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Association between ST-Segment Resolution Following Thrombolysis and Reperfusion of Infarct Related Artery in Coronary Angiogram in Patients with ST-Segment Elevation Myocardial Infarction

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ABSTRACT

Background: ST-segment elevation myocardial infarction (STEMI) is the most critical form of acute coronary syndrome as having the worst overall prognosis. Following thrombolysis, if it is possible to reliably predict about the reperfusion status by means of a non-invasive, readily available tool like ECG, it will help the clinicians to determine the quality of reperfusion and select the next strategy of management. The aim of the study was to assess angiographic findings of TIMI flow in infarct related artery (IRA), compared to the ranges of ST-segment resolution, and determine their association to predict reperfusion in IRA.

Methods: This cross-sectional observational study was conducted in the department of Cardiology at National Institute of Cardiovascular Diseases (NICVD), Dhaka, for 12-months following ethical approval. A total of 116 adult patients with acute STEMI who underwent thrombolysis with streptokinase were enrolled by convenient sampling method after taking written informed consent. The percent resolution of ST-segment deviation from baseline to 60 minutes following thrombolysis was compared with angiographic IRA TIMI flow grade in index hospitalization. Detailed history, thorough clinical examination and necessary investigations were carried out in each patient and recorded in predesigned structured questionnaire. Data were analyzed by SPSS 26.0.

Results: The mean age of the patients was 50.8 ± 8.8 years with male predominance (77.6%). Among all, 45.7% had >70% ST resolution followed by 29.3% had 30-70% and 25% had <30% ST resolution. Regarding TIMI grade flow, 59.1% had grade-3, 22.7% had grade-2 and 18.2% had grade 0 or 1. TIMI grade flow significantly increased with the increased ST-segment resolution. A cut off value of ST-segment resolution ≥57.5% (AUC=0.771, 95% CI=0.684-0.858, p<0.001) in the prediction of TIMI grade flow 3 showed 67.69% sensitivity, 66.67% specificity, 74.58% PPV, 58.82% NPV and 67.27% accuracy. Multivariate logistic regression shows that timing of thrombolysis, >70% ST resolution showed higher odds ratio and >70% ST resolution showed statistically significant p-value for predicting TIMI grade flow 2 or 3.

Conclusion: ST-segment resolution in electrocardiogram following thrombolysis has significant positive association with TIMI flow of infarct related artery in coronary angiogram. However, further larger study is recommended.

KEYWORDS: STEMI, Thrombolysis, ST-segment resolution, TIMI flow grade, Infarct related artery

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INTRODUCTION

A prompt diagnosis with an aim of immediate reperfusion of the infarct-related artery (IRA) is needed to improve the survival in case of ST-segment elevation myocardial infarction (STEMI). Primary PCI has higher rate of success in reperfusion and lower rate of adverse outcome as compared to thrombolysis, when performed in timely manner, in high-volume, experienced centers.[1] In Bangladesh, thrombolysis is currently the most practiced form of reperfusion method due to resource constraints. However, in only 60% - 70% of patients of acute STEMI, thrombolytic therapy results in grade III flow as per the thrombolysis in MI (TIMI) classification system.[2] Angiography is a gold standard technique to measure the patency and reperfusion of infarct-related artery (IRA).[2] Following thrombolysis, if it is possible to reliably know about the reperfusion status by means of a non-invasive, readily available tool like ECG, it will help the clinicians to determine the quality of reperfusion and select the next strategy of management (i.e., pharmacoinvasive strategy) more effectively and efficiently in a limited resource environment. De Lemos et al. showed in their study that a >70% reduction in the ST-segment resolution at 90 minutes after thrombolysis was a useful indicator of the outcome of reperfusion.[3] However, recent data are limited showing association between TIMI flow and ranges of ST-segment resolution (<30%, 30-70%, >70%) following thrombolysis with streptokinase, ensuing current guideline directed medical therapy. In this study, we assessed angiographic findings of TIMI flow in IRA, compared to the ranges of ST-segment resolution, and determined their association to predict reperfusion in IRA.

METHODOLOGY

This cross-sectional observational study carried out in the Department of Cardiology at National Institute of Cardiovascular Diseases (NICVD), Dhaka, Bangladesh from September 2022 to August 2023. Inclusion criteria: Adult patients presenting within 12 hours of symptom onset to the emergency department who met the electrocardiographic (ECG) criteria for STEMI and underwent thrombolysis with streptokinase and subsequently underwent coronary angiogram in index hospitalization. Exclusion criteria: Patients with non-persistent ST segment elevation (<20 mins), ST-segment elevation in aVR and/or V1 coupled with ST depression ≥ 1 mm in eight or more surface leads, true posterior STEMI, conditions precluding the evaluation of ST segment, or with prior history of STEMI, NSTEMI, PTCA, PCI, CABG were excluded. Patients who underwent thrombolysis elsewhere other than NICVD was also excluded.

PROCEDURE

A total of 116 adult patients with acute STEMI who underwent thrombolysis with STK were finally enrolled in this study. Baseline characteristics were noted. 12 lead resting ECG was done at a paper speed of 25 mm/s and 10mm/mV standardization at admission (Wuhan Zoncare Bio-medical Electronics Co., Ltd). Diagnosis of STEMI was made following standard ECG criteria. Within 10 minutes of diagnosis of acute STEMI, patients received intravenous STK 1.5 million units over 30 minutes after excluding any contraindication. After 60 minutes of administration of intravenous STK, 12 lead resting ECG was done once again at a paper speed of 25 mm/s and 10 mm/mV standardization. Both ST-segment elevation and depression at J-point from baseline was measured in millimeters using Slide caliper Set before thrombolysis and one hour after thrombolysis. Summation of elevation and depression had provided the ST-segment deviation. Percentage of follow-up ST deviation to baseline ST deviation was finally be deducted from 100% to find out ST-segment resolution in percentage. Coronary angiography was performed through trans femoral or trans radial approach (Judkins technique) within the index hospitalization using the Trinias system for Interventional Angiography, SHIMADZU. Epicardial blood flow was assessed angiographically using the thrombolysis in myocardial infarction (TIMI) score for qualitative grading of coronary flow by visual estimation. Two expert cardiologists who were blinded of the ECG changes had evaluated the CAG images.

STATISTICAL METHODS

Continuous data were expressed as mean. Categorical data were expressed as frequency and percentage and comparison was done by using Chi-square test and if necessary, Fisher's exact test. Univariate and multivariate logistic regression analysis were done for detecting factors associated with TIMI grade flow 2 or 3. An online calculator (MedCalc, Ostend, Belgium) was used to calculate the sensitivity, specificity, positive and negative predictive value for ST-resolution in predicting the success of thrombolysis. Statistical analysis was carried out by using SPSS 26.0 in Windows operating system. A level of $P<0.05$ was considered statistically significant.

RESULT

The mean age of the study population was 50.8 ± 8.8 years. Majority (90 patients) were male. Among all, 48.3% were current smokers, 32.8% had hypertension, 24.1% had DM, 12.1% had renal disease and 26.1% had BMI >25kg/m2. 45.7% had anterior infarction and 54.3% had inferior infarction. ST resolution pattern among the cases are shown in table 1.

Table 1: Distribution of the patients according to ECG findings (n=116)

ST-segment deviation	Frequency (n)	Percentage (%)
>70% ST resolution	53	45.7
30% -70% ST resolution	34	29.3
<30% ST resolution	29	25

ST resolution more than 70% was significantly higher in inferior infarction than anterior infarction. ST-segment resolution was significantly higher among the patients who had thrombolysis within 6 hours.

Majority of the patients (63.6%) underwent coronary angiogram within 24 hours of thrombolysis followed by 20.9% within 24 to 48 hours and 15.5% within 48 to 72 hours. No significant association was found between time delay of coronary angiogram and TIMI grade flow. Regarding TIMI grade flow, the majority (59.1%) had grade 3, 22.7% had grade 2 and 18.2% had grade 0 or 1. No significant difference was found between TIMI grade flow with age, gender and smoking habit. Hypertension and DM were significantly associated with TIMI grade flow (table 2).

Table 2: Association of TIMI grade flow with comorbidity (n=110)

Comorbidity	TIMI grade flow			p-value*
	0/1 (n=20)	2 (n=25)	3 (n=65)	
Hypertension	10 (50)	12 (48)	14 (21.5)	0.010*
Diabetes mellitus	9 (45)	7 (28)	11 (16.9)	0.036*
Renal disease	2 (10)	4 (16)	7 (10.8)	0.718**
BMI>25kg/m^2	5 (25)	6 (24)	11 (16.9)	0.492*

p-value was determined by *chi-square test and **Fisher exact test. Data was presented with frequency (%) and within parenthesis percentage over column.

Increased ST-segment resolution was significantly associated with increased TIMI flow (Figure I)

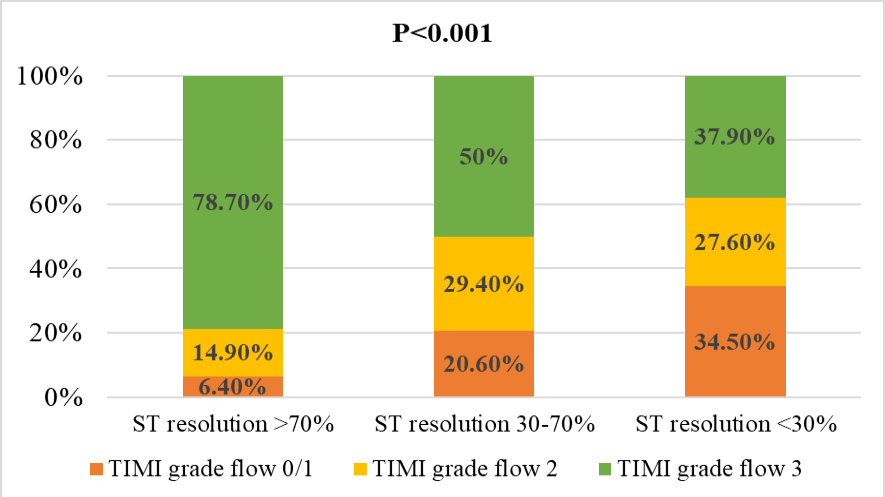

Figure I: Distribution of the patients according to TIMI grade flow in different ST-segment resolution groups (n=110)

TIMI grade flow significantly increases with the increased ST-segment resolution (table 3).

Table 3: Association of ST-segment resolution with TIMI Grade Flow (n=110)

TIMI grade	ST-segment resolution			p-value
	>70% (n=47)	30%-70% (n=34)	<30% (n=29)	
0/1	3 (6.4)	7 (20.6)	10 (34.5)	
2	7 (14.9)	10 (29.4)	8 (27.6)	<0.001*
3	37 (78.7)	17 (50)	11 (37.9)	

p-value was determined by *Fisher exact test and chi-square test. Data was presented with frequency (%) and within parenthesis percentage over column.

Univariate logistic regression shows that DM, timing of thrombolysis, >70% ST resolution were significantly associated with TIMI grade flow (Table 4).

Table 4: Univariate logistic regression analysis for factors associated with TIMI grade flow 2 or 3

	Odds ratio	95% CI	p-value*
Hypertension	2.462	0.917-6.611	0.074
Diabetes mellitus	3.273	1.179-9.087	0.023
Timing of thrombolysis	3.347	1.037-10.801	0.043
>70% ST resolution	4.372	1.355-14.103	0.014

P-value was determined by Univariate logistic regression.

Multivariate logistic regression showed that timing of thrombolysis, >70% ST resolution showed higher odds ratio, whereas >70% ST resolution was statistically significant for predicting advanced TIMI grade flow (Table 5).

Table 5: Multivariate logistic regression analysis for factors associated with TIMI grade flow 2 or 3

	Odds ratio	95% CI	p-value*
Hypertension	0.467	0.151-1.446	0.187
Diabetes mellitus	0.336	0.104-1.082	0.067
Timing of thrombolysis	2.782	0.778-9.948	0.115
>70% ST resolution	2.209	0.334-14.593	0.011

P-value was determined by Multivariate logistic regression.

ST resolution above 50% showed higher sensitivity for both TIMI grade 2 or 3 or for grade 3 (table 6)

Table 6: Prediction of TIMI grade flow by ST- resolution (n=110)

	Sensitivity	Specificity	PPV	NPV
TIMI grade flow at 60 min For grade 2,3				
>70% ST resolution	53.33%	85%	94.11%	28.8%
>50% ST resolution	66.67%	70%	90.91%	31.81%
For Grade 3				
>70% ST resolution	58.46%	71.11%	74.51%	54.23%
>50% ST resolution	69.23%	53.33%	68.18%	54.56%

A cut off value of ST-segment resolution ≥57.5% (AUC=0.771, 95% CI=0.684-0.858, p<0.001) in the prediction of TIMI grade flow 3 showed 67.69% sensitivity, 66.67% specificity, 74.58% PPV, 58.82% NPV and 67.27% accuracy (Figure II).

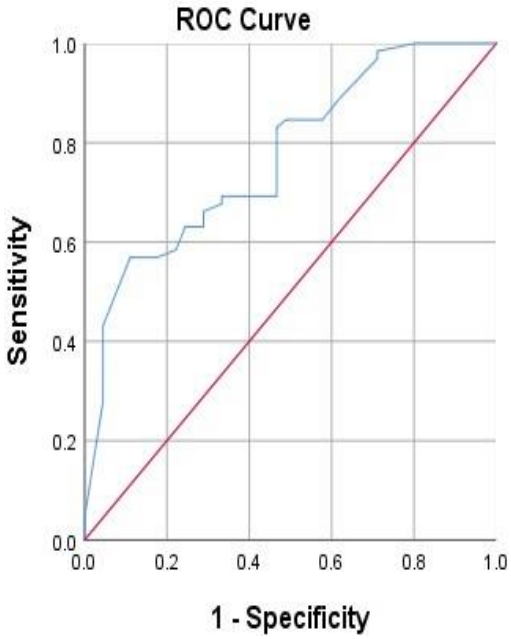

Figure II: ROC curve analysis of ST-segment resolution in the prediction of TIMI grade flow 3 (n=110)

DISCUSSION

This cross-sectional study was conducted to determine the association between ST segment resolution following thrombolysis and TIMI grade flow of IRA in patients with STEMI. A total of 116 patients were enrolled, among them 6 patients were discarded from the study due to lost in follow-up. Age and gender distribution was almost similar to the previous study.[3] In our study, all patients underwent thrombolysis with streptokinase, on the other hand in de Lemos et al. different thrombolytic combinations were used: abciximab alone, alteplase alone, abciximab with reduced doses of alteplase, and abciximab with reduced doses of streptokinase, but in Zeymer et al. streptokinase alone was used as thrombolytic.[3, 4]

Majority of the patients (45.7%) had complete ST resolution. Regarding TIMI grade flow, the majority (59.1%) had grade 3 flow. In the previous studies, the majority also had complete ST resolution and TIMI grade 3 flow, although the proportion of different groups varied due to the condition of enrolled patients during the study.[4, 5]

In our study, we found positive correlation between TIMI grade flow with the ST-segment resolution. Patients who met the criteria of complete ST-segment resolution from baseline ECG at 60 minutes of thrombolysis had shown very high

probability (94.11%) of IRA patency. This is similar with the previous studies.[4, 5] Although significant ST-segment resolution accurately predicted the IRA patency, we did not find absence of significant ST-segment resolution accurately predict the IRA occlusion. In fact, most patients without resolution of ST segment deviation had patent IRA at the time of coronary angiogram. These findings are consistent with previous de Lemos et al study and signify that persistent ST segment deviation is not merely a reflection of reduced epicardial blood flow rather a reflection of extensive tissue and microvascular injury.[5] So, absence of ST resolution designates either no myocardial reflow or epicardial artery occlusion that may warrant immediate rescue PCI or pharmacological treatment. At the other end, in those few patients who had complete ST resolution yet persistent occlusion (TIMI grade 0/1) in IRA, may have effective collateral circulation that may attenuate myocardial ischemia.

Univariate logistic regression shows that DM, timing of thrombolysis, complete ST resolution were significantly associated with advanced TIMI grade flow. Multivariate logistic regression shows that timing of thrombolysis and complete ST resolution showed higher odds ratio, whereas only complete ST resolution was statistically significant for predicting advanced TIMI grade flow. After the impact of all baseline factors, quick reperfusion therapy and resolution of ST deviation were linked with a significantly favorable result with regard to all outcome variables.[3, 6]

In our study, complete ST resolution was significantly higher in inferior infarction than anterior infarction. Previous study also revealed that patients with inferior MI were significantly more likely to have complete ST resolution than were patients with anterior MI.[3] Study of Barbash et al. also observed the similar findings.[6] Those with anterior MI may have more extensive microvascular injury due to interruption of perfusion in larger area of myocardium causing less ST resolution. In addition, either in healthy or in pathological condition, the J point is typically found higher in anterior precordial leads which may explain the reason ST resolution is less sensitive in patients with anterior MI than those with inferior MI as a measure of epicardial reperfusion.[7]

ST resolution above 50% showed higher sensitivity for predicting both TIMI grade 2 or 3 and for only grade 3 flow compared to above 70% ST resolution which was consistent with the previous study.[3] In our study, a cut off value of ST-segment resolution ≥ 57.5% (AUC=0.771, 95% CI=0.6840.858, p<0.001) in the prediction of TIMI grade flow 3 showed higher sensitivity, specificity, PPV, NPV with 67.27% accuracy. In Zeymer et al., the best cut off was around 40%.[4]

Despite some important methodological differences, this study yielded similar findings that were found in some previous studies, suggesting ST-segment resolution had significant positive association with TIMI flow of infarct related artery in coronary angiogram and is a highly accurate marker of IRA patency (positive predictive value ≥90%) yet inaccurate for predicting IRA occlusion (negative predictive value near to 30%). Combination of ST resolution with other noninvasive predictors like the chest pain resolution, rapid washout of serum cardiac biomarkers may improve the predictive value for IRA occlusion. However, since previous studies like de Lemos et al. showed no or partial ST resolution was associated with higher 30-day mortality, this may warrant rescue PCI or routine early PCI as the next strategy of management for these specific patients.[5]

CONCLUSION

Study results show that ST-segment resolution in electrocardiogram following thrombolysis has significant positive association with TIMI flow of infarct related artery in coronary angiogram. ST-segment resolution ≥57.5% was found to be the best cut-off in the prediction of TIMI grade flow 3.

RECOMMENDATIONS

- ST-segment resolution can be a useful tool for clinicians to determine the quality of reperfusion and select the next strategy of management.
- Further randomized multicenter studies with larger sample size are recommended.

LIMITATIONS OF THE STUDY:

- All samples were collected from a single centre.
- TIMI flow grade was assessed by visual observation, so there was every chance of interobserver variation.

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