

Risk Factors for Poor Prognosis in Acute Coronary Syndrome Admitted in the Emergency Department: A Retrospective Cohort Study

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ABSTRACT

Background: In the present study, we aimed to identify risk factors of poor prognosis for patients with acute coronary syndrome in the emergency department.

Methods: The study included 2667 patients, who were admitted to the Emergency Department of Chest Pain Center, Fujian Provincial Hospital, due to chest pain from January 1, 2017 to March 31, 2020. Logistic regression was used to identify factors of poor prognosis for patients with ACS in the ED. Receiver operating characteristic (ROC) curve was plotted to assess the performance of the multivariate logistic regression model. Subgroup analysis was used to analyze the difference of SBP in ACS patients with different characteristics.

Results: The final analysis included 2667 patients, of whom 2,057 patients (77.8%) had poor prognosis. STEMI (compared with UA) (OR=20.139; 95% CI:12.448-32.581; $P < 0.001$), NSTEMI (compared with UA) (OR=7.430; 95% CI:5.159-10.700; $P < 0.001$), respiratory rate ≥ 20 bpm (compared with < 20 bpm) (OR=1.334; 95% CI: 1.060-1.679; $P = 0.014$), and use of antiplatelets (OR=1.557; 95% CI:1.181-2.053; $P = 0.002$) was associated with increased likelihood of poor prognosis for ACS patients in ED. SBP ≥ 140 mmHg (compared with < 140 mmHg) (OR=0.574; 95% CI: 0.477-0.690; $P < 0.001$) was associated with decreased likelihood of poor prognosis for ACS patients in the ED. The area under curve (AUC) of the predictive efficacy of logistic regression model was 0.825 (95% CI: 0.795-0.833, $P < 0.001$).

Conclusion: This study found that STEMI, NSTEMI, respiratory rate ≥ 20 bpm, and use of antiplatelets were associated with increased likelihood of poor prognosis for ACS patients in the ED. It also found that SBP ≥ 140 was associated with decreased likelihood of poor prognosis. Our study may be useful for doctors to make clinical decisions for ACS patients.

Received September 12, 2022; accepted October 7, 2022.

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INTRODUCTION

Acute coronary syndrome (ACS), including unstable angina (UA), non-ST segment elevation myocardial infarction (NSTEMI), and ST-segmental elevation infarction (STEMI), is the leading cause of mortality and disability [Kibos 2011; Hasdai 2003; Bertrand 2000]. Although the mortality rate of ACS greatly has declined [Krumholz 2009], it still is estimated that 40% of patients with coronary events will die within 5 years, and the mortality risk in patients with recurrent events is five to six times higher [Rogers 2000; Thom 2006]. The overall trend of acute myocardial infarction mortality was on the rise from 2002 to 2015 and began to rise rapidly in 2005 in China [China's Health Statistical Yearbook 2016].

Many factors affect the clinical outcome of ACS patients. A previous study found that age, use of diuretics at admission, type 1 diabetes, serum creatinine level, lower systolic blood pressure (SBP), and STEMI and NSTEMI categories are associated with higher mortality risk in ACS patients [Nikus 2007]. A retrospective study found that age, Killip class, SBP, ST-segment deviation, cardiac arrest during presentation, serum creatinine level, positive initial cardiac enzyme findings, and heart rate accounted for 89.9% of the prognostic information of ACS patients with and without ST-segment elevation [Granger 2003]. Blood pressure is a key determinant of adverse events in patients with cardiovascular disease [Dawber 2015]. In the case of acute cardiovascular disease (including ACS), SBP is a powerful predictor of mortality risk [Granger 2003; Eagle 2004]. Another study found there was a significant correlation between the blood pressure of ACS patients on admission and the prognosis of the patients [Roffi 2016]. The results of the PRavastatin OR atorVastatin Evaluation and Infection Therapy-Thrombolysis in Myocardial Infarction (PROVE IT-TIMI) 22 trial showed that after the occurrence of ACS, there was a J-shaped or U-shaped curve correlation between blood pressure and the risk of future cardiovascular events. The lowest event rates were found in SBP range of 130 to 140 mmHg, and the diastolic blood pressure (DBP) range of about 80 to 90 mmHg. With an SBP of 110 to 130 mmHg and a DBP of 70 to 90 mmHg, patients may be at higher risk for cardiovascular events [Bangalore 2010].

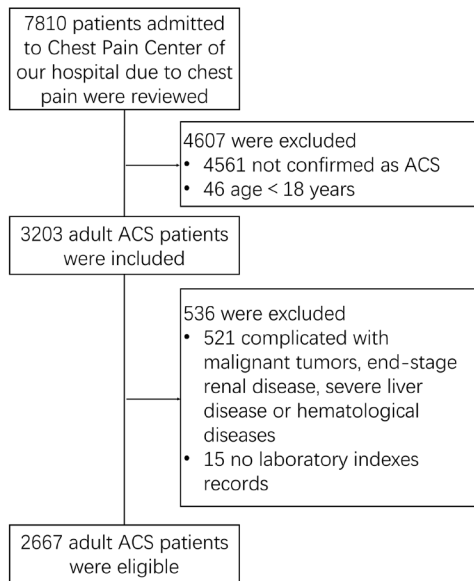


Figure 1. Flow chart of the study

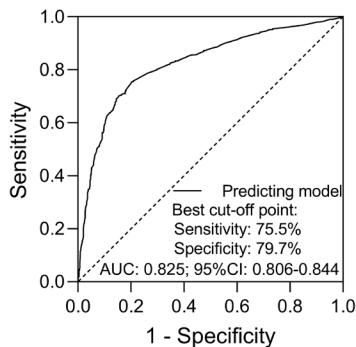


Figure 2. The performance of multivariate logistic regression model in predicting poor prognosis. The AUC was 0.825 (95% CI: 0.806-0.844, $P < 0.001$), sensitivity was 0.755, and specificity was 0.797. ROC, receiver operating characteristic; SBP, systolic blood pressure; NSTEMI, non-ST-segment elevation myocardial infarction; ACS, acute coronary syndrome; AUC, area under curve

Few studies have focused on the risk factors of poor prognosis for patients with ACS in the emergency department (ED). In this study, we aimed to do this as well as offer suggestions to improve prognosis of ACS patients.

METHODS

Participants and study design: This is a retrospective cohort study. A total of 2667 patients, who were admitted to the Chest Pain Center (ED), Fujian Provincial Hospital due to chest pain from January 1, 2017 to March 31, 2020, were included. Research data was extracted from the hospital information system, laboratory information management system, clinical data repository, and intensive care unit database of Fujian Provincial Hospital. Inclusion criteria were

Table 1. Baseline characteristics

Items	ACS patients (N = 2667)
Age (years), mean±SD	64.7±13.0
Gender, n (%)	
Female	835 (31.3)
Male	1832 (68.7)
Diagnosis, n (%)	
UA	1134 (42.5)
STEMI	841 (31.5)
NSTEMI	692 (25.9)
Laboratory indexes median (IQR)	
Respiratory rate (bpm)	20.0 (19.0-20.0)
Pulse rate (bpm)	79.0 (70.0-89.0)
Heart rate (bpm)	79.0 (69.0-89.0)
SBP (mmHg)	135.0 (121.0-153.0)
DBP (mmHg)	80.0 (71.0-89.0)
cTn I (ng/mL)	0.05 (0.01-0.84)
Medication, n (%)	
Aspirin	2547 (95.5)
Clopidogrel	291 (10.9)
Ticagrelor	2243 (84.1)
Antiplatelet	2055 (77.1)
Statin	2243 (84.1)
β-receptor blocker	39 (1.5)

ACS, acute coronary syndrome; SD, standard deviation; UA, unstable angina; STEMI, ST-segment elevation myocardial infarction; NSTEMI, non-ST elevation myocardial infarction; IQR, interquartile range; SBP, systolic blood pressure; DBP, diastolic blood pressure; cTn I, cardiac troponin I

age≥18 years and admission to the hospital with a diagnosis of ACS. Exclusion criteria were pregnancy, patients with malignant tumors, end-stage renal disease, severe liver disease or hematological diseases, and patients with non-cardiogenic chest pain. The selection process for participants is shown in Figure 1. (Figure 1) The study was approved by the Ethical Committee of Fujian Provincial Hospital. The informed consent requirement was waived since the study only involved the use of past clinical data.

Variables and definitions: The study variables included demographic characteristics, physical examination, laboratory testing, and medications. ACS was defined, according to the 2020 European Society of Cardiology (ESC) Guidelines [Collet 2020]. Patients who presented with acute chest pain accompanied by persistent (>20 minutes) elevation of the ST-segment were defined as ST-segment elevation ACS (STE-ACS). Patients with acute chest discomfort but no continuous ST-segment elevation in the electrocardiogram were defined as non-ST-segment elevation ACS (NSTEMI-ACS), which can

Table 2. Univariate logistic regression model analysis of factors predicting disease aggravation

Items	Univariate logistic regression model			
	P-value	OR	95% CI	
			Lower	Higher
Age (≥ 65 years vs. < 65 years)	0.069	0.843	0.702	1.014
Gender (male vs. female)	< 0.001	1.649	1.364	1.994
Diagnosis				
UA				
STEMI	< 0.001	19.796	13.643	28.723
NSTEMI	< 0.001	7.956	5.977	10.591
Respiratory rate (≥ 20 bpm vs. < 20 bpm)	< 0.001	1.419	1.174	1.715
Pulse rate (≥ 100 bpm vs. < 100 bpm)	0.122	1.260	0.940	1.688
Heart rate (≥ 100 bpm vs. < 100 bpm)	0.119	1.262	0.942	1.692
SBP (≥ 140 mmHg vs. < 140 mmHg)	< 0.001	0.574	0.477	0.690
DBP (≥ 90 mmHg vs. < 90 mmHg)	0.840	0.978	0.787	1.215
cTn I (≥ 0.1 ng/mL vs. < 0.1 ng/mL)	< 0.001	5.017	3.946	6.379
Aspirin (yes vs. no)	0.055	0.607	0.364	1.010
Clopidogrel (yes vs. no)	< 0.001	2.924	1.958	4.365
Ticagrelor (yes vs. no)	< 0.001	0.409	0.299	0.559
Antiplatelet (yes vs. no)	< 0.001	1.680	1.369	2.061
Statin (yes vs. no)	< 0.001	0.507	0.378	0.680
β -receptor blocker	0.163	1.956	0.761	5.023

OR, odds ratio; CI, confidence interval; UA, unstable angina; STEMI, ST-segment elevation myocardial infarction; NSTEMI, non-ST elevation myocardial infarction; SBP, systolic blood pressure; DBP, diastolic blood pressure; cTn I, cardiac troponin I

manifest as ST-segment transient elevation, ST-segment persistent or transient depression, T-wave inversion, flat T waves, pseudo-normalization of T waves, or normal electrocardiography. UA is defined as myocardial ischemia at rest or on minimal exertion in the absence of acute cardiomyocyte injury/necrosis.

In the present study, patients labeled with "poor prognosis" were compared to patients with a "good prognosis." The definition of "good prognosis" consisted of those with successful thrombolysis or percutaneous coronary intervention (PCI) and transferred to the general ward. The standard of successful thrombolysis and PCI were consistent with the latest guidelines and research results [Sibbing 2017; Zhang 2019].

Statistical analysis: Continuous variables were summarized as mean \pm standard deviation (SD) or median (IQR), according to their distribution. Categorical variables were displayed by counts and percentages. Univariate logistic regression was applied to screen the factors predicting disease aggravation, then variables with $P < 0.10$ were further analyzed using multivariate logistic regression. The receiver operating characteristic (ROC) curve was plotted, and the area under curve (AUC) (95% confidence interval),

sensitivity and specificity at the best cut-off point also were calculated to assess the performance of multivariate logistic regression model in predicting disease aggravation. SBP was a major predictor for disease aggravation, which was observed in the multivariate logistic regression model. So, the correlation of SBP with disease aggravation was analyzed using univariate logistic regression in different subgroup subsequently. All statistical tests were two-sided, and $P < 0.05$ was regarded as statistically significant. The analyses were conducted using SPSS 24.0 (SPSS Inc., Chicago, Illinois, USA). The figures were plotted with utilization of GraphPad Prism 7.01 software (GraphPad Software Inc., San Diego, California, USA).

RESULTS

Patient characteristics: In total, 2667 patients were included, of whom 2,057 patients (77.8%) had a poor prognosis, while 592 patients (22.2%) did not. Overall, patients included in the final analysis cohort were 64.7 ± 13.0 years old; this was comprised of 1832 (68.7%) males and 835 (31.3%)

Table 3. Multivariate logistic regression model analysis of factors independent predicting disease aggravation

Items	Multivariate logistic regression model			
	P-value	OR	95% CI	
			Lower	Higher
Age (≥ 65 years vs. < 65 years)	0.439	0.915	0.730	1.146
Gender (male vs. female)	0.503	0.924	0.734	1.164
Diagnosis				
UA	Reference	-	-	-
STEMI	< 0.001	20.139	12.448	32.581
NSTEMI	< 0.001	7.430	5.159	10.700
Respiratory rate (≥ 20 bpm vs. < 20 bpm)	0.014	1.334	1.060	1.679
SBP (≥ 140 mmHg vs. < 140 mmHg)	< 0.001	0.601	0.480	0.753
cTn I (≥ 0.1 ng/mL vs. < 0.1 ng/mL)	0.529	1.113	0.797	1.554
Aspirin (yes vs. no)	0.600	1.860	0.183	18.897
Clopidogrel (yes vs. no)	0.708	0.635	0.059	6.832
Ticagrelor (yes vs. no)	0.305	0.293	0.028	3.066
Antiplatelet (yes vs. no)	0.002	1.557	1.181	2.053
Statin (yes vs. no)	0.599	0.890	0.576	1.375

Factors with P -value < 0.1 in univariate logistic regression model were further analyzed in the multivariate logistic regression model. OR, odds ratio; CI, confidence interval; UA, unstable angina; STEMI, ST-segment elevation myocardial infarction; NSTEMI, non-ST elevation myocardial infarction; SBP, systolic blood pressure; cTn I, cardiac troponin I

females. Of these patients, 42.5% were diagnosed with UA, 31.5% with STEMI, and 25.9% with NSTEMI. More details about baseline characteristics are shown in Table 1. (Table 1)

Univariate and multivariate logistic regression analysis of risk factors for poor prognosis of ACS patients in the ED: Logistic regression analysis was used to analyze factors associated with the poor prognosis of ACS patients in the ED. Univariate logistic regression analysis found male (compared with female) (OR=1.649; 95% CI: 1.364-1.994; $P < 0.001$), STEMI (compared with UA) (OR=19.796; 95% CI: 13.643-28.723; $P < 0.001$), NSTEMI (compared with UA) (OR=7.956; 95% CI: 5.977-10.591; $P < 0.001$), respiratory rate ≥ 20 bpm (compared with < 20 bpm) (OR=1.419; 95% CI: 1.174-1.715; $P < 0.001$), cardiac troponin I (cTnI) ≥ 0.1 ng/mL (compared with < 0.1 ng/mL) (OR=5.017; 95% CI: 3.946-6.379; $P < 0.001$), use of clopidogrel (OR=2.924; 95% CI: 1.958-4.365; $P < 0.001$), use of antiplatelets (OR=1.680; 95% CI: 1.369-2.061; $P < 0.001$), SBP ≥ 140 mmHg (compared with < 140 mmHg) (OR=0.574; 95% CI: 0.477-0.690; $P < 0.001$), use of ticagrelor (OR=0.409; 95% CI: 0.299-0.559; $P < 0.001$), and statin (OR=0.507; 95% CI: 0.378-0.680; $P < 0.001$) were significantly associated with poor prognosis of patients in the ED. (Table 2)

Multivariate logistic regression analysis revealed that STEMI (compared with UA) (OR=20.139; 95% CI: 12.448-32.581; $P < 0.001$), NSTEMI (compared with UA) (OR=7.430; 95% CI: 5.159-10.700; $P < 0.001$), respiratory

rate ≥ 20 bpm (compared with < 20 bpm) (OR=1.334; 95% CI: 1.060-1.679; $P = 0.014$), and use of antiplatelets (OR=1.557; 95% CI: 1.181-2.053; $P = 0.002$) were associated with increased likelihood of poor prognosis for ACS patients in the ED. SBP ≥ 140 mmHg (compared with < 140 mmHg) (OR=0.601; 95% CI: 0.480-0.753; $P < 0.001$) was associated with decreased likelihood of poor prognosis for ACS patients in the ED. (Table 3)

The ROC curve of multivariate logistic regression model: Variates with $P < 0.05$ in multivariate logistic regression analysis were used to construct a regression model. The result showed that the AUC was 0.825 (95% CI: 0.806-0.844, $P < 0.001$), the sensitivity was 0.755, and specificity was 0.797. (Figure 2)

The influence of different SBP groups on poor prognosis of ACS patients in the ED: Considering SBP ≥ 140 mmHg was associated with decreased likelihood of poor prognosis and there was limited study on the impact of SBP in ACS patients, we conducted further subgroup analysis. The results showed that the correlation between SBP and poor diagnosis was statistically significant in almost all subgroups. (Table 4)

DISCUSSION

With the use of multivariate logistic regression, we found that diagnosis with STEMI or NSTEMI, respiratory rate ≥ 20

Table 4. Correlation of SBP with disease aggravation in different subgroup

Items	N	SBP stratification (≥ 140 mmHg vs. < 140 mmHg)		
		P-value	OR	95% CI
Age				
<65 years	1250	0.011	0.697	0.527-0.921
≥ 65 years	1417	<0.001	0.502	0.391-0.645
Gender				
Female	835	<0.001	0.555	0.409-0.753
Male	1832	<0.001	0.614	0.486-0.775
Diagnosis				
UA	1134	<0.001	0.542	0.427-0.687
STEMI	841	0.352	1.451	0.663-3.178
NSTEMI	692	0.047	0.585	0.345-0.993
Respiratory rate				
<20 bpm	888	<0.001	0.543	0.401-0.735
≥ 20 bpm	1768	<0.001	0.604	0.478-0.763
Pulse rate				
<100 bpm	2335	<0.001	0.577	0.475-0.701
≥ 100 bpm	328	0.018	0.509	0.291-0.892
Heart rate				
<100 bpm	2307	<0.001	0.579	0.475-0.704
≥ 100 bpm	329	0.031	0.540	0.309-0.944
DBP				
<90 mmHg	2058	<0.001	0.511	0.412-0.634
≥ 90 mmHg	609	0.033	0.539	0.305-0.952
cTn I				
<0.1 ng/mL	1354	<0.001	0.575	0.458-0.722
≥ 0.1 ng/mL	1032	0.010	0.569	0.372-0.872

SBP, systolic blood pressure; OR, odds ratio; CI, confidence interval; UA, unstable angina; STEMI, ST-segment elevation myocardial infarction; NSTEMI, non-ST elevation myocardial infarction; DBP, diastolic blood pressure; cTn I, cardiac troponin I

bpm, use of antiplatelets, and SBP ≥ 140 mmHg were independent predictive factors for poor prognosis of patients in the ED. Secondly, we established a regression model, and the ROC curve was done. It showed good sensitivity and specificity. Finally, we performed a subgroup analysis on SBP and found statistical significance in almost all the different subgroups.

It was obvious that the clinical characteristics of STEMI patients were different from those of NSTEMI. Compared with STEMI, NSTEMI had better short-term outcomes [Chan 2009; Steg 2002; Hasdai 2002]. Compared with STEMI and NSTEMI patients, UA patients have lower short-term mortality risk [Puelacher 2019; Giustino 2015]. A large prospective study showed that at 30 days, all-cause mortality in UA was substantially lower as compared with NSTEMI (0.7% vs. 7.4%) [Puelacher 2019]. In our study,

patients in the ED with STEMI or NSTEMI had a greater risk of poor prognosis than those with UA. We can infer that the poor prognosis in the ED was correlated and consistent with later mortality risk.

A previously published study indicated that respiratory rate had a close relationship with coronary disease. Ponikowski et al. declared that abnormal respiratory response is an indicator of adverse prognosis in heart disease [Ponikowski 2001]. Increase in the respiratory rate can be seen as a reflection of disturbed autonomic control, to some extent, predicting an adverse prognosis in patients with ACS [Barthel 2013].

A multicenter cohort study based on Chinese patients showed that parenteral anticoagulation therapy was not associated with a lower risk of all-cause death or myocardial infarction but significantly associated with a higher risk of

major bleeding for NSTEMI [Chen 2019]. Randomization to warfarin and aspirin was associated with a significantly greater rate of major bleeds, representing an NNH of 100 patients to cause a major bleeding [Andreotti 2006]. In our study, antiplatelet was a risk factor for poor prognosis, too.

In the end, we would like to highlight the result of SBP. SBP \geq 140 mmHg was associated with decreased possibility of poor prognosis for ACS patients in the ED. This was in line with other studies. Lee et al. found that lower SBP was independently associated with the mortality risk of patients with non-ST-elevation ACS [Lee 2013]. A Korean clinical study found that STEMI patients with normal SBP (100-139 mmHg) have a higher risk of in-hospital mortality compared with higher SBP (\geq 140 mmHg) [Park 2015]. Lower blood pressure in ACS patients also was significantly associated with an increased risk of hospitalization for cardiovascular events [Bangalore 2009]. The possible mechanisms for the clinical benefits of SBP \geq 140 mmHg were as follows: For patients with impaired coronary perfusion, lowering blood pressure may reduce blood flow to target organs [Bangalore 2009]. Hypotension may be associated with underlying chronic disease-related symptoms and increased morbidity and mortality. In addition, hypotension is a marker of cardiogenic shock and associated with an increased risk of cardiovascular events [Bangalore 2009]. Patients with higher blood pressure may be more likely to be attended sooner by clinicians. Clinicians may then take some interventions to lower blood pressure, making it easier for these patients to be improved in the ED. All in all, there still is a lack of research about the impact of SBP on ACS patients' improvement in the ED. Our study can fill the gap in literature about the impact of SBP on ACS patients' prognosis in the ED.

The study had several limitations. First, this was a retrospective study; hence, the results need to be verified by a prospective clinical trial. Second, our study was a single-center study; therefore, the research results need to be further verified by multi-center clinical studies. Third, there was also a lack of clinical biochemical variables in the study, which could be further addressed in future research.

In conclusion, STEMI, NSTEMI, and respiratory rate \geq 20 bpm were independent risk factors of poor prognosis for patients in the ED, while SBP \geq 140 mmHg was associated with decreased likelihood of poor prognosis. Furthermore, SBP \geq 140 was an independent predictive factor in most subgroups.

ACKNOWLEDGEMENT

Funding: The present study was supported by 2018 Pilot Project of Sci-Tech Innovation of Fujian Provincial Science & Technology Department (Grant number: 2018Y0009), 2020 Provincial Natural Science Foundation of Fujian (2020J011058) and 2020 High-level hospital foster grants from Fujian Provincial Hospital, Fujian province, China (Grant number: 2020HSJJ12).

We would like to thank all the staff of Chest Pain Center (Emergency Department), Fujian Provincial Hospital who

contributed to the study. We also would like to express our appreciation to Shanghai Synyi Medical Technology Co., Ltd. for providing the data analysis and statistical platform.

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