by NT-proBNP (r = -0.263, P = 0.035), blood glucose (r = -0.090, P = 0.049) and systolic blood pressure (r = 0.012, P = 0.030). As for AHFREF patients, systolic blood pressure (r = 0.047, P = 0.014) and LVEF (r = 10.991, P = 0.037) were the predominant factors; as for AHFPEF patients, NT-proBNP was the major risk factor (r = -0.319, P = 0.033). High NT-proBNP, high blood sugar and low systolic blood pressure at visits are the risk factors for short-term prognosis of AHF patients. Due to different LVEF baseline levels of AHFREF and AHFPEF, the prognosis factors also vary. Low systolic blood pressure and LVEF are the risk factors of AHFREF, while high NT-proBNP is risk factor of AHFPEF.

Keywords: Systolic blood pressure, N-terminal pro-brain natriuretic peptide, blood glucose, ejection fraction, acute heart failure, prognosis

Introduction

Acute heart failure (AHF) is a kind of acute critical illness in clinics, with higher re-hospitalization rate and mortality. Previous studies on cardiac dysfunction have shown that, the majority of conventional treatment for heart failure focuses on heart failure with reduced ejection fraction, but the incidence of heart failure with preserved ejection fraction is higher than heart failure with reduced ejection fraction [1-4]. Heart failure with reduced ejection fraction and heart failure with preserved ejection fraction have different pathogenesis and therapeutic strategies, although their clinical manifestations are similar. Therefore clinical treatment of the two has been widely concerned. This study aims to explore risk factors of short-term prognosis after AHF and compare the difference between acute heart failure with reduced ejection fraction (AHFREF) and acute heart failure with preserved ejection fraction (AHFPEF), in a broader attempt to understand AHF characteristics and improve the prognosis.

Subjects and methods

Subjects and grouping

Eligible patients were hospitalized patients in our hospital between April 2012 and January 2013 due to AHF (including incipient AHF and acute exacerbation of chronic heart failure), and they received conventional treatment after discharge. The medical records of the involved patients were retrospectively analyzed and AHF was diagnosed in accordance with the diagnostic criteria of European Society of Cardiology in 2012. All patients aged more than 18 years old, without malignancy, acute pulmonary embolism, heart valve diseases (such as mild valvular regurgitation), severe renal insufficiency, and N-terminal pro-brain natriuretic peptide (NT-proBNP) < 300 pg/ml. AHFREF group (LVEF < 0.5) and AHFPEF group (LVEF ≥ 0.5) were classified depending on the left ventricular ejection fraction (LVEF). After discharge, patients were followed up *via* telephone contact and consult of medical recording. Unfavorable prognosis was defined upon cardiac death and re-hospitalization within 6 months, otherwise they had favorable short-term prognosis.

Outcome measures

We measured systolic blood pressure, diastolic blood pressure, heart rate of AHF patients in semi-reclining position. N-terminal pro-brain natriuretic peptide (NT-proBNP) and blood glucose were monitored. Heart ultrasound LVEF and cardiothoracic ration in chest radiograph within 1 day after visit were recorded. Roche CARDIAC®proBNP+ was applied to quantitatively detect NT-proBNP levels in heparinized venous whole blood. The test range of NT-proBNP (60-9,000 pg/ml) was classified into five levels: 1: 300-2250; 2: > 2250-4500; 3: > 4500-6750; 4: > 6750-9000; 5: > 9000.

Statistical analysis

Data were statistically analyzed using IBM SPSS 19.0 software. Measurement data were expressed as mean ± standard deviation ($\bar{x} \pm S$) if they met normal distribution, otherwise data were represented as the median and interquartile range [M (P_{25}, P_{75})]. Count data were expressed as the absolute frequency and constituent ratio. The ratio was compared with chi-square test. Binary Logistic regression analysis was performed taking patient's age, gender, systolic blood pressure, diastolic blood pressure, heart rate, NT-proBNP, blood glucose, LVEF, cardiothoracic ratio, history of hypertension, coronary heart disease and diabetic mellitus as independent variables, and short-term prognosis of AHF as dependent variables. Statistically significant independent variables were screened by univariate logistic regression analysis with Enter method, and then multivariate logistic regression analysis was performed using backward condition method. Independent variables filtered by step remove probability of 0.10 into multivariate logistic regression model. A $P < 0.05$ level was considered statistically significant and $P > 0.05$ as insignificant difference.

Results

General information of subjects

A total of 130 AHF patients were enrolled in this study, including 79 male (60.8%) and 51 female (39.2%). The average age of all involved patients was 74.0 years [M (P_{25}, P_{75}) = 64.0, 80.0]. Fifteen cases (11.5%, including 3 deaths) had unfavorable prognosis and 35 cases (27.0%) had favorable prognosis in the AHFREF group. While 31 cases (23.8%, including 3 deaths) had unfavorable prognosis and 49 cases (37.7%) had favorable prognosis in the AHFPEF group (**Tables 1-3**). There was no significant difference in the short-term prognosis and mortality between the two groups ($\chi^2 = 1.030$, $P = 0.310$; $\chi^2 = 0.022$, $P = 0.881$).

Logistic regression analysis of risk factors

After screened by univariate logistic regression analysis, independent variables of multivariate logistic regression analysis for AHF included systolic blood pressure, diastolic blood pressure, NT-proBNP and blood glucose (**Table 1**); independent variables for AHFREF were systolic blood pressure, diastolic blood pressure, LVEF and history of hypertension (**Table 2**); independent variable for AHFPER was NT-proBNP (**Table 3**). Multivariate logistic regression analysis showed that, the risk factors of short-term prognosis of AHF patients were mainly NT-proBNP, blood glucose, systolic blood pressure; the prognosis of AHFREF cases was influenced by systolic blood pressure and LVEF; and the

Table 1. Univariate logistic regression analysis on the indexes of AHF and short-term prognosis

	Age (years)	Gender (male)	SBP (mmHg)	DBP (mmHg)	HR (bpm)	NT-proBNP (pg/ml)	GC (mmol/L)	LVEF	CTR	HP	CHD	Diabetes
AHF (n = 130)	74.0 [64.0, 80.0]	79 (60.8%)	143.0 [124.7, 176.0]	89.0 [72.7, 103.2]	103.5 [87.7, 123.2]	6396 [2427, > 9000]	9.6 [7.9, 12.3]	0.54 [0.40, 0.63]	0.59 ± 0.07	84 (64.6%)	78 (60.0%)	33 (25.4%)
FPG (n = 84)	74.0 [61.8, 79.8]	54 (64.3)	151.0 [127.0, 179.5]	90.0 [87.0, 105.8]	101.0 [87.0, 121.8]	5226 [2006, > 9000]	9.0 [7.7, 11.5]	0.52 [0.40, 0.63]	0.59 ± 0.07	58 (69.0)	50 (59.6)	19 (22.6)
UFPG (n = 46)	74.5 [65.5, 81.3]	25 (54.3)	135.0 [115.0, 168.3]	84.0 [71.8, 95.3]	110.0 [88.0, 127.8]	8553 [3411, > 9000]	10.8 [8.6, 13.5]	0.58 [0.36, 0.62]	0.58 ± 0.07	26 (56.5)	28 (60.9)	14 (30.4)
P	0.567	0268	0.043	0.099	0.434	0.05	0.068	0795	0.493	0.155	0.881	0.329

Values are *M* (P_{25}, P_{75}), n (%), ($\overline{x} \pm S$) or *P*. SBP: systolic blood pressure; DBP: diastolic blood pressure; HR: heart rate; NT-proBNP: N-terminal pro-brain natriuretic peptide; GS: computer blood glucose; LVEF: left ventricular ejection fraction; CTR: cardiothoracic ration in chest radiograph; HP: hypertension; CHD: coronary heart disease; AHF: acute heart failure; FPG: favourable prognosis group; UFPG: unfavourable prognosis group.

Table 2. Univariate logistic regression analysis on the indexes of AHFREF and short-term prognosis

	Age (years)	Gender (male)	SBP (mmHg)	DBP (mmHg)	HR (bpm)	NT-proBNP (pg/ml)	GC (mmol/L)	LVEF	CTR	HP	CHD	Diabetes
AHF (n = 50)	72.5 [59.0, 77.3]	33 (66.0%)	133.0 [119.8, 177.3]	92.0 [76.5, 106.5]	115.0 [98.0, 131.3]	9000 [5456, > 9000]	9.7 [8.0, 11.9]	0.37 [0.30, 0.43]	0.59 ± 0.07	31 (62.0%)	30 (60.0%)	12 (24.0%)
FPG (n = 35)	73.0 [59.0, 77.0]	25 (71.4%)	153.0 [127.0, 189.0]	93.0 [78.0, 112.0]	115.0 [92.0, 131.0]	9000 [4077, > 9000]	9.6 [7.8, 11.0]	0.40 [0.33, 0.44]	0.59 ± 0.07	25 (71.4%)	21 (60.0%)	7 (20.0%)
UFPG (n = 15)	71.0 [59.0, 78.0]	8 (53.3%)	117.0 [104.0, 126.0]	85.0 [72.0, 93.0]	115.0 [104.0, 133.0]	> 9000 [7589, > 9000]	10.9 [8.3, 13.5]	0.28 [0.21, 0.38]	0.60 ± 0.07	6 (40.0%)	9 (60.0%)	5 (33.3%)
P	0.844	0.220	0.004	0.021	0.545	0.249	0.124	0.003	0.796	0.041	1.000	0.316

AHFREF: acute heart failure with reduced ejection fraction; SBP: systolic blood pressure; DBP: diastolic blood pressure; HR: heart rate; NT-proBNP: N-terminal pro-brain natriuretic peptide; GS: computer blood glucose; LVEF: left ventricular ejection fraction; CTR: cardiothoracic ration in chest radiograph; HP: hypertension; CHD: coronary heart disease; AHF: acute heart failure; FPG: favorable prognosis group; UFPG: unfavorable prognosis group.

Table 3. Univariate logistic regression analysis on the indexes of AHFPEF and short-term prognosis

	Age (years)	Gender (male)	SBP (mmHg)	DBP (mmHg)	HR (bpm)	NT-proBNP (pg/ml)	GC (mmol/L)	LVEF	CTR	HP	CHD	Diabetes
AHF (n = 80)	75.0 [68.3, 80.8]	46 (57.5%)	144.0 [127.0, 175.3]	85.0 [72.0, 98.0]	96.0 [84.3, 117.8]	4879 [1555, > 9000]	9.3 [7.9, 12.8]	0.60 [0.55, 0.64]	0.59 ± 0.08	53 (66.3%)	48 (60.0%)	21 (26.3%)
FPG (n = 49)	74.0 [66.5, 80.0]	29 (59.2%)	145.0 [127.0, 173.0]	82.0 [72.0, 98.0]	95.0 [83.5, 116.0]	4267 [1384, 6749]	8.8 [7.6, 12.2]	0.60 [0.54, 0.66]	0.59 ± 0.08	33 (67.3%)	29 (59.2%)	12 (24.5%)
UFPG (n = 31)	75.0 [73.0, 84.0]	17 (54.8%)	142.0 [127.0, 182.0]	86.0 [71.0, 100.0]	101.0 [86.0, 126.0]	6319 [1722, > 9000]	10.8 [8.7, 14.1]	0.60 [0.57, 0.63]	0.58 ± 0.07	20 (64.5%)	19 (61.3%)	9 (29.0%)
P	0.484	0.702	0.867	0.906	0.386	0.033	0.256	0.666	0.353	0.794	0.851	0.653

AHFPEF: acute heart failure with preserved ejection fraction; SBP: systolic blood pressure; DBP: diastolic blood pressure; HR: heart rate; NT-proBNP: N-terminal pro-brain natriuretic peptide; GS: computer blood glucose; LVEF: left ventricular ejection fraction; CTR: cardiothoracic ration in chest radiograph; HP: hypertension; CHD: coronary heart disease; AHF: acute heart failure; FPG: favorable prognosis group; UFPG: unfavorable prognosis group.

Table 4. Related factors of short-term prognosis for AHF, AHFREF and AHFPEF by multiple factor logistic regression model*

	AHF				AHFREF			AHFPEF	
	SBP	NT-proBNP	GC	constant	SBP	LVEF	constant	NT-proBNP	constant
r	0.012	-0.263	-0.090	0.737	0.047	10.991	-9.024	-0.319	1.369
P	0.030	0.035	0.049	0.459	0.014	0.037	0.002	0.033	0.006
OR	0.988	1.301	1.094	0.478	0.954	0.000	8297.615	1.375	0.254
95% CI	0.978-0.999	1.018-1.662	1.000-1.196		0.918-0.991	0.000-0.515		1.025-1.845	

Assignment 1 for FPG, 0 for UFPG. AHF: acute heart failure; AHFPEF: acute heart failure with preserved ejection fraction; AHFPEF: acute heart failure with preserved ejection fraction; SBP: systolic blood pressure; NT-proBNP: N-terminal pro-brain natriuretic peptide; GS: computer blood glucose; LVEF: left ventricular ejection fraction; FPG: favorable prognosis group; UFPG: unfavorable prognosis group. *There were the same results for variables filtered by step remove probability 0.10 and 0.25 into multiple factor logistic regression model.

prognosis of AHFPEF cases was mediated by NT-proBNP (**Table 4**).

Discussion

NT-proBNP is a sensitive indicator of early cardiac function impairment, bedside detection of NT-proBNP levels contributes to distinguish cardiac dyspnea from non-cardiac dyspnea, especially under the condition of ambiguous symptoms and various diseases coexist [5, 6]. Growing evidence have shown that plasma NT-proBNP levels in HFREF patients were higher than that in HFPEF patients, indicating that NT-proBNP is an independent predictor for the prognosis after AHF [6, 7]. This conclusion is supportive by our findings. However, high NT-proBNP level is regarded risk factor for short-term prognosis of AHFPEF cases only. This can be explained by that, NT-proBNP has different prognostic values in AHFREF and AHFPEF due to different LVEF baseline levels.

Blood pressure of AHF patients at visit is critically associated with LVEF, lower systolic blood pressure at admission indicates higher probability of lower LVEF, and some scholars demonstrated that systolic blood pressure at the level of < 120 mmHg was another indicator [8-11]. The results of this study showed that low systolic blood pressure was a high-risk factor of AHF, low systolic blood pressure and LVEF are high-risk factors HFREF, indicating that systolic blood pressure is associated with LVEF. The low blood pressure levels triggered cardiovascular events (including cardiac death and re-hospitalization) within 6 months after discharge in AHF patients, especially AHFREF cases. Blood pressure at acute exacerbation reflects compensatory ability of the heart, activation of neuroendocrine system may increase blood pressure and enhance heart function, low blood pressure at acute attack of heart failure is indicator of severe cardiac dysfunction and impaired compensatory ability, leading to unfavorable prognosis.

Studies have revealed that high blood sugar levels are highly involved in the prognosis of cardiovascular diseases, regardless of the diabetes, high blood sugar levels are predictors of poor prognosis after coronary heart disease [12, 13]. Furthermore high blood glucose levels at admission contributed to increase 2 year all cause mortality risk in diabetic patients with acute coronary events [14]. A previous study among 6212 AHF patients demonstrated that, elevated blood glucose at admission is a strong, independent predictor for 30-day mortality of AHF patients [15]. In this study, we found that elevation of blood glucose levels was an indicator of short-term unfavorable prognosis of AHF patients, which deserves wide concerns from clinicians.

Heart rate at resting plays a crucial role on the diagnosis of chronic heart failure, rapid heart rate is critically involved in disease occurrence, development and prognosis of heart failure patients, controlling heart rate may significantly improve the prognosis after cardiac dysfunction. Close monitoring of heart rate can guide clinical diagnosis and predict the prognosis of heart failure, thus providing effective evidence for determining therapeutic effect. The correlation between heart rate and prognosis after AHF is rarely reported, and we did not find any association between heart rate and short-term prognosis in this study. This evidence implies that, high heart rate is possible a compensatory response of the body to AHF, the compensatory role of cardiac output raised by elevated heart rate after LVEF is reduced may vary from the prognostic role of heart rate in chronic heart failure.

The limitations of the present study are small sample size. Troponin is a prognostic indicator of heart failure, but we only detected troponin levels in a portion of patients at emergency department, so troponin levels were not included in our retrospective study. Severe renal insufficiency significantly affects the excretion of NT-proBNP and NT-proBNP is a hot topic of current study, we excluded AHF patients with severe renal insufficiency in the present study, so renal function was not included in the present study. In addition, a small amount of AHFREF patients were enrolled in this study compared with AHFPEF patients, because AHFREF patients are prone to accompany malignancy, acute pulmonary embolism, valvular heart disease (including mild valvular regurgitation) and severe renal insufficiency, these diseases were excluded from this study.

In summary, high NT-proBNP, high blood sugar and low systolic blood pressure at visits are risk factors for short-term prognosis after AHF. AHFREF and AHFPEF have different risk factors of short-term prognosis due to different LVEF baseline levels, the prognosis of AHFREF patients is mediated by low systolic blood pressure and LVEF, while the prognosis of AHFPEF patients is mainly influenced by high NT-proBNP.

Disclosure of conflict of interest

None.

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References

[1] Fonarow GC, Stough WG, Abraham WT, Albert NM, Gheorghiade M, Greenberg BH, O'Connor CM, Sun JL, Yancy CW and Young JB. Characteristics, treatments, and outcomes of patients with preserved systolic function hospitalized for heart failure: a report from the OPTIMIZE-HF Registry. J Am Coll Cardiol 2007; 50: 768-777.

[2] Aronow WS. Epidemiology, Pathophysiology, Prognosis, And Treatment of Systolic And Diastolic Heart Failure. Cardiol Rev 2006; 14: 108-124.

[3] Owan TE and Redfield MM. Epidemiology of Diastolic Heart Failure. Prog Cardiovasc Dis 2005; 47: 320-332.

[4] Lam CS, Donal E, Kraigher-Krainer E and Vasan RS. Epidemiology And Clinical Course of Heart Failure With Preserved Ejection Fraction. Eur J Heart Fail 2011; 13: 18-28.

[5] Januzzi JL Jr, Camargo CA, Anwaruddin S, Baggish AL, Chen AA, Krauser DG, Tung R, Cameron R, Nagurney JT, Chae CU, Lloyd-Jones DM, Brown DF, Foran-Melanson S, Sluss PM, Lee-Lewandrowski E and Lewandrowski KB. The N-terminal Pro-BNP investigation of dyspnea in the emergency department (PRIDE) study. Am J Cardiol 2005; 95: 948-954.

[6] Januzzi JL, van Kimmenade R, Lainchbury J, Bayes-Genis A, Ordonez-Llanos J, Santalo-Bel M, Pinto YM and Richards M. NT-proBNP testing for diagnosis and short-term prognosis in acute destabilized heart failure: an international pooled analysis of 1256 patients: the International Collaborative of NT-proBNP Study. Eur Heart J 2006; 27: 330-337.

[7] Golcuk Y, Golcuk B, Velibey Y, Oray D, Atilla OD, Colak A, Kurtulmus Y, Yildirim A and Eren M. Predictive cutoff point of admission N-terminal pro-B-type natriuretic peptide testing in the ED for prognosis of patients with acute heart failure. Am J Emerg Med 2013; 31: 1191-1195.

[8] Gheorghiade M, Abraham WT, Albert NM, Greenberg BH, O'Connor CM, She L, Stough WG, Yancy CW, Young JB and Fonarow GC. Systolic blood pressure at admission, clinical characteristics, and outcomes in patients hospitalized with acute heart failure. JAMA 2006; 296: 2217-2226.

[9] Kajimoto K, Sato N, Sakata Y and Takano T. Relationship between systolic blood pressure and preserved or reduced ejection fraction at admission in patients hospitalized for acute heart failure syndromes. Int J Cardiol 2013; 168: 4790-4795.

[10] Buiciuc O, Rusinaru D, Levy F, Peltier M, Slama M, Leborgne L and Tribouilloy C. Low systolic blood pressure at admission predicts long-term mortality in heart failure with preserved ejection fraction. J Card Fail 2011; 17: 907-915.

[11] Murphy M. Low blood pressure and preserved systolic function in elders with heart failure. J Cardiovasc Nurs 2010; 25: 405-410.

[12] Haffner SM, Lehto S, Ronnemaa T, Pyorala K and Laakso M. Mortality from coronary heart disease in subjects with type 2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. N Engl J Med 1998; 339: 229-234.

[13] Nusca A, Patti G, Marino F, Mangiacapra F, D'Ambrosio A and Di Sciascio G. Prognostic role of preprocedural glucose levels on short- and long-term outcome in patients undergoing percutaneous coronary revascularization. Catheter Cardiovasc Interv 2012; 80: 377-384.

[14] Svensson AM, McGuire DK, Abrahamsson P and Dellborg M. Association between hyper- and hypoglycaemia and 2 year all-cause mortality risk in diabetic patients with acute coronary events. Eur Heart J 2005; 26: 1255-1261.

[15] Mebazaa A, Gayat E, Lassus J, Meas T, Mueller C, Maggioni A, Peacock F, Spinar J, Harjola VP, van Kimmenade R, Pathak A, Mueller T, Tavazzi L, Disomma S, Metra M, Pascual-Figal D, Laribi S, Logeart D, Nouira S, Sato N, Parenica J, Deye N, Boukef R, Collet C, Van den Berghe G, Cohen-Solal A and Januzzi JL Jr. Association between elevated blood glucose and outcome in acute heart failure: results from an international observational cohort. J Am Coll Cardiol 2013; 61: 820-829.