ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 03, 2021

Prognostic effects of ST-segment resolution after primary percutaneous coronary intervention in patients with acute ST-segment elevation myocardial infarction in Erbil.

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Abstract

Background: Although ST-segment resolution (STR) after primary percutaneous coronary intervention (PPCI) in patients with acute ST-segment elevation myocardial infarction (STEMI) was considered a useful marker for assessing reperfusion efficiency, its prognostic effect remains a topic of controversy.

Objectives: The main purpose of this study was to evaluate the prognostic effects of STR after PPCI in patients with acute STEMI.

Patients and Methods: In this cohort study, STR was assessed 30 minutes after PPCI in 300 patients with acute STEMI. Patients were divided into two groups according to the degree of STR; group I, 225 patients with complete STR (≥ 50%), and group II, 75 patients with incomplete STR (< 50%). Both groups were assessed and compared regarding baseline, angiographic and outcomes up to two years of follow-up.

Results: Group II patients were more hypertensive, diabetic, hypercholesterolemic, and with a high incidence of prior myocardial infarction. Besides, they had a high prevalence of Killip II and III classes, a high percentage of anterior and double wall infarctions, more heart rate, less hemoglobin level, high blood urea creatinine, and troponin levels. Moreover, left ventricular ejection fraction during follow-up was significantly lower in them. In addition, the mean sum of ST-segment elevation was higher in group II compared to group I. Patients of group I had a shorter door-to-balloon time , a higher rates of post-interventional TIMI flow grade 3. Group II patients had more non-fatal MI events, and a higher death rate in the end of the study.

Conclusion: ST-segment resolution accomplished early after PPCI is an easy, effective and inexpensive method for predicting the outcomes in patients with acute STEMI.

Keywords: ST-segment resolution, ST-segment myocardial infarction, primary percutaneous coronary intervention.

Introduction:

Despite the great medical progress in the health awareness about the dangers of heart disease and modern methods for early diagnosis of coronary arteriosclerosis as well as the great development in finding effective therapeutic procedures, coronary artery disease (CAD) remains a major challenge. Globally, CAD still considered one of the main causes of morbidity and mortality.[1] Although the mortality is decreasing in some countries; it is growing in many others .[2] In developed countries nearly half of the total mortalities is due to ischemic heart disease; while it is nearly one third in developing countries.[3] In United States, about 20% of those over 65 had CAD[4] .There are several types of CAD, but the most dangerous one is acute ST-segment elevation myocardial infarction (STEMI) which present in 25-40% of the cases.[5] In Iraq, limited data are available regarding surveillance studies for CAD as compared to other Middle East countries.[6] Most recent studies mentioned that the mortality of cardiovascular disease in Iraq was 33%.[7, 8] While the prevalence of STEMI was higher (67.4%) among Iraqi people compared to the above mentioned rate.[9] Primary percutaneous coronary intervention (PPCI) can returns the flow to the injured epicardial coronary arteries in a large number of patients with STEMI. To evaluate whether PPCI was successful or not, this can be determined by either coronary angiography to assess the Thrombolysis in Myocardial infarction

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(TIMI) flow or electrocardiographically (ECG) by measuring ST-segment resolution (STR).[10] Although getting TIMI flow grade 3 after PPCI indicates a successful procedure and that normal epicardial blood flow was restored, adequate myocardial reperfusion was not assured; because this needs a perfusion at the level of the coronary microcirculation and myocytes.[11] Those patients usually presented with persistent ST-elevation or inadequate STR. Hence, adequate or complete STR after PPCI is considered an important foreteller of patency of infarct related artery (IRA) and of efficient microcirculatory as well as myocytic perfusion.[12] Despite the fact that there are several methods to ensure the perfusion effect of PPCI on occluded coronary arteries, the STR is considered one of the simple, easy and inexpensive measures for that purpose.[13] Many studies correlated between incomplete STR on the ECG and poor prognosis in acute myocardial infarction represented by increase death rate, impaired left ventricular ejection fraction, and reinfarction.[14,15] To the best of our knowledge, there was no previous study done in Iraq regarding the same subject. Accordingly, the aim of this study was to assess whether STR on the ECG recorded 30 minutes after initiation of PPCI predicts in-hospital and long term outcomes in patients with STEMI.

Patients and Methods: This prospective-cohort study was conducted from May 2019 to May 2021 in Hawler hospital for surgical specialties/Kurdistan region/Iraq. A convenience sample of 300 adult patients with acute STEMI and who were treated successfully with PPCI (successful PPCI was defined as constant patency of the culprit epicardial coronary artery with TIMI flow grade ≥2) were included in this study. The diagnosis of STEMI required chest pain duration of ≥20 min and ST-segment elevation of ≥1 mm in at least two extremity ECG leads or ≥ 2 mm in at least two contiguous precordial leads or new onset left bundle branch block (LBBB).[16] All included patients were underwent 12-lead ECG, before and 30 minutes after PPCI. The ST-segment elevation resolution was calculated as the initial sum of ST-segment elevation minus the sum of ST-segment elevation on the second ECG divided by the initial sum of ST-segment elevation and expressed as a percentage.[17] Patients were divided into two groups according to the degree of ST-segment resolution: group I, included 225 patients with ≥ 50% ST-segment resolution (complete STR), and group II, composed of 75 patients with < 50% ST-segment resolution (incomplete STR).[18] Coronary angiography was performed according to ACC/AHA Guidelines.[19] PPCI and periprocedural care was performed according to the standard criteria.[20] Patients with pacemaker, heart failure, old LBBB and cardiogenic shock were excluded. Risk factors of cardiovascular diseases (hypertension, type 2 diabetes mellitus, hypercholesterolemia, prior MI, smoking, age and family history of ischemic heart disease), baseline characteristics (gender, Killip class[21], infarct location [such as Anterior, Inferior, and double wall] , heart rate, hemoglobin level, blood urea, serum creatinine, troponin level, left ventricular ejection fraction [LVEF], time-to-admission interval, and sum of ST-segment elevation), angiographic characteristic (door-to-balloon time, occluded coronary artery, number of affected coronary artery, TIMI flow grade, and number of stents), and outcomes (mortality, heart failure with reduced ejection fraction (HFrEF), renal failure, target lesion re-vascularization and non-fatal myocardial infarction) were evaluated and compared between complete and incomplete STR groups. The TIMI groups were defined as: TIMI 0, no reperfusion; TIMI 1, penetration without perfusion; TIMI 2, partial reperfusion; and TIMI 3, complete perfusion.[22] Transthoracic echocardiographic examination was performed by an expert cardiologist in the left lateral position. Standard M-mode, 2-Dimensional and Doppler echocardiographies were performed using commercially available echocardiographic machine to assess LV ejection fraction (LVEF). Heart failure was defined as ejection fraction ≤ 40% according to the standards of the American Society of Echocardiography.[23] The end point of the study was mortality, heart failure with reduced ejection fraction (HFrEF), renal failure, target lesion re-vascularization and non-fatal myocardial infarction after two years of follow-up. The follow-up information was gathered from the patients through an interview, if possible, or by phone contact. Information on deaths was obtained from hospital records or phone contact with relatives of the patient.

Ethical considerations:

This study was authorized by the Ethical Committee of the College of Medicine - Hawler Medical University.

Statistical analysis

The statistical package for social sciences (SPSS, version 22) was used for data analysis. The results were analyzed using frequency of distribution. Chi square test of association was used to compare proportions, and a 95% C.I. reference range was calculated. Fisher's exact test was used when the expected count of

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 03, 2021

more than 20% of the cells of the table was less than 5. Appropriate tables and graphs were used for data representation .P-value of ≤ 0.05 was considered statistically significant.

Results: A convenience sample of 300 patients with acute STEMI in which they were treated successfully by PPCI was enrolled in the current study. According to the degree of ST-segment resolution (STR) , before and 30 minutes after balloon inflation, patients were divided into two groups. In group I, there were 225(75%) patients with complete STR (≥ 50% STR improvement of baseline value), and 75 (25%) patients with incomplete STR (<50% STR improvement of baseline value) in group II. Table 1 shows the baseline characteristics between the two groups. Group I patients were predominantly males, and generally looked younger, but with no statistical significance (P=0.4, and 0.37 respectively). Significant statistical differences were found regarding cardiovascular risk factors. Group II patients were more hypertensive (P=0.001), more diabetic (P=0.001), more hypercholesterolemic (P=0.003), and with a high incidence of prior myocardial infarction (P=0.011). Besides, group II patients had a high prevalence of Killip II and III classes (P=0.001), a high percentage of anterior and double infarction (P=0.001), more heart rate (P=0.001), less hemoglobin level (P=0.002), high blood urea (P=0.001), creatinine (P=0.001), and troponin levels (P=0.001). Moreover, LVEF after PPCI and during follow-up was significantly lower in group II patients (P=0.002, and 0.001 respectively). In addition, the mean sum of ST-segment elevation was higher (P=0.002) in group II patients compared to group I. The remaining characteristics showed no statistical differences.

Table 1: Baseline characteristics among patients with complete STR and incomplete STR.

characteristics	Group I Complete STR (n=225, %)	Group II Incomplete STR (n=75, %)	P
Gender: male	147 (65.3%)	42 (56%)	0.403
female	78 (34.7%)	33 (44%)	
Age, years	57.43 ± 11.54	59.64 ± 8.04	0.377
Hypertension	126 (56%)	69 (92%)	**0.001**
Diabetes mellitus	48 (21.3%)	60 (80%)	**0.001**
Hypercholesterolemia	168 (74.7%)	75 (100%)	**0.003**
Family history of IHD	15 (6.7%)	3 (4%)	0.999
Prior MI	24 (10.7%)	27 (36%)	**0.011**
Smoking	78 (34.7%)	24 (32%)	0.589
Killip class			
I(No HF)	57 (25.3%)	0(0%)	
II(basal rales)	150 (66.7%)	54 (72%)	**0.001**
III (acute, severe HF)	18 (8%)	21 (28%)	
Infarct location			
Anterior	130 (57.8%)	50 (66.7%)	
Inferior	83 (36.9%)	10 (13.3%)	**0.001**
Double	12 (5.3%)	15 (20 %)	
Heart rate, bpm	76.80±6.86	89.44±10.89	**0.001**
Hemoglobin level	13.51±0.73	12.40±1.41	**0.002**
BU, md/dl	39.27±4.61	52.24±18.46	**0.001**
S. creatinine, mg/dl	0.68±0.21	1.15±0.36	**0.001**
Troponin level	0.18±0.14	0.47±0.22	**0.001**
LVEF (%) after PPCI	58.64±3.02	54.72±5.41	**0.002**
LVEF (%) Follow up	61.53±4.46	47.40±5.86	**0.001**
Time-to-admission interval, h	9.49±1.76	10.28±2.11	0.070
Sum of ST-segment elevation, mm	8.04±2.07	9.92±2.53	**0.002**
ST-segment resolution, %	67.43±9.56	32.12±6.84	**0.001**

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Table 2 shows the angiographic characteristics among patients with complete STR and incomplete STR. Patients with the group I had a shorter door-to-balloon time (P=0.006), a lower incidence of the occluded left main and left anterior descending arteries (P=0.001) , a higher incidence of occluded left circumflex artery (P=0.001) , a lesser number of occluded coronary arteries (P=<0.001) and stents usage (P=<0.001), a lesser rates of pre-interventional TIMI flow grade 0 (P=0.002), and a higher rates of post-interventional TIMI flow grade 3 (P=<0.001).

Table 2: Angiographic characteristics among patients with complete STR and incomplete STR.

characteristics	Group I Complete STR (n=225)	Group II Incomplete STR (n=75)	P
Door-to-balloon time , h	1.78±0.27	1.92±0.18	**0.006**
Occluded coronary artery			
Left main(LM)	3 (1.3%)	5 (6.7%)	
Left anterior descending(LAD)	112 (49.9%)	42 (56%)	**0.001**
Left circumflex (LCX)	55 (24.4%)	8(10.7%)	
Right coronary artery (RCA)	55 (24.4%)	20 (26.6%)	
Number of occluded arteries			
1	180 (80%)	9 (12%)	**<0.001**
2	45 (20%)	33 (44%)	
3	0 (0%)	33 (44%)	
Number of stents			
1	165(73.3%)	12 (16%)	**<0.001**
2	54 (24%)	33 (44%)	
3	6 (2.7%)	30 (40%)	
TIMI flow grade (Pre-intervention)			
0	75 (33.3%)	51 (68%)	
1	150 (66.7%)	24 (32%)	**0.002**
2	0	0	
3	0	0	
TIMI flow grade (Post-intervention)			
0	0	0	
1	0	0	**<0.001**
2	21 (9.3%)	57 (76%)	
3	204 (90.7%)	18 (24%)	

Table 3 demonstrates the distribution of the patients between the studied groups according to the clinical outcomes during the period of the study. During in-hospital period, the only significant difference (P= <0.001) was in the number of patients with renal failure, as their number was ten in the incomplete STR group compared to zero patient in group I. No significant differences were found regarding mortality, heart failure, the need for re-vascularization to target lesion(s), or non-fatal MI. At the end of the first year, there were 3 deaths in the incomplete SRT group and nil death in the complete STR group (P=<0.001). Heart failure occurred in 12 patients, all of them belonging to the incomplete STR group (P=<0.001). Renal failure was recorded in 10 patients from the incomplete STR group, compared to nil patient in group I (P=<0.001). Revascularization to the target lesion(s) was required in 12 patients with incomplete STR, and 9 patients with complete STR (P=<0.001). There were 10 non-fatal MI events among incomplete STR patients and no events were detected in group I (P=<0.001). In the second year of follow-up, 6 patients died in group II while there were zero patients in group I (P=<0.001). Regarding heart failure, 15 patients were affected in group II compared to 6 patients in group I (P=<0.001). There were 10 patients with renal failure

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in group II compared to zero patients in group I (P=<0.001). 23 patients out of 75 were in the need for new re-vascularization in group II compared to 27 patients out of 225 in group I (P=<0.001). Non-fatal MI happened in 33 patients in group II and 6 patients in group I (P=<0.001), as shown in Table 4.

Table 3: Distribution of the patients between complete STR and incomplete STR groups according to the clinical outcomes during the study period.

Variable	Categories	Group I Complete STR (No.=225)	Group II Incomplete STR (No.=75)	P-value
Mortality	In-hospital	0	0	**0.014**
	1 year	0	3	
	2 years	0	6	
Heart failure	In-hospital	0	0	**< 0.001**
	1 year	0	12	
	2 years	6	15	
Renal failure	In-hospital	0	5	**< 0.001**
	1 year	0	10	
	2 years	0	10	
Stroke	No stroke	0	0	N.A
Revascularization	In-hospital	0	0	**< 0.001**
	1 year	9	12	
	2 years	27	23	
Non-fatal MI	In-hospital	0	0	**< 0.001**
	1 year	0	10	
	2 years	6	23	

Discussion:

There has always been a need to find an easy, effective and inexpensive method for predicting the outcomes of patients presented with acute STEMI after successful PPCI.[13] In this study we tried to evaluate the prognostic effects of STR in patients with acute STEMI after successful PPCI throughout the two-year study period and over different intervals. The results of the current study confirm the fact that incomplete STR after successful PPCI carries a lot of bad consequences represented by early onset renal failure, high incidence of long-term heart failure, the more need for future re-vascularization to the target lesion(s) , more non-fatal MI events, and a higher death rate. The results of this study are similar to some extent with many other studies. In 1997, a study was published by van't Hof et al in *Lancet* found that the relative risk for cardiovascular mortality was high (6.4 at 3.1±1.9 years) in patients with incomplete STR.[24] Another study that was published in 1999 by Claeys and colleagues in *Circulation,* found that there was a 3.4-fold risk of MACE in patients with persistent ST-segment elevation.[25] Increased death rate and more heart failure was also reported by Matelzky et al in patients with persistent ST-elevation after primary PTCA.[26] In 2004, Prasad and his colleagues found an association between failure of ST-segment recovery and increased MACE but not death.[27] The prognostic value of incomplete STR after successful primary angioplasty was evaluated in Promer Domingo et al study.116 patients with acute MI were followed for one-year. The study confirmed that those patients with persistent ST-segment elevation after primary angioplasty had a worse prognosis, with a more extensive MI, bad long-term ventricular function, and more death rates.[28] Another study done by Bendary and his colleagues in 2018, in which the impact of ST-segment resolution on clinical outcome was assessed in 110 patients with STEMI .There was a significant reduction in rates of re-hospitalization due to heart failure in patients with complete STR. They also found that incomplete STR was a significant independent predictor for 30-day MACE.[29] Sejersten and his

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colleagues in their study (the DANAMI-2 study) tried to determine the long-term prognostic value of ST-segment resolution in 1421 patients with STEMI treated with fibrinolysis or PPCI. They mentioned that the STR at 4 hours correlated with decreased mortality only among patients receiving fibrinolytic therapy, and no association was observed for PPCI patients.[30] In our study, a lot of these bad clinical predictors were observed in patients with incomplete STR, and we believe that they collectively have affected their bad clinical outcome. What was noted in the current study that patients with incomplete STR had the worst risk factors on admission. They were more hypertensive, diabetic, hypercholesterolemic, and had more exposure to previous MI. These findings were noticed by many previous studies.[15,31,32] Increased heart rate, low hemoglobin level, renal impairment presented by elevated blood urea and serum creatinine, and longer ischemic time presented by elevated time-to-admission interval, were considered other important clinical predictors of incomplete STR. These results were supported by other studies.[33] Our patients with incomplete STR were presented with higher Killip II and III classes, which was seen also in previous studies.[34] Individuals with a high Killip class are more likely to die within the first 30 days after their myocardial infarction (mortality rate was found to be 17%-38 %).[21] Not only short-term mortality can be predicted by this classification, but can also predict the mortality rate at mean follow-up of 5 years post-AMI in some studies.[35] High prevalence of anterior wall infarction in our patients with incomplete STR was observed in many other studies.[32,34,36] A good prognostic marker to detect late risk stratification in patients with STEMI consists of an assessment of left ventricular function by echocardiography at admission. People with persistently depressed LVEF are at high risk for arrhythmic and non-arrhythmic deaths.[37] In this study, patients with incomplete STR presented with lower LVEF at admission than those with complete STR, and complicated by heart failure earlier than patients with complete STR. Another important finding to be mentioned in this study is that the degree of STR had a good impact on LVEF at the end of the study. A significant improvement was noticed in the cardiac function of patients with complete STR, and in contrast to that, an obvious deterioration in the cardiac function of the second group. The correlation between the STR% and LVEF was mentioned in Kiron and George study. In their study, there was a good positive correlation between STR% and the LVEF (correlation coefficient was 0.59). The STR% was a useful surrogate marker in prognosticating patients with STEMI.[38] The mean sum of ST-segment elevations in the current study was higher in patients with incomplete STR than those with complete STR. Higher ST-segment elevations on the admission in patients with STEMI was considered a strong marker of myocardial damage, and was significantly associated with infarct size and impaired myocardial salvage, and was independently correlated with MACE.[39]

Concerning angiographic findings, patients with incomplete STR had more left main and left anterior descending arteries lesions. STEMI outcomes are influenced by the location of the culprit vessel with worse outcomes portended with a LAD culprit lesion.[40] While the LAD artery is the most common artery affected in patients with incomplete STR by many studies[32,34,36] , it is not the case for the left main artery. According to Xu et al study, AMI caused by left main coronary artery lesions is complicated by high incidence of mortality.[41] Although our patients in this study were included after successful PPCI and getting a suitable flow in the culprit artery, TIMI flow grade 3 post PPCI was achieved in 90.7% in patients with complete STR compared to only 24% in group II patients. That means there was unsuccessful restoration of full epicardial blood flow to maintain sufficient perfusion at the myocyte level in patients with incomplete STR. This phenomenon is called myocardial “no-reflow”, which was first described by Kloner et al in 1974.[42] In this study, 25% of our patients had incomplete STR despite having angiographically successful PPCI. This finding is almost identical to what was found in other studies.[28,33] The method we used to classify the response of STR after PPCI (a value of 50%) has been used in many previous studies.[21,28,43,44]

Conclusions:

ST-segment resolution accomplished early after PPCI is an easy, effective and inexpensive method for predicting the outcomes in patients with acute STEMI.

Conflict of interest: The authors have none to declare.

Source of funding: The researchers did not receive any financial support.

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