Does Continuous ST-Segment Monitoring Add Prognostic Information to the TIMI, PURSUIT, and GRACE Risk Scores?

Pedro Carmo, M.D., Jorge Ferreira, M.D., Carlos Aguiar, M.D.,
António Ferreira, M.D., Luís Raposo, M.D., Pedro Gonçalves, M.D.,
João Brito, M.D., and Aniceto Silva, M.D.

From the Department of Cardiology, Hospital de Santa Cruz, Carnaxide, Portugal

Background: Recurrent ischemia is frequent in patients with non-ST-elevation acute coronary syndromes (NST-ACS), and portends a worse prognosis. Continuous ST-segment monitoring (CSTM) reflects the dynamic nature of ischemia and allows the detection of silent episodes. The aim of this study is to investigate whether CSTM adds prognostic information to the risk scores (RS) currently used.

Methods: We studied 234 patients with NST-ACS in whom CSTM was performed in the first 24 hours after admission. An ST episode was defined as a transient ST-segment deviation in ≥ 1 lead of ≥ 0.1 mV, and persisting ≥ 1 minute. Three RS were calculated: Thrombolysis in Myocardial Infarction (TIMI; for NST-ACS), Platelet glycoprotein IIb/IIIa in Unstable angina: Receptor Suppression Using Integrilin (PURSUIT; death/MI model), and Global Registry of Acute Coronary Events (GRACE). The end point was defined as death or nonfatal myocardial infarction (MI), during 1-year follow-up.

Results: ST episodes were detected in 54 patients (23.1%) and associated with worse 1-year outcome: 25.9% end point rate versus 12.2% (Odds Ratio [OR] = 2.51; 95% Confidence Interval [CI], 1.18–5.35; $P = 0.026$). All three RS predicted 1-year outcome, but the GRACE (c-statistic = 0.755; 95% CI, 0.695–0.809) was superior to both TIMI (c-statistic = 0.632; 95% CI, 0.567–0.694) and PURSUIT (c-statistic = 0.644; 95% CI, 0.579–0.706). A GRACE RS > 124 showed the highest accuracy for predicting end point. The presence of ST episodes added independent prognostic information the TIMI RS (hazard ratio [HR] = 2.23; 95% CI, 1.13–4.38) and to PURSUIT RS (HR = 2.03; 95% CI, 1.03–3.98), but not to the GRACE RS.

Conclusions: CSTM provides incremental prognostic information beyond the TIMI and PURSUIT RS, but not the GRACE risk score. Hence, the GRACE risk score should be the preferred stratification model in daily practice.

Ann Noninvasive Electrocardiol 2011;16(3):239–249

ST-segment monitoring; acute coronary syndromes prognosis; risk scores

ST-SEGMENT MONITORING

Patients with non-ST-elevation acute coronary syndromes (NSTE-ACS) constitute a heterogeneous population regarding diagnosis and prognosis. Risk stratification is essential to identify patients at higher risk, who require immediate admission to an intensive care unit and more aggressive diagnostic and therapeutic procedures. On the other hand, low-risk patients may be discharged early or transferred to less differentiated levels of care, hence saving financial resources. The process of

risk stratification should begin at the time of admission.^{1,2} However, in most cases, the level of risk is not clear on the initial assessment, raising the need for extended observation for a few hours after presentation.

In the absence of the ideal risk marker, several scores are available for risk stratification in NSTE-ACS. Such scores include variables from the medical history, physical examination, electrocardiogram (ECG), and biochemical markers of myocardial injury. The scores commonly used in clinical practice are the Global Registry of

Address for correspondence: Pedro Miguel Lopes do Carmo, M.D., Hospital de Santa Cruz, Av Prof Doutor Reinaldo dos Santos, 2794-035 Carnaxide, Portugal. Fax: 351 214241388; E-mail: p.lopecarmo@gmail.com

Acute Coronary Events (GRACE)³, Thrombolysis in Myocardial Infarction (TIMI)⁴, and Platelet glycoprotein IIb/IIIa in Unstable angina: Receptor Suppression Using Integrilin (PURSUIT).⁵

The GRACE score has been shown to be the most accurate risk score in a real-world setting, and furthermore to aid in the selection of patients with NSTEMI-ACS who most benefit from myocardial revascularization.⁶⁻⁸ For these reasons, the GRACE score is preferred by the European Society of Cardiology.² However, an important limitation of all the above-mentioned risk scores (RS) is the fact that variables are assessed at the time of admission, thus not reflecting the dynamic nature of the risk in NSTEMI-ACS.

Recurrent myocardial ischemia is a common complication in the early hours after a NSTEMI-ACS; although it is more often clinically silent, it is nevertheless associated with poor prognosis. Continuous monitoring of the ST segment is an effective way of detecting silent myocardial ischemia, providing immediate results and reflecting the dynamic nature of myocardial ischemia and coronary thrombosis. The occurrence of ischemic episodes identified by continuous monitoring is an established marker of worse prognosis.⁹⁻¹⁷

The purpose of this study is to determine whether continuous monitoring of ST segment adds prognostic value to RS routinely used in clinical practice for NSTEMI-ACS.

METHODS

Patient Selection

All consecutive patients admitted between January 2006 and October 2007 in the Cardiac Intensive Care Unit of our institution were eligible for this prospective study. The inclusion criteria were: at least one episode of chest pain within 24 hours of admission, or other symptoms suggestive of ACS occurring at rest and lasting ≥ 20 minutes.

We excluded patients with: (1) ST-segment elevation on admission, (2) ECG abnormalities that preclude the detection of ischemia by ST-segment analysis (left bundle branch block, ventricular pacing), (3) history of myocardial infarction (MI) or revascularization procedure (surgical or percutaneous) within 14 days prior to admission to the hospital.

The study population represents on average 39% of patients admitted with ACS in our unit.

All patients consented to participate in the study before inclusion. Clinical data were collected prospectively. The therapeutic approach was individualized and coronary angiography was performed according to clinical indications.

Baseline ECG

A resting 12-lead ECG was obtained at admission, and then at least daily during hospitalization. Whenever symptoms suggestive of ongoing myocardial ischemia were present an ECG was also obtained.

ST-segment depression was defined as a deviation ≥ 0.1 mV below the isoelectrical line in at least two contiguous leads.

Continuous ST-Segment Monitoring

The ST-segment monitoring was performed continuously during 24 hours after admission, using the Siemens SC 9000 system (Siemens, Danvers, MA, USA). This equipment analyzes the changes in ST segment in three leads, stores this information, and can show real-time trends of ST deviation (in the form of a graph displaying the changes in the ST-segment level over a period of 1, 2, 4, 8, 12, or 24 hours). Two of the three examined leads were DI and aVF in all studied patients. The third lead was always the precordial lead with the most severe ST-segment deviation at admission or V₅.

We compared the changes in the ST segment during continuous monitoring with baseline ECG. The baseline ECG, was called the "nonischemic ECG" that corresponds to the admission ECG if there were no ischemic reversible ST-segment deviation, or to the first ECG after ST-segment normalization. Every minute, the device calculates the median QRS-T complex from the last 10 seconds of monitoring. The ST-segment deviation was measured 60 milliseconds after the J point (Fig. 1).¹⁸ The ST trends were available during the stay in the Cardiac Intensive Care Unit, and therefore the attending physicians were aware of that information.

Analysis of ST-Segment Monitoring and Definition of ST Events

The trends of the ST segment of each patient were examined by a cardiologist blinded to the clinical findings. Artifacts were eliminated before analysis.

Figure 1. Trends show three ST-segment deviation events (A) and none event (B).

We defined ST-segment deviations due to postural changes as sudden shifts in the ST segment with concomitant changes of the QRS amplitudes, and T wave.

"ST event" was defined as a transient ST-segment deviation (elevation or depression) in at least one lead, measuring ≥ 0.1 mV, and lasting ≥ 1 minute (Fig. 1).

Risk Scores

We calculated the three RS—TIMI, PURSUIT, and GRACE—for each patient from the clinical history, ECG, and laboratory findings at admission (Table 1).

For the purpose of the TIMI score, we considered that the prior history of MI in patients not submitted to coronary angiography was equivalent to the existence of significant coronary artery disease, as has been validated by the authors of this score.¹⁹ TIMI risk score was calculated by the arithmetic sum of each of the present variables.⁴

We used the PURSUIT simplified score for death and MI, which was calculated by adding the points assigned to each present variable.⁵

The software (GRACE ACS Risk Model calculator application) that is available on the web site http://www.outcomes-umassmed.org/grace/acs_risk.cfm was used to calculate GRACE risk score.

Clinical End Points

We recorded adverse events that occurred in the first year of follow-up after admission. The primary end point was death from any cause or nonfatal MI. Nonfatal MI was defined as a typical rise of an myocardial necrosis biomarker—troponin

I (cTnI) or creatine kinase MB isoenzyme (CK-MB)—associated with ischemic symptoms at rest and/or de novo ischemic ECG changes. Recurrent MI was defined according to the universal definition of MI.²⁰

Table 1. Risk Scores

PURSUIT (0–18)	
Age, separate points for enrolment diagnosis decade	Worst CCS-class in previous 6 weeks:
[UA (MI)]	No angina or CCS I/III = 0
50 = 8/11	CCS III/IV = 2
60 = 9/12	Signs of heart failure = 2
70 = 11/13	
80 = 12/14	
Sex:	ST-depression on presenting ECG = 1
Male = 1	
Female = 0	
TIMI (0–7)	
Age ≥ 65 years = 1	>1 episode of rest angina in <24 h = 1
≥ 3 risk factors for CAD = 1	ST-segment deviation = 1
Use of ASA (last 7 days) = 1	Elevated cardiac markers = 1
Known CAD (stenosis $\geq 50\%$) = 1	
GRACE (0–258)	
Age (years):	Heart rate (bpm):
<40 = 0	<70 = 0
40–49 = 18	70–89 = 7
50–59 = 36	90–109 = 13
60–69 = 55	110–149 = 23
70–79 = 73	150–199 = 36
$\geq 80 = 91$	>200 = 46
Systolic BP (mmHg):	Creatinine (mg/dL):
<80 = 63	0–0.39 = 2
80–99 = 58	0.4–0.79 = 5
100–119 = 47	0.8–1.19 = 8
120–139 = 37	1.2–1.59 = 11
140–159 = 26	1.6–1.99 = 14
160–199 = 11	2–3.99 = 23
$\geq 200 = 0$	>4 = 31
Killip class:	Cardiac arrest at admission = 43
Class I = 0	Elevated cardiac markers = 15
Class II = 21	ST-segment deviation = 30
Class III = 43	
Class IV = 64	

All clinical events were validated by two cardiologists without knowledge of the clinical baseline status or the ST-segment monitoring results. The event analysis was completed for the entire study population.

Statistical Analysis

Continuous variables were expressed as mean $\pm$ standard deviation when of normal distribution (Shapiro-Wilks test) or as median (interquartile range) if otherwise. Categorical variables were expressed as frequencies and percentages.

The statistical comparison of categorical baseline characteristics and rates of clinical events was performed using the chi-square test with Yates' correction or the Fisher's exact test, when appropriate. Continuous variables were compared using two-tailed Student's *t*-test. We used the Mann-Whitney test to compare unpaired variables with nonparametric distribution.

We constructed receiver operating characteristic (ROC) curves to relate the scores with the incidence of primary end points at 1 year. The area under the curve (AUC) was used to express the accuracy of each risk score. The relative performance of each test was evaluated with the 95% confidence interval (CI) for the difference between two AUCs. The cutoff points identified with the ROC curves for each score were used to divide the studied population into low- and high-risk patients.

For the purpose of time-to-end point analyses, we used the Kaplan-Meier method and the log rank test when comparing patients by risk category ("High" and "Low" risk for each risk score) and by the occurrence of ST events.

Cox regression analysis was used to assess the weight and independence of each risk score and of ST events for the risk of death or nonfatal MI at 1-year follow-up.

For all statistical comparisons, we considered a *P* value <0.05 as statistically significant. Statistical analysis was performed with SPSS version 13.0 (SPSS Inc., Chicago, IL, USA) and MedCalc version 9.3.8.0 (MedCalc Software, Mariakerke, Belgium).

RESULTS

Baseline Characteristics and In-Hospital Treatment

We included 234 patients (mean age 64.0 years), of whom 53 (22.6%) are female. The final diagno-

sis of the ACS was unstable angina in 89 patients (38.0%) and non-ST elevation MI in 145 patients (62.0%) (Table 2).

We detected at least one ST event in 54 patients (23.1%). Patients with ST events were older, more often had a prior history of MI or coronary artery bypass grafting (CABG), and more often presented heart failure manifestations at admission, and ST-segment depression in the initial ECG. The values of all three RS were higher in patients with ST events.

Coronary angiography was performed in 87% patients (Table 3). The prevalence and severity of coronary artery disease were higher in patients with ST events. Pharmacological therapy and the use of revascularization strategies were similar in patients with and without ST events (Table 3).

End Points and Their Relation with Risk Scores

By 1-year follow-up, 19 patients had died (8.1%), and death or nonfatal MI had occurred in 36 patients (15.4%).

The median value of the TIMI risk score was 4 (3, 5) and of the PURSUIT score was 13 (11, 15). The mean value of the GRACE risk score was 126 ± 35 . Any of the three scores performed well in predicting the primary end point at 1-year follow-up (Table 4 and Fig. 2), but the GRACE score showed the greatest accuracy (Table 5).

End Points and Their Relation to ST Events

Both total mortality and the combined incidence of death or nonfatal MI were significantly higher in patients with ST events during the 24 hours of monitoring. In univariate analysis, the presence of ST events increased the risk of death (hazard ratio [HR] = 2.72, 95% CI: 1.10 to 6.77) and of death or nonfatal MI (HR = 2.50, 95% CI: 1.28 to 4.89). These increased risks were evident early after admission, as shown by the early separation of the Kaplan-Meier curves (Fig. 3).

End Points, Risk Scores, and ST-Segment Monitoring

When adjusted for the best cutoff value of TIMI and PURSUIT RS, the presence of ST events during the first 24 hours of admission remained a predictor

Table 2. Baseline Characteristics

	All n = 234	ST Events n = 54	No ST Events n = 180	P
Age, years	64.0 ± 10.5	66.7 ± 9.4	63.4 ± 10.7	0.043
Male gender, n (%)	181 (77.4)	47 (87.0)	134 (74.4)	NS
Risk factors, n (%)				
Diabetes mellitus	54 (23.1)	14 (25.9)	40 (22.2)	NS
Smoking	49 (20.9)	10 (18.5)	39 (21.7)	NS
Hypertension	139 (59.4)	32 (59.3)	107 (59.4)	NS
Hypercholesterolemia	145 (62.0)	34 (63.0)	111 (61.7)	NS
Previous history, n (%)				
MI	102 (43.6)	31 (57.4)	71 (39.4)	0.028
PCI	72 (30.8)	13 (24.1)	59 (32.8)	NS
CABG	54 (23.1)	19 (35.2)	35 (19.4)	0.026
ST segment depression at admission, n (%)	137 (58.5)	41 (75.9)	95 (52.8)	0.003
Killip-Kimbal class, n (%)				0.009
I	200 (85.5)	39 (72.2)	161 (89.4)	
II	16 (6.8)	6 (11.1)	10 (5.6)	
III or IV	18 (7.7)	9 (16.7)	9 (5.0)	
GRACE score	126 ± 35	141 ± 33	122 ± 34	<0.001
TIMI score	4 (3; 5)	4 (3; 5)	4 (3; 4)	<0.001
PURSUIT score	13 (11; 15)	15 (13; 16)	13 (11; 14)	<0.001
cTnI +, n (%)	145 (62.0)	39 (72.2)	106 (58.9)	NS

MI = myocardial infarction; PCI = percutaneous coronary intervention; CABG = coronary artery bypass grafting; cTnI = cardiac troponin I.

of the primary end point. However, when adjusted for the best cutoff value of GRACE risk score, ST events no longer added prognostic information (Table 6, and Fig. 4).

Heart Failure and Creatinine: Prognostic Value

The superiority of GRACE risk score and the inability of ST-segment monitoring to improve its prognostic value justified further analysis. In this population, Killip-Kimbal (KK) class—which is part of the GRACE score, but not the TIMI and PURSUIT scores—was strongly associated with the incidence of the primary end points at 1 year (unadjusted HR = 2.41, 95% CI: 1.63 to 3.57). The variable KK class presented a similar distribution in low- and high-risk patients according to TIMI and PURSUIT best cutoff values. On the contrary, we found a significant association between KK class and ST monitoring: KK class was higher among patients with ST events (Table 7).

Similarly, the serum creatinine level at admission—which is part of the GRACE score, but not the TIMI and PURSUIT scores—was as-

sociated with the primary end point (unadjusted HR = 1.30, 95% CI: 1.53 to 1.46). The GRACE and PURSUIT scores, but not the TIMI score, discriminated patients with higher baseline creatinine (Table 7).

When adjusted for the presence of ST events and the best cutoff value of TIMI and PURSUIT scores, KK class and creatinine were independent prognostic markers and supplanted the prognostic effect of ST events, without affecting the value of each individual score.

Risk Scores and ST Monitoring—Interaction with Revascularization

Despite their higher prevalence and severity of coronary artery disease, patients with ST events were managed invasively with coronary angiography and revascularization before discharge at similar rates as those patients without ST events (Table 2).

The primary end point occurred at similar rates in patients submitted or not to revascularization during hospitalization (14.3% vs 17.2%, HR = 0.81,

Table 3. In-Hospital Management and Primary End Points at 1 Year

	All n = 234	ST Event n = 54	No ST Event n = 180	P
Drug therapy, n (%)				
ASA	226 (96.6)	52 (96.3)	174 (96.7)	NS
Dual antiplatelets	217 (92.7)	51 (94.4)	166 (92.2)	
UFH/LMWH	226 (96.6)	53 (98.1)	173 (96.1)	NS
GP IIb/IIIa inhibitor	75 (32.1)	19 (35.2)	56 (31.1)	NS
Nitrate	214 (91.5)	50 (92.6)	164 (91.1)	NS
Beta-blocker	200 (85.5)	46 (85.5)	154 (85.6)	NS
Calcium channel Blocker	23 (9.8)	9 (16.7)	14 (7.8)	NS
ACE inhibitor	183 (78.2)	42 (77.8)	141 (78.3)	NS
Statin	226 (96.6)	51 (94.4)	175 (97.2)	NS
Coronariography, n (%)	204 (87.2)	49 (90.7)	155 (86.1)	NS
CAD, n (%)*	208 (93.3)	52 (100)	156 (91.2)	0.025
Multivessel CAD, n (%)	168 (76.7)	49 (94.2)	119 (71.3)	<0.001
Revascularization, n (%)				
PCI	103 (44.0)	24 (44.4)	79 (43.9)	NS
CABG	45 (19.2)	14 (25.9)	40 (22.2)	NS
Primary end point at 1-year follow-up				
Death or MI, n (%)	36 (15.4)	14 (25.9)	22 (12.2)	0.019
Death, n (%)	19 (8.1)	8 (14.8)	11 (6.1)	0.044

ASA = Aspirin; UFH = unfractionated heparin; LMWH = low-molecular-weight heparin; GP = glycoprotein; ACE = angiotensin-converting enzyme; CAD = coronary artery disease; Multivessel CAD = at least one stenosis >50% in two or more epicardial coronary arteries or in left main artery or prior CABG; PCI = percutaneous coronary intervention; CABG = coronary artery bypass grafting.

*Eleven patients were never submitted to coronary angiography.

95% CI: 0.42 to 1.57). However, we found a significant interaction between the result of ST segment continuous monitoring and the prognostic effect of revascularization during hospitalization: only patients with ST events benefited from revascularization (Fig. 5).

DISCUSSION

This prospective study of patients with NSTEMI-ACS shows that the detection of ST-segment deviation episodes using continuous monitoring of three leads, predicts long-term outcome above and beyond the TIMI and PURSUIT RS, but not the GRACE risk score. Hence, this study underscores

the superiority of the GRACE risk score versus the TIMI and PURSUIT scores for predicting hard clinical events such as death or nonfatal MI by 1-year follow-up.

Table 4. Predictive Accuracy of Each Risk Score at 1-Year Follow-Up

	AUC (95% CI)	Best Cutoff	Odds Ratio (95% CI)
GRACE	0.76 (0.70–0.81)	>124	6.88 (2.67–17.69)
PURSUIT	0.64 (0.58–0.71)	>11	7.19 (1.73–29.94)
TIMI	0.63 (0.57–0.69)	>3	2.48 (1.13–5.44)

Figure 2. ROC curves of each risk score.

Table 5. Comparison of the Predictive Accuracy of the Risk Scores at 1-Year Follow-Up

	Δ AUC	95% CI	P
GRACE vs PURSUIT	0.11	−0.01 a 0.23	0.068
GRACE vs TIMI	0.12	−0.001 a 0.25	0.051
PURSUIT vs TIMI	0.01	−0.11 a 0.13	0.842

Δ AUC = difference between the AUC of the two scores.

Previous studies in patients with NSTEMI-ACS showed the prognostic value of dynamic ST-segment deviations during the first hours of monitoring.^{9,15,21–23} Its independent value from other prognostic factors such as baseline clinical characteristics, ST-segment deviations on baseline ECG, cTn levels, left ventricular function, and severity of coronary disease has also been demonstrated.^{10,14,15,17,24–27}

This is the first study to demonstrate the prognostic value of three leads continuous ST-segment monitoring beyond the TIMI and PURSUIT RS, and the first to compare it with the GRACE risk score in an unselected population. Furthermore, whereas prior studies on continuous ST-segment monitoring have assessed short-term outcomes, the present study evaluated the long-term prognostic value.^{16,28,29}

Figure 3. Kaplan-Meier curves for the primary end point according to the presence of ST events during 24-hour monitoring.**Table 6.** Prognostic Value of ST Events During 24-Hours Monitoring

Adjusted For:	Hazard Ratio (95% CI)	P
GRACE > 124	1.68 (0.85–3.33)	0.13
TIMI > 3	2.23 (1.13–4.38)	0.02
PURSUIT > 11	2.03 (1.03–3.98)	0.04

In an attempt to understand why ST monitoring added prognostic information to the TIMI and PURSUIT, but not the GRACE risk score, we performed exploratory analyses. Although the three RS share many variables, two variables—the KK class³⁰ and baseline creatinine³¹—are exclusive to GRACE, and seem to explain a significant part of its prognostic value.³ In the present study, the occurrence of ST events was associated not only with worse outcome, but with a higher KK class and baseline creatinine. The PURSUIT score assesses the presence of heart failure at admission, but does not consider its clinical severity. Our study suggests that the KK class adds prognostic value to the PURSUIT score.

The prognostic value of continuous ST-segment monitoring compared to the GRACE score was evaluated in a selected group of patients included in the INTERACT study.^{16,32} In this study, the occurrence of ST events added prognostic information to the GRACE score, a finding that is in contrast with our results. This discrepancy merits two comments. First, all patients of INTERACT received a glycoprotein IIb/IIIa inhibitor as part of their standard treatment, a drug that is currently recommended only for high-risk patients^{1,2}, and which is administered to only 20.8% of patients with NSTEMI-ACS.³³ By contrast, our study population is more representative of the real world, because we included patients with all levels of risk, treated or not with a glycoprotein IIb/IIIa inhibitor. Second, despite the high-risk profile of the INTERACT patients, their incidence of ST events was half (19% in 48 hours) of that seen in our study, suggesting that potent platelet inhibition reduces the frequency of silent ischemia. Hence, ST events probably identified the very high-risk patients in INTERACT.

ST episodes were detected during the 24 hours after admission in 54 patients (23.1%). In previous studies, the incidence of ST episodes during continuous monitoring varies considerably (15% to 77%), probably due to differences in

Figure 4. Distribution of the primary end point for each risk score—dichotomized into low- and high-risk categories—and according to the presence of ST-segment events. Patients with ST-segment events had a higher incidence of primary end points, but the difference is more striking when they are distributed according to TIMI or PURSUIT risk score, than the GRACE risk score.

Table 7. Heart Failure and Creatinine: Prognostic Value

	All Patients n = 234	TIMI ≤ 3 n = 93	TIMI > 3 n = 141	P
Killip-Kimbal class	1 (1; 1)	1 (1; 1)	1 (1; 1)	NS
Creatinine, mg/dL	1.1 (1.0; 1.3)	1.1 (0.9; 1.3)	1.2 (1.0; 1.3)	NS
	All patients n = 234	PURSUIT ≤ 11 n = 65	PURSUIT > 11 n = 169	P
Killip-Kimbal class	1 (1; 1)	1 (1; 1)	1 (1; 1)	NS
Creatinine, mg/dL	1.1 (1.0; 1.3)	1.0 (0.9; 1.2)	1.2 (1.0; 1.4)	<0.001
	All patients n = 234	ST events n = 180	No ST events n = 54	P
Killip-Kimbal class	1 (1; 1)	1 (1; 1)	1 (1; 2)	0.001
Creatinine, mg/dL	1.1 (1.0; 1.3)	1.1 (1.0; 1.3)	1.2 (1.0; 1.5)	0.028
	All patients n = 234	Without primary end point n = 198	With primary end point n = 36	P
Killip-Kimbal class	1 (1; 1)	1 (1; 1)	1 (1; 3)	0.001
Creatinine, mg/dL	1.1 (1.0; 1.3)	1.1 (1.0; 1.3)	1.3 (1.1; 1.9)	<0.001

Figure 5. Distribution of the primary end point according to performance of a revascularization procedure during hospitalization.

inclusion criteria, therapeutic strategies, and duration of monitoring.^{14,16,17,24,26,34–36} We found ST episodes more often in older patients, with previous history of MI or CABG, with ST-segment depression on admission ECG, heart failure, and more severe coronary artery disease—all factors of poor prognosis. These results are consistent with findings of previous studies.^{16,17,35}

Clinical Implications

Our results support the use of the GRACE risk score in all patients with suspected NSTEMI-ACS. Continuous monitoring of the ST segment in the first hours after admission for ACS is a good method for detection of recurrent ischemia, and may guide the management strategy especially when patients are initially stratified by TIMI or PURSUIT risk score, and possibly when they are treated with glycoprotein IIb/IIIa inhibitors. Furthermore, our study suggests that the most appropriate treatment for patients with ST events is invasive stratification using coronary angiography, followed by revascularization when appropriate.

Study Limitations

Patients with ECG abnormalities that compromise the detection of ischemia by ST-segment

analysis—left bundle branch block and ventricular pacing—were not included.

The physicians involved in treatment decisions had access to the results of the ST-segment trends. This may have influenced the management of patients, and underestimated the prognostic value of ST monitoring.

The sensitivity of ST-segment continuous monitoring using 12-leads is superior to 3-leads.³⁶

CONCLUSION

Continuous monitoring of the ST segment in the first 24 hours after NSTEMI-ACS provides long-term prognostic information beyond the initial stratification with TIMI and PURSUIT RS, but not GRACE risk score. The GRACE score is thus superior to the TIMI and PURSUIT scores for long-term risk stratification.

REFERENCES

1. Anderson JL, Adams CD, Antman AM, et al. ACC/AHA 2007 guidelines for the management of patients with unstable angina/non-ST-elevation myocardial infarction: A report of the American College of Cardiology/American Heart Association Task Force on practice guidelines (Writing Committee to revise the 2002 guidelines for the management of patients with unstable angina/non-ST-elevation myocardial infarction): Developed in collaboration with the American College of Emergency Physicians, American College of Physicians, Society for Academic Emergency Medicine,

- Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. *J Am Coll Cardiol* 2007;50:e1-e157.
2. Hamm C, Ardissino D, Boersma E, et al. Guidelines for the diagnosis and treatment of non-ST-segment elevation acute coronary syndromes: The task force for the diagnosis and treatment of non-ST-segment elevation acute coronary syndromes of the European Society of Cardiology. *Eur Heart J* 2007;28:1598-1660.
3. Granger CB, Goldberg RJ, Dabbous OH, et al. For the Global Registry of Acute Coronary Events Investigators. Predictors of hospital mortality in the global registry of acute coronary events. *Arch Intern Med* 2003;163:2345-2353.
4. Antman EM, Cohen M, Bernink PJLM, et al. The TIMI risk score for unstable angina/non-ST elevation MI. *J Am Med Assoc* 2000;284:835-842.
5. Boersma E, Pieper KS, Steyerberg EW, et al. For the PURSUIT Investigators. Predictors of outcome in patients with acute coronary syndromes without persistent ST-segment elevation. Results from an international trial of 9461 patients. *Circulation* 2000;101:2557-2567.
6. de Araujo Goncalves P, Ferreira J, et al. TIMI, PURSUIT, and GRACE risk scores: Sustained prognostic value and interaction with revascularization in NSTEMI-ACS. *Eur Heart J* 2005;26:865-872.
7. Wong CK, White HD. Value of community-derived risk models for stratifying patients with non-ST elevation acute coronary syndromes. *Eur Heart J* 2005;26:851-852.
8. Yan AT, Yan RT, Tan M, et al. In-hospital revascularization and one year outcome of acute coronary syndrome patients stratified by the GRACE risk score. *Am J Cardiol* 2005;96:913-916.
9. Gottlieb SO, Weisfeldt ML, Ouyang P, et al. Silent ischemia as a marker for early unfavorable outcomes in patients with unstable angina. *N Engl J Med* 1986;314:1214-1219.
10. Langer A, Freeman MR, Armstrong PW. ST segment shift in unstable angina: Pathophysiology and association with coronary anatomy and hospital outcome. *J Am Coll Cardiol* 1989;13:1495-1502.
11. Langer A, Minkowitz J, Dorian P, et al. Pathophysiology and prognostic significance of Holter-detected ST segment depression after myocardial infarction. The Tissue Plasminogen Activator: Toronto (TPAT) Study Group. *J Am Coll Cardiol* 1992;20:1313-1317.
12. Andersen K, Eriksson P, Dellborg M. Non-invasive risk stratification within 48 h of hospital admission in patients with unstable coronary disease. *Eur Heart J* 1997;18:780-788.
13. Holmvang L, Andersen K, Dellborg M, et al. Relative contributions of a single-admission 12-lead electrocardiogram and early 24-hour continuous electrocardiographic monitoring for early risk stratification in patients with unstable coronary artery disease. *Am J Cardiol* 1999;83:667-674.
14. Norgaard BL, Andersen K, Dellborg M, et al. Admission risk assessment by cardiac troponin T in unstable coronary artery disease: Additional prognostic information from continuous ST segment monitoring. TRIM study group. *Thrombin Inhibition in Myocardial Ischemia. J Am Coll Cardiol* 1999;33:1519-1527.
15. Jernberg T, Lindahl B, Wallentin L. The combination of a continuous 12-lead ECG and troponin T: A valuable tool for risk stratification during the first 6 hours in patients with chest pain and a nondiagnostic ECG. *Eur Heart J* 2000;21:1464-1472.
16. Yan A, Yan R, Tan M, et al. Long-term prognostic value and therapeutic implications of continuous ST-segment monitoring in acute coronary syndrome. INTERACT Investigators. *Am Heart J* 2007;153:500-506.
17. Aguiar C, Ferreira J, Seabra-Gomes R. Prognostic value of continuous ST segment monitoring in patients with non-ST-segment elevation acute coronary syndromes. *Ann Noninvasive Electrocardiol* 2002;7:29-39.
18. Drew BJ, Krucoff MW. Multilead ST-segment monitoring in patients with acute coronary syndromes: A consensus statement for healthcare professionals. ST Segment Monitoring Practice Guideline International Working Group. *Am J Crit Care* 1999;6:372-386.
19. Morrow DA, Antman EM, Snapinn SM, et al. An integrated clinical approach to predicting the benefit of tirofiban in non-ST elevation acute coronary syndromes. Application of the TIMI risk score for UA/NSTEMI in PRISM-PLUS. *Eur Heart J* 2002;23:223-229.
20. Thygesen K, Alpert JS, White HD. On behalf of the Joint ESC/ACCF/AHA/WHF Task Force for the Redefinition of Myocardial Infarction. Universal definition of myocardial infarction. *Eur Heart J* 2007;28:2525-2538.
21. Cohn PF, Fox KM, Daly C. Silent myocardial ischemia. *Circulation* 2003;108:1263-1277.
22. Krucoff MW, Johanson P, Baeza R, et al. Clinical utility of serial and continuous ST-segment recovery assessment in patients with acute ST-elevation myocardial infarction: Assessing the dynamics of epicardial and myocardial reperfusion. *Circulation* 2004;110:e533-e539.
23. Akkerhuis KM, Klootwijk PA, Lindeboom W, et al. Recurrent ischaemia during continuous multilead ST-segment monitoring identifies patients with acute coronary syndromes at high risk of adverse cardiac events: Meta-analysis of three studies involving 995 patients. *Eur Heart J* 2001;22:1997-2006.
24. Patel DJ, Holdright DR, Knight CJ, et al. Early continuous ST-segment monitoring in unstable angina: Prognostic value additional to the clinical characteristics and the admission electrocardiogram. *Heart* 1996;75:222-228.
25. Langer A, Singh N, Freeman MR, et al. Detection of silent ischemia adds to the prognostic value of coronary anatomy and left ventricular function in predicting outcome in patients with unstable angina. *Can J Cardiol* 1995;11:117-122.
26. Jernberg T, Lindahl B, Wallentin L. ST-segment monitoring with continuous 12-lead ECG improves early risk stratification in patients with chest pain and ECG nondiagnostic of acute myocardial infarction. *J Am Coll Cardiol* 1999;34:1413-1419.
27. Shaun GG, Barr A, Sobtchouk A, et al. Low molecular weight heparin decreases rebound ischemia in unstable angina or non-Q-wave myocardial infarction: The Canadian ESSENCE ST Segment Monitoring Substudy. *J Am Coll Cardiol* 2000;36:1507-1513.
28. Romeo F, Rosano GM, Martuscelli E, et al. Unstable angina: Role of silent ischemia and total ischemic time (silent plus painful ischemia), a 6-year follow-up. *J Am Coll Cardiol* 1992;19:1173-1179.
29. Pozzati A, Bugiardini R, Borghi A, et al. Transient ischaemia refractory to conventional medical treatment in unstable angina: Angiographic correlates and prognostic implications. *Eur Heart J* 1992;13:360-365.
30. Steg PG, Dabbous OH, Feldman LJ, et al. For the Global Registry of Acute Coronary Events Investigators. Determinants and prognostic impact of heart failure complicating acute coronary syndromes: Observations from the Global Registry of Acute Coronary Events (GRACE). *Circulation* 2004;109:440-442.
31. Santopinto JJ, Fox KA, Goldberg RJ, et al. for the Global Registry of Acute Coronary Events Investigators. Creatinine clearance and adverse hospital outcomes in patients with acute coronary syndromes: Findings from Global Registry of Acute Coronary Events (GRACE). *Heart* 2003;89:1003-1008.

32. Goodman SG, Fitchett D, Armstrong PW, et al. Randomized evaluation of the safety and efficacy of enoxaparin versus unfractionated heparin in high-risk patients with non-ST-segment elevation acute coronary syndromes receiving the glycoprotein IIb/IIIa inhibitor eptifibatide. *Circulation* 2003;107:238-244.
33. Mandelzweig L, Battler A, Boyko V, et al. Euro Heart Survey Investigators. The second Euro Heart Survey on acute coronary syndromes: Characteristics, treatment, and outcome of patients with ACS in Europe and the Mediterranean Basin in 2004. *Eur Heart J* 2006;27:2285-2293.
34. Akkerhuis KM, Maas AC, Klotwijk PA, et al. Recurrent ischemia during continuous 12-lead ECG-ischemia monitoring in patients with acute coronary syndromes treated with eptifibatide: Relation with death and myocardial infarction. PURSUIT ECG-Ischemia Monitoring Substudy Investigators. Platelet glycoprotein IIb/IIIa in unstable angina: Receptor suppression using integrilin therapy. *J Electrocardiol* 2000;33:127-136.
35. Patel DJ, Knight CJ, Holdright DR, et al. Pathophysiology of transient myocardial ischemia in acute coronary syndromes. Characterization by continuous ST-segment monitoring. *Circulation* 1997;95:1185-1192.
36. Klotwijk P, Meij S, von Es GA, et al. Comparison of usefulness of computer assisted continuous 48-h 3-lead with 12-lead ECG ischaemia monitoring for detection and quantitation of ischaemia in patients with unstable angina. *Eur Heart J* 1997;18:931-940.