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Comparative clinical implications of admission electrocardiographic findings for patients with non-ST-segment elevation myocardial infarction

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Abstract

Early risk stratification is crucial for appropriate management using invasive strategies in non-ST elevation myocardial infarction (NSTEMI), and electrocardiography (ECG) has been widely used for risk stratification. However, ECG findings in NSTEMI vary, and there is a need to define the clinical characteristics and outcomes according to ECG.

We analyzed the admission ECGs of 345 NSTEMI patients who underwent coronary angiography from 2006 to 2013. Demographics, procedural characteristics, and clinical outcomes were analyzed.

The ST-segment depression, T-wave inversion, and no ECG change groups included 114, 90, and 141 patients, respectively. The ST-segment depression group trended toward older, nonsmoking, and female, with a lower body mass index (BMI) and a higher incidence of comorbidities, than the no ECG change group. The ST-segment depression group also had a higher Killip class, a lower left ventricular ejection fraction, a higher regional wall motion score index (RWMSI), and 3-vessel coronary artery disease angiographically, than the no ECG change group. Patients with T-wave inversion trended toward older, female, lower BMI, less smoking, lower creatine kinase MB, and more left anterior descending (LAD) artery involvement, than the no ECG change group. In clinical outcomes, the ST-segment depression group had a higher mortality rate at 30 days and 12 months after the index procedure than the no ECG change group, whereas the T-wave inversion group showed similar clinical outcomes.

Patients with ST-segment depression have a greater burden of comorbidities with risk factors and worse clinical outcomes, whereas patients with T-wave inversion have an intermediate number of risk factors but similar outcomes, compared with the no ECG change group. Further study is necessary to evaluate the prognostic impact of the baseline ECG on admission.

Abbreviations: ACEi = angitension-converting enzyme Inhibitor, ARB = angiotension receptor blocker, BMI = body mass index, CABG = coronary artery bypass graft, CK = creatine kinase, CKMB = creatine kinase MB, ECG = electrocardiogram, GPCRs = G-protein-coupled receptors, GRKs = G-protein-coupled receptor kinases, LAD = left anterior descending artery, LBBB = left bundle branch block, LVEF = left ventricular ejection fraction, NSTEMI = non-ST-segment elevation myocardial infarction, PCI = percutaneous coronary intervention, RWMSI = regional wall motion score index.

Keywords: coronary artery disease, myocardial infarction, percutaneous coronary intervention

1. Introduction

As non-ST-segment elevation myocardial infarction (NSTEMI) encompasses a wide spectrum of clinical presentations with different clinical characteristics and outcomes, early risk stratification is crucial for appropriate management using invasive strategies. In a real-world practice, the electrocardiogram (ECG) on admission has been widely used for rapid risk stratification of patients presenting with chest pain, due to its simplicity, easy accessibility, safety, and low cost. ECG findings in NSTEMI at presentation show several variations, including ST-segment depression, T-wave inversion, and no ECG change. ST-segment depression and T-wave inversion are relatively well studied,[1–3] but limited data are available on the clinical characteristics and outcomes of patients with NSTEMI presenting with no ECG change.

Therefore, we analyzed and compared demographics, procedural characteristics, and clinical outcomes of NSTEMI with ST-segment depression, T-wave inversion, and no ECG change.

2. Material and methods

2.1. Study populations

Of 400 patients diagnosed with NSTEMI, 347 (86.7%) underwent coronary angiography from June 2006 to May 2013. The decision to perform coronary angiography was at the physician's discretion, based on the patient's medical history and clinical status.

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Patients were divided into 3 subgroups according to initial ECG on admission: T-wave inversion, ST-segment depression, and no change. ST-segment depression was defined as new, or presumed new, horizontal, or downsloping ST-segment depression >0.05 mV in 2 contiguous leads below the isoelectric line on the ECG. T-wave inversion was defined as new, or presumed new, T-wave inversion of >0.1 mV in 2 contiguous leads, with a prominent R wave or R/S ratio >1 within the first 24 hours of presentation. The ECG was considered to have no ischemic change if the first ECG did not reveal ST-segment depression or T-wave inversion. ST-segment depression accompanied by T-wave inversion was defined as ST-segment depression. Left bundle branch block (LBBB) in the initial ECG was excluded from analysis because a subgroup cannot be categorized.

Basic demographics, procedural characteristics, and clinical outcomes were compared between the 2 groups. This study was approved by the institutional review board of Kyung Hee University Hospital at Gangdong, and the requirement for informed consent was waived due to the retrospective nature of the analysis.

2.2. Intervention procedure

Plain balloons were used in percutaneous coronary intervention (PCI) when the culprit artery was <2.5 mm. Drug-eluting stents were implanted exclusively when the culprit artery was ⩾ 2.5 mm. Stent implantation was performed according to standard techniques, and stents were selected at the physician's discretion. Complete lesion coverage was recommended, in addition to angiographic optimization with <20% residual stenosis by visual estimate. During the procedure, patients received a bolus of 100 IU/kg heparin, with a repeated bolus of 3000 IU heparin to maintain an activated clotting time ≥300 seconds. All patients were treated daily with 100 mg aspirin indefinitely, and 75 mg clopidogrel or 100 mg ticagrelor daily for at least 12 months.

2.3. Definition

NSTEMI was defined as typical symptoms within 12 hours, with elevated creatine kinase (CK)-MB or troponin-I, without ST-segment elevation in the ECG. The culprit lesion was determined at angiography by 2 independent physicians. An occluded artery was defined as a lesion with 100% stenosis with Thrombolysis In Myocardial Infarction (TIMI) flow 0. Chronic kidney disease was defined as serum creatinine levels greater than 1.4 mg/dL. A quantitative assessment of left ventricular systolic function was performed using the biplane modified Simpson method to calculate the ejection fraction. Congestive heart failure was defined as a left ventricular ejection fraction (LVEF) <40% on echocardiography.

2.4. Statistical analysis

Data are expressed as the mean ± SD for continuous variables and frequencies for categorical variables. Continuous variables were compared using an unpaired Student t test and categorical variables with a Chi-square test. A P value of <0.05 was considered statistically significant. The analyses were performed using SPSS (version 12.5; SPSS Inc., Chicago, IL).

3. Results

NSTEMI was suspected in 400 patients; of these, 347 underwent coronary angiography and were confirmed as having NSTEMI. The number of patients with ST-segment depression, T-wave inversion, or no change was 114, 90, and 141, respectively. Two patients with LBBB were excluded from the analysis. Baseline characteristics are summarized in Table 1.

Patients with ST depression trended toward older, female, lower body mass index (BMI), less smoking, and more comorbidities such as hypertension, diabetes, chronic kidney disease, congestive heart failure, and cerebrovascular accidents, than those with no ECG change. The ST-depression group also showed a higher Killip class (III or IV), a more rapid heart rate, a lower LVEF, and a higher regional wall motion score index (RWMSI), than the no ECG change group. Patients with T-wave inversion trended toward older, female, lower BMI, less smoking, lower diastolic blood pressure on admission, and lower CKMB than the no ECG change group. Angiographic data are presented in Table 2. The ST-segment depression group had a higher incidence of 3-vessel coronary artery disease, while left anterior descending (LAD) artery involvement was higher in the T-wave inversion group, than the no ECG change group.

The data of clinical outcomes are presented in Table 3. The ST-segment depression group showed higher 30-day and 12-month mortalities than the no ECG change group. In contrast, the T-wave inversion group and the no ECG change group showed similar clinical outcomes.

The ST-depression group was divided into 2 subgroups: PCI within 24 hours and PCI more than 24 hours after admission. A total of 89 patients (78.0%) underwent PCI within 24 hours of admission. The incidence of in-hospital mortality did not differ between the 2 groups (30-day mortality: within 24 hours vs more than 24 hours, 17.5% vs 8.7%, $P=0.296$; 12-month mortality: within 24 hours vs more than 24 hours, 19.7% vs 13.0%, $P=0.457$) (data not shown).

The Kaplan–Meier curves in Fig. 1 show that death- and event-free survival within 1 year were significantly higher in the ST-depression group than in the other 2 groups.

Univariate and multivariate analyses were performed for death at 12 months. Age, type of ECG at admission, weight, hypertension, Killip class, LVEF at index admission, RWMSI at admission, LAD culprit lesion, and 3-vessel disease were associated with death at 12 months in univariate analysis. In multivariate analysis, age [odds ratio (OR) = 1.165, 95% confidence interval (95% CI) = 1.053–1.290, $P=0.003$], LAD culprit lesion (OR = 20.359, 95% CI = 1.528–271.190, $P=0.023$), and hypertension (OR = 10.407, 95% CI = 1.072–101.063, $P=0.043$) were independent predictors of death at 12 months.

4. Discussion

The present study shows that the ST-segment depression group was associated with older age, higher incidence of comorbidities, and severe coronary artery disease than the no ECG change group. The T-wave inversion group had an intermediate number of risk factors compared with the no ECG group. The ST-segment depression group showed poor clinical outcomes, whereas the T-wave group showed similar clinical outcomes, compared with the no ECG change group.

In previous studies,[1–4] ST-segment depression has been a predictor of poor outcomes in NSTEMI. In particular, short-term and long-term incidences of death or myocardial infarction were higher in patients with acute coronary syndrome presenting with ST-segment depression, compared with those presenting with T-wave inversion or no ECG change. The reason that ST-segment

Table 1

Baseline characteristics of the study population.

	ST-segment depression (n = 114)	T-wave inversion (n = 90)	No ECG change (n = 141)
Age, y	69.7 ± 11.3†	64.7 ± 12.4*	60.1 ± 12.5
Males, (%)	70 (61.4%)†	51 (56.6%)†	115 (81.5%)
Height, cm	161 ± 8†	161 ± 9*	165 ± 8
Weight, kg	60.8 ± 11.1†	63.6 ± 12.2*	68.5 ± 11.8
BMI	23.2 ± 3.9*	24.3 ± 3.5	24.8 ± 3.5
Hypertension, (%)	78 (68.4%)*	56 (62.2%)	75 (53.1%)
Diabetes, (%)	51 (44.7%)*	26 (28.9%)	40 (28.3%)
Smoking, (%)	55 (48.2%)*	47 (52.2%)*	102 (72.3%)
Dyslipidemia, (%)	16 (14.0%)	19 (21.1%)	22 (15.6%)
Previous PCI, (%)	10 (8.7%)	6 (6.6%)	9 (6.3%)
Previous CABG, (%)	1 (0.8%)	0	0
Peripheral artery disease, (%)	3 (2.6%)	0	0
Chronic kidney disease, (%) (Creatinine >1.4 mg/dL)	21 (18.4%)*	10 (11.1%)	6 (4.2%)
Congestive heart failure, (%)	10 (8.7%)†	1 (1.1%)	0
Cerebrovacular disease, (%)	24 (21.0%)*	7 (7.7%)	14 (9.9%)
Killip class, (%)			
I	78 (68.4%)*	76 (84.4%)	122 (86.5%)
II	0	1 (1.1%)	4 (2.8%)
III	20 (17.5%)*	9 (10%)	9 (6.3%)
IV	16 (14.0%)*	4 (4.4%)	6 (4.2%)
LVEF, %	53.5 ± 12.7†	56.4 ± 12.3	58.8 ± 9.9
LVEF <40% on index echocardiogram, (%)	14 (12.2%)	7 (7.7%)	10 (7.0%)
Regional wall motion score index (RWMSI)	1.41 ± 0.39*	1.36 ± 0.36	1.29 ± 0.33
Heart rate on admission, bpm	85 ± 23*	76 ± 18	77 ± 19
Systolic blood pressure on admission, mm Hg	136 ± 30	134 ± 26	137 ± 28
Diastolic blood pressure on admission, mm Hg	78 ± 16	77 ± 13*	81 ± 15
CKMB on admission, mg/dL	22.5 ± 50.0	17.4 ± 29.1*	24.9 ± 44.8
CKMB at peak, mg/dL	66.6 ± 87.9	38.9 ± 63.4†	69.0 ± 84.0
Troponin-I on admission, mg/dL	4.6 ± 7.9	3.8 ± 6.9	4.1 ± 8.5
Time from admission to angiography within 24 h, (%)	89 (78.0%)	71 (78.8%)	114 (80.8%)
Medications			
Aspirin	108 (94.7%)	88 (97.7%)	136 (96.4%)
Thienopyridine	109 (95.6%)	88 (97.7%)	136 (96.4%)
Beta blocker	80 (70.1%)	61 (67.7%)	100 (70.9%)
ACEi or ARB	86 (75.4%)	67 (74.4%)	99 (70.2%)
Statin	99 (86.8%)	88 (97.7%)	132 (93.6%)

ACEi = angitension-converting enzyme Inhibitor, ARB = angiotension receptor blocker, BMI = body mass index, CABG = coronary artery bypass graft, CKMB = creatine kinase MB, LVEF = left ventricular ejection fraction, PCI = percutaneous coronary intervention.

* *P* values are <0.05 in comparison with the no ECG change group.

† *P* values are <0.001 in comparison with the no ECG change group.

depression is related to poor clinical outcomes may be accompanying comorbidities. In the present study, underlying comorbidities, including diabetes, chronic kidney disease, congestive heart failure, Killip class ≥III, and older average age were significantly more common, and disease severity as seen on angiography was more severe in the ST-depression group than in the no ECG change group. Previous studies have also shown similar baseline and clinical characteristics in the ST-segment depression group.[4,5] In particular, these comorbidities in the ST-depression group and the no ECG change group were more distinct than those seen in previous studies,[4,5] which may suggest that our study population is a real-world practice, including more high-risk patients than other randomized studies. However, some studies[6,7] reported that hospital mortality increased as the number of cardiovascular risk factors declined. But these results are not matched with our results or those of others,[2,4,8–10] and they did not evaluate factors such as metabolic syndrome, novel risk markers, and infarct size, as well as the severity of elevated blood pressure, plasma glucose, and plasma lipids even though they considered 5 traditional significant risk factors.[11]

On the contrary, the T-wave inversion group seemed to have an intermediate number of risk factors, but in-hospital cardiovascular events were similar to those in the no ECG change group. These results are well matched with those of a previous study,[4] which showed that isolated negative T waves on the admission ECG were associated with less severe coronary disease and relatively benign prognosis, as compared with ST-segment changes among patients with acute coronary syndrome.

Overall, early aggressive medical and interventional treatment including coronary angiography in patients with ST-segment change could help improve clinical outcomes. However, in our study, early invasive treatment within 24 hours of admission did not improve the clinical outcome compared with a delayed invasive strategy in the ST-depression group. In a recently published study,[12] the primary outcome was shown to be significantly better in the early intervention group than in the delayed intervention group in higher-risk patients, even though the routine early intervention group did not show a significant difference in the primary outcome, compared with the delayed intervention group in acute coronary syndrome. The reason why the early invasive strategy in our study did not improve early and

Table 2

Angiographic characteristics of the study population.

	ST-segment depression (n = 114)	T-wave inversion (n = 90)	No ECG change (n = 141)
Lesion characteristics			
Culprit coronary vessel, (%)			
Left anterior descending	50 (43.8%)	52 (55.5%)*	50 (35.4%)
Left circumflex	26 (22.8%)	10 (11.1%)*	48 (34.0%)
Right coronary	34 (29.8%)	27 (30.0%)	39 (27.6%)
Left main	4 (3.5%)	1 (1.1%)	4 (2.8%)
Culprit location, (%)			
Proximal	57 (50.0%)	38 (42.2%)	52 (36.8%)
Middle	29 (25.4%)	44 (48.8%)	45 (31.9%)
Distal	28 (24.6%)	18 (20.0%)	44 (31.2%)
Number of diseased vessels, (%)			
Single	29 (25.4%)*	31 (34.4%)	61 (43.2%)
Double	24 (21.0%)	31 (34.4%)	33 (23.4%)
Triple	61 (53.5%)*	28 (31.1%)	47 (33.3%)
Revascularization	112 (98.2%)	88 (97.7%)	136 (96.4%)
Successful PCI, (%)	100 (87.7%)	85 (94.4%)	133 (94.3%)
Pre-PCI TIMI 0, (%)	27 (23.6%)	21 (23.3%)	30 (21.2%)
Post-PCI TIMI 3, (%)	108 (94.7%)	88 (97.7%)	138 (97.8%)
Quantitative coronary angiography			
Reference vessel diameter, mm	2.8 ± 0.4	3.1 ± 2.0	2.7 ± 0.4
Stent length, mm	21.8 ± 7.8	23.2 ± 0.7	21.4 ± 7.8
Stent diameter, mm	2.8 ± 0.4	2.9 ± 0.3	2.7 ± 0.4
Number of stent, mm	1.3 ± 0.7	1.4 ± 0.7	1.3 ± 0.6

PCI = percutaneous coronary intervention.

* *P* values are <0.05 in comparison with the no ECG change group.

long-term clinical outcomes in the ST-depression group is unclear, but we suspect that high-risk patients may undergo earlier revascularization at the physician's discretion. The population in the ST-depression group was heterogeneous, and the revascularization rate was higher than in a previous study,[12] which also could affect the results. However, the number of patients involved was relatively small and this study had a retrospective design; therefore, further large-scale, prospective randomized studies are necessary to evaluate this hypothesis.

In some individuals, coronary artery disease is not associated with risk factors, suggesting that other genetic factors contribute to a predisposition to coronary atherosclerosis and thrombotic complications. Clinical and experimental studies have suggested that certain genetic polymorphisms are associated with vascular function and coronary artery disease, including CaMK4,[13] glycoprotein IIIa PIA2,[14,15] and G-protein coupled receptor kinases (GRKs).[16,17] In particular, PIA1/A2 has been one of the most investigated GP IIIa genetic polymorphisms that can influence both platelet activation and aggregation.[18] GRKs classically desensitize receptor signal transduction, thus preventing hyperactivation of G-protein coupled receptors (GPCRs) in second-messenger cascades. Changes in GRK expression have featured prominently in many cardiovascular pathologies, and GRKs have been intensively investigated as potential diagnostic and therapeutic targets.[19]

There were several limitations to our study. First, this analysis is a retrospective, small-sized, single-center investigation, and it is possible that both identified and unidentified confounders, such as drug compliance, inflammatory biomarkers, and genetic factors may have influenced the outcomes. Hence, the results cannot be generalized to other populations. Second, the culprit lesion was located on data collection by 2 independent physicians without central adjudication. This may have led to bias, particularly for patients with multi-vessel disease. Third, approximately 15% of the patients did not have a coronary angiogram, which could be included in selection bias. We did not analyze their clinical

Table 3

Clinical outcomes at 12 months.

	ST-segment depression (n = 114)	T-wave inversion (n = 90)	No ECG change (n = 141)
30-day clinical outcomes			
Death, 30 days, (%)	18 (15.7%)†	2 (2.2%)	5 (3.5%)
Stroke, 30 days, (%)	0	0	1 (0.7%)
12-month clinical outcomes			
Death, 12 months, (%)	24 (21.0%)*	8 (8.8%)	13 (9.2%)
Myocardial Infarction, 12 months, (%)	5 (4.3%)	3 (3.3%)	5 (3.5%)
Stroke, 12 months, (%)	1 (0.8%)	4 (4.4%)	3 (2.1%)
Readmission, 12 months, (%)	17 (14.9%)	11 (12.2%)	17 (12.0%)

* *P* values are <0.05 in comparison with the no ECG change group.

† *P* values are <0.001 in comparison with the no ECG change group.

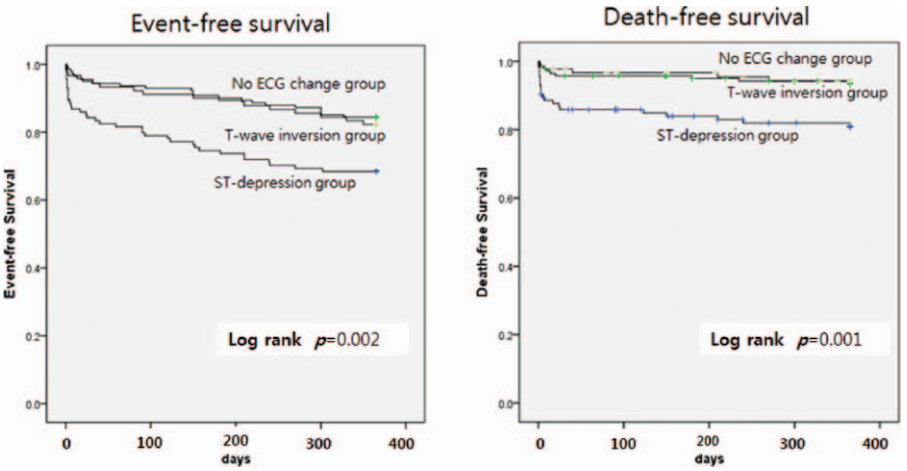

Figure 1. Kaplan–Meier curves.

characteristics and outcomes, which could have affected group characteristics and clinical outcomes according to ECG type. Finally, quantitative ECG analysis was not performed. But there is controversy over the usefulness of quantitative ECG analysis, as it requires more expertise and is more time-consuming than qualitative ECG analysis. Several studies showed that quantitative and qualitative ECG characteristics were independently associated with long-term outcomes.[9,10,20] However, recently published studies showed that quantitative ECG analysis may provide no or only weak incremental prognostic value compared with qualitative ECG analysis.[8,21]

In conclusion, patients with ST-segment depression showed different demographic features with multiple cardiac comorbidities, and had a higher risk of in-hospital and 12-month mortality, than the no ECG change group. The T-wave inversion group had an intermediate burden of baseline findings. However, the clinical outcomes in the T-wave inversion group and no ECG change group were similar. Further study is necessary to evaluate the prognostic impact of the baseline ECG on admission.

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