

# A new prognostic evaluation of patients with acute ST-elevation myocardial infarction undergoing primary angioplasty: combined Zwolle and Syntax score

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## Abstract

**Background:** The Zwolle score (Zs) is a validated risk score used to identify low-risk patients with acute ST-elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (PCI). The Syntax score (Ss) is an angiographic score that evaluates the complexity of coronary artery disease.

**Aim:** We aimed to create a simple risk score by combining these two scores for risk stratification in patients with STEMI undergoing primary PCI.

**Methods:** 299 consecutive STEMI patients (mean age  $57.4 \pm 11.7$  years, 240 men) who underwent primary PCI were prospectively enrolled into the present study. The study population was divided into tertiles based on admission Zs and Ss. A high Zs ( $> 3$ ) and high Ss ( $> 24$ ) were defined as values in the third tertiles. A low Zs and low Ss were defined as values in the lower two tertiles. Patients were then classified into four groups: high Zs and high Ss (HZsHSs,  $n = 26$ ), high Zs and low Ss (HZsLSs,  $n = 29$ ), low Zs and high Ss (LZsHSs,  $n = 48$ ), and low Zs and low Ss (LZsLSs,  $n = 196$ ). In-hospital cardiac outcomes were then recorded.

**Results:** In-hospital cardiovascular mortality was higher in HZsHSs (50%) compared to the HZsLSs (27.5%), LZsHSs (0%), and LZsLSs (0.5%) groups. After adjustment for potentially confounding factors, HZsHSs (OR 77.6, 95% CI 6.69–113.1,  $p = 0.001$ ), and HZsLSs (OR 28.9, 95% CI 2.77–56.2,  $p = 0.005$ ) status, but not LZsHSs and LZsLSs status, remained independent predictors of in-hospital cardiovascular mortality.

**Conclusions:** STEMI patients with HZsHSs represent the highest risk population for in-hospital cardiovascular mortality.

**Key words:** Syntax score, Zwolle score, acute myocardial infarction

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## INTRODUCTION

Acute coronary syndrome (ACS) usually results from a ruptured coronary atherosclerotic lesion with a superimposed acute thrombosis that decreases coronary blood flow abruptly. ST-elevation myocardial infarction (STEMI) is one of the most dangerous forms of ACS. Despite the improvement of different therapeutic modalities, major adverse cardiac events (MACE) are still 8.7% [1]. Various risk scores have been introduced in STEMI over time [2–5], most of which were developed before

the primary percutaneous coronary revascularisation (PCI) era. The Syntax score (Ss) has been validated as an angiographic scoring system in stable coronary artery disease (CAD) [6]. Subsequently, it was studied in STEMI patients, and it was shown that the Ss yielded a similar prognostic value in STEMI [7–10]. The Zwolle score (Zs) is a scoring system that consists of clinical and angiographic variables, and it helped in the prognostic assessment of STEMI [3]. The present study was aimed to evolve a simple, practical, and sensitive risk score

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by including factors of clinical and angiographic relevance in STEMI patients undergoing primary PCI.

## METHODS

### *Patient population*

Our population was composed of a total of 299 consecutive patients with acute STEMI who were admitted to Bezmialem Vakif University Faculty of Medicine (Istanbul) and underwent urgent cardiac catheterisation. Patients were included in the study if they met the following criteria: (1) they presented within 12 h (18 h for cardiogenic shock) from the onset of symptoms (typical chest pain lasting for > 30 min); (2) there was ST-segment elevation of at least 1 mm in at least two contiguous electrocardiography (ECG) leads or new onset of complete left bundle-branch block; and (3) they had primary PCI (angioplasty and/or stent deployment). The patients in whom decisions for coronary artery bypass graft surgery (CABG) and medical treatment were made were excluded from the study. The study protocol was approved by the hospital's ethics committee.

### *Analysis of patient data*

Baseline clinical characteristics and blood biochemistry parameters that were studied at hospital admission were recorded. Blood biochemistry and complete blood count measurements were carried out using standard methods. The glomerular filtration rate was estimated by the simplified modification of diet in renal disease equation [11]. Thrombolysis In Myocardial Infarction (TIMI) risk score was calculated from medical history, angiographic and haemodynamic values. A transthoracic echocardiography was performed using a Philips HD11 XE (Philips Medical Systems, Andover, MA, USA) with a 2.5-MHz phased-array transducer. Recordings were taken with patients positioned in the left lateral decubitus position. The left ventricular ejection fraction (LVEF) was measured using modified Simpson's rule [12].

### *Coronary angiography, primary angioplasty and stenting*

All patients received 300-mg chewable aspirin and 600-mg loading dose of clopidogrel before coronary angiography. Emergency coronary angiography was performed by the percutaneous femoral approach. In all cases, a nonionic low-osmolality contrast media was used. The infarct-related artery was graded according to TIMI classification [13]. The grade of coronary collateral development was determined according to the Cohen-Rentrop method [14]. Heparin (100 U/kg) was administered when coronary anatomy was first assessed. The usage of tirofiban was left to the opinion of the operator.

### *Syntax and Zwolle score*

Syntax score was calculated for all coronary lesions with a diameter stenosis greater than 50% in vessels larger than

1.5 mm [6]. Angiographic variables relevant to Ss calculation were computed by two interventional cardiologists who did not know the patients' characteristics and clinical outcome, in the diagnostic angiogram phase. When disagreement existed, a third investigator was asked to interpret and a final decision was made by consensus. All lesions were scored before any intervention (prewiring). Total occlusion in infarct-related artery was scored as < 3-months' duration. In-stent restenosis was scored as de-novo lesions. All other parameters of Ss were applied as usual. Zwolle score was calculated from the risk factors such as Killip class (Killip 1, zero point; Killip 2, four points; Killip 3–4, nine points), post-TIMI flow grade (3, zero point; 2, one point; 1, two points), age ( $\geq 60$ , two points), three-vessel disease (one point), anterior myocardial infarction (MI) (one point) and ischaemic time > 4 h (one point) [3].

### *Definitions*

Contrast-induced nephropathy (CIN) was defined as a relative increase in baseline serum creatinine of greater than 25% and/or an absolute increase of 0.5 mg/dL within 72 h after contrast administration [15]. Advanced heart failure was defined as a New York Heart Association classification of at least 3. Cardiovascular mortality was defined as unexplained sudden death or death as a result of acute MI, heart failure or arrhythmia. Reinfarction was defined as an acute MI that occurs during the in-hospital period of an incident- or recurrent MI that was confirmed by elevation of serum troponin enzyme levels with the other evidence of myocardial necrosis (European Society of Cardiology definition). Target-vessel revascularisation was defined as either percutaneous or surgical revascularisation of the target vessel after the initial intervention. Hypertension was defined as resting systolic or diastolic blood pressure of at least 140/90 mm Hg or physician-diagnosed hypertension. Diabetes mellitus (DM) was defined as a previous diagnosis, use of diet or antidiabetic medicines, or a fasting venous blood glucose levels 126 mg/dL on two occasions. Hypercholesterolaemia was defined as total cholesterol of at least 200 mg/dL. Anemia was defined as a baseline haemoglobin < 13 mg/dL in men and < 12 mg/dL in women.

### *Follow-up*

Cardiovascular mortality, MACE, reinfarction, repeat target vessel revascularisation (percutaneous or surgical), ventricular tachycardia/fibrillation (VT/VF), stroke, cardiopulmonary resuscitation, advanced heart failure, atrioventricular block needing transient pace intervention, intraaortic balloon pump, new atrial fibrillation, renal failure requiring dialysis, inotrope usage, ventilator usage and mechanical complications of MI were recorded during the in-hospital stay.

### *Statistical analysis*

The study group was divided into tertiles based on admission Zs and Ss. A high Zs (> 3) and high Ss (> 24) were defined as

**Table 1.** Baseline characteristics of study patients

Variables	LZsLSs (n = 196)	LZsHSs (n = 48)	HZsLSs (n = 29)	HZsHSs (n = 26)	P
Age [years]	55.5 (10.3)	56.7 (13)	63.9 (14.8)	65.5 (13.4)	< 0.001
Men	156 (79.5)	43 (89.5)	23 (79.3)	18 (69.2)	0.2
Diabetes mellitus	40 (20.4)	9 (18.7)	4 (13.7)	15 (57.6)	< 0.001
Hypertension	81 (41.3)	22 (45.8)	15 (51.7)	11 (42.3)	0.73
Family history	42 (21.4)	12 (25)	4 (13.7)	2 (7.6)	0.25
Hyperlipidaemia	21 (10.7)	6 (12.5)	2 (6.8)	4 (15.3)	0.77
Current smoking	139 (70.9)	30 (62.5)	15 (51.7)	11 (42.3)	0.01
MI history	2 (1)	4 (8.3)	0 (0)	0 (0)	0.009
PCI history	14 (7.1)	7 (14.5)	2 (6.8)	0 (0)	0.14
Anterior MI	69 (35.2)	32 (66.6)	13 (44.8)	21 (80.7)	< 0.001
RV MI	13 (6.6)	1 (2)	8 (27.5)	3 (11.5)	< 0.001
Killip > 1	1 (0.5)	2 (4.1)	8 (27.5)	10 (38.4)	< 0.001
Zwolle score	1.15 (1.01)	1.76 (1.06)	8.1 (3.77)	10.3 (4.3)	< 0.001
Syntax score	13.7 (5.7)	28.2 (4.3)	17.5 (4.3)	35.4 (7.6)	< 0.001
Pain-to-balloon time [min]	259.8(189.2)	240.9 (192.3)	316.1 (156.1)	304.2 (201.6)	0.25
TIMI score	1.9 (1.6)	2.1 (1.7)	5.9 (2.6)	7.6 (2.8)	< 0.001
QRS duration at admission [ms]	85.7 (12.8)	94.3 (16.8)	98.5 (24.7)	113.7 (33.1)	< 0.001

Mean values (SD) and % (n) are reported for continuous and categorical variables, respectively. LZsLSs — low Zwolle low Syntax; LZsHSs — low Zwolle high Syntax; HZsLSs — high Zwolle low Syntax; HZsHSs — high Zwolle high Syntax; MI — myocardial infarction; PCI — percutaneous coronary intervention; RV — right ventricular; TIMI — Thrombolysis In Myocardial Infarction

a value in the third tertile and low Zs ( $\leq 3$ ) and low Ss ( $\leq 24$ ) were defined as a value in the lower two tertiles. In addition, the study group was divided into subgroups according to Zs and Ss: high Zs and high Ss (HZsHSs, n = 26), high Zs and low Ss (HZsLZs, n = 29), low Zs and high Ss (LZsHSs, n = 48), low Zs and low Ss (LZsLSs, n = 196). Qualitative variables were expressed as percentages (%), and quantitative variables were expressed as mean value  $\pm$  standard deviation (SD). Comparison of parametric values between the two groups was performed by means of a two-tailed Student's t test. Categorical variables were compared by the likelihood-ratio  $\chi^2$  or Fisher's exact test. Backward stepwise multivariate logistic regression analysis, which included variables with p value less than 0.1, was performed to identify independent predictors of in-hospital cardiovascular mortality. The receiver operating characteristics (ROC) curve was used to identify the best threshold value for both continuous variables that were independent predictors of in-hospital cardiovascular mortality. A p value of less than 0.05 was considered statistically significant. All statistical studies were carried out with the program SPSS (version 15.0, SPSS, Chicago, IL, USA).

## RESULTS

The baseline characteristics of patients are set out in Table 1. Among the 299 study patients (mean age  $57.4 \pm 11.7$  years, range 31–92; 240 men and 59 women), Zs ranged from

0 to 15 (mean  $2.7 \pm 3.6$ ) and Ss ranged from 2 to 49 (mean  $18.3 \pm 9.3$ ). Patients in the HZsHSs group were more likely to be older and had more commonly DM, anterior MI, Killip class > 1, high TIMI score and high QRS duration. Right ventricular (RV) MI were higher in the HZsLSs group. Smoking was higher in the LZsLSs group. MI history was higher in the LZsHSs group.

Laboratory findings of patients are depicted in Table 2. Admission glucose and high density lipoprotein cholesterol (HDL-C) were higher in the HZsHSs group. Admission creatinine was higher in the HZsLSs group.

Angiographic and procedural characteristics are given in Table 3. Patients in the HZsHSs group more commonly had left main and left anterior descending artery culprit lesions, three-vessels disease, higher post TIMI 0/1 grade, lower LVEF and higher usage of tirofiban.

Table 4 presents the in-hospital adverse outcomes after primary PCI. The in-hospital cardiovascular mortality, MACE, renal failure requiring dialysis, VT/VF, cardiopulmonary resuscitation, advanced heart failure, inotrope usage, intraaortic balloon pump usage, mechanical complication, complete atrioventricular block requiring transient pacemaker and ventilator usage were higher in patients in the HZsHSs group than the other groups (Fig. 1). CIN and new atrial fibrillation development were higher in the HZsLSs group. Time of hospital stay was not different in the general group.

**Table 2.** Laboratory findings of patients

Variables	LZsLSs (n = 196)	LZsHSs (n = 48)	HZsLSs (n = 29)	HZsHSs (n = 26)	P
Admission creatinine	0.92 (0.22)	0.99 (0.34)	1.47 (1.35)	1.15 (0.9)	< 0.001
Peak CK-MB [U/L]	144.8(114.9)	229.5 (188.3)	186.1 (169.7)	164.4 (156.7)	0.16
TC [mg/dL]	199.6 (36.8)	188.2 (32.6)	175.3 (18.8)	220.8 (38.1)	0.08
LDL-C [mg/dL]	138.4 (35.6)	132.1 (38)	119.9 (38.1)	130.2 (30.8)	0.29
HDL-C [mg/dL]	38.4 (10.6)	37.4 (11.2)	39.7 (11.9)	58.6 (8.1)	0.04
TG [mg/dL]	118.3 (88.1)	92.2 (58.1)	82.5 (39.7)	109.8 (62.2)	0.42
Admission glucose [mg/dL]	159.1 (163.7)	142.9 (41.6)	195.9 (100.4)	251.2 (108.5)	< 0.001
WBC (×10 <sup>9</sup> /L)	11.7 (3.3)	12.5 (2.9)	11.7 (4.4)	13.2 (5.9)	0.27
GFR (mL/min/1.73 m <sup>2</sup> )	113.5 (61.3)	106.1 (43.2)	73.1 (36.3)	80.9 (41.6)	0.23
Admission anemia	50 (25.5)	9 (18.7)	11 (37.9)	9 (34.6)	0.19

Mean values (SD) and % (n) are reported for continuous and categorical variables, respectively. LZsLSs — low Zwolle low Syntax; LZsHSs — low Zwolle high Syntax; HZsLSs — high Zwolle low Syntax; HZsHSs — high Zwolle high Syntax; CK-MB — creatine kinase-MB; TC — total cholesterol; LDL-C — low density lipoprotein cholesterol; HDL-C — high density lipoprotein cholesterol; TG — trygliceride; WBC — white blood cell; GFR — glomerular filtration rate

**Table 3.** Angiographic and procedural characteristics of patients

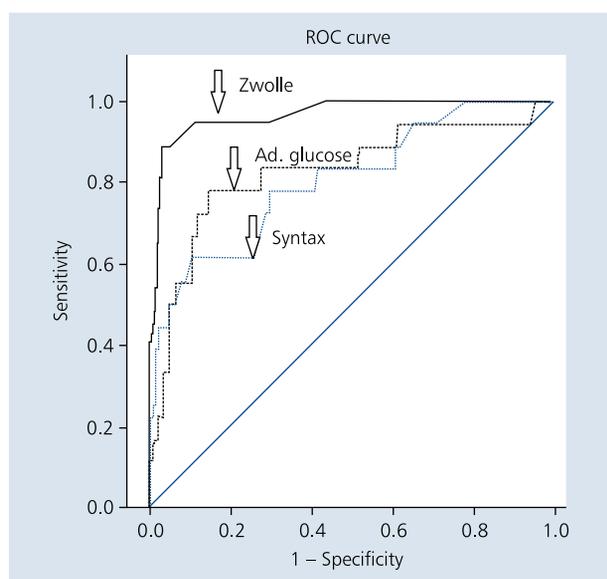
Variables	LZsLSs (n = 196)	LZsHSs (n = 48)	HZsLSs (n = 29)	HZsHSs (n = 26)	P
Culprit lesion:					< 0.001
LMCA	1 (0.5)	0 (0)	0 (0)	4 (15.3)	
LAD	68 (34.6)	32 (66.6)	13 (44.8)	17 (65.3)	
Cx	28 (14.2)	6 (12.5)	6 (20.6)	1 (3.8)	
RCA	96 (48.9)	10 (20.8)	8 (27.5)	4 (15.3)	
Diagonal/intermediate	3 (1.5)	0 (0)	2 (6.8)	0 (0)	
No. of diseased vessels:					< 0.001
1	116 (59.1)	11 (22.9)	15 (51.7)	3 (11.5)	
2	63 (32.1)	20 (41.6)	9 (31)	6 (23)	
3	17 (8.6)	17 (35.4)	5 (17.2)	17 (65.3)	
Pre TIMI grade:					0.2
0/1	151 (77)	45(93.7)	26 (89.6)	24 (92.3)	
2	36 (18.3)	3 (6.2)	2 (6.8)	2 (7.6)	
3	9 (4.5)	0 (0)	1(3.4)	0 (0)	
Post TIMI grade:					< 0.001
0/1	4 (2)	1 (2)	4 (13.7)	9 (34.6)	
2	39 (19.8)	13 (27)	8 (27.5)	7 (26.9)	
3	153 (78)	34 (70)	17 (58.6)	10 (38.4)	
Stent [%]	186 (94.8)	46 (95.8)	26 (89.6)	22 (84.6)	0.08
Stent length [mm]	21.1 (15.6)	22.6 (6.8)	23.6 (4.6)	32.7 (7.9)	0.29
Stent diameter [mm]	3.1 (0.46)	3.3 (0.55)	2.98 (0.45)	3.12 (0.58)	0.06
DES	135 (68.8)	29 (60.4)	19 (65.5)	18 (69.2)	0.73
LVEF [%]	48.3 (8.9)	40.9 (9.8)	42.9 (8.6)	37.1 (10.2)	< 0.001
Tirofiban	10 (5.1)	4 (8.3)	2 (6.8)	6 (23)	0.01
Rentrop > 1	7 (3.5)	2 (4.1)	0 (0)	0 (0)	0.77

Mean values (SD) and % (n) are reported for continuous and categorical variables, respectively. LZsLSs — low Zwolle low Syntax; LZsHSs — low Zwolle high Syntax; HZsLSs — high Zwolle low Syntax; HZsHSs — high Zwolle high Syntax; LMCA — left main coronary artery; LAD — left anterior descending; Cx — circumflex; RCA — right coronary artery; TIMI — Thrombolysis In Myocardial Infarction; DES — drug eluting stent; LVEF — left ventricular ejection fraction

**Table 4.** In-hospital cardiac events and complications

Variables	LZsLSs (n = 196)	LZsHSs (n = 48)	HZsLSs (n = 29)	HZsHSs (n = 26)	P
In-hospital cardiovascular mortality	1 (0.5)	0 (0)	8 (27.5)	13 (50)	< 0.001
Reinfarction	0 (0)	1 (2)	0 (0)	0 (0)	0.16
Target-vessel revascularisation	0 (0)	1 (2)	0 (0)	0 (0)	0.16
Major adverse cardiac events	1 (0.5)	1 (2)	8 (27.5)	13 (50)	< 0.001
Contrast-induced nephropathy	6 (3)	2 (4.1)	7 (24.1)	6 (23)	< 0.001
Stroke	1 (0.5)	0 (0)	0 (0)	0 (0)	0.91
Cardiopulmonary resuscitation	3 (1.5)	0 (0)	9 (31)	14 (53.8)	< 0.001
VT/VF	7 (3.5)	0 (0)	9 (31)	13 (50)	< 0.001
Advanced heart failure	4 (2)	5 (10.4)	7 (24.1)	11 (42.3)	< 0.001
Inotrope usage	1 (0.5)	1 (2)	9 (31)	12 (46.1)	< 0.001
Intraaortic balloon pump	0 (0)	1 (2)	3 (10.3)	9 (34.6)	< 0.001
Renal failure requiring dialysis	0 (0)	0 (0)	1 (3.4)	4 (15.3)	< 0.001
New atrial fibrillation	6 (3)	3 (6.2)	4 (13.7)	3 (11.5)	0.04
Mechanical complication	0 (0)	0 (0)	1 (3.4)	1 (3.8)	0.03
Complete atrioventricular block requiring transient pacemaker	10 (5.1)	0 (0)	4 (13.7)	8 (30.7)	< 0.001
Blood transfusion	6 (3)	0 (0)	1 (3.4)	1 (3.8)	0.65
Ventilator usage	1 (0.5)	0 (0)	7 (24.1)	10 (38.4)	< 0.001
Time of hospital stay [days]	3.7 (1.3)	3.8 (1.1)	3.9 (2.4)	3.9 (2.3)	0.92
Time of hospital stay (dead patients excluded) [days]	3.7 (1.3)	3.8 (1.1)	4.3 (1.3)	5.1 (1.6)	< 0.001

Mean values (SD) and % (n) are reported for continuous and categorical variables, respectively. LZsLSs — low Zwolle low Syntax; LZsHSs — low Zwolle high Syntax; HZsLSs — high Zwolle low Syntax; HZsHSs — high Zwolle high Syntax; VT/VF — ventricular tachycardia/fibrillation



**Figure 1.** In-hospital cardiovascular mortality and major adverse cardiac events in high Zwolle score (Zs) high Syntax score (Ss) (HZsHSs), high Zs low Ss (HZsLSs), low Zs high Ss (LZsHSs) and low Zs low Ss (LZsLSs) groups; Ad. — admission; ROC — receiver operating characteristics

However, it was significantly higher in the HZsHSs group ( $5.1 \pm 1.6$  days,  $p < 0.001$ ) when the 22 patients who died in hospital were excluded.

Table 5 shows univariate and multivariate predictors of in-hospital cardiovascular mortality. Multivariate logistic regression analysis was performed by including DM, smoking, female gender, family history, admission QRS duration, admission glucose, RV MI, tirofiban usage, admission creatinine, CIN, HZsLSs and HZsHSs. A significant association was noted between HZsHSs and the adjusted risk of in-hospital cardiovascular mortality (odds ratio [OR] 77.6, 95% confidence interval [CI] 6.69–113.1,  $p = 0.001$ ). Other independent predictors of cardiovascular mortality were determined by logistic regression analysis (Table 5). In a ROC curve analysis, higher area under curves (AUC) with regard to cardiovascular mortality were determined for Zs (AUC 0.966, 95% CI 0.925–1.006,  $p < 0.001$ ), admission glucose (AUC 0.825, 95% CI 0.706–0.943,  $p < 0.001$ ) and Ss and (AUC 0.802, 95% CI 0.686–0.918,  $p < 0.001$ ) (Table 6, Fig. 2).

## DISCUSSION

The major findings of the present single-centre study, which is the first to examine the impact of the combined Zs and Ss in patients undergoing primary PCI for STEMI, are as follows:

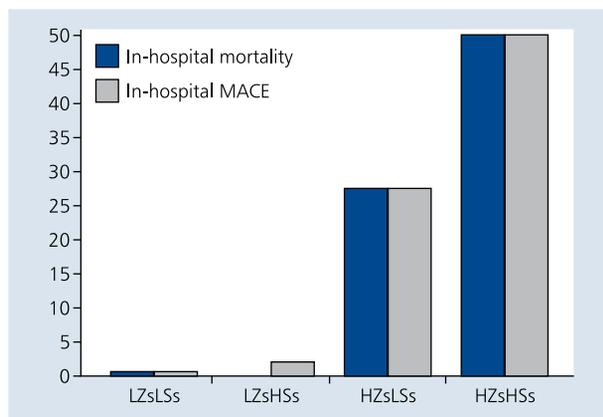
**Table 5.** Effects of multiple variables on in-hospital cardiovascular mortality in univariate and multivariate logistic regression analyses

Variables	Unadjusted OR	95% CI	P	Adjusted OR*	95% CI	P
Diabetes mellitus	2.56	1.04–6.27	0.04			
Smoking	0.414	0.173–0.995	0.05			
Female gender	2.53	1.01–6.4	0.04			
Family history	0.176	0.023–1.335	0.09			
QRS	1.05	1.03–1.07	< 0.001			
Admission glucose	1.01	1.008–1.02	< 0.001	1.016	1.004–1.028	0.007
RV MI	5.07	1.78–14.5	0.002			
Tirofiban	3.3	1.007–10.9	0.04			
Admission creatinine	1.71	0.96–3.04	0.07			
CIN	8.667	3.045–24.667	< 0.001			
HZsLSs	74.3	8.9–156.1	< 0.001	28.9	2.77–56.2	0.005
HZsHSs	195	23.6–276.8	< 0.001	77.6	6.69–113.1	0.001

\*Adjusted for DM, smoking, female gender, family history, admission QRS duration, admission glucose, RV MI, tirofiban usage, admission creatinine, CIN, HZsLSs, HZsHSs; OR — odds ratio; CI — confidence interval; RV MI — right ventricular myocardial infarction; CIN — contrast induced nephropathy; HZsLSs — high Zwolle low Syntax; HZsHSs — high Zwolle high Syntax

**Table 6.** Receiver operating characteristics analyses for variables

	Area under curve	95% confidence interval	P
Zwolle score	0.966	0.925–1.006	< 0.001
Admission glucose	0.825	0.706–0.943	< 0.001
Syntax score	0.802	0.686–0.918	< 0.001



**Figure 2.** The receiver operating characteristics curve with regard to in-hospital cardiovascular mortality for Zwolle score (Zs) (AUC 0.966, 95% CI 0.925–1.006,  $p < 0.001$ ), admission glucose (AUC 0.825, 95% CI 0.706–0.943,  $p < 0.001$ ) and Syntax score (Ss) (AUC 0.802, 95% CI 0.686–0.918,  $p < 0.001$ ); MACE — major adverse cardiac events; rest abbreviations as in Table 1

(1) Patients with a HZsHSs have the greatest risk for in-hospital mortality and MACE. Moreover, compared to an isolated HSs, an isolated HZs indicates a poorer prognosis for the in-hospital period; (2) After adjustments for potential confounders, HZsHSs was the most powerful independent predictor of in-hospital cardiovascular mortality; and (3) The present findings confirm previous trials showing that a high Zs, either with or without a high Ss, is associated with excessive in-hospital mortality in patients with STEMI.

The Ss depends only on the characteristics of angiographic lesions. It was designed to grade the complexity of CAD in patients undergoing PCI and to aid communication between surgeons and interventional cardiologists in identifying the optimal revascularisation strategy in patients with complex lesions [6, 16]. The findings of initial studies, which were performed in patients with stable CAD, revealed that the Ss is an independent long-term predictor of mortality and MACE [17–19]. Later studies were conducted in patients with STEMI. In a study of 807 patients with acute STEMI undergoing primary PCI, Garg et al. [8] discovered that the incidence of all clinical outcomes, including mortality, MACE, and stent thrombosis, after one year was highest in patients in the top Ss tertile ( $> 16$ ). Magro et al. [9] argued that STEMI patients with a high Ss were at high risk for long-term mortality and MACE, and that these patients may need more intensive therapy because the Ss provides additional risk stratification of standard risk scores. In addition, they found an independent association between a high Ss ( $> 21$ ) and no reflow after primary PCI [10]. Palmerini et al. [20] reported that in patients with a non-STEMI undergoing PCI, the Ss was an independent predictor of the one-year rate of death, cardiac death, MI, and tricuspid valve replacement. In a recent study by

our team [7], patients with a high Ss ( $> 21.75$ ) undergoing primary angioplasty for STEMI had poorer in-hospital survival, and a high Ss was an independent risk factor for in-hospital cardiovascular mortality.

The Ss cannot be used to determine the effect of clinical factors such as age, renal impairment or cardiogenic shock because it is based solely on angiographic variables. Therefore, some researchers have developed risk scores using the Ss and clinical variables. For example, Garg et al. [8] compared the Ss in isolation and in combination with the primary angioplasty in MI score (a clinical-based score) [4]. Together, the Ss and primary angioplasty in MI score led to a net reclassification improvement in mortality and MACE in patients undergoing primary PCI. Another study evaluated the ability of the Ss and clinical Ss (CSs) to predict long-term outcomes in all populations receiving drug-eluting stents [21]. The CSs was calculated by combining the Ss with variables such as age, baseline LVEF, and creatinine clearance. The CSs advanced the predictivity of the Ss for five-year all-cause mortality. Using the data from the Fractional Flow Reserve Versus Angiography for Multivessel Evaluation (FAME) study, Nam et al. [22] calculated the Ss by incorporating only ischaemia-producing lesions as determined by a fractional flow reserve  $\leq 0.80$ ; they called this score the functional Ss (FSs). The FSs decreased the number of higher-risk patients by moving one-third of them to a lower risk category, and compared to the Ss, the FSs had better predictive accuracy for MACE at one-year follow-up. Capodanno et al. [23] produced another risk score called the global risk classification system, which was created by combining the Ss and EuroSCORE strata. The inclusion of the EuroSCORE in an Ss-based model significantly improved the prediction of cardiac mortality [23]. These studies demonstrate the significant increase in prognostic value obtained by adding clinical information to the Ss.

In the era of primary PCI, several different clinical scores have been used, including the Global Registry of Acute Coronary Events [24], primary angioplasty in MI [4], TIMI-STEMI [2], Zs [3], and controlled abciximab and device investigation to lower late angioplasty complications (CADILLAC) risk score [5]. The first three of these scores have become outdated because of insufficient data about procedural variables such as post-TIMI flow. The CADILLAC risk score has been useful in terms of its prognostic accuracy (c statistic: 0.83 for 30-day mortality and 0.79 for one-year mortality). In the CADILLAC scoring system, patients admitted with cardiogenic shock and a complex coronary anatomy (e.g. left main or bifurcation disease) were excluded. Also, pain-to-balloon time, which is associated with survival [25], was not evaluated. The Zs, which was created by De Luca et al. [3], can be used to identify a large cohort (73.4%) of low-risk ( $\leq 3$  points) patients, with a good discriminatory capacity (c statistic for 30-day mortality: 0.902). In their study, the mortality rate was 0.1% after two days and 0.2% between two and ten days

in patients with a score  $\leq 3$ . The Zs comprises Killip class, post-TIMI flow, age, three-vessel disease, anterior infarction, and pain-to-balloon time.

After evaluating the literature, we decided that combining the Zs and Ss may be a wise approach for obtaining more information about a patient's coronary anatomy and clinical situation.

One interesting result of our study is that the 'smoking paradox' was clearly seen between groups. The smoking paradox became known through studies showing that smokers, compared to non-smokers, experienced a better outcome following an acute MI [26]. However, the paradox could not be verified in all cases. For example, Weisz et al. [27] argued that the protective effect of smoking may be explained by differences in baseline risk rather than smoking status per se. Cornel et al. [28] revealed that habitual smoking was associated with a greater risk of subsequent stent thrombosis in patients hospitalised with ACS. It seems that conflicting results will continue.

Not surprisingly, in the high Zs and high Ss (HZSHSs) group, there were additional risk factors, including a higher Killip class, higher TIMI score, longer QRS duration on admission, older age, and more common occurrences of DM, anterior MI, three-vessel disease, and left main disease. A worse clinical outcome and higher mortality were detected in the HZSHSs group, as a HZs is a valuable prognostic marker and the Ss score potentiates the Zs as a marker of diffuse atherosclerosis. The lower LVEF in the HZSHSs group clarifies the association between these scores and mortality. Also, a poorer post-TIMI flow may be a sign of diffuse and long lesions as well as a cause of higher tirofiban usage. Patients with a HZs, regardless of their Ss, had a greater number of RV MIs and poorer renal function. This is because isolated proximal right coronary artery lesions may cause RV MI without a Hs. Poorer renal function may be the result of HZs representing worse clinical parameters that impact upon renal perfusion. We are uncertain of the reasons for the higher HDL-C level in the HZSHSs group. Interestingly, the in-hospital cardiovascular mortality rate was '0' in the LZSHSs group. As only one cardiovascular death occurred in the LZSLs group, we cannot explain these conflicting results based on the information we have. The influence of some unknown factor is possible.

### **Limitations of the study**

This study has several limitations. This was a single-centre study with a small sample size. Additionally, we conducted no long-term follow-up. Reperfusion markers such as myocardial blush grade or ST-segment resolution could not be determined. Patients with a history of CABG were excluded because the Ss is applicable only for native coronary vessels. In this study, we used the current calculation algorithm for the Ss. In other words, the culprit lesion was scored using angiographic views of the infarct-related artery before any

intervention. Garg et al. [8] measured pre-and post-wiring scores and suggested using the pre-wiring score. Although the Ss is useful for risk stratification, it has some limitations. For example, it is not completely comprehensive, has poor calibration, does not include clinical parameters, does not discriminate ischaemia, has only moderate reproducibility, and is time-consuming to determine [29]. In the CADILLAC score, LVEF is the most powerful prognostic predictor, but the Zs does not include LVEF.

## CONCLUSIONS

In this study, we combined the Zs and Ss for the first time. This combination accurately predicted in-hospital cardiovascular mortality. Our findings show that in the setting of primary PCI, the lesion complexity, procedural outcome, and evaluation of clinical parameters significantly enhanced the risk stratification. In summary, the combined Zs and Ss system is a useful and powerful prognostic factor in patients undergoing primary PCI for STEMI. We expect that this risk model will be improved in future studies.

**Conflict of interest:** none declared

## References

- Räber L, Kelbæk H, Ostojic M et al. Effect of biolimus-eluting stents with biodegradable polymer vs bare-metal stents on cardiovascular events among patients with acute myocardial infarction: the COMFORTABLE AMI randomized trial. *JAMA*, 2012; 308: 777–787.
- Morrow DA, Antman EM, Charlesworth A et al. TIMI Risk Score for ST-elevation myocardial infarction: a convenient, bedside, clinical score for risk assessment at presentation. *Circulation*, 2000; 102: 2031–2037.
- De Luca G, Suryapranata H, van't Hof AW et al. Prognostic assessment of patients with acute myocardial infarction treated with primary angioplasty: implications for early discharge. *Circulation*, 2004; 109: 2737–2743.
- Addala S, Grines CL, Dixon SR et al. Predicting mortality in patients with ST-elevation myocardial infarction treated with primary percutaneous coronary intervention (PAMI risk score). *Am J Cardiol*, 2004; 93: 629–632.
- Halkin A, Singh M, Nikolsky E et al. Prediction of mortality after primary percutaneous coronary intervention for acute myocardial infarction: the CADILLAC risk score. *J Am Coll Cardiol*, 2005; 45: 1397–1405.
- Sianos G, Morel MA, Kappetein AP et al. The SYNTAX Score: an angiographic tool grading the complexity of coronary artery disease. *EuroIntervention*, 2005; 1: 219–227.
- Kul S, Akgul O, Uyarel H et al. High SYNTAX score predicts worse in-hospital clinical outcomes in patients undergoing primary angioplasty for acute myocardial infarction. *Coron Artery Dis*, 2012; 23: 542–548.
- Garg S, Sarno G, Serruys PW et al. Prediction of 1-year clinical outcomes using the SYNTAX score in patients with acute ST-elevation myocardial infarction undergoing primary percutaneous coronary intervention: a substudy of the STRATEGY (Single High-Dose Bolus Tirofiban and Sirolimus-Eluting Stent Versus Abciximab and Bare-Metal Stent in Acute Myocardial Infarction) and MULTISTRATEGY (Multicenter Evaluation of Single High-Dose Bolus Tirofiban Versus Abciximab With Sirolimus-Eluting Stent or Bare-Metal Stent in Acute Myocardial Infarction Study) trials. *J Am Coll Cardiol Intv*, 2011; 4: 66–75.
- Magro M, Nauta S, Simsek C et al. Value of the SYNTAX score in patients treated by primary percutaneous coronary intervention for acute ST-elevation myocardial infarction: the MI SYNTAX score study. *Am Heart J*, 2011; 161: 771–781.
- Magro M, Nauta ST, Simsek C et al. Usefulness of the SYNTAX Score to Predict “No Reflow” in Patients Treated With Primary Percutaneous Coronary Intervention for ST-Segment Elevation Myocardial Infarction. *Am J Cardiol*, 2012; 109: 601–606.
- Stevens LA, Coresh J, Greene T et al. Assessing kidney function—measured and estimated glomerular filtration rate. *N Engl J Med*, 2006; 354: 2473–2483.
- Schiller NB, Shah PM, Crawford M et al. Recommendations for quantitation of the left ventricle by twodimensional echocardiography. American Society of Echocardiography Committee on Standards, Subcommittee on Quantitation of Two-Dimensional Echocardiograms. *J Am Soc Echocardiogr*, 1989; 2: 358–367.
- Chesebro JH, Knatterud G, Roberts R et al. Thrombolysis in Myocardial Infarction (TIMI) Trial, Phase I: a comparison between intravenous tissue plasminogen activator and intravenous streptokinase. Clinical findings through hospital discharge. *Circulation*, 1987; 76: 142–154.
- Rentrop KP, Cohen M, Blanke H et al. Changes in collateral channel filling immediately after controlled coronary artery occlusion by an angioplasty balloon in human subjects. *J Am Coll Cardiol*, 1985; 5: 587–592.
- Pucelikova T, Dangas G, Mehran R. Contrast-induced nephropathy. *Catheter Cardiovasc Interv*, 2008; 71: 62–72.
- Serruys PW, Onuma Y, Garg S et al. Assessment of the SYNTAX score in the SYNTAX study. *EuroIntervention*, 2009; 5: 50–56.
- Valgimigli M, Serruys PW, Tsuchida K et al.; for the ARTS II Investigators. Cyphering the complexity of coronary artery disease using the SYNTAX score to predict clinical outcome in patients with three-vessel lumen obstruction undergoing percutaneous coronary intervention. *Am J Cardiol*, 2007; 99: 1072–1081.
- Serruys PW, Onuma Y, Garg S et al.; for the ARTS II Investigators. 5-year clinical outcomes of the ARTS II (Arterial Revascularization Therapies Study II) of the sirolimus-eluting stent in the treatment of patients with multivessel de novo coronary artery lesions. *J Am Coll Cardiol*, 2010; 55: 1093–1101.
- Capodanno D, Di Salvo ME, Cincotta G et al. Usefulness of the SYNTAX score for predicting clinical outcome after percutaneous coronary intervention of unprotected left main coronary artery disease. *Circ Cardiovasc Interv*, 2009; 2: 302–308.
- Palmerini T, Genereux P, Caixeta A et al. Prognostic value of the SYNTAX score in patients with acute coronary syndromes undergoing percutaneous coronary intervention: analysis from the ACUITY (Acute Catheterization and Urgent Intervention Triage Strategy) trial. *J Am Coll Cardiol*, 2011; 57: 2389–2397.
- Palmerini T, Caixeta A, Genereux P et al. Comparison of clinical and angiographic prognostic risk scores in patients with acute coronary syndromes: Analysis from the Acute Catheterization and Urgent Intervention Triage Strategy (ACUITY) trial. *Am Heart J*, 2012; 163: 383–391.
- Nam CW, Mangiacapra F, Entjes R et al.; FAME Study Investigators. Functional SYNTAX score for risk assessment in multivessel coronary artery disease. *J Am Coll Cardiol*, 2011; 58: 1211–1218.
- Capodanno D, Miano M, Cincotta G et al. EuroSCORE refines the predictive ability of SYNTAX score in patients undergoing left main percutaneous coronary intervention. *Am Heart J*, 2010; 159: 103–109.
- Granger CB, Goldberg RJ, Dabbous O et al.; Global Registry of Acute Coronary Events Investigators. Predictors of hospital mortality in the global registry of acute coronary events. *Arch Int Med*, 2003; 163: 2345–2353.
- Antoniucci D, Valenti R, Migliorini A et al. Relation of time to treatment and mortality in patients with acute myocardial infarction undergoing primary coronary angioplasty. *Am J Cardiol*, 2002; 89: 1248–1252.

26. Sparrow D, Dawber TR. The influence of cigarette smoking on prognosis after a first myocardial infarction. A report from the Framingham study. *J Chronic Dis*, 1978; 31: 425–432.
27. Weisz G, Cox DA, Garcia E et al. Impact of smoking status on outcomes of primary coronary intervention for acute myocardial infarction: the smoker's paradox revisited. *Am Heart J*, 2005; 150: 358–364.
28. Cornel JH, Becker RC, Goodman SG et al. Prior smoking status, clinical outcomes, and the comparison of ticagrelor with clopidogrel in acute coronary syndromes—insights from the PLATelet inhibition and patient Outcomes (PLATO) trial. *Am Heart J*, 2012; 164: 334–342.
29. Capodanno D, Tamburino C. Does the SYNTAX score get on your nerves? Practical considerations on how and when avoiding it to maximize its usefulness with no waste of time. *Int J Cardiol*, 2012; 159: 165–168.

## Nowa metoda oceny prognostycznej chorych z ostrym zawałem serca z uniesieniem odcinka ST poddanych pierwotnej angioplastyce wieńcowej: połączenie skal Zwolle i Syntax

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### Streszczenie

**Wstęp:** Skala Zwolle (Zs) jest zweryfikowaną skalą ryzyka stosowaną do identyfikowania chorych z grupy małego ryzyka z ostrym zawałem serca z uniesieniem odcinka ST (STEMI) poddanych pierwotnej przeszłokornej interwencji wieńcowej (PCI). Skala Syntax (Ss) stanowi angiograficzną skalę służącą do oceny złożoności choroby wieńcowej (CAD).

**Cel:** Celem badania było stworzenie prostej skali oceny ryzyka przez połączenie dwóch skal w celu stratyfikacji ryzyka u chorych ze STEMI poddanych pierwotnej PCI.

**Metody:** Do badania włączono w sposób prospektywny 299 kolejnych chorych ze STEMI (śr. wieku  $57,4 \pm 11,7$ ; 240 mężczyzn) poddanych pierwotnej PCI. Badaną populację podzielono na tercyle w zależności od punktacji w skalach Zs i Ss przy przyjęciu do szpitala. Do górnego tercyla kwalifikowano osoby z wysoką punktacją Zs ( $> 3$ ) i Ss ( $> 24$ ). Niską punktacją Zs i Ss definiowano jako dwa dolne tercyle wartości. Następnie chorych podzielono na cztery grupy: wysoka punktacja Zs i wysoka punktacja Ss (HZsHSs,  $n = 26$ ); wysoka punktacja Zs i niska punktacja Ss (HZsLSs,  $n = 29$ ); niska punktacja Zs i wysoka punktacja Ss (LZsHSs,  $n = 48$ ); niska punktacja Zs i niska punktacja Ss (LZsLSs,  $n = 196$ ). Zebrano dane dotyczące kardiologicznych punktów końcowych.

**Wyniki:** Śmiertelność wewnątrzszpitalna z przyczyn sercowo-naczyniowych była wyższa w grupie HZsHSs (50%) niż w grupach HZsLSs (27,5%), LZsHSs (0%) i LZsLSs (0,5%). Po skorygowaniu względem możliwych czynników zakłócających przynależność do grup HZsHSs (OR 77,6; 95% CI 6,69–113,1;  $p = 0,001$ ) i HZsLSs (OR 28,9; 95% CI 2,77–56,2;  $p = 0,005$ ) nadal stanowiła niezależny czynnik predykcyjny wewnątrzszpitalnego zgonu sercowo-naczyniowego, natomiast przynależność do grup LZsHSs i LZsLSs nie miała takiego znaczenia prognostycznego.

**Wnioski:** Pacjenci ze STEMI zakwalifikowani do grupy HZsHSs charakteryzują się największym ryzykiem zgonu wewnątrzszpitalnego z przyczyn sercowo-naczyniowych.

**Słowa kluczowe:** skala Syntax, skala Zwolle, ostry zawał serca

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