

# Relationship between TIMI myocardial perfusion grade and ST resolution in evaluating the coronary reperfusion

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## ABSTRACT

The current research was conducted and implemented to evaluate the relationship between TIMI grade and STR after PCI. By reviewing the medical record of 112 patients with diagnosis of acute coronary syndrome and under coronary angiography, the primary characteristics of the patients were extracted in this research. Coronary flow was evaluated after PCI by 200 µg nitroglycerin bolus intracoronary prescribing. TIMI value was determined based on the contrast opacification dynamics of coronary microcirculation. By aggregating the total values in increase in ST in all infarction leads and reduction in reciprocal leads, SSTD value was determined. Relative SSTD value, which means percentage of reduction in SSTD (SSTD%) compared to its base value, was calculated. Strong and significant correlation was found between TIMI variations after PCI and SSTD (correlation coefficient=0.340, P = 0.001). Additionally, a strong and significant correlation was found between TIMI variations after PCI and SSTD% (correlation coefficient =0.442, P = 0.001). Based on the analysis of area under the ROC curve, evaluation of SSTD (AUC = 0.699) and SSTD% (AUC = 0.621) could predict improvement in TIMI flow in patients after PCI. According to the analysis of area under ROC curve, evaluation of SSTD (AUC = 0.667) and SSTD% (AUC = 0.873) could predict the occurrence of mortality in patients after PCI. Measuring STR can predict TIMI grade variations strongly after performing the PCI process. In addition, determining STR has great value in predicting the mortality after the mentioned procedure.

**Keywords:** TIMI myocardial perfusion, ST resolution, coronary reperfusion, primary PCI

## Introduction

In early years of the current century, it was revealed that the occurrence of ischemic heart damage is due to an imbalance between oxygen distributed for myocardial tissue and demand of the tissue for oxygen [1]. Animal research conducted by induction of coronary artery stenosis, elevation of ST segment in the electrocardiogram was associated with reduced heart creatinine kinase activity [2], and we observed myocardial tissue necrosis in histological evaluation [3]. ST segment elevation in case of necrosis or ischemia is regarded as a useful index to evaluate the ischemic myocardial damage severity [4]. Along with coronary artery occlusion in animal models, myocardial reperfusion was associated with improvement and fast return of

ST segment to its own initial position [5]. Along with improvement and development in thrombolytic therapies of acute myocardial infarction in last decade, our observations in human studies were recorded and reported [6]. ST segment resolution or STR has been used as an accurate criterion to evaluate and predict coronary arteries patency related to infarction [7-11], while coronary artery angiography is still regarded as gold standard to evaluate the impact of reperfusion regimes. Observation-based research conducted recently indicates the feasibility of using STR evaluation in predicting and monitoring the ST segment variations after MI with ST elevation or STEMI. Some observations indicated that high-precision STR could predict mortality rate and heart congestive failure in patients underwent fibrinolytic therapy [12-15]. Moreover, some research indicated significant relationship between STR degree and occurrence of mortality [13, 16]. Second, it has been found that providing the epicardial normal blood flow for appropriate myocardial reperfusion is not adequate, since providing the reperfusion through coronary microcirculation and myositis is also required. The modern regimes of coronary reperfusion have been developed increasingly in the recent years, and these regimes have been integrated with fibrinolytic and antiplatelet therapies [16-18], and these regimes have even been used even in coronary microcirculation [19, 20]. It has been recognized that patients with

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fibrinolytic therapy failure with the aim of achieving to normal grade 3 TIMI in epicardial blood flow are always at the risk of mortality and heart congestive failure [21, 22]. Accordingly, data on the supporting role of emergency PCI in patients suffering from coronary artery occlusion are very limited [23, 24], and clinical trial studies have also been carried out using small sample size [25]. Unfortunately, it is impossible to evaluate the useful impact of rescue PCI directly, because researchers did not show high tendency to consider intervention, except for conducting PCI, after the diagnosis and identification of obstructed coronary artery associated with infarction through angiography [26], but the current research suggests high value of rescue PCI in rescuing the patients with moderate to high risk following the fibrinolytic therapy [26]. Moreover, in light of using GP IIb/IIIa inhibitors [27] and angioplasty [28], the benefits of using rescue PCI have increased. These developments have led to reduction in probability of rescue PCI failure, which is about 30 to 50% in the normal cases [29-31]. PCI rescue role in TIMI II patients has not been recognized yet clearly, since stenosis and remaining thrombosis might have a secondary role in the pathogenesis of TIMI II. Many TIMI II patients experience slow flow because of increased resistance to microvascular hospitalization not due to local stenosis of coronary arteries after reperfusion therapy [32]. In some of the clinical trials conducted, performing the PCI rescue for TIMI II patients did not lead to improvement in clinical outcome of patients [26, 33]. There are simple and available evaluations to determine the success or failure of epicardial reperfusion for identifying and determining the PCI rescue candidates. STR is used widely in this regard [7-11]. In general, recent research has shown that measuring and evaluating the STR is a strong predictor for coronary arteries patency (with a positive predictive value of higher than 90%, it has not been so much accurate to predict coronary artery occlusion related to infarction (negative predictive value of lower than 50% [34-36]. Recent research revealed significant relationship between higher STR and higher values of patency values and TIMI III [37, 38]. After introducing the tPA, 35 to 40% patients are faced with complete 90-minute STR based on Schröder criteria [39]. In contrast, following the use of streptokinase, almost 25% of patients reach to complete 90-minute STR [40]. Considering 180-minute time, both protocols of tPA and streptokinase led to achieving complete STR only in 50% of patients [40]. In total, in patients with complete 90-minute STR, the probability of achieving to desired coronary patency related to infarction area is between 92% and 94%, and this probability is between 70 and 80% in achieving TIMI III [37, 38]. However, lack of STR will not predict coronary occlusion related to infarction area, and this is seen merely in half of the patients. Another interesting point is the effect of infarction position on the relationship between STR and TIMI grade. There is a significant difference between the anterior and inferior MIs in terms of STR in this regard [41-43]. Patients with anterior MI experience significantly lower STR compared to patients with inferior MI. In fact, STR has less value in predicting reperfusion in anterior MI patients compared to that in inferior MI patients [41]. This issue might be related to technical factors such as increased J point in the anterior leads. Moreover, MI anterior wall is often associated with a wider infarct size and ischemic damage to inferior abdominal wall. Additionally, difference in STR threshold level might be more desired for anterior MI compared to that for inferior MI [41]. STR deviation to more than 70% is considered an acceptable threshold for inferior MI patients, while in anterior MI patients; threshold more than 50% can be

considered desired [38]. In terms of prognosis, higher degree of STR has been associated with reduced mortality in both the anterior and inferior wall MI groups [12, 13]. Investigating the STR in distinguishing two groups with TIMI II and TIMI III has been valuable. TIMI III patients have higher STR compared to patients with TIMI II [44]. In general, the probability of TIMI III is only 70-80% in patients with complete STR or STR higher than 70%. Thus, while complete STR confirms the presence of patent coronary arteries, complete STR does not confirm the presence of TIMI III completely. Another important point is that the mortality rate in TIMI III and TIMI II patients with similar level of STR is completely same [38]. STR deficiency alone to diagnose the patients with epicardial reperfusion failure caused that other factors such as chest pain resolution or fast removing of heart enzymes combined with STR to be used [45-48]. However, continuous chest pain after fibrinolytic therapy could predict coronary artery occlusion. This index has no adequate accuracy in clinical prediction of cardiovascular consequences [49]. Among the heart markers, early measuring of the myoglobin is more accurate than CK-MB or troponin for evaluating the reperfusion [50-54]. Evaluating the rate of increase in the serum level of myoglobin during 60 to 90 minutes after fibrinolysis or the ratio of myoglobin 60 to 90 minutes to that baseline time was very accurate in evaluating coronary patency related to the infarction area [54]. Using more specialized molecules, including the protein bound to speculated fatty acids of the heart did not lead to increased diagnostic accuracy, in comparison to myoglobin [55]. Additionally, some research stressed on increasing the accuracy and efficacy of two combined indices of STR and heart biomarkers in determining the candidates to perform the rescue PCI [56]. In other words, STR combined with determination of myoglobin concentration with high accuracy could predict the failure of epicardial reperfusion [49]. Three indices have been generally introduced for predicting the epicardial reperfusion failure, including the STR less than 50% during 90 minutes, continuous chest pain during 90 minutes, and the ratio of 60-minute myoglobin to baseline lower than 4. Combination of three indices would be able to predict epicardial reperfusion failure with probability of 76%. However, about 60% of patients with only one of these indices or none of them were faced with 6% risk for coronary artery occlusion [57-60]. It should be also noted that TIMI III alone is considered as an independent predictor for success of reparation, and other indices will play auxiliary role [61-63]. Another important point is STR role in prediction of prognosis of patients with CAD. Some researchers have shown that almost two thirds of the patients with STR more than 50% during the 4 hours after the thrombolysis experienced 3.5% mortality, while patients with lower STR experienced 7.4% mortality [64] additionally, a strong relationship was found between STR degree during the 180 minutes and long-term mortality of patients with CAD [40]. Recent investigations have indicated that evaluating STR even during 3 to 4 hours of fibrinolytic therapy was effective in determining the risk level of mortality or morbidity caused by CAD [65-68]. Additionally, patients with complete STR during 60 minutes experienced significantly less mortality or heart failure compared to patients with STR during 90 minutes [65-68]. In addition, STR degree could predict the level dysfunction in left ventricle. Increased STR has been associated with reduction in infarct size and increase in ejection fraction of left ventricle [69, 70]. Among the methods used to evaluate the success of reperfusion after PCI in STEMI patients, both methods of electrocardiography and coronary angiography are used widely. Both angiographic

evaluation methods of coronary blood flow provide important prognostic information in infarction site arteries and initial variations in segment resolution [71,72]. Reperfusion of coronary arteries can be evaluated through angiography or through scoring system of Myocardial Blush Grade (MBG) and grading system of TIMI. While MBG scoring system often indicates opacification severity, TIMI system has mainly dynamic base. When we are faced with TMBG 0 or 1 in this regard, we are faced with high infarction and mortality even at the presence of TIMI III. In this regard, TMBG 3 would mean complete reperfusion of microcirculation [73]. The most common method of ECG used to evaluate the reperfusion is the analysis of STR in ECGs, recorded after reperfusion therapy. There is a high relationship between STR severity and rate of re-infarction and early mortality in patients treated with PCI [74-76]. ST segment variations, either in the form of sum of variations of ST segment in all leads or searching the highest variations in ST segment, are possible in one lead [74-80]. Moreover, ST segment variations can be examined with regard to variations observed before or after reperfusion [77]. In general, it was found that remaining variations on STR after PCI would predict worse outcome in patients. After reperfusion therapy, the simultaneous occurrence of TIMI III, microcirculation angiographic reperfusion, and complete ST resolution variations can be observed in less than one fifth of the patients [78, 81-86]. Some research suggests that inconsistency and simultaneity between STR and tissue reperfusion angiographic degree happens in 40% of the patients [79]. Review of research conducted in this regard indicates some evidence on the rate of resolution evaluated by TIMI flow and value of STR, while this evidence is limited. Thus, the current research was conducted to evaluate the relationship between TIMI grade and STR after PCI.

## Methodology

This is a retrospective research conducted by reviewing the medical record of 112 patients with diagnosis of acute coronary syndrome, and the demographic characteristics of the patients were derived from their medical record and recorded in the project questionnaire. The demographic characteristics of the patients included height, weight, BMI, history of heart disease risk factors such as family history of heart disease, hypertension, hyperlipidemia, diabetes mellitus, smoking, drug using history of patients, especially heart drugs, history of cardiovascular events, history of myocardial infarction, history of heart failure, history of cerebrovascular events, history of kidney failure, history of peripheral vascular failure, and chronic obstructive pulmonary disease. In addition, information related to coronary angiography (number and extent of involved coronary arteries) was recorded. Evaluating the coronary flow after PCI was performed through 200 µg nitroglycerin bolus intracoronary prescribing. The value of TMPG was determined based on coronary microcirculation contrast opacification dynamics. ECG bands of the patients were evaluated in two stages of before PCI and during 30 minutes after transferring of the patient to ICU. The elevation cases of ST were determined in leads I, aVL, V1-V6 (in anterior or anterolateral) or leads II, III, aVF, and V5-V6 (in inferior or inferior-lateral MI). In addition, ST lowering cases were determined in reciprocal leads. By aggregating total values of ST elevation in all infarction leads and ST lowering in reciprocal leads, SSTD value was determined. Relative value of

SSTD means reduction percentage of SSTD (SSTD %) compared to its baseline value. Then, the correlation between TIMI and two indices of SSTD and SSTD% was determined and the median of these two indices was compared between different scores of TIMI.

## Inclusion criteria of research

Inclusion criteria of research included all patients affected with STEMI and admitted to Seyyedol Shohada Hospital of Urmia, who underwent primary PCI successfully. The successful primary PCI process was defined in the form of achieving to TIMI III after PCI with stenosis less than 20% and in absence of dissection, thrombosis, or perforation.

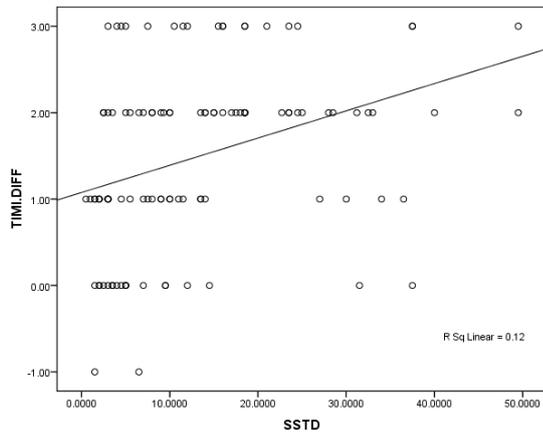
## Exclusion criteria of research

Exclusion criteria of research included shock before revascularization, fibrinolytic therapy during 2 weeks ago and death of patient during the performing the PCI. In addition, patients who had history of heart block were excluded from study.

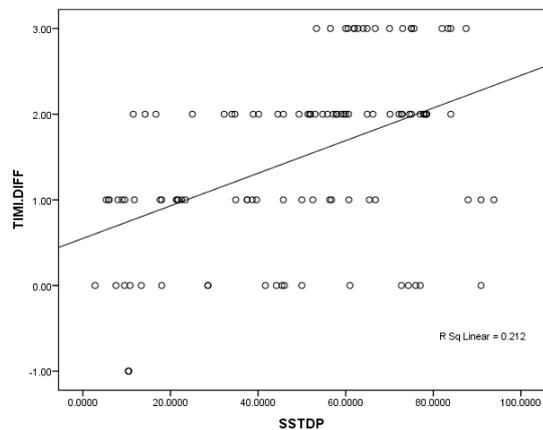
After collecting the data, SPSS 21 software was used to analyze the current research data.

## Findings

In the current research, 112 patients were examined. In this regard, 92 of the subjects (82.1%) were male and 20 of them (17.9%) were female. The mean age of the patients was obtained to be  $58.889 \pm 13.67$  years in the range of 33 to 87 years. The mean TIMI grade before performing the PCI was  $0.78 \pm 0.86$ , so that TIMI 0 was found in 53 (47.3%) patients, TIMI I was found in 34 (30.4%) patients, TIMI II was found in 22 (19.6%) patients, and TIMI III was found in 3 (2.7%) patients. After performing the PCI, the mean of TIMI was increased to  $2.24 \pm 0.81$ , so that TIMI 0 was reported in 6 (5.4%) patients, TIMI I was found in 34 (7.1%) patients, TIMI II was found in 51 (45.5%) patients, and TIMI III was found in 47 (42%) patients. In total, the mean of TIMI variations after the procedure compared to before procedure was evaluated to be  $1.46 \pm 1.06$ . In general, increase in TIMI was found in 89 cases (79.5%), while it remained unchanged in 20 (17.9%) cases, and it was reduced in 3 cases (2.7%). The mean of SSTD in the examined patients was obtained to be  $13.66 \pm 11.37$  in the range of 0.5 to 49.5. In addition, the mean of SSTD% was obtained to be  $51.03 \pm 24.35\%$ , which varied in the range of 2.78 to 93.84%. In terms of involvement of dominant coronary arteries in angiography report, LAD in involvement was reported in 57 cases (50.9%), RCA involvement was reported in 41 cases (36.6%), LCX involvement was reported in 12 cases (10.7%), LMCA involvement was reported in 1 case (0.9%) and diagonal involvement was reported in 1 case (0.9%). In terms of frequency after PCI procedure, mortality was found in 4 cases (3.6%) and the need for performing the CABG was reported in 1 case (0.9%).

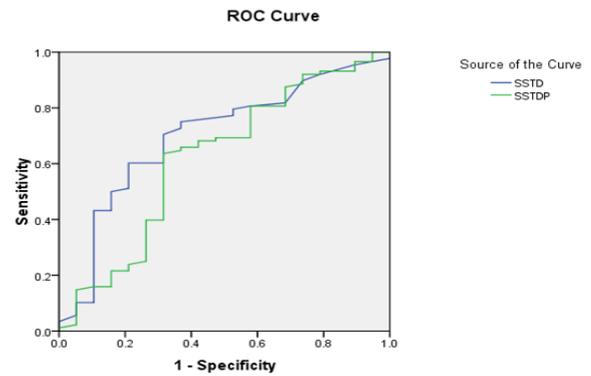


**chart.1:** Linear correlation between TIMI variations before procedure and STR



**Chart 2:** Linear correlation between TIMI variations after procedure and STR

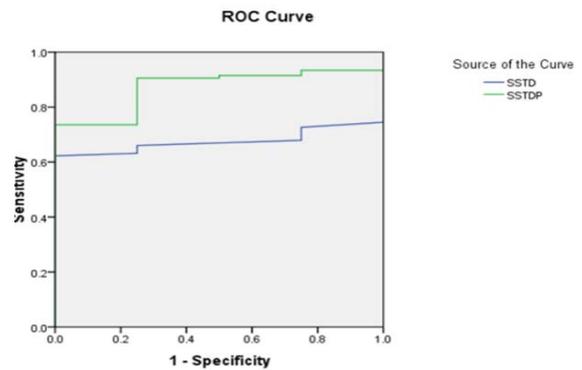
High and significant correlation was found between TIMI variations after PCI and SSTD (correlation coefficient = 0.340, P = 0.001). Additionally, high and significant correlation was found between TIMI variations after PCI and SSTD% (correlation coefficient = 0.442, P = 0.001). Based on the analysis of area under the ROC curve, evaluation of SSTD (AUC = 0.699) and SSTD% (AUC = 0.621) could predict improvement in TIMI flow in patients after PCI. In general, the best cut-off point for SSTD to predict TIMI flow improvement was estimated to be 5.25, which in this cut-off point, it showed the sensitivity of 75% and specificity of 63.2%. In addition, the best cut-off point for SSTD% to predict the TIMI flow improvement was determined to be 45%, which in this cut-off point, it showed the sensitivity of 69.3% and specificity of 52.6% (Charts 1 and 2).



Area Under the Curve

**Chart 3:** area under curve ROC in predicting TIMI variations by SSTD and SSTD%

Test Result Variable(s)	Area	Std. Error	Asymptotic Sig.b	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
SSTD	.699	.067	.007	.569	.830
SSTD%	.621	.077	.099	.471	.771



Area Under the Curve

**Chart 4:** area under curve ROC in predicting mortality by SSTD and SSTD%

Test Result Variable(s)	Area	Std. Error	Asymptotic Sig.b	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
SSTD	.676	.048	.234	.582	.770
SSTD%	.873	.048	.012	.778	.968

The mean SSTD in patients who finally died and living patients was  $9.57 \pm 9.88$  and  $17.40 \pm 10.71$ , respectively, which was significantly lower in patients who died (P value = 0.002). Additionally, mean SSTD% in patients who died and living patients was  $37.23 \pm 26.29$  and  $57.10 \pm 17.97$ , respectively, which was significantly lower in patients who died (P = 0.001). According to the analysis of area under ROC curve, evaluation of SSTD (AUC = 0.667) and SSTD% (AUC = 0.873) could predict the occurrence of mortality in patients after PCI. Based on the analysis of area under the ROC curve, evaluation of SSTD (AUC = 0.676) and SSTD% (AUC = 0.873) could predict occurrence of mortality in patients after

PCI. In general, the best cut-off point for SSTD to predict TIMI flow improvement was estimated to be 6.0, that in this cut-off point, it showed the sensitivity of 67% and specificity of 50%. In addition, the best cut-off point for SSTD% to predict the TIMI flow improvement was determined to be 35%, that in this cut-off point, it showed the sensitivity of 75.5% and specificity of 75% (Charts 1 and 2).

## Discussion and conclusion

Researcher followed two main objectives in the current research. First, the correlation between TIMI flow variations and SSTD and also SSTD% was tested, and the importance of assessing these two indices, including SSTD and SSTD%, in predicting the improvement in the TIMI index as an applied criterion in evaluating the myocardial reperfusion was evaluated. Then, the role of SSTD and SSTD% in predicting the procedural mortality was investigated after determining the frequency of patient mortality after the PCI procedure. Our research confirmed the significant role of two indices of SSTD and SSTD% in predicting the improvement in TIMI and improvement of reperfusion in patients underwent PCI, so that they predicted the TIMI grade improvement with acceptable sensitivity and specificity. An interesting point was determining two indices of SSTD and SSTD with acceptable sensitivity and specificity in predicting the mortality following the PCI in these patients. Thus, the final role of STR in evaluating the value of TIMI flow and predicting the post-PCI death was completely confirmed. As stated before, findings revealed that measuring and evaluating STR is a stronger predictor for patency of coronary arteries involved. Recent research revealed a significant relationship between higher STR and higher values of patency and TIMI III<sup>[37, 38]</sup>. In fact, investigating the STR in differentiating two groups with TIMI II and TIMI III was very valuable, so that patients with TIMI III showed higher STR compared to the patients with TIMI II, which this result is in line with our research<sup>[44]</sup>. The research conducted by Gibson *et al.* in 2004 revealed that occurrence of STR was associated with improved TIMI on angiography<sup>[80]</sup>. In a research carried out by Aasa *et al.*, STR value was more than 50% in 73% of the patients, which showed a significant correlation with TIMI<sup>[81]</sup>. Our research also revealed that measuring the STR and its variation was strong predictor for occurrence of the post-PCI mortality. Unlike our research, in the research conducted by Ndrepepa *et al.*, in 2012<sup>[82]</sup> and the research conducted by van der Zwaan *et al.* in 2010<sup>[83]</sup>, it was found that determining the STR in patients with STEMI could predict post-PCI mortality. However, similar to our research, in the research conducted by Wang *et al.* in 2015, increase in STR led to significant improvement in MACE in patients underwent PCI due to STEMI<sup>[84, 92]</sup>. It seems that the differences in results obtained in different studies on role of STR in predicting the PCI outcome might be due to different reasons, such as the number of samples examined, type of research performed in terms of being cross-sectional or prospective, inclusion and exclusion criteria of research, sampling method, and follow-up time of patients. It could be concluded that measuring the STR can be a strong predictor of TIMI grade variations after the PCI procedure. In addition, determining the STR will have high value in predicting the mortality after the mentioned procedure.

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