Association of electrocardiographic changes with severity of coronary artery disease and short term outcome in patients with non-ST-segment elevation acute coronary syndromes

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ABSTRACT

الأهداف: تقييم العلاقة بين تغيرات تخطيط القلب الكهربائي (ECG) في المرضى المصابين بمتلازمة الشريان التاجي الحاد NSTE-ACS مع عدم ارتفاع وصلة ST، و شدة مرض الشريان التاجي (CAD)، و النتائج قصيرة المدى.

الطريقة: اشتملت هذه الدراسة المقطعية الوصفية 111 مريض يراجعون مستشفى شهيد مدني للقلب خلال الفترة من مارس 2005 حتى مارس 2007م و تسجيل من يعانون من متلازمة الشريان التاجي الحادة مع عدم ارتفاع وصلة ST، و خضعوا لتصوير الأوعية الشريانية خلال مؤشر الحدث.

النتائج: اشتملت هذه الدراسة على 111 مريض (64 ذكر، و 47 أنثى) مع نتائج قصيرة المدى و سجل مقدار معدل فترة المراجعة 4.6 ± 1.8 شهر. ارتفع معدل الوفاة لدى المرضى المراجعين الذي يعانون من ارتفاع وصلة ST-T بمقدار 16.7 مقابل 2.7% بقيمة إحصائية p=0.01، و ارتفعت الذبحة المتكررة 36.1مقابل 6.7% بقيمة إحصائية p=0.001، و وذمة الرئة 8.3 مقابل 1.3% بقيمة إحصائية p=0.045. يعد LVEF للمرضى الذين يعانون من تغيرات ECG أقل من الذين لا يعانون من تغيرات ECG بقيمة إحصائية p=0.001. كان قلس المترالي MR منتشر بين الذين يعانون من تغيرات ECG بقيمة إحصائية p=0.006. في التحليل الإحصائي لمتعدد المتغيرات، يعد ضيق صمام ST في تخطيط القلب الكهربائي المنبئ المستقل لقرب الوفاة، و من النتائج الضائرة السريرية لهذا الحدث.

خاتمة: في المرضى المصابين بمتلازمة الشريان التاجي الحاد NSTE-ACS مع عدم ارتفاع وصلة ST، يرتبط انحراف وصلة ST مع النتائج القليلة قصيرة المدى و التي تشمل أمراض الشريان المزمنة CAD، و انخفاض الكسر القذفي للبطين الأيسر LVEF، و انتظام المترالي بشكل منتشر MR.

Objectives: To assess the association between electrocardiogram (ECG) changes in non-ST-segment elevation acute coronary syndrome (NSTE-ACS) patients with severity of coronary artery disease (CAD) and short-term outcome.

Methods: In this cross-sectional descriptive-analytical study, 111 patients admitted to the Cardiology Department of Shahid Madani Heart Hospital, Tabriz, Iran between March 2005 and March 2007 with first NSTE-ACS, and had undergone coronary angiography during index event were evaluated.

Results: One hundred and eleven patients (64 males, and 47 females) were enrolled, and their in-hospital and short-term outcome with a mean follow-up period of 4.6 ± 1.8 months was evaluated. Patients with ST-T changes on admission had higher rates of death (16.7 versus 2.7%, p=0.01), recurrent angina (36.1 versus 6.7%, p=0.001), and pulmonary edema (8.3 versus 1.3%, p=0.045). The mean left ventricular ejection fraction (LVEF) of patients with ECG changes were significantly lower than those without ECG changes (p=0.001). Mitral regurgitation (MR) was also more common among those with ECG changes (p=0.006). In a multivariate regression analysis, the only independent predictor of short-term mortality and adverse clinical event was ST depression on ECG (p=0.001).

Conclusion: In patients with first NSTE-ACS, ST deviation is associated with adverse short-term outcome including more severe CAD, lower LVEF, and more common MR.

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Acute myocardial infarctions are categorized according to admission electrocardiography as ST-elevation myocardial infarction (STEMI) and non-ST elevation myocardial infarction (NSTEMI). This classification is essential, since prognostic and therapeutic implications for each subtype are different.[1] To triage patients presenting with ischemic symptoms, physicians trust the 12-lead electrocardiogram (ECG) to rapidly determine whether patients have an acute STEMI that would benefit from urgent reperfusion.[2] Although unstable angina and NSTEMI were previously considered as separate diagnostic entities, they are now regarded as sharing a common pathophysiologic basis as manifestations along a spectrum of severity of the same disease. Accordingly, the term "non-ST segment elevation acute coronary syndromes" (NSTE-ACS) is now applied for description of these 2 closely related cardiovascular syndromes. The major distinction between unstable angina (UA) and NSTEMI is that in the setting of NSTEMI, macro or microvascular coronary flow is diminished enough to produce detectable myocardial necrosis, which presents with elevation of cardiac enzymes.[3] The ECG remains an important tool that helps rapidly establish a working diagnosis for patients with ischemic symptoms. Other methods of risk stratification such as echocardiography, nuclear scintigraphy, or computed tomographic coronary angiography can provide complementary diagnostic and prognostic information, but are limited by time intensiveness, and limited 24-hour availability.[2] The ST-segment depression and T-wave inversion on admission ECG are important predictors of outcome in patients with NSTE-ACS.[4] The ST-segment depression on admission ECG of patients with NSTE-ACS is associated with higher mortality.[5] Cumulative ST-segment deviation of at least one mm on admission ECG identifies patients at risk for subsequent adverse cardiac events.[6] In this study, we aimed to assess the relation between ECG changes of patients with NSTE-ACS and severity of coronary artery disease (CAD), as well as short-term outcomes.

Methods. This is a single institutional cross-sectional descriptive-analytical study on the association of electrocardiographic changes with severity of CAD, and short-term morbidity and mortality in patients with NSTE-ACS who underwent coronary angiography. In this study, demographic data, basic and clinical parameters, in-hospital and short-term mortality and morbidity of patients who was admitted with NSTE-ACS in the Cardiology Department of Shahid Madani Heart Hospital, Tabriz, Iran, between March 2005 and March 2007 with a mean follow up period of 4.6 ± 1.8 months were evaluated. The ethics committee of Madani Heart Hospital of Tabriz University of Medical Sciences approved the study. Inclusion criteria were first time admission with NSTE-ACS and coronary angiography during index event, and 18 years of age or older. Patients with a previous history of revascularization (percutaneous transluminal coronary angioplasty or coronary artery bypass graft [CABG]), valvular heart disease, cardiomyopathy, history of STEMI, bundle branch block pattern, or evidence of pre-excitation in ECG were excluded from the study. We excluded patients who underwent elective angiography before admission, and those who were taking digoxin. Among 554 patients, 111 cases met the criteria and were enrolled in the study. Patients data including age, gender, previous history of anginal chest pain, diabetes mellitus (DM), hypertension (HTN), history of smoking, family history of CAD, hyperlipidemia, clinical findings on admission, ECG findings on admission, angiographic findings, cardiac events (re-infarction, congestive heart failure, recurrence of angina), and need for revascularization during hospitalization, and in a short-term follow-up period were collected in the questionnaires. Two cardiologists reviewed the coronary angiograms. Diameter stenosis of more than 50% in the left main stem, and more than 60% in other coronary arteries were considered as significant, which is similar to the study of Mueller et al.[4] The ST-segment depression was defined as J-point depression ≥1 mm followed by a horizontal or downsloping ST segment for at least 0.08 seconds. The T-wave inversion was defined as T-wave deviation ≥1 mm from baseline.[4] A more than 2-fold increase in creatine kinase-myocardial band, or a cardiac troponin-I (CTn-I) level of more than 0.2 ng/ml was considered as myocardial infarction. Cardiogenic shock was defined as hemodynamic instability with systolic blood pressure (SBP) less than 80 mm Hg with capillary wedge pressure exceeding 20 mm Hg.

Statistical analyses were performed by the Statistical Package for Social Sciences version 15 software (SPSS Inc., Chicago, IL., USA). Results are presented as mean values and standard deviation (SD). Chi-square analysis was used to compare categorical variables, and comparisons between 2 continuous variables by using student t test. Multivariate logistic regression was used to identify predictors of in-hospital outcome. A *p*-value less than 0.05 was considered statistically significant.

Results. One hundred and eleven patients were enrolled in the study. The mean age of participants was 58.63 ± 11.29 years with a male to female ratio of 64:47. Findings of ECG on admission in different leads are summarized in **Table 1**. Seventy-five patients had no ST-T changes, and 36 patients had ST-T change in at least one ECG lead. Baseline clinical characteristic of patients with, or without ST-changes are summarized in

Table 2. Patients with ECG changes were older and more frequently female, or smokers. They also had higher mean SBP on admission, and more frequently had S_3 gallop on heart auscultation during admission. Other clinical findings and patients' characteristics (notably history of HTN and DM) were not significantly different between the 2 groups. **Table 3** summarizes the short-term events in patients with, and without ECG changes on admission. Patients with ST-T changes on admission had higher rates of death (p=0.01), recurrent angina (p=0.001), and pulmonary edema p=0.045). Although not statistically meaningful, other adverse events were also more frequently observed in patients with ST-T changes. In multivariate regression analysis, the only independent predictor of in-hospital mortality and adverse clinical events was ST depression on ECG (p=0.001). Cardiac catheterization and echocardiographic data are shown in **Table 4**. Mean left ventricular ejection factor (LVEF) of patients with ECG changes was significantly less than those without ECG changes (p=0.001). Mitral regurgitation (MR) was also more common among those with ECG changes (p=0.006). The CAD was found in 80.6% of patients with ST-T changes, and 84% of those without ECG changes. This difference was not statistically meaningful (p=0.654). However, severe forms of CAD including 3 vessel and left main disease were more common in those with ST-T changes (p=0.006). Twenty-one patients in ST-T changes group, and 24 patients among those without ECG changes had 3 vessel involvement on coronary angiography. This difference was statistically significant. However, 2 vessel involvement and one vessel involvement were significantly more common in patients without ECG changes. Frequency of neither culprit arteries was statistically significant among 2 groups. Among 36 patients with ST changes, the recommendation of the cardiologist was CABG in 17, and percutaneous coronary intervention (PCI) in 9 patients, and among those without ST changes, the recommendation for CABG was 19 and 35 for PCI (p=0.06). There was no significant difference in patients undergoing CABG or PCI between 2 groups during hospital course (**Table 3**). Patients with ST elevation in aVR lead among diseased one vessel was one (7.1%), 2 vessel was 3 (21.4%), and 3 vessel was 10 (71.4%) cases. There was no statistically significant difference among them (p=0.106).

Table 1 - Findings of patients' electrocardiogram on admission in different leads.

Lead	ST-depression		T inversion without ST-depression		ST-elevation	
	n (%)					
I	4	(3.6)	-	-	-	-
II	10	(9)	1	(0.9)	-	-
III	5	(4.5)	1	(0.9)	-	-
aVR	1	(0.9)	-	-	15	(13.5)
aVL	7	(6.3)	2	(1.8)	-	-
aVF	7	(6.3)	1	(0.9)	-	-
V_1	-	-	-	-	10	(9)
V_2	6	(5.4)	7	(6.3)	-	-
V_3	14	(12.6)	9	(8.1)	1	(0.9)
V_4	23	(20.7)	13	(11.7)	1	(0.9)
V_5	30	(27)	13	(11.7)	-	-
V_6	16	(14.4)	8	(7.2)	-	-

T - T wave, aVR - augmented voltage left arm, aVL - augmented voltage left arm, aVF - augmented voltage foot, V - voltage

Table 2 - Clinical signs and demographics of patients with and without electrocardiogram changes.

Findings	Patients with ST changes (n=36)	Patients without ST changes (n=75)	*P*-value
	n (%)		
Age (years) (mean ± SD)	62.32 ± 10.70	57 ± 11.22	0.021
Gender (female)	20 (55.6)	27 (36.0)	0.020
History of angina pectoris	25 (69.4)	52 (69.3)	0.528
History of diabetes mellitus	12 (33.3)	16 (21.3)	0.105
History of hypertension	24 (66.7)	39 (52.0)	0.051
History of smoking	27 (75.0)	5 (6.7)	0.021
Positive familial history	0 (0)	3 (4.0)	0.552
History of hyperlipidemia	15 (41.7)	43 (57.3)	0.205
Heart rate/minute (mean ± SD)	82.39 ± 17.81	76.24 ± 15.70	0.074
Systolic blood pressure (mean ± SD)	140.45 ± 28.18	127.04 ± 21.37	0.008
Diastolic blood pressure (mean ± SD)	85 ± 14.47	79.41 ± 13.34	0.053
Third heart sound (S_3) on admission	6 (16.7)	2 (2.7)	0.01
Pulmonary edema on admission	4 (11.1)	2 (2.7)	0.064

Table 3 - Comparison of short-term events between cases with and without electrocardiogram changes.

In-hospital events	Patients with ST changes (n=36)	Patients without ST changes (n=75)	*P*-value
	n (%)		
Mortality rate	6 (16.7)	2 (2.7)	0.01
STEMI	1 (2.8)	0 (0)	0.306
Recurrent AP	13 (36.1)	5 (6.7)	0.001
Pulmonary edema	3 (8.3)	1 (1.3)	0.045
Cardiogenic shock	2 (5.6)	1 (1.3)	0.222
Heart failure	3 (8.3)	2 (2.6)	0.167
Need for CABG	4 (11.1)	5 (6.7)	0.452
Need for PTCA	4 (11.1)	17 (22.7)	0.201

STEMI - ST-elevation myocardial infarction, AP - angina pectoris, CABG - coronary artery bypass graft, PTCA - percutaneous transluminal coronary angioplasty

Table 4 - Catheterization findings of patients with and without ECG changes.

Catheterization findings	Patients with ST changes (n=36)	Patients without ST changes (n=75)	*P*-value
	n (%)		
LVEF (%) (mean ± SD)	42.35 ± 9.47	50.42 ± 8.09	0.001
Coronary vessels involvement	29 (80.6)	63 (84.0)	0.654
MR	16 (44.4)	12 (16.0)	0.006
Severity of CAD			0.006
1 vessel disease	3 (8.3)	24 (32.0)	
2 vessel disease	5 (13.9)	15 (20.0)	
3 vessel disease	21 (58.3)	24 (32.0)	
LMA lesion	4 (11.1)	2 (2.7)	

LVEF - left ventricular ejection fraction, MR - mitral regurgitation, CAD - coronary artery disease, LMA - left main artery

Discussion. For patients with NSTE-ACS, the goals for the physician must stratify risk and decide optimal therapeutic interventions, based on the level of risk. To achieve the goals of risk assessment history, physical examinations, as well as results from ECG, or CTn are available.[3] The ECG predicts the location and size of the injured zone during STEMI. Particularly, ST segment deviations reflect myocardial ischemia, with important information on first-line treatment and severity of disease.[7] The baseline ECG has an important prognostic value for ACS, as the risk of new or reversible ST segment depression greater or equal to 0.5 mm has comparable risks to transient ST elevation, or new left bundle branch block and increased mortality up to 2-fold.[8] It also increases the risk for myocardial infarction (MI) or recurrent rest ischemia, as well as failure of medical therapy from 3 to 6-fold.[9] Sub analysis of the Fast Revascularization during Instability in Coronary artery disease trial (FRISC II) population showed that patients with NSTE-ACS and ST-segment deviation on the admission ECG had poor prognosis.[6] In these patients, angiography and subsequent revascularization were beneficial in reducing mortality and the incidence of MI.[6] In a subgroup analysis of the Treat Angina with Aggrastat and Determine Cost of Therapy with an Invasive or Conservative Strategy-Thrombolysis in Myocardial Infarction (TACTICS-TIMI) 18 trial,[10] the additional information of ST segment deviation and troponin T concentration was assessed. The magnitude of ST-segment deviation and the degree of troponin T elevation predicted the likelihood of failure of a conservative strategy, the extent of CAD, and the likelihood of death or MI in a 6 months follow up. Furthermore, the extent of ST-segment deviation, when added to the degree of troponin T elevation and other baseline characteristics, provided statistically significant additional value regarding the degree of benefit of early invasive management.[10] In patients with NSTEMI, the study by Barrabés et al[11] showed that ST depression in 2 lateral leads (I, aVL, V5, and V6) was associated with

lower LVEF and left main (LM) coronary artery or 3-vessel disease more often than in patients without ST depression in the lateral leads. In a study carried out by Diderholm et al[12] in 2002 in patients with UA, ST depression in ECG on admission is associated with a 100% increase in the prevalence of 3 vessel CAD. In the present study, we concluded that in severe CADs (3 vessel disease), ST depression was significantly more common. In our study, 36 (32.4%) patients had significant ST depression, and this was 38.2% in the study of Muller et al,[4] and 46.2% in the FRISC II study[12] however, it should be noted that significant ST depression was defined as ≥1 mm in the first 2 studies, and ≥0.5mm in the latter.

In this study in patients with NSTE-ACS, mitral insufficiency, recurrent angina pectoris, and S_3 on auscultation occurred more frequently in patients with ST changes in ECG on admission. There are several studies, which have shown that some major post-NSTE-ACS complications are more common in cases with ST depression, as compared with those without ST changes.[11,12] Also, Savonitto et al[13] showed that ST-segment depression provides more information than the simple qualitative assessment of ST-segment depression. Over the years, many criteria have been developed to strengthen the predictive value of ECG.[7] There are several studies that have reported that ST changes of ECG on admission occur more commonly in those NSTE-ACS patients with LMA lesion.[11,14,15] The available evidence proposes that ST elevation in aVR is useful when suspecting LM lesion in patients with NSTEMI, in the sense that its absence largely excludes LM as culprit artery; although this notion is based on data from a limited amount of patients.[7] In the present study, although the frequency of patients with ST elevation in aVR was higher in patients with 3 vessel disease, this was not statistically significant. The combination of ST-segment depression and T-wave inversion is a potent predictor of poorer outcome. This ECG pattern, particularly when recorded in leads V4 and V5 in patients without tachycardia and with concomitant ST-segment elevation in lead aVR, was shown to represent circumferential ischemia often associated with left main or 3 vessel disease.[13]

Combining the subgroup of patients with T-wave inversion, or nonspecific electrocardiographic findings with those who have ST-segment depression has been criticized, because the latter has been shown to be associated with a poorer prognosis.[1,16] Some studies have shown that T-wave inversion was associated with higher mortality.[17] Two studies[18,19] showed that T-wave inversion had no clinical significance when it was associated with ST depression. In contrast, isolated T-wave inversion without ST depression was associated with adverse outcome.[18,19] Mueller et al[4] in a 3-year follow-up of 1,450 consecutive patients with NSTE-ACS, reported mortality rates of 8% in patients with no ECG changes, 19.9% in patients with ST depression, and only 5.1% in patients with T-wave inversion. In our study, patients with on admission ST changes in their ECG had a greater inpatient mortality compared to those without ECG changes.

The present study has some limitations that deserve to be mentioned. One pertains to the restriction of clinical outcomes to short term follow up, with no further follow-up. The relatively small group size is also a limitation. Further studies of a larger population and long-term follow-up are necessary.

In conclusion, the standard 12-lead admission ECG remains as an easy, widely available, and inexpensive method of risk stratifying in patients with NSTE-ACS. The only independent predictor of short- term mortality and adverse clinical events was ST depression on ECG. In patients with first NSTE-ACS, ST deviation is associated with adverse outcome including more severe CAD, lower LVEF, and more common MR.

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