The added value of ST-elevation in lead aVR to clinical thrombolysis in myocardial infarction risk score in predicting the angiographic severity and extent of coronary artery disease in patients with non-ST-elevation acute coronary syndrome

Mohammad F. Badry[a], Khaled M. Elmaghraby[b], Hatem A. Helmy[b], Salwa R. Demitry[b]

[a]Department of Cardiology, Sohag Heart and GIT Center, Sohag, [b]Department of Cardiology, Assiut University, Assiut, Egypt

Correspondence to Hatem A. Helmy, MD
Cardiology, Assist. Prof. of Cardiology,
Department of Cardiology,
Faculty of Medicine, Assiut University,
Assiut, Egypt
Mobile: 01005212162;
e-mail: hatem19652007@yahoo.com

Received 12 February 2018
Accepted 10 April 2018

Journal of Current Medical Research and Practice
May-August 2018, 3:100–105

Introduction
The use of ST-segment elevation (STE) in lead aVR in addition to thrombolysis in myocardial infarction (TIMI) risk score may improve the early risk stratification and the management of patients at high-risk coronary artery disease, with subsequent effect on morbidity and mortality.

Patients and methods
A total of 65 patients who underwent coronary angiograms in Sohag Heart Specialized Center in the period between September 2013 and March 2014 were the participants of the study. All patients were subjected to full history taking, clinical evaluation, laboratory investigations, ECGs, TIMI scoring, and coronary angiography by femoral approach.

Results
Of the 65 patients, 59 patients were found to have significant coronary artery disease with 39 of them had STE in aVR lead, and none of the normal coronary angiography (CA) cases had STE in this lead. Of the 39 with STE-aVR, 13 patients had left main disease and 30 of them had multivessel disease. ST-aVR was elevated in 17 cases with low or intermediate risk according to TIMI score (9.1 and 55% of both groups, respectively), and was normal in three (12%) of the patients with high-risk TIMI score. Thus, STE-aVR could predict another 28.8% of high-risk cases that would not be detected by TIMI.

Conclusion
STE in lead aVR has a diagnostic and prognostic value in patients with non-STE acute coronary syndrome and may provide an additional prognostic value to the conventional cardiovascular risk factors, particularly in patients from the TIMI low-risk and intermediate-risk groups.

Keywords:
acute coronary syndrome, angiography, aVR, coronary, infarction, non-ST-segment elevation, TIMI , ECG

J Curr Med Res Pract 3:100–105

2357-0121

Introduction

The term acute coronary syndrome (ACS) refers to any group of clinical symptoms compatible with acute myocardial ischemia and includes unstable angina (UA), non-ST-segment elevation myocardial infarction (NSTEMI), and ST-segment elevation myocardial infarction (STEMI) [1]. In the spectrum of ACS, UA/NSTEMI is defined by ECG ST-segment depression or prominent T-wave inversion and/or positive biomarkers of necrosis (e.g. troponin) in the absence of ST-segment elevation (STE) and in an appropriate clinical setting (chest discomfort or angina equivalent) [2].

In patients with NSTEMI, ST-segment depression has also been related to the presence of extensive coronary artery disease (CAD) and to a greater benefit of an early invasive therapeutic approach. STE in lead aVR, in combination with other repolarization changes, has been associated with severe coronary artery lesions in patients with UA or STEMI. However, the prognostic significance of this finding is unknown [3].

A number of risk assessment tools have been developed to assist in assessing risk of death and ischemic events in patients with UA/NSTEMI, thereby providing a basis for therapeutic decision making. Antman *et al*. [4] developed the thrombolysis in myocardial infarction (TIMI) risk score, which is a simple tool composed of 7 (1/point) risk indicators that are rated on presentation.

TIMI risk score has been correlated with the severity of CAD with each increase in the score; nevertheless, it was found to lack sensitivity in low-risk and intermediate-risk groups; among them, high-risk CAD was diagnosed by coronary angiography [5]. Moreover, TIMI and many risk scores failed to predict the presence of a culprit lesion [6].

Aim

The aim was to investigate the added value of the presence of STE in lead avR of the 12-lead admission ECG to the TIMI clinical scoring system in predicting the angiographic severity of CAD in patients admitted with NSTEACS.

Patients and methods

Patients

Our study includes 65 patients (37 male and 28 female) with non-STE-segment elevation acute coronary syndrome (NSTEACS) who were presenting to the CCU of Sohag Heart Specialized Center in the period from September 2013 to March 2014.

Inclusion criteria

Inclusion criteria were patients with typical chest discomfort attributed to cardiac ischemia lasting at least 20 min and involving an unstable pattern of pain, including rest pain, new onset, severe, or frequent angina (accelerating angina), as well as ECG of NSTEACS including depressed ST-segment or deeply symmetrical inverted T-wave.

Exclusion criteria

Patients with STE in the surface ECG, patients with conditions precluding the evaluation of QRS duration or ST-segment changes on ECG (left bundle branch block, left ventricular hypertrophy, ventricular pacing, ventricular pre-excitation, nonischemic cardiomyopathy, and antiarrhythmic drugs), and patients with nonischemic or atypical chest pain were excluded from the study.

Methods

All patients were subjected to full history taking with special emphasis on demographic criteria including age and sex; a detailed medical and cardiac history including smoking, hypertension, history of diabetes, either type I or II, previous ischemic heart disease either STEMI or NSTEACS (documented by an old ECG showing evidence of ischemia as STE or depression, pathological Q waves, biochemical markers of necrosis or radioisotope scan showing an area of infarction), and previous coronary artery bypass grafting operation; and clinical examination including local cardiac examination.

ECG was done on admission of the patients at a paper speed of 25 mm/s and amplification of 10 mm/mV. The evaluation of all ECGs was done by an investigator blinded to all other clinical data. ST-segment shifts were measured 80 ms after the J-point for ST-segment depression using the preceding TP segment as the baseline. ST-segment deviation greater than 0.5 mm in any lead is considered significant [7]. Each ECG will be analyzed to assess the following:

(1) The presence and degree of STE in lead aVR (ST-segment shifts measured 20 ms after J-point for STE using the preceding TP segment as the baseline [3]
(2) The presence and degree of ST-segment depression in leads other than lead aVR, and the number of leads showing this depression.

Cardiac troponin I level

Risk stratification was done through TIMI scoring system. All patients underwent risk stratification for CAD according to 7 (1/point) indicators of the clinical scoring system TIMI (4). The seven indicators are as follows: (1) age greater than 65 years, (2) three or more risk factors for CAD, (3) known CAD (CA showing stenosis ≥50%), (4) severe anginal symptoms (≥2 anginal events in preceding 24 h), (5) use of aspirin in the last 7 days; (6) ST-segment deviation greater than 0.05 mV; and (7) elevated serum cardiac markers of necrosis.

Coronary angiography is done either immediately on admission in patients with unstable hemodynamics caused by ischemic attacks and in whom ischemic attacks cannot be controlled by intensive drug treatment or after the patient's condition stabilizes with drug treatment. All coronary angiographies were assessed by an experienced operator blinded to all other clinical data. The angiography is assessed for the severity and distribution of coronary affection where stenosis greater than or equal to 50% in the diameter of the left main coronary artery [8] or stenosis greater than or equal to 70% in one or more of the major epicardial vessels or their main branches was considered clinically significant [9].

The study protocol was agreed by the local Ethical Committee of Faculty of Medicine, Asyut University.

An informed written consent was taken from all patients before inclusion in the study.

Statistical analysis

Statistical package for the social sciences (IBM-SPSS), version 24 IBM (May 2016; SPSS Inc., Chicago, Illinois, USA), and Microsoft Excel 2016 (Microsoft Corporation, Chicago, Illinois, USA) were used for statistical data analysis.

Data are expressed as mean, SD, number, and percentage. Mean and SD were used as descriptive value for quantitative data, whereas number and percentage were used to describe qualitative data.

Student's *t*-test was used to compare the mean between two groups, and Pearson's χ^2 was used to compare percentages of qualitative data.

Sensitivity statistics were used for the possible predictors of coronary involvement.

The level of significance (*P* value) was considered to be 0.05.

Results

The mean age of all patients in our study was approximately 60 years and SD of 9 years only. Of the different risk factors, ischemic heart disease, dyslipidemia, male sex, and diabetes mellitus were significantly associated with increased risk of CAD (Table 1). The patients of the study were divided according to TIMI risk score into three groups as follows: (a) score 0–2: low risk [17% of cases (*n* = 11 patients]; (b) score 3–4: intermediate risk [44.6% of cases (*n* = 29 patients)]; and (c) score 5–7: high risk [38.5% of cases (*n* = 25 patients)]. Of the 65 cases included in the study, 59 (90.8%) had CAD. Most cases had multivessel disease (58.5%, *n* = 38 patients), with only approximately one-sixth of the cases having either single vessel (15.4%, *n* = 10 patients) or two vessel diseases (16.9%, *n* = 11 patients). Left main disease was seen in 16 (24.6%) cases.

STE in lead aVR was found in approximately 60% of cases (*n* = 39 patients). STE in lead aVR was increasing in frequency with the rise of TIMI score, and the relation between the increasing TIMI score and the possibility of elevated ST at aVR was highly significant. Most cases (66.1%, *n* = 39 patients) of CAD had STE in lead aVR, with none of the normal CA cases had elevated ST in this lead (Table 2). Moreover, the number of vessels affected and the risk of left main artery involvement were significantly associated with STE-aVR. As shown in Table 3, STE-aVR was found in 17 cases with low-risk or intermediate-risk TIMI score, whereas it was absent in three of the patients with high-risk TIMI score. As shown in Table 4, STE-aVR was not found in any of patients with normal coronaries, whereas it was absent in 20 patients with significant CAD.

Table 1 Risk factors in relation to coronary artery involvement

Factors	No coronary involvement [*n* (%)]	Coronary involvement [*n* (%)]	χ^2	*P*
Age				
<65 years	6 (12)	44 (88)	1.983	0.322 (NS)
>65 years	0	15 (100)		
Sex				
Male	1 (2.7)	36 (97.3)	4.369	0.037 (S)
Female	5 (17.9)	23 (82.1)		
DM				
Yes	1 (2.5)	39 (97.5)	5.623	0.028 (S)
No	5 (20)	20 (80)		
HTN				
Yes	3 (6.7)	42 (93.3)	1.148	0.361 (NS)
No	3 (15)	17 (85)		
Dyslipidemia				
Yes	3 (5.4)	53 (94.6)	7.243	0.007 (S)
No	3 (33.3)	6 (66.7)		
IHD				
Yes	0	35 (100)	7.712	0.005 (S)
No	6 (20)	24 (80)		
Smoking				
Yes	1 (3.4)	28 (96.6)	2.090	0.148 (NS)
No	5 (13.9)	31 (86.1)		
Obesity				
Normal	1 (4.2)	23 (95.8)	4.535	0.099 (NS)
Overweight	1 (8.3)	11 (91.7)		
Obese	1 (5.9)	16 (94.1)		
Morbid obese	3 (25)	9 (75)		
Family history				
Yes	1 (7.1)	13 (92.9)	0.093	0.616 (NS)
No	5 (9.8)	46 (90.2)		

DM, diabetes mellitus; HTN, hypertension; IHD, ischemic heart disease; S, significant.

Table 2 Relation between ST-segment elevation-aVR and coronary involvement

Factors	ST-elevation in aVR lead [*n* (%)]		χ^2	*P*
	No	Yes		
Normal coronaries	6 (100)	0	9.915	0.002
Coronary involvement	20 (33.9)	39 (66.1)		
One vessel involvement	6 (60)	4 (40)	17.321	<0.001
Two vessels involvement	6 (54.5)	5 (45.5)		
Multivessels involvement	8 (21.1)	30 (78.9)		
Left main artery involvement	3 (18.7)	13 (81.3)	3.993	0.046

Table 3 The frequency of ST-segment elevation-aVR and high-risk thrombolysis in myocardial infarction score in the study group, either alone or combined

	n (%)
None	23 (35.4)
High-risk TIMI only	3 (4.6)
Positive STE-aVR only	17 (26.2)
High-risk TIMI and positive STE-aVR	22 (33.8)
Total	65 (100.0)

STE, ST-segment elevation; TIMI, thrombolysis in myocardial infarction.

Of all 65 patients of the study group, 34 (57.6%) patients of non-high-risk TIMI group were found to have significant CAD, whereas none of the normal coronary patients were defined by TIMI score as high-risk patients (Table 5).

Sensitivity increased when combining both STE-aVR and high-risk TIMI score for prediction of significant coronary artery involvement, as shown in Table 6.

As shown in Table 5, STE-aVR could detect 17 cases with high-risk coronary involvement that could not be detected as having high-risk TIMI score; thus, STE-aVR could predict another 28.8% of high-risk cases that are not at high-risk TIMI score. On the contrary, TIMI detected alone three cases as having high risk for coronary involvement. None of the two predictors falsely considered a low-risk patient as a high-risk one. Finally, there are still 17 cases that already developed coronary diseases but failed to be detected by any of the two predictors.

Of all 65 patients of this study, four patients died soon after coronary angiography, and all of them had been considered as high risk by the two predictors (high-risk TIMI score and positive STE-aVR).

Table 4 Sensitivity statistics of ST-segment elevation-aVR as a predictor of coronary involvement

Factors	ST-elevation in lead aVR	
	No	Yes
Normal coronaries [*n* (%)]	6 (100)	0
Coronary involvement [*n* (%)]	20 (33.9)	39 (66.1)
Sensitivity	39/(39+20)	66.1%
Specificity	6/(6+0)	100%
Positive predictive value	39/(39+0)	100%
Negative predictive value	6/(6+20)	23.1%
Accuracy	Sensitivity+specificity/2	83.1%

Table 5 Sensitivity statistics of high-risk thrombolysis in myocardial infarction score as a predictor of coronary involvement

Factors	High-risk TIMI score	
	No	Yes
Normal coronaries [*n* (%)]	6 (100)	0
Coronary involvement [n (%)]	34 (57.6)	25 (42.4)
Sensitivity	25/(25+34)	42.4%
Specificity	6/(6+0)	100%
Positive predictive value	25/(25+0)	100%
Negative predictive value	6/(6+34)	15%
Accuracy	Sensitivity+specificity/2	71.2%

TIMI, thrombolysis in myocardial infarction.

Table 6 Sensitivity statistics of combined ST-segment elevation-aVR and high-risk thrombolysis in myocardial infarction score as predictors of coronary involvement

Factors	ST-elevation by aVR lead and/or high-risk TIMI score	
	No	Yes
Normal coronaries [*n* (%)]	6 (100)	0
Coronary involvement [*n* (%)]	17 (28.8)	42 (71.2)
Sensitivity	42/(42+17)	71.2%
Specificity	6/(6+0)	100%
Positive predictive value	42/(42+0)	100%
Negative predictive value	6/(6+17)	26.1%
Accuracy	Sensitivity+specificity/2	85.6%

TIMI, thrombolysis in myocardial infarction.

Discussion

Clinical risk factors and risk scores may be used to identify higher risk patients in whom potent antithrombotic agents and early invasive management are particularly advantageous [10]. The use of TIMI risk score in prediction of angiographic severity of CAD was investigated in multiple previous studies. The main finding in our study was that STE in lead aVR was an independent predictor of angiographic severity of CAD, particularly in those patients with LM or multivessel diseases. Moreover, when added to the TIMI clinical risk score, STE-aVR significantly improved the prediction of severity of CAD in low and intermediate TIMI risk group.

Garcia *et al.* [5] studied the correlation between the TIMI risk score and angiographic findings in NSTEACS. Despite correlating well with LM and three-vessel disease in high-risk group with a cut-off point greater than 5, it was found that TIMI score was less sensitive among low-risk and intermediate-risk groups. Similar finding was found in our study.

Our findings are also in agreement with those of Lakhani *et al.* [11] who found 3VD in 63 (44.2%) patients and significant LM stenosis in three (2.1%) patients among patient group with TIMI score less than or equal to 4. This low sensitivity of TIMI score among intermediate-risk and low-risk groups was supported by a previous study of Isilak *et al.* [6] who compared different scoring systems in predicting 3VD and culprit lesions in patients with NSTEACS and concluded that the TIMI and GRACE risk scores have more predictive value than the others but TIMI score has low sensitivity with cut-off value greater than 4. Moreover, they could not show a predictive value of any of the risk assessment or scoring systems for the presence of a culprit lesion. Moreover, Chase *et al.* [12] in their study found that in the low-risk ED population, the modified TIMI risk score outperformed the original TIMI regarding overall diagnostic accuracy. However, both scores are insufficiently sensitive or specific to recommend as the sole means of determining disposition in ED chest pain patients.

Previous studies have found analysis of lead aVR to be useful in estimating the severity of CAD and the

likelihood of LM or three-vessel disease. The relation of STE-aVR to the culprit lesion was shown by Engelen *et al.* [13], who found that STE-aVR was very specific to proximal LAD occlusion proximal to S1 branch in patients with acute anterior myocardial infarction. A study by Barrabes *et al.* [3] supported the idea that lead aVR plays an important role in the diagnosis of ACS in patients with NSTEMI. Yamaji *et al.* [14] found a higher incidence of lead aVR STE in the left main coronary artery (LMCA) group than in other groups, as well as a significant relationship between the amplitude of lead aVR STE and the patients' clinical outcomes in the LMCA group. Kosuge *et al.* [15] have shown that the predictive value of STE-aVR for mortality is based on its relationship with multivessel disease and left main coronary artery obstruction. In our study, 39 (60%) patients with significant CAD had STE in lead aVR, with none of the normal CA cases had elevated ST in this lead. Moreover, the number of vessels affected and the risk of left main artery involvement were significantly associated with elevated ST-aVR. STE-aVR was found in 30 (78.9%) cases of patients with multivessel disease and 13 (81.3%) cases of patients with LM disease. ST-aVR was elevated in 17 cases with low-risk or intermediate-risk TIMI score (9.1 and 55% of both groups, respectively) and was normal in three (12%) of the high-risk TIMI score patients.

Thus, STE-aVR could predict another 28.8% of high-risk cases that could not be detected by TIMI. On the contrary, TIMI detected alone three cases as having high risk for coronary involvement in whom there were no STE in lead aVR. None of the two predictors falsely considered a low-risk patient as a high-risk one. Early suspicion of multivessel or left main disease should be carried out with patients having STE in lead aVR. This may be useful in their management and decision making about early invasive strategy or even urgent bypass surgery.

Finally, for those patients thought to have a potential ACS, our data suggest that among low TIMI risk and intermediate TIMI risk groups, some patients may be still at higher risk CAD than addressed by TIMI score. Those patients may need to be re-stratified by another tool for their risk and the decision of a specific urgent strategy for their treatment.

The current study has the following limitations: it included a single medical center (Sohag Heart and GIT specialized center). The study included only 65 patients, which is a relatively small number; therfore, it will be useful to confirm our findings by larger studies. Although being assessed by an experienced operator, the angiographic results were reported according to the visual assessment method without applying the recently developed standard scores. In our study, we did not examined the relation of findings to different magnitudes of STE in this lead. Moreover, we did not investigate with the presence of Q wave and its duration in relation to the findings as done in some studies. Tropnin I was the only cardiac biomarker used in our study, and it was investigated as an included variable among the TIMI risk score rather than as an independent finding.

Conclusion

In conclusion, STE in lead aVR has a diagnostic and prognostic value in patients with NSTEACS and may provide an additional prognostic value to the conventional cardiovascular risk factors, particularly in patients from the TIMI low-risk and intermediate-risk groups.

The use of STE in lead aVR in addition to TIMI risk score may improve the early stratification and management of those patients at high-risk CAD, with subsequent effect on morbidity and mortality.

Acknowledgements

The authors thank all of the participants in this research, without them no medical research could be done.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1 Kumar A, Cannon CP. Acute coronary syndromes: diagnosis and management, part II. Mayo Clin Proc 2009; 84:1021–1036.

2 Wright RS, Anderson JL, Adams CD, Bridges CR, Casey DE Jr, Ettinger SM, *et al.* 2011 ACCF/AHA focused update incorporated into the 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 Foundation/American Heart Association Task Force on Practice Guidelines developed in collaboration with the American Academy of Family Physicians, Society for Cardiovascular Angiography and Interventions, and the Society of Thoracic Surgeons. J Am Coll Cardiol 2011; 57:e215–e367.

3 Barrabes JA, Figueras J, Moure C, Cortadellas J, Soler-Soler J. Prognostic value of lead aVR in patients with a first non-ST-segment elevation acute myocardial infarction. Circulation 2003; 108:814–819.

4 Antman EM, Cohen M, Bernink PJLM, McCabe CH, Horacek T, Papuchis G, *et al.* The TIMI risk score for unstable angina/non-ST elevation MI. JAMA 2000; 284:835.

5 Garcia S, Canoniero M, Peter A, de Marchena E, Ferreira A. Correlation of TIMI risk score with angiographic severity and extent of coronary artery disease in patients with non-ST-elevation acute coronary syndromes. Am J Cardiol 2004; 93:813–816.

6 Isilak Z, Kardesoglu E, Aparci M, Uz O, Yalcin M, Yiginer O, *et al*. Comparison of clinical risk assessment systems in predicting three-vessel coronary artery disease and angiographic culprit lesion in patients with non-ST segment elevated myocardial infarction/unstable angina pectoris. Kardiol Pol 2012; 70:242–250.

7 Wagner GS, Macfarlane P, Wellens H, Josephson M, Gorgels A, Mirvis DM, *et al*. AHA/ACCF/HRS recommendations for the standardization and interpretation of the electrocardiogram: part VI: acute ischemia/infarction: a scientific statement from the American Heart Association Electrocardiography and Arrhythmias Committee, Council on Clinical Cardiology; the American College of Cardiology Foundation; and the Heart Rhythm Society. Endorsed by the International Society for Computerized Electrocardiology. J Am Coll Cardiol 2009; 53:1003–1011.

8 Reeves TJ, Sheffield LT. Natural history of coronary artery disease. Bull NY Acad Med 1972; 48:1109–1125.

9 Lipinski M, Do D, Morise A, Froelicher V. What percent luminal stenosis should be used to define angiographic coronary artery disease for noninvasive test evaluation? Ann Noninvasive Electrocardiol 2002; 7:98–105.

10 Cannon CP, Weintraub WS, Demopoulos LA, Vicari R, Frey MJ, Lakkis N, *et al*. Comparison of early invasive and conservative strategies in patients with unstable coronary syndromes treated with the glycoprotein IIb/IIIa inhibitor tirofiban. N Engl J Med 2001; 344:1879–1887.

11 Lakhani MS, Qadir F, Hanif B, Farooq S, Khan M. Correlation of thrombolysis in myocardial infarction (TIMI) risk score with extent of coronary artery disease in patients with acute coronary syndrome. J Pak Med Assoc 2010; 60:197–200.

12 Chase M, Robey JL, Zogby KE, Sease KL, Shofer FS, Hollander JE. Prospective validation of the Thrombolysis in Myocardial Infarction Risk Score in the emergency department chest pain population. Ann Emerg Med 2006; 48:252–259.

13 Engelen DJ, Gorgels AP, Cheriex EC, de Muinck ED, Ophuis AJ, Dassen WR, *et al*. Value of the electrocardiogram in localizing the occlusion site in the left anterior descending coronary artery in acute anterior myocardial infarction. J Am Coll Cardiol 1999; 34:389–395.

14 Yamaji H, Iwasaki K, Kusachi S, Murakami T, Hirami R, Hamamoto H, *et al*. Prediction of acute left main coronary artery obstruction by 12-lead electrocardiography: ST segment elevation in lead aVR with less ST segment elevation in lead V1. J Am Coll Cardiol 2001; 38:1348–1354.

15 Kosuge M, Kimura K, Ishikawa T. Combined prognostic utility of ST segment in lead aVR and troponin T on admission in nonST-segment elevation acute coronary syndromes. Am J Cardiol 2006; 97:334–339.