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The role of commonly used clinical indicators in the diagnosis of acute heart failure

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Abstract. – OBJECTIVE: Acute heart failure (AHF) is one of the most commonly seen clinical cases, with a high rate of re-hospitalization and mortality. AHF can be divided into two categories based on the systolic function of the left ventricle, which are heart failure with reduced ejection fraction (HFREF) and heart failure with preserved ejection fraction (HFPEF). Pathogenesis and treatment of the two are quite different. In this article we attempted to explore the value of combined use of clinical and laboratory indicators in the differential diagnosis of AHFREF and AHFPEF.

PATIENTS AND METHODS: AHF patients ≥18 years old without valvular heart disease, acute myocardial infarction, renal dysfunction, ongoing hemodialysis or acute pulmonary embolism were chosen. Patients with left ventricular ejection fraction (LVEF) <0.5 fell into AHFREF group, and the remaining were placed in the AHFPEF group. Binary logistic regression analysis of age, gender, systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), NT-proBNP, blood glucose, LVEF and cardiothoracic ratio (CTR) as covariates and AHF types as dependent variables.

RESULTS: 166 patients were enrolled and, among them, 66 cases (39.8%) were in the AHFREF group and 100 cases (60.2%) in the AHFPEF group. We chose age, SBP, DBP, HR and NT-pro BNP as covariates in the binary logistic regression analysis, and obtained the regression equation and the results were statistically significant (χ^2=32.177, p<0.001). Hosmer-Lemeshow model test was (χ^2=8.654, p=0.372). Samples were tested with the remaining approximately 30% of the subjects.

CONCLUSIONS: Combined application of clinical and laboratory indicators, such as age, blood pressure, HR and NT-proBNP play an important role in the differential diagnosis of AHFREF and AHFPEF.

Key Words
Acute heart failure, Emergency medicine, Diagnosis, Clinical indicators.

Introduction

Clinically, heart failure is divided into heart failure with reduced ejection fraction (HFREF) and heart failure with preserved ejection fraction (HFPEF), according to the left ventricular ejection fraction (LVEF). With the deepening of understanding of heart function, it is found that the traditional treatment of heart failure is mainly targeted at the treatment of HFREF, while the incidence of HFPEF is equivalent to or even higher than HFREF[1-3]. Although the clinical manifestations of the two are similar, the pathogenesis and treatment are different, so their identification has important clinical significance, which is recently attracting more attention.

Acute heart failure (AHF) is a severe disease that is often encountered in the emergency with a complex etiology and a very high mortality rate. Therefore, various studies around the world are paying close attention to AHF and its treatment. In 2005, European Society of Cardiology (ESC) issued guidelines for the diagnosis and treatment of AHF[4]. In 2006, ACC/AHA successively released practical guidelines for heart failure[5], which described in detail the assessment and treatment of AHF. In 2008, ESC released the acute and chronic heart failure treatment guidelines[6], followed by updates. However, the clinical LVEF access for emergency care is often in a state of hysteresis. Previous studies showed that when AHF patients arrive at the hospital, some readily available clinical indicators are related to LVEF, suggesting that combined application of these indicators may predict LVEF before ultrasonic cardiac examination. Therefore, to explore the application of commonly used clinical or laboratory indicators for distinguishing AHFREF and AHFPEF, has certain clinical significance.

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Patients and Methods

Patients

166 AHF patients who visited the Emergency Department of Zhongshan City for hospitalization between April 2012 and April 2013, and adhered to conventional treatment after discharge, were enrolled in our research. Their diagnosis and treatment measures conformed to acute and chronic heart failure diagnosis and treatment guidelines (2012) of European Society of Cardiology. Among these patients, there were 103 males (62%) and 63 females (38%), whose average age was 74 (64-79). The major diseases these patients suffered from were hypertension (107 cases, 64.5%), coronary heart disease (97 cases, 58.4%), diabetes (42 cases, 25.3%), arrhythmia (20 cases, 12%), chronic obstructive pulmonary disease with acute exacerbation (11 cases, 6.6%), pulmonary infection (10 cases, 6%), dilated cardiomyopathy (4 cases, 2.4%), infective endocarditis (3 cases, 1.8%) and acute viral myocarditis (3 cases, 1.8%). Patients with the following diseases were excluded: valvular heart disease (including mild or above valvular regurgitation), acute myocardial infarction, renal dysfunction (BUN>9 mmol/L, Cr>178 mol/L), ongoing hemodialysis and acute pulmonary embolism. Peri-operative period AHF patients and patients with a malignant tumor or NT-proBNP<300 pg/ml were also excluded. The diagnosis of AHF, HFREF, and HFPEF was in compliance with the diagnostic criteria (2012) of European Society of Cardiology[7]. BP in semi-reclining position, HR, respiratory rate, transcutaneous oxygen saturation and consciousness of the patients were measured when they visited the emergency room.

Methods

Collection of Cases Materials

The general clinical data of all selected patients were collected, including: hospital number, name, sex, age, detailed medical history and physical examination. Left ventricular end diastolic diameter, as well as LVEF was determined by color Doppler ultrasonography. Moreover, biochemical tests such as blood routine, blood glucose (BG) and liver and renal function were measured.

Establishment of Excel Database

All data were collected by double entry and double-checking in Microsoft Excel.

Statistical Analysis

Data were analyzed using statistical analysis software IBM SPSS 19.0 (SPSS Inc., Chicago, IL, USA). Measurement data in line with normal distribution were shown as mean ± standard deviation ($\bar{x} \pm s$). Measurement data not in line with normal distribution were shown as median and the four-quantile range [M (P_{25}, P_{75})]. Quantitative data are shown as frequency and constituent ratio. Measurement data of normal distribution were compared with the t-test, otherwise the non-parametric test of the independent sample was used. X^2 test was used for comparison of rates. Bivariate correlation analysis was used for analysis of the correlation between each indicator. The non-parametric test was used to compare the grade data. The difference was considered to have statistical significance when $p<0.05$.

Results

Correlation Between LVEF and Clinical Indicators

Our results showed LVEF correlates with clinical indexes commonly used in emergency medicine (Table I). LVEF of AHF patients was negatively correlated with heart rate (r=-0.252, p=0.001) and NT-proBNP (r=-0.286, p=0.000). LVEF of AHFREF patients was positively correlated with

Table I. Correlation analysis between LVEF and clinical indicators of AHF, AHFREF and AHFPEF patients.

Team	Statistics	Age	Gender	SBP	DBP	HR	NT-pro BNP	BG	Hypertension	CHD	Diabetes	C/T
AHF	*r*	0.141	-0.022	0.101	-0.134	-0.252	-0.286	-0.040	-0.038	-0.106	0.011	-0.073
	P	0.071	0.774	0.194	0.084	0.001	0.000	0.611	0.626	0.174	0.888	0.347
AHFREF	*r*	0.416	-0.173	0.392	0.240	-0.242	0.134	-0.082	0.345	0.099	0.273	0.016
	P	0.001	0.164	0.001	0.052	0.050	0.283	0.511	0.005	0.430	0.026	0.895
AHFPEF	*r*	-0.017	0.075	-0.086	-0.054	0.002	0.005	-0.143	-0.164	-0.250	-0.132	-0.170
	P	0.865	0.459	0.395	0.590	0.981	0.960	0.156	0.103	0.012	0.189	0.090

age (r=0.416, p=0.001), SBP (r=0.392, p=0.001), history of hypertension (r=0.345, p=0.005) and history of diabetes (r=0.273, p=0.026). LVEF of AHFPEF patients was negatively correlated with history of coronary heart disease (CHD, r=-0.250, p=0.012).

Characteristics and Comparison of General Clinical Data

We set a random seed number 20140101 and randomly sampled out approximately 70% of the total population as training samples (118 people), the remaining 30% were determined to test samples (48 people).

Clinical Characteristics

166 patients were enrolled, with 103 males (62%) and 63 females (38%), whose average age was 74 (64-79). M (P_{25}, P_{75}) of systolic blood pressure (SBP) was 143 (126.0, 179.3) mmHg and M (P_{25}, P_{75}) of diastolic blood pressure (DBP) was 89 (73, 101.5) mmHg. M (P_{25}, P_{75}) of HR was 102.5 (87.0, 122) beats/min. M (P_{25}, P_{75}) of BG was 9.7 (8.1, 12.2) mmol/L. The cardiothoracic ratio (C/ T) was 0.59 ± 0.07. Of the 166 patients, 107 (64.5%) had a history of hypertension, 97 (58.4%) had CHD, and 42 (25.3%) had a history of diabetes mellitus (Table II-I). 66 cases (39.8%) were in the AHFREF group and 100 cases (60.2%) were in the AHFPEF group. Age (Z=-1.220, p=0.222), gender (χ^2=0.117, p=0.732), SBP (Z=-0.982, p=0.326), BG (Z=-0.393, p=0.695), cardiothoracic ratio (t=-0.821, p=0.413) and history of hypertension (χ^2=0.233, p=0.629), CHD (χ^2=0.213, p=0.645) and diabetes (χ^2=0.065, p=0.799) between the two groups had no significant difference (Table II-I). Compared with AHFPEF group, AHFREF group had higher DBP [92 (77.8, 105.3) mmHg *vs.* 84 (71.3, 97.0) mmHg, Z=-2.342, p=0.019], higher HR [113 (95.8, 130.0) bpm *vs.* 96 (83, 116.5) bpm, Z=-3.186, p=0.001] and higher NT-pro BNP. There were statistically significant differences in BNP NT-pro BNP grade between the two groups (Z=-4.601, p=0.000).

Training Sample

118 patients were enrolled, with 76 males (64.4%) and 42 females (35.6%), whose average age was 74 (64, 78). M (P_{25}, P_{75}) of SBP was 144.5 (127, 181) mmHg and M (P_{25}, P_{75}) of DBP was 91 (76.5, 103.3) mmHg. M (P_{25}, P_{75}) of HR was 102 (87, 122.3) beats/min. M (P_{25}, P_{75}) of BG was 9.8 (8.2, 12.6) mmol/L. The cardiothoracic ratio (C/T) was 0.59 ± 0.07. Of the 118 patients, 75 (63.6%) had a history of hypertension, 70 (59.3%) had CHD, and 33 (28%) had a history of diabetes. AHFREF group had more patients with high grade of NT-pro BNP, whereas AHFPEF group had more patients with low grade of NT-proBNP (Table II-II).

49 cases (41.5%) were in the AHFREF group and 69 cases (58.5%) were in AHFPEF group. Age (Z=-0.894, p=0.371), gender (χ^2=0.030, p=0.863), SBP (Z=-1.491, p=0.136), DBP (Z=-1.475, p=0.140), BG (Z=-0.885, p=0.376), cardiothoracic ratio (t=-0.636, p=0.526) and history of hypertension (χ^2=0.110, p=0.740), CHD (χ^2=0.126, p=0.723) and diabetes (χ^2=0.503, p=0.478) among the two groups had no significant difference (Table II-II). Compared with AHFPEF group, AHFREF group had higher HR [112 (94, 129.5) bpm *vs.* 96 (78, 116), Z=-2.729, p=0.007] and higher NT-proBNP levels. There were statistically significant differences in BNP NT-proBNP levels between two groups (Z=-3.678, p=0.000) (Table II-II).

Comparison of each clinical characteristic of the total population and training sample between AHFPEF and AHFREF groups are shown in Table II-I and Table II-II. There were significant differences in DBP, HR, and NT-pro BNP levels between the groups in the total population (p<0.05), which was not seen in the other indicators. There were significant differences in HR and NT-pro BNP levels between the groups in the training sample (p<0.05), which were not seen among in other indicators.

Screening of Clinical Parameters for AHFREF and AHFPEF Sub-type Diagnosis

Single variable logistic regression analysis of AHFREF and AHFPEF sub-type diagnosis in total population are shown in Table II-III. NT-proBNP grade, DBP and HR were determined to be statistically significant in single variable logistic regression analysis using AHFREF and AHFPEF sub-type as binary classification of dependent variables (p<0.1). Single variable logistic regression analysis of AHFREF and AHFPEF sub-type diagnosis in training samples are shown in Table II-IV. NT-proBNP level and HR were determined to be statistically significant in single variable logistic regression analysis using AHFREF and AHFPEF sub-type as binary classification of dependent variables (p<0.1).

Table II-I. The comparison of general clinical data between groups from the total population.

Index	Descriptions	AHFPEF	AHFREF	Total	Statistics	p
Age	x±s	71.33±13.50	68.32±14.37	70.13±13.88	-1.220	0.222
	Min-Max	28.00-90.00	20.00-89.00	20.00-90.00		.
	P25-P75	66.00-80.00	60.00-77.25	64.00-79.00		.
	Median	74.00	73.50	74.00		.
SBP	x±s	153.17±36.74	148.71±40.36	151.40±38.16	-0.982	0.326
	Min-Max	89.00-270.00	71.00-245.00	71.00-270.00		.
	P25-P75	128.25-177.50	120.75-181.00	126.00-179.25		.
	Median	144.00	140.50	143.50		.
DBP	x±s	86.38±20.00	93.41±24.42	89.17±22.07	-2.342	0.019
	Min-Max	38.00-160.00	43.00-176.00	38.00-176.00		.
	P25-P75	71.25-97.00	77.75-105.25	73.00-101.50		.
	Median	84.00	92.00	89.00		.
HR	x±s	100.69±25.52	112.50±24.61	105.39±25.75	-3.186	0.001
	Min-Max	56.00-167.00	60.00-170.00	56.00-170.00		.
	P25-P75	83.00-116.50	95.75-130.00	87.00-122.00		.
	Median	96.00	113.00	102.50		.
BG	x±s	11.04±4.67	10.34±3.43	10.76±4.23	-3.939	0.695
	Min-Max	3.60-27.70	5.70-26.50	3.60-27.70		.
	P25-P75	8.00-13.05	8.20-11.15	8.10-12.20		.
	Median	9.50	9.75	9.70		.
C/T	x±s	0.59±0.08	0.59±0.06	0.59±0.07	-0.821	0.413
	Min-Max	0.43-0.78	0.46-0.83	0.43-0.83		.
	P25-P75	0.54-0.63	0.55-0.64	0.55-0.63		.
	Median	0.59	0.59	0.59		.
Gender	female	39 (39.0%)	24 (36.4%)	63 (38.0%)	0.117	0.732
	male	61 (61.0%)	42 (63.6%)	103 (62.0%)		.
	total	100 (100.0%)	66 (100.0%)	166 (100.0%)		.
NTproBNP grade	300-2250	33 (33.0%)	4 (6.1%)	37 (22.3%)	-4.601	0.000
	>2250-4500	14 (14.0%)	9 (13.6%)	23 (13.9%)		.
	>4500-6750	21 (21.0%)	7 (10.6%)	28 (16.9%)		.
	>6750-9000	8 (8.0%)	14 (21.2%)	22 (13.3%)		.
	>9000	24 (24.0%)	32 (48.5%)	56 (33.7%)		.
	total	100 (100.0%)	66 (100.0%)	166 (100.0%)		.
Hypertension	no	37 (37.0%)	22 (33.3%)	59 (35.5%)	0.233	0.629
	yes	63 (63.0%)	44 (66.7%)	107 (64.5%)		.
	total	100 (100.0%)	66 (100.0%)	166 (100.0%)		.
CHD	no	43 (43.0%)	26 (39.4%)	69 (41.6%)	0.213	0.645
	yes	57 (57.0%)	40 (60.6%)	97 (58.4%)		.
	total	100 (100.0%)	66 (100.0%)	166 (100.0%)		.
Diabetes	no	74 (74.0%)	50 (75.8%)	124 (74.7%)	0.065	0.799
	yes	26 (26.0%)	16 (24.2%)	42 (25.3%)		.
	total	100 (100.0%)	66 (100.0%)	166 (100.0%)		.

Table II-II. The comparison of general clinical data between groups from the training sample.

Index	Descriptions	AHFPEF	AHFREF	Total	Statistics	p
Age	x±s	71.06±11.89	68.31±13.18	69.92±12.46	-0.894	0.371
	Min-Max	28.00-89.00	38.00-89.00	28.00-89.00		.
	P25-P75	66.00-78.50	59.50-77.00	64.00-78.00		.
	Median	74.00	73.00	74.00		.
SBP	x±s	156.07±36.45	148.55±39.89	152.95±37.93	-1.491	0.136
	Min-Max	89.00-252.00	85.00-245.00	85.00-252.00		.
	P25-P75	134.50-180.50	120.50-181.00	127.00-181.00		.
	Median	150.00	135.00	144.50		.
DBP	x±s	89.25±20.41	94.73±25.59	91.53±22.76	-1.475	0.140
	Min-Max	56.00-160.00	43.00-176.00	43.00-176.00		.
	P25-P75	72.50-99.00	79.50-105.00	76.50-103.25		.
	Median	90.00	93.00	91.00		.
HR	x±s	98.74±24.44	111.24±24.64	103.93±25.19	-2.805	0.005
	Min-Max	56.00-167.00	60.00-170.00	56.00-170.00		.
	P25-P75	78.00-116.00	94.00-129.50	87.00-120.25		.
	Median	96.00	112.00	102.00		.
BG	x±s	11.14±4.36	10.33±3.59	10.81±4.06	-0.885	0.376
	Min-Max	3.60-24.90	5.70-26.50	3.60-26.50		.
	P25-P75	8.05-14.10	8.25-11.20	8.20-12.60		.
	Median	9.80	9.80	9.80		.
C/T	x±s	0.59±0.07	0.60±0.06	0.59±0.07	-0.636	0.526
	Min-Max	0.43-0.75	0.49-0.83	0.43-0.83		.
	P25-P75	0.54-0.63	0.56-0.64	0.55-0.63		.
	Median	0.60	0.60	0.60		
Gender	female	25 (36.2%)	17 (34.7%)	42 (35.6%)	0.030	0.863
	male	44 (63.8%)	32 (65.3%)	76 (64.4%)		.
	total	69 (100.0%)	49 (100.0%)	118 (100.0%)		.
NTproBNP grade	300-2250	20 (29.0%)	3 (6.1%)	23 (19.5%)	-3.678	0.000
	>2250-4500	11 (15.9%)	8 (16.3%)	19 (16.1%)		.
	>4500-6750	16 (23.2%)	6 (12.2%)	22 (18.6%)		.
	>6750-9000	6 (8.7%)	7 (14.3%)	13 (11.0%)		.
	>9000	16 (23.2%)	25 (51.0%)	41 (34.7%)		.
	total	69 (100.0%)	49 (100.0%)	118 (100.0%)		.
Hypertension	no	26 (37.7%)	17 (34.7%)	43 (36.4%)	0.110	0.740
	yes	43 (62.3%)	32 (65.3%)	75 (63.6%)		.
	total	69 (100.0%)	49 (100.0%)	118 (100.0%)		.
CHD	no	29 (42.0%)	19 (38.8%)	48 (40.7%)	0.126	0.723
	yes	40 (58.0%)	30 (61.2%)	70 (59.3%)		.
	total	69 (100.0%)	49 (100.0%)	118 (100.0%)		.
Diabetes	no	48 (69.6%)	37 (75.5%)	85 (72.0%)	0.503	0.478
	yes	21 (30.4%)	12 (24.5%)	33 (28.0%)		.
	total	69 (100.0%)	49 (100.0%)	118 (100.0%)		.

Table II-III. The comparison of general clinical data between groups from the training sample.

Index	Regression coefficient	Standard error	Odds ratio	95% CI	p
Age	-0.016	0.011	0.985	0.963-1.007	0.174
Gender (1=male, 0=female) 1 vs. 0	0.085	0.358	1.119	0.588-2.128	0.732
NTproBNP (1=300-2250, 2≥2250-4500, 3≥4500-6750, 4≥6750-9000, 5>9000)					0.000
NTproBNP 2 vs. NTproBNP 1	1.668	0.680	5.304	1.398-20.122	
NTproBNP 3 vs. NTproBNP 1	1.012	0.686	2.750	0.717-10.553	
NTproBNP 4 vs. NTproBNP 1	2.670	0.690	14.437	3.731-55.874	
NTproBNP 5 vs. NTproBNP 1	2.398	0.594	11.000	3.432-35.260	
SBP	-0.003	0.004	0.997	0.989-1.005	0.461
DBP	0.015	0.007	1.015	1.000-1.030	0.048
HR	0.018	0.007	1.019	1.006-1.032	0.005
BG	-0.041	0.040	0.960	0.888-1.037	0.298
Hypertension (0=no, 1=yes)	0.161	0.333	1.175	0.611-2.257	0.629
CHD (0=no, 1=yes)	0.149	0.323	1.161	0.616-2.185	0.645
Diabetes (0=no, 1=yes)	-0.093	0.367	0.911	0.444-1.869	0.799
C/T	0.715	2.277	2.044	0.024-177.426	0.754

Continuous variables of all the indicators in the total population (age, SBP, DBP, HR, BG and cardiothoracic ratio) were selected for co-linear analysis (Table II-V and II-VI). Our results indicated that there was co-linearity between the 6 variables. Based on clinical experience, cardiothoracic ratio was excluded and co-linear diagnosis was performed later (Table II-VII and II-VIII). Results showed that the co-linearity had been controlled. Qualitative variables in total population were selected for correlation analysis (Table II-IX). Results demonstrated that there was no strong correlation with gender, hypertension, CHD and diabetes (r<0.3), without considering the deleted variables.

Establishing Regression Equation, ROC Curve and the Optimal Diagnostic Cut-off Point

Combined with the results of this study, and the comprehensive consideration of clinical practice, we chose age, SBP, DBP, HR and NT-proBNP as covariates in the binary logistic regression analysis, and obtained the regression equation: p=1/(1+exp (-(-1.218-0.020*Age+0.519*NT proBNP-0.032*SBP+0.046* DBP+0.011*HR))). There was statistical significance in the regression equation (χ^2=32.177, p<0.001), and the coefficient of determination of COX and Snell was 0.239, whereas the coefficient of determination of Nagelkerke was 0.321. Hosmer-Lemeshow model test was (χ^2=8.654, p=0.372). This indicates there was no significant difference between the predictive value and the observed value of the model and the model was established with statistical significance and the fitting effect was good. By selecting the maximum value of Youden index for the ROC curve, we found that the prediction probability of the best diagnostic point was 0.375. The sensitivity was 0.796, the specificity was 0.739 and the prediction accuracy was 76.3%. The area under the curve was 0.804 (p<0.001),

Table II-IV. Univariate logistic regression analysis on typing factors for the training sample.

Index	Regression coefficient	Standard error	Odds ratio	95% CI	p
Age	-0.018	0.015	0.982	0.954-1.012	0.239
Gender (1=male, 0=female)1 vs. 0	0.067	0.391	1.070	0.497-2.301	0.863
NTproBNP (1=300-2250, 2≥2250-4500, 3≥4500-6750, 4≥6750-9000, 5>9000)					0.005
NTproBNP 2 vs. NTproBNP 1	1.579	0.774	4.848	1.063-22.107	
NTproBNP 3 vs. NTproBNP 1	0.916	0.783	2.500	0.539-11.591	
NTproBNP 4 vs. NTproBNP 1	2.051	0.832	7.778	1.522-39.754	
NTproBNP 5 vs. NTproBNP 1	2.343	0.697	10.417	2.657-40.835	
SBP	-0.003	0.004	0.995	0.985-1.005	0.289
DBP	0.011	0.008	1.011	0.994-1.028	0.201
HR	0.021	0.008	1.021	1.005-1.037	0.009
BG	-0.052	0.049	0.949	0.863-1.045	0.287
Hypertension (0=no, 1=yes)	0.129	0.390	1.138	0.530-2.443	0.740
CHD (0=no, 1=yes)	0.135	0.381	1.145	0.542-2.417	0.723
Diabetes (0=no, 1=yes)	-0.299	0.423	0.741	0.324-1.698	0.479
C/T	1.799	2.817	6.044	0.024-1510.774	0.523

and 95% CI was 0.723-0.886 (Figure 1, Table II-X and II-XI). Samples were tested with the remaining 30% of the subjects and the screening criteria were selected based on training samples. The sensitivity and specificity of the screening criteria in the test sample was calculated. The sensitivity of cut-off value for the test sample at 0.375 was 0.765, the specificity was 0.774 and the prediction accuracy was 77.1%. The area under the curve was 0.829 (p<0.001) and 95% CI was 0.713-0.946. These results were consistent with the training samples. The coordinates of part of the training sample predicting the probability curve are shown in Table II-XII.

Model Test

Samples were tested with the remaining 30% of the subjects and the screening criteria were selected based on the training sample. The sensitivity and specificity of the screening criteria in test sample were calculated. The sensitivity of the cut-off value for the test sample at 0.375 was 0.765, the specificity was 0.774 and the prediction accuracy was 77.1%. The area under the curve was 0.829 (p<0.001) and 95% CI was 0.713-0.946. These results were consistent with the training samples and suggest that the model established in this study is reliable, practical and applicable (Table II-XIII and Figure 2).

Discussion

Cardiac ultrasound is the most simple, direct, noninvasive and effective method to diagnose heart failure. There are many indicators to evaluate the systolic and diastolic function of the heart, among which the most sensitive and specific indicator for measuring systolic cardiac function is LVEF[8]. Since diastolic function is complex and involves many factors, there are no concise indicators for the evaluation of diastolic function at present.

Table II-V. First linear diagnostic for typing factors-1.

Model	unstandardized coefficient		Standard coefficient	t	p	95% confidence interval of B		Co linear statistic	
	B	Standard error	Trial version			Lower limit	Upper limit	Tolerance	VIF
Constant	0.164	0.415		0.396	0.693	-0.655	0.984		
Age	-0.003	0.003	-0.081	-1.084	0.280	-0.008	0.002	0.976	1.025
SBP	-0.004	0.001	-0.331	-3.046	0.003	-0.007	-0.001	0.468	2.137
DBP	0.008	0.002	0.358	3.251	0.001	0.003	0.013	0.454	2.202
HR	0.003	0.001	0.163	2.095	0.038	0.000	0.006	0.914	1.094
BG	-0.004	0.009	-0.036	-0.480	0.632	-0.021	0.013	0.980	1.021
C/T	0.147	0.526	0.021	0.279	0.781	-0.893	1.186	0.983	1.018

Table II-VI. First linear diagnostic for typing factors-1.

Model dimension	Eigenvalue	Condition index	Variance ratio						
			constant	age	SBP	DBP	HR	BG	C/T
1.000	6.709	1.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
2.000	0.129	7.218	0.000	0.000	0.010	0.010	0.020	0.820	0.000
3.000	0.068	9.938	0.010	0.080	0.140	0.100	0.100	0.040	0.010
4.000	0.053	11.290	0.000	0.270	0.000	0.000	0.550	0.060	0.000
5.000	0.021	17.776	0.030	0.500	0.010	0.060	0.180	0.030	0.300
6.000	0.015	20.982	0.000	0.020	0.830	0.820	0.090	0.000	0.020
7.000	0.006	34.663	0.960	0.130	0.000	0.010	0.060	0.040	0.660

Table II-VII. Second linear diagnostic for typing factors-1.

Model	unstandardized coefficient		Standard coefficient	t	p	95% confidence interval of B		Co linear statistic	
	B	Standard error	Trial version			Lower limit	Upper limit	Tolerance	VIF
Constant	0.243	0.305			0.796	0.427	-0.359	0.845	
Age	-0.003	0.003	-0.080	-1.072	0.285	-0.008	0.002	0.979	1.021
SBP	-0.004	0.001	-0.328	-3.043	0.003	-0.007	-0.001	0.470	2.126
DBP	0.008	0.002	0.358	3.255	0.001	0.003	0.013	0.454	2.201
HR	0.003	0.001	0.164	2.130	0.035	0.000	0.006	0.920	1.087
BG	-0.004	0.009	-0.037	-0.491	0.624	-0.021	0.013	0.981	1.019

Table II-VIII. Second linear diagnostic for typing factors-2.

Model dimension	Eigenvalue	Condition index	Variance ratio					
			constant	age	SBP	DBP	HR	BG
1.000	5.729	1.000	0.000	0.000	0.000	0.000	0.000	0.000
2.000	0.128	6.689	0.000	0.000	0.010	0.020	0.030	0.810
3.000	0.064	9.446	0.010	0.090	0.140	0.080	0.200	0.030
4.000	0.052	10.500	0.000	0.360	0.000	0.000	0.440	0.070
5.000	0.016	19.163	0.010	0.010	0.780	0.900	0.010	0.020
6.000	0.011	23.008	0.970	0.540	0.070	0.000	0.310	0.070

Table II-IX. Correlation analysis of qualitative indicators (total population).

	Gender	Hypertension	CHD	Diabetes
Gender	1			
Hypertension	r = -0.010 p = 0.897	1		
CHD	r = -0.105 p =0.176	r=0.268 p<0.001	1	
Diabetes	r = -0.116 p =0.137	r=-0.201 p =0.010	r=0.266 p =0.001	1

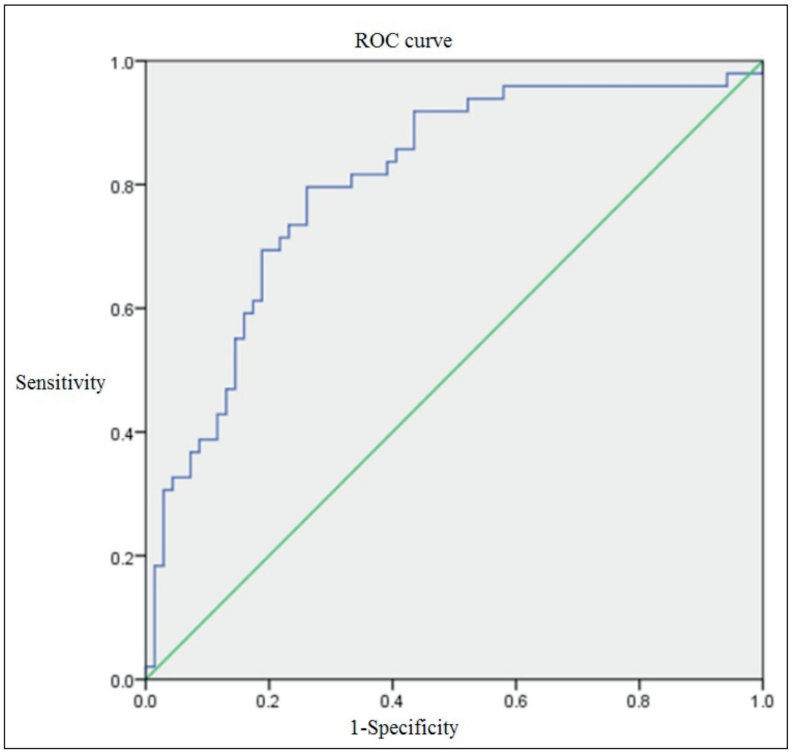

Figure 1. The prediction probability ROC curve of training sample.

Table II-X. Typing factors for AHFREF and AHFPEF by multiple factor logistic regression model.

Index	Regression coefficient	Standard error	Odds ratio	95 % CI	p
Age	-0.020	0.018	0.980	0.946-1.015	0.263
NTproBNP (1=300-2250, 2≥2250-4500, 3≥4500-6750, 4≥6750-9000, 5>9000)	0.519	0.149	1.681	1.225-2.252	0.001
SBP	-0.032	0.010	0.969	0.950-0.988	0.001
DBP	0.046	0.017	1.047	1.012-1.084	0.008
HR	0.011	0.010	1.011	0.992-1.030	0.253
Constant	-1.218	1.928	0.399		0.528

The accepted indicators are the E/A wave ratio of mitral valve flow (MVF) (i.e. MVF filling velocity ratio of early diastole and late diastole) and DT (peak E deceleration time of early diastole)[9]. To guide treatment, heart failure is clinically divided into HFREF (LVEF <50%) and HFPEF (LVEF ≥ 0.5) according to the LVEF measured by cardiac ultrasound. However, the acquisition of LVEF is often in the Emergency Department following AHF. Previous studies showed that when AHF patients arrive at the hospital, some readily available clinical indicators are related to LVEF, suggesting that combined application of these indicators may predict LVEF before ultrasonic cardiac examination.

NT-pro BNP has been widely used in the differential diagnosis of emergency dyspnea. Studies showed[10,11] that as a non-age-dependent intercept point of NT-proBNP, 300 pg/ml can be used to exclude AHF. Thus, this study has excluded patients with NT-proBNP <300 pg/ml. The relationship between NT-proBNP levels and left ventricular systolic dysfunction has been clearly understood and even if there is no systolic dysfunction, NT-proBNP levels are associated with diastolic dysfunction. Clinically, HFREF patients are often given more attention, while HFPEF patients are often misdiagnosed. Among patients with significant or even severe heart failure symptoms, LVEF value is often in the normal range. Therefore, it is of great importance to find an early, effective and accurate method for the diagnosis of HFPEF.

Table II-XI. The area under the prediction probability ROC curve of training sample.

Area	Standard error	p	95 % CI	
			Lower limit	Upper limit
0.804	0.042	0.000	0.723	0.886

Table II-XII. The prediction probability ROC curve of training sample.

Sample No.	Positive If greater than or equal to	Sensitivity	1–Specificity
1	0.000	1.000	1.000
2	0.053	0.980	1.000
3	0.061	0.980	0.986
4	0.075	0.980	0.971
5	0.089	0.980	0.957
.....	.....	.....	.....
57	0.337	0.796	0.333
58	0.341	0.796	0.319
59	0.346	0.796	0.304
60	0.355	0.796	0.290
61	0.367	0.796	0.275
62	0.375	0.796	0.261
63	0.382	0.776	0.261
64	0.389	0.755	0.261
65	0.397	0.735	0.261
66	0.405	0.735	0.246
67	0.407	0.735	0.232
.....	.....	.....	.....
115	0.831	0.061	0.014
116	0.840	0.041	0.014
117	0.850	0.020	0.014
118	0.890	0.020	0.000
119	1.000	0.000	0.000

Table II-XIII. The area under the prediction probability ROC curve of training sample.

Area	Standard error	p	95 % CI	
			Lower limit	Upper limit
0.829	0.059	0.000	0.713	0.946

The present study shows that LVEF negatively correlates with NT-proBNP in AHF patients (r=-0.286, p=0.000). Moreover, NT-proBNP (β=0.519, p=0.001, 95% CI=1.225-2.252) in regression equation indicates that NT-proBNP is of great significance not only for diagnosis of heart failure, but also for differentiating AHFREF and AHFPEF. Patients are more likely to belong to the AHFREF group when their NT-proBNP value is high. This result is consistent with previous studies in that the plasma levels of NT-proBNP in HFREF patients are higher than that of HFPEF patients[12-16].

An investigation using OPTIMIZE-HF demonstrated that patients with systolic blood pressure >140 mmHg, when hospitalized, accounted for more than 50% of AHF patients, of which 56% patients had normal systolic function. Notably, patients with low blood pressure, when hospitalized, accounted for about 5-10% of AHF patients, most of whose heart function was severely damaged resulting in LVEF reduction. This suggests that blood pressure was associated with LVEF in AHF patients at admission, and the higher the systolic pressure is, the higher the LVEF is[17-19]. However, there are also reports[20] that show that this relationship is only evident when systolic blood pressure is <120 mmHg on admission. Our results also indicate that systolic blood pressure is helpful in the differential diagnosis of AHFREF and AHFPEF. Rapid HR has significant influence on the occurrence, development, and prognosis of heart failure. Abnormal increase in HR may cause cardiac output changes and increase in myocardial oxygen consumption, affecting the prognosis of patients with heart failure.

Fox et al[21] observed the correlation of basic resting HR and heart disease using a Cox regression model. Their results showed that patients with HR ≥ 70 bpm had a significant increase in heart disease-related mortality (34%, p=0.0041), heart failure-related hospitalization rate (53%, p<0.05), myocardial infarction-related hospitalization rate (46%, p=0.0066) and coronary revascularization rate (38%, p=0.037). With each increase in resting HR of 5 bpm, the rate of death from heart disease increased by 8% (p=0.0005) and the rate of hospitalization for heart failure increased by 16% (p<0.0001). INVEST found that in patients with

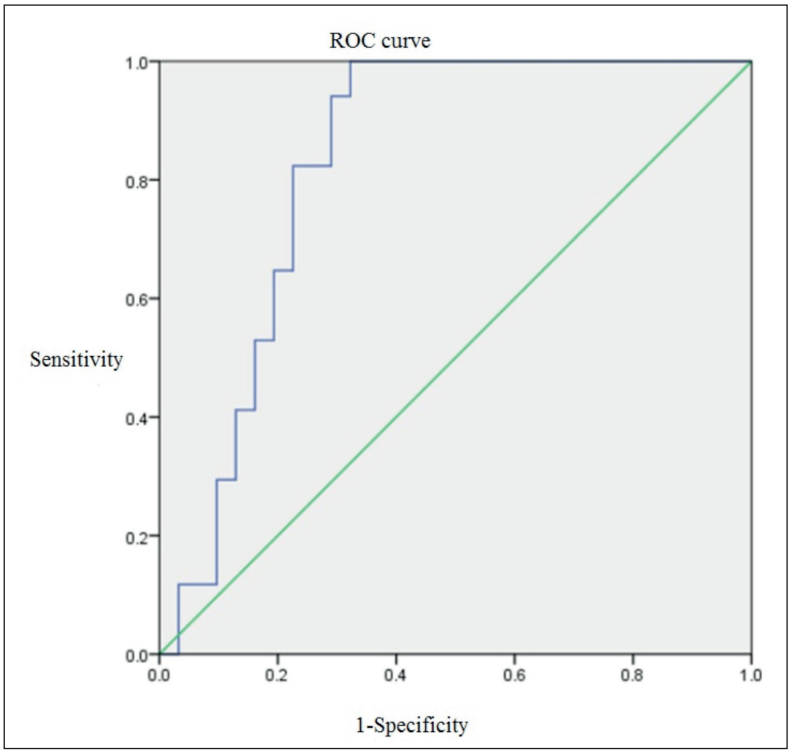

Figure 2. The prediction probability ROC curve of test sample

cardiac disease, the prognosis of patients with HR<59 bpm was not significantly improved than that of patients with HR>60 bpm and prognosis had no significant difference among patients with HR ranging from 55-100 bpm[22].

Studies about the relationship between HR and AHF, especially the relationship between HR and LVEF of AHF patients is rare. Kajimoto et al[23] found that among patients with acute heart failure syndrome, HR of LVEF<40% group (n=2585) was significantly higher than that of LVEF≥40% group (n=2135) (103.7±28.3 *vs.* 92.1±29.1, $p<0.001$). Our study also showed that the HR of AHFREF group was significantly higher than that of AHFPEF group in AHF patients [113 (95.8, 130) bpm *vs.* 96 (83, 116.5) bpm, $Z=-3.186$, $p=0.001$], and HR was inversely related to LVEF ($r=-0.252$, $p=0.001$). Therefore, HR is helpful in the differential diagnosis of these two types of heart failure, but this needs further large sample investigation.

Scholars[24] showed that with an increase in age, the incidence of chronic heart failure was relatively reduced, whereas the rate of acute left heart failure and chronic left heart failure with acute exacerbation was significantly increased, especially in elderly patients. We did not find age to be correlated with LVEF in AHF patients, but was positively correlated with LVEF in AHFREF group (r=0.416, $p=0.001$). This could be due to a part of the patients being excluded, and this also indicates that with an increase in age, only a portion of AHF patients' show a decrease in myocardial contractility and myocardial compliance reduction is part of the reason for heart failure. Therefore in the treatment of senile heart failure, we should not only pay attention to improving myocardial contractility, but also improve myocardial compliance.

Conclusions

This work retrospectively analyzed the role of commonly used clinical indicators in emergency medicine, such as age, sex, BP, HR, BG, NT-proBNP and other indicators in the diagnosis and classification of acute heart failure. Our results could prove to be helpful for early diagnosis of AHF and help to better understand the pathogenesis of the two types of heart failure. In this study, there was a small number of patients with NT-proBNP levels > 9000 pg/ml, which exceed the range of measurement. Thus, part of the information was lost, which exerted an influence on the accuracy of the equation.

Conflict of Interest

The authors declare no conflict of interest.

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