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RESEARCH ARTICLE

Association between Percentage of Neutrophils at Admission and in-Hospital Events in Patients ≥75 Years of Age with Acute Coronary Syndrome

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Abstract

Objective: The study aimed to evaluate the role of the neutrophil percentage (N%) at admission in predicting in-hospital major adverse cardiovascular events (MACE) in patients ≥75 years of age with acute coronary syndrome (ACS).

Methods: A total of 1189 patients above 75 years of age with ACS hospitalized at the Second Xiangya Hospital between January 2013 and December 2017 were enrolled in this retrospective study. Receiver operator characteristic curve analysis was performed to calculate the optimal N% cut-off value for patient grouping. The in-hospital MACE consisted of acute left heart failure, stroke and any cause of death. Multivariable logistic analyses were used to assess the role of N% in predicting MACE in older patients with ACS.

Results: The patients were divided into a high N% group (N% ≥74.17%, n=396) and low N% group (N%<74.17%, n=793) according to the N% cut-off value (N%=74.17%). The rate of MACEs during hospitalization was considerably higher in the high N% group than the low N% group (27.5% vs. 9.6%, P<0.001). After adjustment for other factors, high N% remained an independent risk factor for in-hospital MACE in older patients with ACS (odds ratio 1.779, 95% confidence interval 1.091–2.901, P=0.021).

Conclusion: High N% at admission is an independent risk factor for in-hospital MACE in patients above 75 years of age with ACS.

Keywords: Acute coronary syndrome; percentage of neutrophils; major adverse cardiovascular events; older patients

Introduction

Coronary heart disease (CHD), the leading cause of mortality and disability, has posed a heavy social and economic burden on both developing and developed countries. The number of people experiencing acute coronary syndrome (ACS) has been estimated to be approximately 635,000 each year [1], and a death rate of 40% has been estimated to occur within 5 years after ACS onset in America [2]. The economic burden of ACS is substantial, at approximately 30,000 dollars per patient annually [3]. Therefore, improving outcomes through evidence-based treatment is critical.

ACS spans a large spectrum progressing from unstable angina and non-ST-segment elevation myocardial infarction (NSTEMI) to ST-segment

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elevation myocardial infarction (STEMI). Decreased coronary blood flow resulting from plaque rupture and thrombosis formation is responsible for ACS onset [4]. Advanced age, the strongest risk factor for CHD, independently predicts adverse outcomes of ACS [5]. As a prognostic marker for ACS, age has been applied in many risk scores of ACS, such as the Global Registry of Acute Coronary Events (GRACE) [6]. The incidence of myocardial infarction in patients 50–59 years of age is considerably higher than that in patients <50 years of age (27.4% vs. 18%, $P<0.05$) [7]. Although ACS morbidity and mortality have declined with optimized treatments, the clinical outcomes of vulnerable older patients have not improved.

The infiltration of inflammatory cells in infarcted regions is considered the main mechanism of CHD [8]. The accumulation of leukocytes and the release of mediators such as tumor necrosis factor and interleukins facilitate the formtion of thrombosis and ischemic progression [9]. An elevated white blood cell (WBC) count was associated with CHD severity as early as the 1980s [10, 11]. A prospective study involving 1037 patients has revealed that neutrophils are superior to other leukocyte parameters in predicting AMI mortality, because they directly reflect the extent of myocardial damage [12]. The neutrophil percentage (N%), calculated by dividing the absolute neutrophil count by the total WBC count, is also considered an inflammatory biomarker in the progression of ACS [13]. However, few studies have focused on the association between N% and in-hospital adverse events in older patients with ACS. Therefore, this study was aimed at evaluating the value of N% at admission in predicting major adverse cardiovascular events (MACE) in patients above 75 years of age with ACS.

Methods

Study Population

Clinical data for 1305 patients 75 years of age or older with ACS, who were hospitalized in the Second Xiangya Hospital between January 2013 and December 2017 were collected in the retrospective single-center study. Patients younger than 75 years; those with complications of pericarditis, myocarditis, pulmonary embolism, aortic dissection, pneumothorax, cancer, infection, shock, cancer, immune disease and hematological disease; and those with incomplete data were excluded. A total of 1189 older patients with ACS were finally enrolled and analyzed. In the study, ACS was classified into STEMI and non-ST-elevation ACS (NSTE-ACS), including NSTEMI and unstable angina, according to American College of Cardiology criteria [14].

Measures

Demographic characteristics including age and sex; lifestyle factors including smoking; anthropometrics including body mass index (BMI), systolic blood pressure (SBP) and heart rate (HR); medical history including hypertension, dyslipidemia, type 2 diabetes mellitus (T2DM), chest pain, percutaneous transluminal coronary intervention (PCI) and coronary artery bypass crafting (CABG); biochemistry parameters including hemoglobin, WBC, N%, platelets, albumin, alanine aminotransferase (ALT), creatinine, N-terminal-pro brain natriuretic peptide (NT-proBNP), creatine kinase-myocardial band (CK-MB), total cholesterol (TC), triglycerides (TG), low density lipoprotein cholesterol (LDL-c) and high density lipoprotein cholesterol (HDL-c); ultrasound data including left ventricular ejection fraction (LVEF), hospital course including aspirin, clopidogrel, beta blockers, statins, proton pump inhibitors (PPIs), angiotensin-converting-enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), mechanical ventilation, intra-aortic balloon pump (IABP) and hospital PCI; and angiographic data including left main and three-vessel disease were collected. The blood samples were collected within 1 hour after admission for the measurement of all relevant parameters.

Outcomes

The end point was MACE, a composite outcome including in-hospital acute left heart failure, stroke and any cause of death. Acute left heart failure was defined as the new onset or worsening syndromes, and signs of heart failure including orthopnea, pink bubble sputum cough and hypotension, induced by acute coronary syndrome, arrhythmia or other triggers [15]. Stroke occurs when the brain does not

receive sufficient blood supply because of a cerebral thrombosis or bleed, as determined by imaging or autopsy [16].

Ethics

The study was approved by the human research committee of Second Xiangya Hospital (No. 2022345). Informed consent was obtained from each participant.

Statistical Analysis

The cut-off value of N% to predict in-hospital MACE and determine patient groupings was calculated with receiver operator characteristic (ROC) curve analysis. Continuous variables with a normal distribution are described as mean and standard deviation, whereas continuous variables with a skewed distribution are described as median and interquartile range. Two-sided Student's *t*-test or non-parametric test was performed to compare differences between two groups. Categorical variables, represented as number and percentage, were compared with chi-square tests. Multivariate logistic regression was performed to evaluate the association between risk factors and in-hospital MACE. Estimated odds ratios (OR) and 95% confidence intervals (95% CI) are reported. A P-value below 0.05 was considered to indicate statistical significance. SPSS IBM 28.0 (SPSS Inc., Chicago, USA) was used for statistical analysis.

Results

Patient Groupings

The optimal cut-off value of N% to predict in-hospital MACE was 74.17% [sensitivity 58.9%, specificity 71.4%, area under the curves (AUC) 67.6%], according to ROC curve analysis (Figure 1). The patients were divided according to the N% cut-off value into a low N% group (<74.17%, n=793) and high N% group (≥74.17%, n=396).

Baseline Characteristics of Patients

Baseline characteristics are shown in detail in Table 1. Patients in the high N% group were older than those in the low N% group [79 (77, 82) vs. 78 (76, 80), P=0.007]. The proportion of men in the high N% group was greater than that in the low N% group (65.2% vs. 58.8%, P=0.033). The BMI [22.3 (20.1, 24.5) vs. 23.1 (20.8, 25.3), P=0.004] and SBP [136 (118, 158) vs. 138 (121, 155), P=0.016] were lower, whereas the HR [79 (70, 90) vs. 72 (64, 81)] was higher in the high N% group than the low N% group. Patients in the high N% group were less likely to experience previous chest pain (62.4% vs. 68.6%, P=0.030) and PCI treatment (12.9% vs. 17.6%, P=0.038) than those in the low N% group. In addition, WBC [7.9 (6.2, 9.9) vs. 5.9 (4.9, 7.0), P<0.001], ALT [22.2 (12.8, 40.5) vs. 17.4 (12.2, 26.5), P<0.001], creatinine [97.7 (73.4, 134.5) vs. 87.1 (69.2, 113.4), P<0.001], NT-proBNP [2373.0 (834.1, 5640.5) vs. 670.3 (237.6, 1713.0), P<0.001] and CK-MB [17.0 (12.3, 31.7) vs. 13.0 (10.1, 17.7), P<0.001] were higher in patients with high N% than low N%. However, lower levels of hemoglobin [116 (101, 128) vs. 121 (109, 131), P<0.001], albumin [34.52 (31.4, 37.1) vs. 35.8 (33.4, 38.3), P<0.001] and TG [1.1 (0.8, 1.6) vs. 1.3 (0.9, 1.8), P<0.001] were found in patients with high N%. Compared with the low N% group, the high N% group had a greater percentage of patients

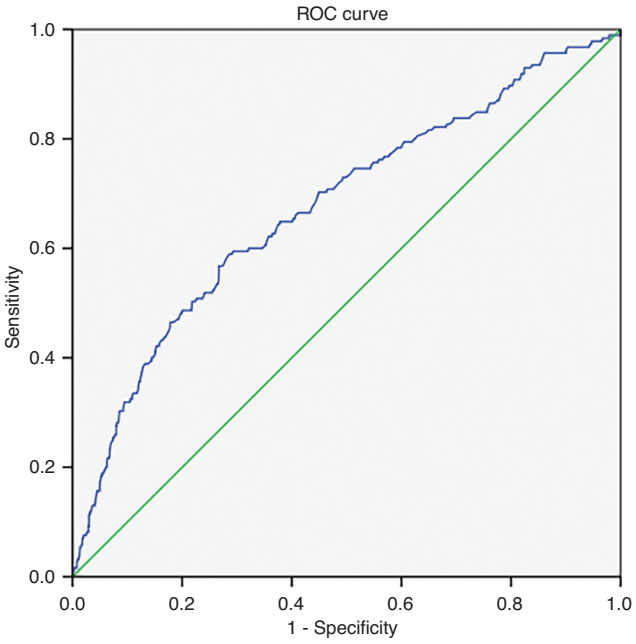

Figure 1 ROC Curve Analysis.
The AUC was 0.676 (95% CI 0.631–0.720, P<0.001), the sensitivity was 0.589, and the specificity was 0.714. AUC: area under the curve; ROC: receiver operator characteristic.

Table 1 Baseline Characteristics of Patients.

	Overall (N = 1189)	Low N% group (n = 793)	High N% group (n = 396)	P-value
Demographic characteristics				
Age (years)	78 (76, 81)	78 (76, 80)	79 (77, 82)	0.007
Male sex (%)	724 (60.9)	466 (58.8)	258 (65.2)	0.033
Lifestyle				
Smoking, yes (%)	423 (35.6)	268 (33.8)	155 (39.1)	0.070
Anthropometrics				
BMI (kg/m^2)	23.0 (20.8, 25.1)	23.1 (20.8, 25.3)	22.3 (20.1, 24.5)	0.004
HR (beats/min)	74 (66, 84)	72 (64, 81)	79 (70, 90)	<0.001
SBP (mmHg)	135 (119, 152)	138 (121, 155)	136 (118, 158)	0.016
Medical history				
Hypertension, yes (%)	895 (75.3)	603 (76.0)	292 (73.7)	0.386
Dyslipidemia, yes (%)	286 (24.1)	190 (24.0)	96 (24.2)	0.914
T2DM, yes (%)	343 (28.8)	216 (27.2)	127 (32.1)	0.083
Chest pain, yes (%)	791 (66.5)	544 (68.6)	247 (62.4)	0.030
PCI, yes (%)	190 (16.0)	139 (17.6)	51 (12.9)	0.038
CABG, yes (%)	18 (1.5)	10 (1.3)	8 (2.0)	0.314
Biochemistry				
Hemoglobin (g/L)	119 (107, 130)	121 (109, 131)	116 (101, 128)	<0.001
WBC (10^9/L)	6.3 (5.2, 7.9)	5.9 (4.9, 7.0)	7.9 (6.2, 9.9)	<0.001
Platelets (10^9/L)	177 (143, 217)	174 (140, 211)	181 (141, 215)	0.520
Albumin (g/L)	35.4 (32.8, 38.1)	35.8 (33.4, 38.3)	34.52 (31.4, 37.1)	<0.001
ALT (U/L)	18.2 (12.4, 29.3)	17.4 (12.2, 26.5)	22.2 (12.8, 40.5)	<0.001
Creatinine (μmoI/L)	89.7 (71.0, 118.0)	87.1 (69.2, 113.4)	97.7 (73.4, 134.5)	<0.001
NT-proBNP (pg/mL)	1020.0 (322.5, 2885.9)	670.3 (237.6, 1713.0)	2373.0 (834.1, 5640.5)	<0.001
CK-MB (IU/L)	14.2 (10.4, 21.4)	13.0 (10.1, 17.7)	17.0 (12.3, 31.7)	<0.001
TC (mmol/L)	3.8 (3.2, 4.5)	3.8 (3.2, 4.4)	3.8 (3.2, 4.5)	0.315
TG (mmol/L)	1.2 (0.9, 1.7)	1.3 (0.9, 1.8)	1.1 (0.8, 1.6)	<0.001
LDL-c (mmol/L)	2.2 (1.7, 2.8)	2.1 (1.6, 2.8)	2.2 (187, 2.8)	0.106
HDL-c (mmol/L)	1.0 (0.9, 1.2)	1.0 (0.9, 1.2)	1.0 (0.9, 1.2)	0.697
Ultrasound data				
LVEF <50%, yes (%)	256 (21.5)	143 (18.0)	113 (28.5)	<0.001
Hospital course				
Aspirin, yes (%)	1016 (85.4)	676 (85.2)	340 (86.3)	0.628
Clopidogrel, yes (%)	1040 (87.5)	685 (86.7)	355 (89.6)	0.146
Beta blocker, yes (%)	821 (69.0)	555 (70.0)	266 (67.2)	0.322
Statin, yes (%)	1152 (96.9)	766 (96.8)	386 (97.7)	0.391
PPI, yes (%)	948 (79.7)	606 (76.4)	342 (86.4)	<0.001
ACEI or ARB, yes (%)	767 (64.5)	505 (63.7)	262 (66.2)	0.400
Mechanical ventilation, yes (%)	30 (2.5)	12 (1.5)	18 (4.5)	0.002
IABP, yes (%)	19 (1.6)	8 (1.0)	11 (2.8)	0.021
Hospital PCI, yes (%)	400 (33.6)	268 (33.8)	132 (33.5)	0.920
Severe heart failure*, yes (%)	594 (50.0)	398 (50.2)	196 (49.5)	0.821
Angiographic data				
Left main, yes (%)	92 (7.7)	69 (10.8)	23 (6.9)	0.052
Three-vessel disease, yes (%)	273 (23.0)	182 (27.4)	91 (26.5)	0.766

Table 1 (continued)

	Overall (N = 1189)	Low N% group (n = 793)	High N% group (n = 396)	P-value
Types of ACS				
STEMI, yes (%)	253 (21.3)	113 (14.2)	140 (35.4)	<0.001
NSTE-ACS, yes (%)	936 (78.7)	680 (85.8)	256 (64.6)	<0.001
Hospital MACE	185 (15.6)	76 (9.6)	109 (27.5)	<0.001
Acute left heart failure, yes (%)	179 (15.1)	75 (9.5)	104 (26.3)	<0.001
Stroke, yes (%)	9 (0.8)	4 (0.5)	5 (1.3)	0.155
Any cause of death, yes (%)	13 (1.1)	2 (0.3)	11 (2.8)	<0.001

*Severe heart failure: heart failure with class 3–4 according to Killip or New York Heart Association classification [17].
N%: percentage of neutrophils; BMI: body mass index; HR: heart rate; SBP: systolic blood pressure; T2DM: type 2 diabetes mellitus; PCI: percutaneous coronary intervention; CABG: coronary artery bypass grafting; WBC: white blood cell; ALT: alanine aminotransferase; NT-proBNP: N-terminal-pro brain natriuretic peptide; CK-MB: creatine kinase-myocardial band; TC: total cholesterol; TG: triglycerides; LDL-c: low density lipoprotein cholesterol; HDL-c: high density lipoprotein cholesterol; LVEF: left ventricular ejection fraction; PPI: proton pump inhibitor; ACEI: angiotensin-converting-enzyme inhibitor; ARB: angiotensin receptor blocker; IABP: intra-aortic balloon pump; STEMI: ST-segment elevation myocardial infarction; NSTE-ACS: non-ST-elevation acute coronary syndrome; MACE: major adverse cardiovascular events.

with LVEF <50% (28.5% vs. 18.0%, P<0.001), PPI treatment (86.4% vs. 76.4%, P<0.001), mechanical ventilation (4.5% vs. 1.5%, P=0.002) IABP (2.8% vs. 1.0%, P=0.021) and STEMI (35.4% vs. 14.2%, P<0.001). Consistently, the incidence of in-hospital MACE was considerably higher in the high N% group than the low N% group (27.5% vs. 9.6%, P<0.001) (Table 1).

Associations Among Risk Factors and in-Hospital MACE

The risk factors for in-hospital MACE were investigated with univariate analysis of the demographic characteristics, lifestyle, anthropometrics, medical history, biochemistry and in-hospital management (Table 2). The following significant factors with P<0.05 in univariate analysis were adjusted for in multivariate logistic regression analysis: age, HR, SBP, WBC, albumin, ALT, creatinine, NT-proBNP, CK-MB, HDL-c, LVEF <50%, clopidogrel, PPI, mechanical ventilation, IABP, severe heart failure and STEMI. High N% was an independent risk factor for in-hospital MACE (OR 1.779, 95% CI 1.091–2.901, P=0.021). Age (OR 1.087, 95% CI 1.025–1.153, P=0.005), WBC (OR 1.112, 95% CI 1.027–1.205, P=0.009), NT-proBNP (OR 1.000, 95% CI 1.000–1.000, P<0.001), LVEF <50% (OR 1.770, 95% CI 1.103–2.840, P=0.018), mechanical ventilation (OR 6.655, 95% CI 2.280–19.425, P<0.001) and severe heart failure (OR 2.032, 95% CI 1.252–3.299, P=0.004) were also independent risk factors for in-hospital MACE (Table 3).

Discussion

The study examined the effects of N% at admission on in-hospital MACE in patients older than 75 years with ACS. Older patients with high N% had a greater incidence of in-hospital MACE than those with low N%, and N% ≥74.17% was an independent risk factor for in-hospital MACE in older patients with ACS. In addition, age, WBC, NT-proBNP, LVEF <50%, mechanical ventilation and severe heart failure were also found to be independent risk factors for in-hospital MACE in patients with ACS.

Risk stratification in patients with ACS is usually based on clinical manifestations including age, SBP, Killip class, ST deviation or elevation, and traditional biomarkers including creatinine and NT-proBNP [18, 19]. After adjustment, SBP and creatinine were no longer risk factors for in-hospital MACE in older patients with ACS. However, age, WBC, NT-proBNP, LVEF <50% and severe heart failure remained prognostic factors for in-hospital MACE in older patients with ACS, in agreement with findings from previous studies [20, 21].

Table 2 Univariable Analyses of Factors Associated with in-Hospital MACE.

	No in-hospital MACE (n = 1004)	With in-hospital MACE (n = 185)	OR	95% CI	P-value
Demographic characteristics					
Age (years)	78 (76, 81)	80 (77, 84)	1.113	1.068–1.160	<0.001
Male sex (%)	609 (60.7)	115 (62.2)	1.066	0.771–1.472	0.700
Lifestyle					
Smoking, yes (%)	361 (36.0)	62 (33.5)	0.898	0.645–1.251	0.524
Anthropometrics					
BMI (kg/m^2)	23.0 (20.8, 25.1)	22.0 (20.3, 25.5)	0.977	0.916–1.042	0.474
HR (beats/min)	73 (65, 82)	82 (72, 92)	1.037	1.027–1.048	<0.001
SBP (mmHg)	139 (121, 156)	124 (114, 146)	0.990	0.983–0.997	0.007
Medical history					
Hypertension, yes (%)	758 (75.5)	137 (74.1)	0.926	0.647–1.326	0.676
Dyslipidemia, yes (%)	245 (24.4)	41 (22.2)	0.882	0.606–1.284	0.513
T2DM, yes (%)	288 (28.7)	55 (29.7)	1.052	0.746–1.483	0.773
Chest pain, yes (%)	668 (66.5)	123 (66.5)	0.995	0.714–1.387	0.976
PCI, yes (%)	168 (16.7)	22 (11.9)	0.671	0.417–1.079	0.099
Biochemistry					
Hemoglobin (g/L)	120 (109, 131)	118 (103, 130)	0.994	0.986–1.002	0.141
Low N%	717 (71.4)	76 (41.1)	0.279	0.202–0.386	<0.001
High N%	287 (28.6)	109 (58.9)	3.583	2.593–4.951	<0.001
WBC (10^9/L)	6.1 (5.0, 7.5)	7.2 (6.0, 9.6)	1.232	1.166–1.301	<0.001
Platelets (10^9/L)	175 (143, 211)	164 (136, 230)	0.999	0.996–1.001	0.349
Albumin (g/L)	35.6 (33.0, 38.3)	34.2 (31.1, 37.1)	0.900	0.865–0.936	<0.001
ALT (U/L)	17.2 (11.7, 26.7)	23.0 (13.0, 48.4)	1.005	1.002–1.008	0.002
Creatinine (μmoI/L)	86.8 (68.1, 112.9)	101.0 (70.9, 148.8)	1.005	1.003–1.006	<0.001
NT-proBNP (pg/mL)	815.8 (312.0, 2015.5)	5029.2 (2336.4, 8765.9)	1.000	1.000–1.000	<0.001
CK-MB (IU/L)	13.4 (10.3, 19.1)	16.7 (11.3, 29.7)	1.002	1.001–1.004	0.004
TC (mmol/L)	3.7 (3.2, 4.4)	3.7 (3.1, 4.4)	0.959	0.812–1.131	0.616
TG (mmol/L)	1.2 (0.9, 1.7)	1.2 (0.8, 1.8)	0.816	0.661–1.007	0.058
LDL-c (mmol/L)	2.2 (1.7, 2.8)	2.1 (1.6, 2.7)	0.964	0.791–1.174	0.714
HDL-c (mmol/L)	1.0 (0.9, 1.2)	1.0 (0.8, 1.2)	0.507	0.281–0.913	0.024
Ultrasound data					
LVEF <50%, yes (%)	172 (17.1)	84 (45.4)	4.023	2.884–5.611	<0.001
Hospital course					
Aspirin, yes (%)	858 (85.5)	158 (85.9)	1.027	0.654–1.612	0.908
Clopidogrel, yes (%)	868 (86.7)	172 (93.0)	2.027	0.121–3.667	0.019
Beta blocker, yes (%)	701 (69.8)	120 (64.9)	0.798	0.573–1.111	0.181
Statin, yes (%)	971 (97.0)	181 (97.8)	1.398	0.487–4.016	0.534
PPI, yes (%)	784 (78.1)	164 (88.6)	2.191	1.358–3.535	0.001
ACEI or ARB, yes (%)	643 (64.0)	124 (67.0)	1.141	0.818–1.591	0.436
Mechanical ventilation, yes (%)	8 (0.8)	22 (12.0)	16.907	7.402–38.621	<0.001
IABP, yes (%)	7 (0.7)	12 (6.6)	9.985	3.876–25.719	<0.001
Hospital PCI, yes (%)	348 (34.7)	52 (28.3)	0.741	0.524–1.048	0.090
Severe heart failure*, yes (%)	472 (47.0)	122 (65.9)	2.183	1.572–3.031	<0.001

Table 2 (continued)

	No in-hospital MACE (n = 1004)	With in-hospital MACE (n = 185)	OR	95% CI	P-value
Angiographic data					
Left main, yes (%)	79 (9.7)	13 (8.4)	0.862	0.467–1.593	0.637
Three-vessel disease, yes (%)	238 (28.0)	35 (22.4)	0.745	0497–1.117	0.154
Types of ACS					
STEMI, yes (%)	179 (17.8)	74 (40.0)	3.073	2.197–4.298	<0.001
NSTE-ACS, yes (%)	825 (82.2)	111 (60.0)	0.325	0.233–0.455	<0.001

*Severe heart failure: heart failure with class 3–4 according to Killip or New York Heart Association classification.
MACE: major adverse cardiovascular events; OR: odds ratios; 95% CI: 95% confidence intervals; BMI: body mass index; HR: heart rate; SBP: systolic blood pressure; T2DM: type 2 diabetes mellitus; PCI: percutaneous coronary intervention; CABG: coronary artery bypass grafting; WBC: white blood cell; ALT: alanine aminotransferase; NT-proBNP: N-terminal-pro brain natriuretic peptide; CK-MB: creatine kinase-myocardial band; TC: total cholesterol; TG: triglycerides; LDL-c: low density lipoprotein cholesterol; HDL-c: high density lipoprotein cholesterol; LVEF: left ventricular ejection fraction; PPI: proton pump inhibitor; ACEI: angiotensin-converting-enzyme inhibitor; ARB: angiotensin receptor blocker; IABP: intra-aortic balloon pump; STEMI: ST-segment elevation myocardial infarction; NSTE-ACS: non-ST-elevation acute coronary syndrome; N%: percentage of neutrophils.

Table 3 Multivariable Analyses of the Factors Associated with in-Hospital MACE.

	OR	95% CI	P-value
Age	1.087	1.025–1.153	0.005
HR	1.014	1.000–1.029	0.057
SBP	0.993	0.984–1.003	0.181
WBC	1.112	1.027–1.205	0.009
Albumin	1.037	0.981–1.097	0.200
ALT	0.999	0.996–1.001	0.273
Creatinine	1.001	0.999–1.003	0.434
NT-proBNP	1.000	1.000–1.000	<0.001
CK-MB	1.000	0.998–1.002	0.960
HDL-c	0.523	0.247–1.106	0.090
LVEF <50%	1.770	1.103–2.840	0.018
Clopidogrel	1.850	0.850–4.028	0.121
PPI	1.226	0.631–2.384	0.548
Mechanical ventilation	6.655	2.280–19.425	<0.001
IABP	2.005	0.508–7.913	0.321
Severe heart failure*	2.032	1.252–3.299	0.004
STEMI	1.751	1.042–2.942	0.034
High N%	1.779	1.091–2.901	0.021

*Severe heart failure: heart failure with class 3–4 according to Killip or New York Heart Association classification.
OR: odds ratio; 95% CI: 95% confidence interval; HR: heart rate; SBP: systolic blood pressure; WBC: white blood cell; ALT: alanine aminotransferase; NT-proBNP: N-terminal-pro brain natriuretic peptide; CK-MB: creatine kinase-myocardial band; HDL-c: high density lipoprotein cholesterol; LVEF: left ventricular ejection fraction; PPI: proton pump inhibitor; IABP: intra-aortic balloon pump; STEMI: ST-segment elevation myocardial infarction; N%: percentage of neutrophils.

Numerous studies have explored the association of WBC and outcomes of CHD. Friedman et al. first reported that upregulated WBC increases the risk of AMI [22]. Subsequently, associations of WBC and its subtypes with adverse cardiovascular events in ACS were observed [12, 23, 24]. For example, a high neutrophil lymphocyte ratio has been found to predict the angiographic severity of ACS, as evaluated by the SYNTAX score [25]. Studies have revealed that the activity of WBC in AMI is attributable primarily to neutrophils, which participate in all aspects of AMI, including plaque rupture, reperfusion injury and myocardium remodeling [12]. High N% values at admission have been found to be an independent predictor of long-term mortality in patients with STEMI who underwent primary PCI [26]. However, the half-life of neutrophils, the main inflammatory cells, has been estimated to be only 6–12 hours in the circulation [27]; thus neutrophils with a short half-life do not have value in predicting long-term adverse events in CHD. Therefore, our study was aimed at clarifying the association between N% and MACE in patients with ACS during hospitalization. A high N% was an independent risk factor for in-hospital MACE in older patients with ACS after adjustment for possible factors, thereby providing evidence-based support for the treatment of patients over 75 years of age with ACS.

However, the study has several limitations. First, the clinical data were retrospectively collected from

a single center in Chinese Han populations. Further validation remains to be conducted in multicenter and multiracial populations. Second, owing to the limited samples, a strict standard to select potential variables for multivariate logistic analysis was set, i.e., $P<0.05$; therefore, some effective predictive factors might have been missed.

Conclusion

In conclusion, older patients with ACS with high N% face elevated risk of in-hospital MACE. Further large-scale studies are needed to clarify this relationship.

Data Availability

The data in the study are available from the corresponding author upon reasonable request.

Ethics Statement

This study was approved and conducted by the Ethics Committee of the Second Xiangya Hospital of Central South University. All patients provided written informed consent.

Author's Contributions

Dr. Zhu contributed to the design of the study. Dr. Tian was responsible for the conception, data collection, statistical analysis and first draft of this manuscript. Drs. Xie, Wei, Fang, Hu and Zhou reviewed the manuscript. The final manuscript was approved by all authors.

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Not available.

Conflicts of Interest

The authors have no conflicts of interest to disclose.

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