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# Evaluation of the Prognostic Role of the Wall Motion Score Index and the SYNTAX Score II in Patients with Acute Coronary Syndrome Following Percutaneous Coronary Intervention by Evaluation of Major Adverse Cardiovascular Events at 12-Month Follow-Up

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Data Collection B  
Statistical Analysis C  
Data Interpretation D  
Manuscript Preparation E  
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**Background:** This study aimed to evaluate the wall motion score (WMS) index and the SYNTAX score II (SSII) in patients with acute coronary syndrome (ACS) following percutaneous coronary intervention (PCI) by evaluation of major adverse cardiovascular events (MACEs) at the 12-month follow-up at a single center.


**Material/Methods:** An observational study of 430 patients with ACS undergoing PCI at the Second Affiliated Hospital of Soochow University over a 1-year period was performed. Baseline data including WMS and SSII were recorded and compared with the rates of MACEs in the study group. WMS and SSII were stratified by the tercile from low to high.

**Results:** Both WMS and SSII were associated with the rates of MACEs ( $P < 0.001$  and  $P = 0.003$ , respectively). The incidence of MACEs was positively correlated with terciles of the WMS and SSII groups (3.7% vs 1.6% vs 7.0% [ $P < 0.001$ ] and 2.6% vs 5.8% vs 11.6% [ $P < 0.001$ ], lowest to highest, respectively). Logistic regression analyses identified combined predictors for 12-month outcome, including WMS and SSII. The use of a model combining both scores yielded a higher predictive value (area under the curve [AUC]=0.78; 95% confidence interval [CI], 0.733-0.835;  $P < 0.001$ ) than the use of either score alone. Using WMSs alone, the AUC was 0.73 (95% CI, 0.660-0.793;  $P < 0.001$ ). Using SSII alone, the AUC was 0.71 (95% CI, 0.649-0.769;  $P < 0.001$ ).

**Conclusions:** This study showed that the combined methods of the WMS index and the SSII were predictive factors of MACEs in patients with ACS following PCI at the 12-month follow-up.

**Keywords:** **Acute Coronary Syndrome • Coronary Angiography • Echocardiography**

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## Background

A variety of risk factors, including age, tobacco use, hypertension, diabetes mellitus, and dyslipidemia, contribute to increased rates of major adverse cardiovascular events (MACEs) in patients undergoing coronary revascularization. The use of the SYNTAX score, which is based upon angiographic findings, has been helpful in determining the risks and outcomes associated with percutaneous coronary intervention (PCI) and coronary artery surgery. This score has been further refined. The SYNTAX study documented the efficacy of using the SYNTAX score II (SSII) in determining the risk for cardiac death at 10 years and MACEs [1,2]. Similarly, wall motion scores (WMSs) have been useful in the assessment of MACEs in patients undergoing revascularization [3,4]. The degree of impairment of left ventricular function has also been correlated with adverse cardiovascular outcomes, and recent studies have assessed the role of the WMS in predicting MACEs in patients undergoing PCI. The use of a tool combining WMS and SSII has not been well studied, and it remains uncertain whether a combined score would be useful in predicting clinical outcomes in patients undergoing PCI.

Based on the recommendation of the American Society of Echocardiography, the WMS is calculated using a 17-segment model, in which the left ventricle is divided into specific segments to detect myocardial systolic function. The contractility of each segment is scored as follows: 1, normal; 2, hypokinesia; 3, akinesia; 4, dyskinesia; and 5, ventricular aneurysm. All variables are analyzed by 2 independent experienced cardiologists [5,6].

SSII is based on the SYNTAX score (SS) with the addition of age, sex, left ventricular ejection fraction (LVEF), estimated glomerular filtration rate, peripheral arterial disease, chronic obstructive pulmonary disease, and left main coronary artery disease. The online version (<http://www.syntaxscore.org/>) was used for calculation. Given that previous studies found that SSII was superior to SS in predicting clinical outcomes in patients with complex coronary artery disease (CAD), it was necessary to incorporate other parameters into the SSII model to evaluate the prognostic role and stratify the risk of acute coronary syndrome (ACS) patients with MACEs [7-9].

## Material and Methods

### Study Design and Participants

This single-center observational cohort study was included all patients undergoing PCI for ACS at the Second Affiliated Hospital of Soochow University between January 1, 2018, and December 31, 2018. After strict screening by 2 independent

experts, a total of 550 eligible patients with an ACS diagnosis were retrospectively enrolled. A total of 430 consecutive patients were ultimately enrolled and completed the follow-up (with 12 patients lost to follow-up). Patients were excluded from study if they had a diagnosis of myocarditis, any type of cardiomyopathy (dilated cardiomyopathy, hypertrophic cardiomyopathy, and restrictive cardiomyopathy), congenital heart disease, pericardial disease, or valvulopathy (hemodynamically significant aortic or mitral valve disease); a cardiac pacemaker; severe infection; or a malignant tumor. The study was approved by the Institutional Review Board of the Second Affiliated Hospital of Soochow University, and all participants provided written informed consent.

### Data Acquisition

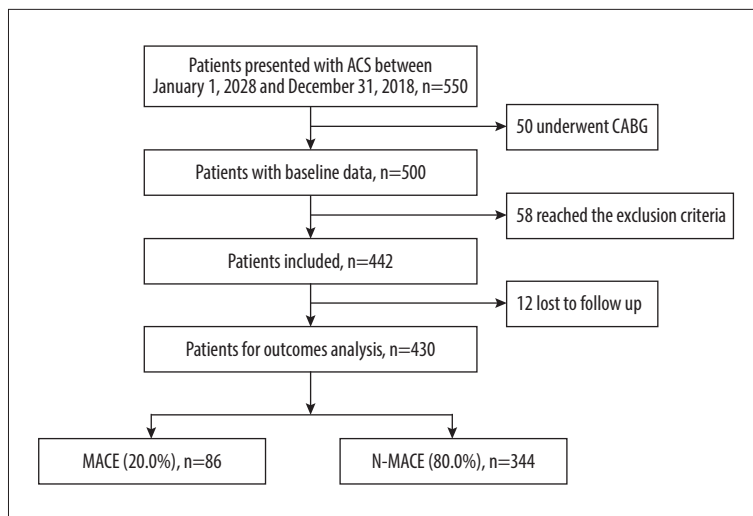
Clinical characteristics were retrospectively collected from the medical database of the Second Affiliated Hospital of Soochow University. Coronary angiography and echocardiography were independently assessed in the Emergency Department or after admission by 2 specialists who were blinded to the study. Subsequently, WMS and SSII were respectively measured based on the clinical data.

All patients admitted to our hospital with angina and elevated cardiac biomarkers or with clinical findings of ongoing cardiac ischemia and over 70% stenosis by coronary angiography are recommended to undergo coronary revascularization. Patients who experience the onset of angina within 12 h of presentation or who demonstrate hemodynamic instability are recommended for emergency PCI. According to the current guidelines, dual antiplatelet therapy with aspirin and P2Y<sub>12</sub> receptor inhibitor are recommended after PCI for all patients for at least 12 months.

### WMS and SSII Calculation

WMS is measured according to the 17-segment model described above. Each segment is graded by contractility on a 1- to 5-point scale, and the WMS is based on the sum of all segments.

The SS is measured according to the online SS calculator by a trained cardiologist blinded to the study. The SS calculator includes 12 main questions: (1) dominance; (2) number of lesions; (3) segments involved per lesion; (4) total occlusion; (5) trifurcation; (6) bifurcation; (7) aorto-ostial lesion; (8) severe tortuosity; (9) length (>20 mm); (10) heavy calcification; (11) thrombus; and (12) diffuse disease/small vessels. The SS is based on the sum of these points, and the other 6 variables as clarified above are subsequently collected for the calculation of SSII.



**Figure 1.** Flow chart of the study population.

ACS – acute coronary syndrome; CABG – coronary artery bypass grafting; MACE – major adverse cardiovascular events; N-MACE – no major adverse cardiovascular events.

Since SSII reflects the complexity of a patient's coronary heart disease and WMS indicates the myocardial contractility, all variables that worsen ACS and lead to poor outcomes can cause high WMS and SSII.

### Follow-Up and Clinical Endpoint

For assessment of clinical outcomes over time, all subjects were followed up by scheduled outpatient visits, rehospitalization, and telephone contact to track disease development. The endpoint of the study was a MACE, including recurrent myocardial ischemia, myocardial infarction, malignant arrhythmia (sustained ventricular tachycardia, ventricular fibrillation, advanced atrioventricular block), or heart failure, and all-cause mortality.

### Statistical Analysis

Continuous variables were expressed as mean±standard deviation (SD) and compared using 2-tailed *t* test. Categorical variables are expressed as frequency (percentage) and were compared using the chi-square or Fisher's exact test. Multivariate regression analysis was used to identify the independent predictors of clinical outcome. To analyze the relationship between specific MACEs and the predictors by stratification, we divided WMS and SSII into 3 groups by tercile, and all subjects developing a MACE fell into 1 of 3 groups according to the score from low to high. The chi-square test was applied to assess the intergroup differences. For the prediction models, we used the receiver-operating characteristic (ROC) curves to evaluate the prognostic value of WMS and SSII, separately and jointly. Nomogram was added to assess the survival probability of the combined predictors objectively. Statistical analysis was conducted using SPSS (version 20.0), GraphPad Prism (8.0), and R (version 4.0). All statistics tests were 2-tailed, and  $P<0.05$  was considered to indicate statistical significance.

## Results

### Study Population and Baseline Characteristics

The study flowchart is shown in **Figure 1**. From January 1, 2018, to December 31, 2018, we identified 430 patients who met inclusion criteria, of whom were divided into MACE and no MACE (N-MACE) groups. The patients developing MACEs were then divided into categories based on terciles for the WMS and SSII, from low to high.

The study's demographic and baseline clinical characteristics are shown in **Table 1**. Overall, the mean age was  $63.40\pm 12.45$  years, and 81.6% of the participants were men. Risk factors for ACS were assessed, and we found that 61.4% of the participants were tobacco smokers, 64.4% had a history of hypertension, and 27.0% had diabetes.

Among patients with a documented MACE in 1 year of follow-up, patients were documented to have lower LVEF and/or estimated glomerular filtration rate and higher B-type natriuretic peptide and cardiac troponin T. Patients experiencing a MACE tended to have a higher prevalence of smoking, hypertension, and diabetes. Those patients sustaining a MACE in follow-up who presented with an acute myocardial infarction were graded with a higher Killip class. Results of coronary angiography in patients with a MACE demonstrated a higher prevalence of left anterior descending branch and left main coronary artery (64.0% vs 48.3%,  $P=0.009$ , 11.7% vs 2.9%,  $P=0.001$ ). Interestingly, the number of diseased vessels was not statistically significant. The mean WMS and SSII were  $21.04\pm 4.86$  and  $46.64\pm 7.02$ . The MACE group presented with higher WMS and SSII ( $24.76\pm 7.46$  vs  $20.11\pm 3.38$ ,  $P<0.001$ ,  $50.43\pm 6.69$  vs  $45.69\pm 6.78$ ,  $P<0.001$ ) As is shown in **Table 2**.

**Table 1.** Baseline patient characteristics.

Variables	All (N=430)
Age (years)	63.40±12.45
Sex (Male), n (%)	351 (81.6)
Risk factors	
Tobacco use, n (%)	264 (61.4)
Hypertension, n (%)	277 (64.4)
Family history, n (%)	30 (7.0)
Dyslipidemia, n (%)	286 (89.8)
Diabetes, n (%)	116 (27.0)
Blood text index	
cTnT (pg/ml)	2969.1±3320.0
BNP (pg/ml)	1542.6±2886.2
Creatnine (µmol/l)	73.96±32.98
eGFR (ml/min/1.73 m <sup>2</sup> )	97.08±34.25
Echocardiography	
LAD (mm)	44.69±9.86
LVDs (mm)	31.30±8.35
LVDd (mm)	47.56±7.36
LVEF (%)	58.67±11.83
Pulmonary artery pressure(mmHg)	30.35±8.67
Heart rate (bpm)	79.54±16.31
Systolic pressure (mmHg)	130.92±23.35

Variables	All (N=430)
Angiographic data	
LAD lesion, n (%)	221 (51.4)
LCX lesion, n (%)	81 (18.8)
RCA lesion, n (%)	173 (40.2)
LM lesion, n (%)	20 (4.7)
Single-vessel disease, n (%)	106 (24.7)
Two-vessel disease, n (%)	135 (31.4)
Multivessel disease, n (%)	189 (44.0)
Reperfusion therapy	
Emergency PCI, n (%)	193 (44.9)
Selective PCI, n (%)	237 (55.1)
Balloon dilatation, n (%)	35 (8.1)
PTCA, n (%)	53 (12.3)
Bare stents, n (%)	40 (9.3)
Drug-eluting stents, n (%)	362 (84.2)
SYNTAX score II	46.64±7.02
Wall motion score	21.04±4.86
MACE, n (%)	86 (20.0)
Recurrent angina	53 (12.3)
Acute myocardial infarction	11 (2.6)
Malignant arrhythmia	19 (4.4)
Heart failure	14 (3.3)
Cardiac death	3 (0.7)

BNP – brain natriuretic peptide; cTnT – troponin T; eGFR – effective glomerular filtration rate; LAD – left atrial diameter; LVDs – left ventricular end systolic diameter; LVDd – left ventricular end diastolic diameter; LVEF – left ventricular ejection fraction; LAD – left anterior descending coronary artery; LCX – left circumflex coronary artery; RCA – right coronary artery; LM – left main coronary artery; PCI – percutaneous coronary intervention; PTCA – percutaneous transluminal coronary angioplasty; MACE – major adverse cardiovascular events.

**Patients with a MACE in Tercile with WMS and SSII**

Eighty-six patients were documented to have a MACE in follow-up; 12.3% presented with recurrent angina, 2.6% with acute myocardial infarction, 4.4% with malignant arrhythmia, 3.3% with heart failure, and 0.7% with cardiac death. The difference among the groups with stratified WMS and SSII are shown in **Figure 2**. In general, MACEs were more prevalent in the elevated WMS (4.9% vs 2.6% vs 12.5%, *P*<0.001) and SSII groups (2.6% vs 5.8% vs 11.6%, *P*<0.001) as defined by terciles. For the WMS group, patients with a MACE were stratified according to tercile, with a low group (≤19), a moderate group (20-21), and a high group (≥22). No significant difference was found in the high WMS group except for recurrent angina (3.7% vs 1.6% vs 7.0%, *P*<0.001) and cardiac death (0.0% vs 0.0% vs 0.7%, *P*=0.031). In the SSII group (low, ≤42.9;

moderate, 43.0-48.7; high, ≥48.8), recurrent angina, (3.3% vs 3.0% vs 6.0%, *P*=0.033), malignant arrhythmia (0.0% vs 1.4% vs 3.0%, *P*=0.001), and heart failure (0.0% vs 1.4% vs 1.8%, *P*=0.021) showed significant differences.

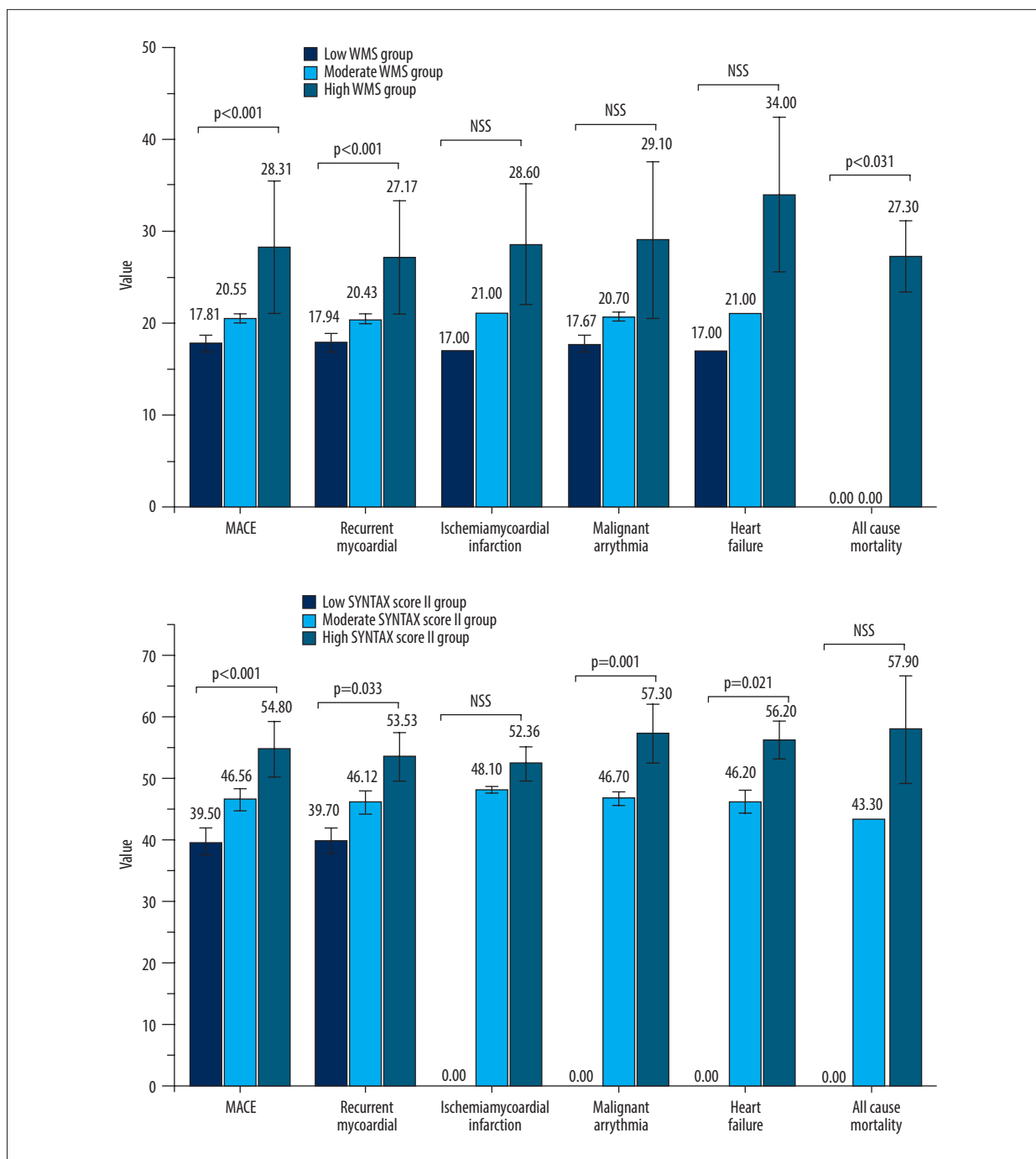
**Multivariate Cox Regression Analysis**

The results of the Cox proportional hazard regression analysis are presented in **Table 3**. First, we included all related variables from the univariate analysis with a widened probability range. Then, added with sudden cardiac arrest, both WMS and SSII were identified to be powerful independent predictors for the occurrence of a MACE in ACS (WMS, hazard ratio [HR]: 1.056, 95% confidence interval [CI]: 1.019-1.094, *P*=0.003; SSII, HR: 1.058, 95% CI: 1.028-1.089, *P*<0.001).

**Table 2.** Comparison of clinical characteristics between different groups.

Variables	MACE (n=86)	N-MACE (n=344)	P value
SYNTAX score II	50.43±6.69	45.69±6.78	<0.001
WMS	24.76±7.46	20.11±3.38	<0.001
LVEF (%)	52.18±11.88	60.30±11.26	<0.001
Age (years)	67.22±11.10	62.45±12.61	0.001
Sex			0.191
Male [n (%)]	66 (76.7)	285 (82.8)	
Female [n (%)]	20 (23.3)	59 (17.2)	
Creatinine (µmol/l)	83.64±65.59	71.54±16.28	0.090
eGFR (ml/min/1.73 m <sup>2</sup> )	87.21±40.99	99.55±31.94	0.003
BNP (pg/ml)	2594.24±3056.70	1279.65±2785.50	<0.001
cTnT (pg/ml)	3462.97±3550.74	2845.57±3253.41	0.150
Tobacco use			0.488
Yes [n (%)]	50 (58.1)	214 (62.2)	
No [n (%)]	36 (41.9)	130 (37.8)	
Hypertension			0.365
Yes [n (%)]	59 (68.6)	218 (63.4)	
No [n (%)]	27 (31.4)	126 (36.6)	
Diabetes			0.910
Yes [n (%)]	24 (27.9)	94 (27.3)	
No [n (%)]	62 (72.1)	250 (72.7)	
Cardiac arrest			<0.001
Yes [n (%)]	15 (17.4)	3 (0.9)	
No [n (%)]	71 (82.6)	341 (99.1)	
LAD			0.009
Yes [n (%)]	55 (64.0)	166 (48.3)	
No [n (%)]	31 (36.0)	178 (51.7)	
LCX			0.579
Yes [n (%)]	18 (20.9)	63 (18.3)	
No [n (%)]	68 (79.1)	281 (81.7)	
LM			0.001
Yes [n (%)]	10 (11.7)	10 (2.9)	
No [n (%)]	76 (88.3)	334 (97.1)	
PTCA			0.340
Yes [n (%)]	8 (9.3)	45 (13.1)	
No [n (%)]	78 (90.7)	299 (86.9)	
Extent of disease			0.651
Single-vessel disease [n (%)]	25 (29.1)	81 (23.5)	
Multivessel disease [n (%)]	61 (70.9)	263 (76.5)	

BNP – brain natriuretic peptide; cTnT – troponin T; eGFR – effective glomerular filtration rate; LVEF – left ventricular ejection fraction; LAD – left anterior descending coronary artery; LCX – left circumflex coronary artery; RCA – right coronary artery; LM – left main coronary artery; PTCA – percutaneous transluminal coronary angioplasty.

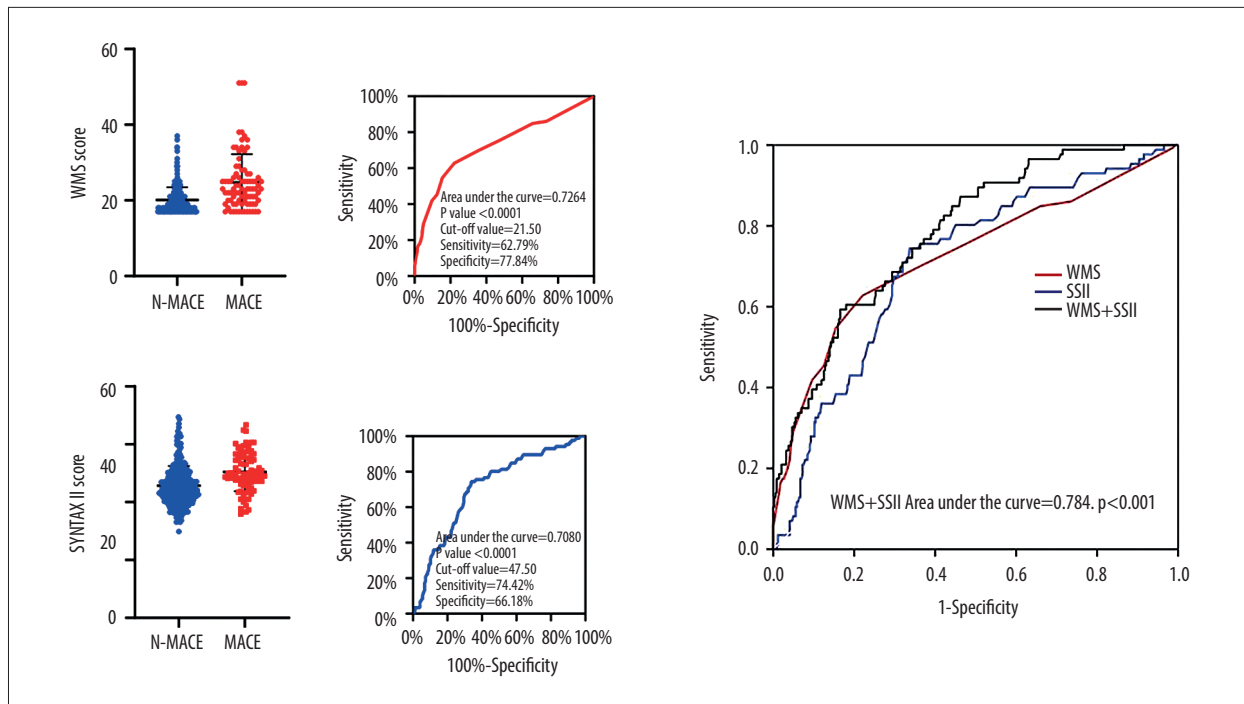


**Figure 2.** Comparison of major adverse cardiovascular events among the 3 wall motion score (WMS) and SYNTAX score II (SSII) groups. NSS – no statistic significance; MACE – major adverse cardiovascular events.

**Table 3.** Multivariate Cox regression analysis.

Variables	B value	HR	95% CI	p Value
SYNTAX score II	0.054	1.056	1.019~1.094	0.003
WMS	0.057	1.058	1.028~1.089	<0.001
Sudden cardiac arrest	-2.072	0.126	0.071~0.224	<0.001





**Figure 3.** Receiver-operating characteristic curve (ROC) for wall motion score (WMS), SYNTAX score II (SSII), and the combined models in predicting long-term major adverse cardiovascular events (MACE). WMS – wall motion score; SSII –SYNTAX score II; MACE – major adverse cardiovascular events; N-MACE – no major adverse cardiovascular events.

### ROC Curve of WMS and SSII in predicting MACEs

As shown in **Figure 3**, the ROC analysis indicated that both WMS and SSII had a positive prognostic function for the outcomes of ACS after PCI (WMS, area under the curve [AUC]=0.73, 95% CI: 0.660-0.793,  $P < 0.001$ ; SSII, AUC=0.71, 95% CI: 0.649-0.769,  $P < 0.001$ ). Moreover, the combination of WMS and SSII increased the predictive value (AUC=0.78, 95% CI: 0.733-0.835,  $P < 0.001$ ). To predict the occurrence of MACEs, we identified a threshold value of 21.5 for the WMS and 47.5 for the SSII.

### Nomogram Analysis

Subsequently, the nomogram was constructed, as shown in **Figure 4**. The results demonstrated that both WMS and SSII were valuable factors to evaluate the prognosis in patients with ACS.

## Discussion

This study evaluated adverse outcomes in patients with ACS treated with PCI. First, abnormalities in WMS and SSII were associated with adverse outcomes in patients with ACS treated with PCI. Second, WMS and SSII assessments may be useful to stratify the MACE risk of patients with PCI and ACS. Third, while both WMS and SSII in patients with ACS who underwent PCI were associated with MACE risk in our patients, an

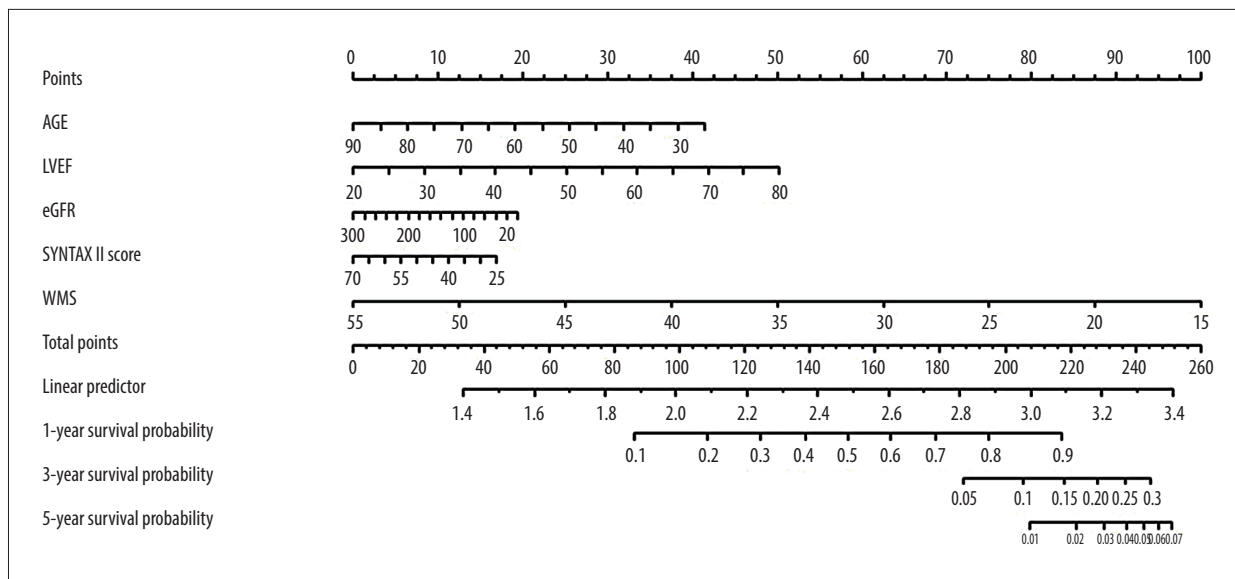
analysis based on both scores showed that their combination better reflected MACE risk at 1 year of follow-up.

The morbidity of MACEs from ACS was 20.0%, which accorded with previous results [10,11].

Given that clinical manifestation, physical examination, and serology testing are inadequate for a full assessment, cardiologists now pay more attention to estimating the severity of CAD through radiography and ultrasound technology. Thus, new scoring systems derived from angiography and echocardiography are desperately needed for comprehensive assessment of ACS [12-14].

The SS is now widely used in evaluating the severity of clinical CAD because of its strong predictive accuracy for complex CAD, especially for patients undergoing revascularization [15,16]. Nevertheless, studies showed that SSII had a stronger predictive effect for hospitalization and long-term mortality in hospitalized patients with both ST-segment elevation myocardial infarction and non-ST-segment elevation myocardial infarction than SS [7,17,18]. Other studies also elucidated that, the latter is more capable of evaluating complex CAD and even better than other risk-scoring systems including GRACE and TIMI scores [7,19], motivating us to further explore the role of SSII.

Our findings were in line with the previous literature. Specifically, the MACE group had a higher SSII compared with



**Figure 4.** Nomogram to predict the clinical outcomes in patients undergoing percutaneous coronary intervention (PCI).

the N-MACE group and there was a statistically significant difference in heart failure; however, recurrent angina with malignant arrhythmia was not the same as in previous studies [10,20]. We attributed this variation to individual differences and the treatment strategies of different research centers.

At present, WMS is the most used and validated index in echocardiography, and it provides an optimal alternative as an approach to quantifying systolic function after acute myocardial infarction [21]. Jurado-Román et al [22] reported that the analysis of wall motion segments, compared with LVEF, might be a more accurate marker in the prognostic stratification, especially with a smaller extent of myocardial damage.

WMS was also identified to be a prognostic marker in patients with ACS. Figueras et al [23] demonstrated that the severity of WMS was associated with ST-segment depression and increased worsening of WMS was associated with short-term mortality.

In terms of the prognostic value of WMS for ACS, our results are consistent with previous studies [24-27]. The unique point of our research was that we not only focused on the long-term mortality but also attached great importance to other adverse events, which improved the outcomes of ACS.

In summary, several studies have shown that WMS and SSII have a positive impact on the predictive value for CAD. However, the predictive ability of SSII for ACS patients was limited, and no one studied the combined effect of WMS and SSII on predicting the outcomes of ACS. We evaluated the predictive effect

of the combination of these scores and assessed survival probability of patients with ACS for the first time. We found the combination was stronger than either score alone in predicting development of a MACE in patients with ACS, and both scores could be used to predict the survival probability.

## Conclusions

The combined methods of the WMSI and the SSII were predictive factors of MACEs in patients with ACS following PCI at the 12-month follow-up.

## Limitations

Several limitations of the study need to be mentioned. First, this study had a retrospective design and was based on results in a single center from specific population. Therefore, our findings may lack predictive value in the prognosis of a broader population of patients with ACS. Second, selective bias in the nonrandomized study could affect the accuracy of our results. Lastly, the follow-up was not long enough, and the study population needs to be followed for a much longer period.

## Declaration of Figures Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.



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