

Resolution of Reciprocal ST Segment Depression as Predictor for Major Cardiovascular Events in Stemi Patients Treated with Alteplase

Aldino S. Adhitya*¹, Harris Hasan¹, Andika Sitepu¹, Zulfikri Mukhtar¹

¹Department of Cardiology and Vascular Medicine, University of Sumatera Utara, Adam Malik Hospital, Medan, Indonesia

Abstract : Background: ST Elevation Myocardial Infarction (STEMI) may cause Major Cardiovascular Events (MACEs). Revascularization needs to be done in all STEMI patients to restore coronary blood flow, hence saving myocardial perfusion. Reciprocal ST Segment Depression (STSD) is associated with poor prognosis in STEMI patients receiving fibrinolytic therapy. The main purpose of this study is to evaluate MACE in STEMI patients receiving alteplase as fibrinolytic therapy using resolution in STSD.

Methods: This cohort prospective study with 60 subjects of STEMI patients which are evaluated for MACEs (death, heart failure, and rehospitalization) within 30 days after myocardial infarction. Resolution in reciprocal STSD is defined as resolution \geq 50% STSD in reciprocal leads within 90 minutes after fibrinolytic therapy.

Results: Bivariate analysis showed that Ejection fraction (EF) $<$ 40% with OR 8,32 (2,11-32,74), $p=0,001$; smoking with OR 4,17 (1,05-16,57), $p=0,034$; Anterior STEMI with OR 3,94 (1,11-13,90), $p=0,027$; Creatinine $>$ 1,97 mg/dl with OR 3,69 (1,18-11,55), $p=0,022$; complete outpatient medication with OR 5,23 (1,61-17,01), $p=0,004$; fragmented QRS with OR 5,23 (1,61-17,01), $p=0,001$; resolution in STSD with OR 26,35 (5,16-134,40), $p<0,001$; resolution in ST Segment Elevation with OR 10,5 (2,97-37,24), $p<0,001$; are proven to be determining factor for MACE within 30 days. Multivariate analysis showed that among those determining factors for MACEs, resolution in STSD in reciprocal leads is evidently the most dominant factor for predicting MACEs within 30 days in STEMI patients receiving fibrinolytic therapy [OR 11.47 (1.14-115.10), $p=0.038$].

Conclusion: There is significant difference in MACEs within 30 days after myocardial infarction (MI) between patients with and without resolution in STSD. The subjects without resolution in STSD showed higher MACEs incidence. Resolution in STSD is evidently an independent predictor for MACEs within 30 days after myocardial infarction in STEMI patients.

Keywords : Resolution in STSD, MACE, STEMI, Fibrinolytic.

Introduction

ST Elevation Myocardial Infarction (STEMI) is a part of Acute Coronary Syndrome resulting from total occlusion of coronary artery by thrombus formation as a result from ruptured atherosclerotic plaque. STEMI can cause sudden cardiac death or other MACEs during or after hospitalization. Nowadays, MACEs occur in 10.3% STEMI patients receiving reperfusion therapy.¹

Revascularization needs to be done to restore blood flow in coronary artery. This can be done by one of two options, which are Primary PCI strategy, or fibrinolytic therapy. Revascularization is indicated for all STEMI patients with new onset, which is below 12 hours of presentation.^{2,3} In H Adam Malik General Hospital (HAMGH) reperfusion therapy is achieved 91% by fibrinolytic therapy⁴, but the success rate of this therapy and MACEs occurring after receiving fibrinolytic have never been studied before. This is related to success criterias of fibrinolytic therapy, which are resolution in more than 50% of ST Segment Elevation level, the significantly diminishing of angina, and the presence of reperfusion arrhythmia such as idioventricular rhythm. Of all these criterias for successful fibrinolytic, only the presence of reperfusion arrhythmia can be objectively evaluated. The other criteria such as resolution of ST segment elevation is still in the gray area, and whether it is considered resolved even with the development of pathological Q wave. This was not stated clearly.

ECG findings are still considered to be the main key of making diagnosis of STEMI. ECG is the gold standard in locating the STEMI area. Even more information can be obtained from ECG findings, such as infarct size, and long term prognosis in STEMI patients.^{5,6} There are typical ECG findings that we can see in STEMI patients, such as ST segment elevation morphology in corresponding lead, and reciprocal ST segment depression as mirror image from non infarcted area of the myocardium with the prevalence of 54-82%.^{7,8,9} The presence of reciprocal ST segment depression (STSD) are often seen in inferior STEMI (72%) compared to anterior STEMI (37%). Reciprocal STSD are also more frequently seen in STEMI with complication and even larger infarct area.¹⁰

At first, reciprocal STSD are considered as benign electrical phenomenon.^{11,12} With advancing techniques of coronary angiography and non invasive cardiac imaging, it is easier to evaluate ventricular function globally and segmentally.¹¹ There are a lot of experimental studies to prove this benign electrical phenomenon theory. But unfortunately still with inconsistent results. Most of the studies give an alternative theory that reciprocal STSD shows even larger infarct area resulted from occluded coronary culprit. This is proven with higher level of increasing cardiac enzyme, more extensive wall motion abnormality, and even more reduced LV EF, compared to STEMI patients without reciprocal STSD. STEMI with reciprocal STSD are associated with poorer in hospital and long term prognosis, and even higher mortality compared to those without reciprocal STSD.^{13,14,15,16,17}

Stevenson *et al*, tried to prove that reciprocal STSD in STEMI patients receiving fibrinolytic are associated with poorer prognosis. Buller *et al*, stated that resolution in reciprocal STSD soon after primary PCI turned out to be a simple prognostic parameter.¹⁹ There has been a study in HAMGH which stated the presence of reciprocal STSD as a prognostic marker in patients with inferior STEMI.²⁰ Nevertheless, for subjects with inferior STEMI, recent studies showed that resolution in reciprocal STSD is far more important than the elevation in ST segment itself as short-term prognostic marker.²¹

Considering the importance of resolution in reciprocal STSD as a simple parameter, but efficient, for predicting prognosis in patients with STEMI receiving early reperfusion, the author wants to compare the MACEs outcome between those with and without resolution in reciprocal STSD.

Methods

Study Design

This prospective cohort study included subjects with STEMI patients receiving alteplase as fibrinolytic therapy in Cardiology Department HAMGH. Inclusion criteria was STEMI patients with reciprocal STSD receiving fibrinolytic therapy by alteplase, below 12 hour of onset, and never had any episode of myocardial infarction before. ECGs that cannot be interpreted were excluded. ECGs were made soon after admission in the

ER, and 90 minutes after fibrinolytic started, with ECG calibrated at 25 mm/s and 10 mm/mV using ECG GE MAC 2000.

From March 2017 until December 2017, 108 subjects were included. 48 subjects were excluded due to history of myocardial infarction before and some not feasible ECG recordings. Leaving 60 subjects of STEMI patients studied.

Study Procedure

Samples collection was done using consecutive sample method. Baseline characteristics, subject identities, and history of illness and medication were recorded. ECGs were evaluated soon after admission, and 90 minutes after fibrinolytic started. Pre-fibrinolytic STSD was calculated at 80ms after J points from isoelectrical baseline. STSD was evaluated using 150 mm Krisbow micrometer dial caliper (KW0600352) and magnifying glass. The result of STSD evaluation was reported in mm. Resolution in reciprocal STSD was calculated with :

$$\text{Resolution } \sum \text{DSST } (\%) = \frac{\sum \text{DSST pre fibrinolytic} - \sum \text{DSST post fibrinolytic}}{\sum \text{DSST pre fibrinolytic}} \times 100$$

based on ECG recordings, the subjects were divided by two groups, which are STEMI with reciprocal STSD and STEMI without reciprocal STSD. Evaluation of the ECG was done by resident in charge at the ER and validated by cardiologist.

Subjects were then followed up for 30 days after admission. Followed up was done by interview and medical check up for detecting MACEs after myocardial infarction.

Statistical Analysis

Data was extracted and analysed by statistical computer software. Categorical data was presented with number or frequency (n) and percentage (%). Numeric data was presented with mean and standard deviation for normally distributed data. Normality test was done using Kolmogorov-Smirnov with $n > 50$. Comparison between two groups on dependent and independent categorical variable was done using Chi Square test. Fisher test was done if Chi Square conditions are not fulfilled. Comparison between two groups on independent categorical variable and dependent numeric variable was done using unpaired T test. Mann Whitney test was done if unpaired T test conditions are not met. Significant variable in bivariate analysis was tested in multivariate analysis. Those with significant result in multivariate analysis was presented with Odds Ratio (OR) with 95% CI.

Results

Baseline Characteristics

Subjects were divided into 2 groups, which are STEMI with resolution in reciprocal STSD (50%, $n=30$), and STEMI without resolution in reciprocal STSD (50%, $n=30$). Mean age is 54 years old for STEMI with resolution in reciprocal STSD resolution, and 53 years old for STEMI without resolution in reciprocal STSD resolution. In the STEMI with resolution in reciprocal STSD group, 22 patients (73.3%) are male. Compared to the STEMI without resolution in reciprocal STSD group, 24 patients (80%) are male. Mean systolic blood pressure is 130 mmHg in the STEMI with resolution in reciprocal STSD group, and 120 mmHg in the STEMI without resolution in reciprocal STSD group. Mean heart rate on admission is 77 times per minute in the STEMI with resolution in reciprocal STSD group, and 76 times per minute in the STEMI without resolution in reciprocal STSD group.

There was no significant difference in the blood work up between two groups. This accounts on leukocyte count, ureum and creatinine level. There is also no significant difference in the coronary risk factor between two groups.

This study showed there is significant difference in anterior MI and LV ejection fraction (LV EF) between two groups. STEMI without resolution in reciprocal STSD tend to happen in anterior MI (83.3%, n=25). Compared to the other group, which showed lower rate of anterior MI in STEMI with resolution in reciprocal STSD (33.3%, n=10). STEMI with resolution in reciprocal STSD tend to have higher LV EF compared to the other group, which is 52% and 43% respectively ($p < 0.001$). Baseline characteristic is showed on table 1.

Subject Characteristic Based on MACEs

From 60 subjects, 40 had MACEs and 19 did not. With the proportion of heart failure was 11 subjects (18%), rehospitalization was 6 subjects (10%), and death was 4 subjects (7%) in 30 days after myocardial infarction.

Characteristic of ECG Findings Based on MACEs

There was significant difference in ECG findings between subjects with and without MACEs. This accounts on QRS fragmentation, resolution in ST segment elevation, and resolution in reciprocal ST segment depression.

Fragmented QRS was found in 13 subjects with MACEs (68.4%) and 10 subjects without MACEs (24.4%) with p value 0.001. Resolution in ST segment elevation was found in 6 subjects with MACEs (31.6%) and 34 subjects without MACEs (82.9%) with p value < 0.001 . Resolution in reciprocal ST segment depression was found in 1 subject with MACEs (5.3%) and 32 subjects without MACEs (78%). Characteristic of ECG findings is showed on table 2.

Comparison of MACEs in 30 days after STEMI treated with Alteplase with and without resolution in reciprocal STSD

STEMI without resolution in reciprocal STSD had higher incidence of MACEs (85.9%, n=17) compared to STEMI with resolution in reciprocal STSD (10.5%, n=2). STEMI without resolution in reciprocal STSD were more likely to have MACEs within 30 days after myocardial infarction (OR 18.3) compared to STEMI with resolution in reciprocal STSD (figure 1).

Resolution in reciprocal STSD as Predictor for MACEs in 30 days after STEMI treated with Alteplase

Based on bivariate analysis, resolution in reciprocal STSD can be used as a predictor for MACEs in 30 days after myocardial infarction (Table 4). There is significant difference in MACEs between STEMI with and without resolution in reciprocal STSD. STEMI without resolution in reciprocal STSD had higher incidence of MACEs compared to those with resolution in reciprocal STSD.

Bivariate analysis showed 8 risk factors determining MACEs in STEMI population, which are LV EF (p value 0.001), smoker (p value 0.034), anterior STEMI (p value 0.027), serum creatinine level (p value 0.022), drug compliance (p value 0.004), QRS fragmentation (p value 0.001), resolution in reciprocal STSD (p value 0.001), and resolution in ST segment elevation (p value < 0.001).

Multivariate analysis was done to these variables. There are 3 variables proven significant amongst all variables, which are resolution in reciprocal STSD, drug compliance, and serum creatinine level. Resolution in reciprocal STSD is evidently the most dominant predictor for MACEs in 30 days after myocardial infarction with OR 11.47 ((1.14-115.10), p value 0.038).

Discussion

The most evidently significant ECG findings for predicting MACEs are QRS fragmentation, resolution in ST segment elevation, and resolution in reciprocal STSD. Data acquired from TIMI-4 study showed QRS fragmentation was correlated with larger infarct size and more extensive myocardial scarring proven by sestamibi Tc-99m scanning.⁵ In the era of primary PCI and fibrinolytic therapy, resolution in ST segment elevation is a marker for reperfusion and patency of coronary artery (estimated by TIMI flow), hence showing smaller infarct size.^{22,23,24} Lately, the presence of ST segment depression (other than ST segment elevation) and

resolution to these ST segment depression appear to be an important prognostic marker. This represents ischemia in other region of myocardium, or reciprocal to the location of ST segment elevation. The presence of this STSD is associated with larger infarct area and poorer prognostic outcome.^{5,25,26,27}

This study showed that STEMI without resolution of ST segment depression had higher rate of MACEs in 30 days after myocardial infarction compared to those with resolution in ST segment depression. This result is consistent with other study showing higher rate of in-hospital mortality in STEMI patients without resolution in ST segment depression, compared to those with resolution in ST segment depression²⁸. Other studies proved that inferior STEMI with reciprocal ST segment depression has larger infarct area, compared to those without reciprocal ST segment depression³⁰. Now, it is concluded that not only elevation and resolution in ST segment that accounts for infarct area, as well as prognostic marker, for STEMI patients. Depression and resolution in reciprocal ST segment also contributes to the infarct area, hence affect the management strategy for STEMI patients.

After being adjusted to other variable affecting MACEs in 30 days after myocardial infarction, resolution in reciprocal STSD is proven dominant in predicting MACEs. This is consistent with studies done by Tjandrawidjaja et al, 2010³¹; Wong et al, 2015³²; and Reinstadler et al, 2015³³. Which stated that absence of resolution in STSD is associated with higher rate of MACEs in reperfused STEMI patients. We can conclude that resolution in reciprocal STSD can be used as predictor for MACEs in 30 days after myocardial infarction in STEMI patients treated with Alteplase.

Conclusion

This study concluded that STEMI patients without resolution in reciprocal STSD had higher rate of MACEs in 30 days after myocardial infarction. Resolution in reciprocal STSD can be used as predictor for MACEs with OR 11.47.

Limitations

Considering the limited number of STEMI patients treated with alteplase, caused by advancing facility in hospital for doing primary PCI, larger studies with larger population is required to get better and more reliable results.

Table 1. Baseline Characteristic Classified by Resolution on Reciprocal STSD

	subjects N=60	Resolution on STSD		
		Presence n = 30	Absence n = 30	p
Age (years)	54 ± 9	54 ± 8	53 ± 9	0,526
Male (number, %)	46 (77)	22 (73,3)	24 (80)	0,542
Body weight (kg)	70 (50-87)	70 (50-87)	69 (50-85)	0,480
SBP (mmHg)	129 (70-200)	130 (100-200)	120 (70-170)	0,594
Heart rate (beat per minute)	77 ± 15	77 ± 12	76 ± 17	0,815
Smoker (number, %)	39 (65)	18 (60)	21 (70)	0,417
DiabetesMelitus(number, %)	24 (40)	11 (36,7)	13 (43,3)	0,598
Hypertension (number, %)	35 (58)	16 (53,3)	19 (63,3)	0,432
Dyslipidemia (number, %)	45 (75)	25 (83,3)	20 (66,7)	0,136
Obesity (number, %)	11 (18)	6 (20)	5 (16,7)	0,739
Anterior STEMI(number, %)	35 (58)	10 (33,3)	25 (83,3)	<0,001
Ejection fraction (% , %)	48 (25-60)	52 (25-60)	43 (26-54)	<0,001
Leukocyte (mm ³)	12647 ± 3778	13231 ± 2979	12063 ± 4411	0,234
Ureum (mg/dl)	24 (9-105)	21 (9-105)	25 (13-90)	0,426
Creatinine (mg/dl)	0,90 (0,59-6,61)	0,90 (0,59-6,61)	0,89 (0,60-3,61)	0,827

Table 2. Characteristic of ECG Findings Based on MACEs

ECG Findings	MACEs (+) n = 19	MACEs (-) n = 41	<i>p</i>
Left Ventricle Hypertropy (n, %)	1 (5,3)	2 (4,9)	1
QRS Fragmentation (n, %)	13 (68,4)	10 (24,4)	0,001
Rs Configuration (n, %)	6 (31,6)	6 (14,6)	0,127
T Wave Inversion (n, %)	12 (62,3)	20 (48,8)	0,299
Resolution in STE (n, %)	6 (31,6)	34 (82,9)	<0,001
Resolution in STSD (n, %)	1 (5,3)	32 (78)	<0,001
Resolution of T Wave Inversion (n, %)	3 (15,8)	10 (24,4)	0,452
Pathological Q Wave Post (n, %)	17 (89,5)	33 (80,5)	0,385
Resolution on STE with Pathological Q Wave	6 (96,7)	28 (82,4)	0,264

Table 3. Bivariate Analysis on STSD Resolution with MACEs in 30 Days after STEMI Treated with Alteplase

Resolution on Reciprocal STSD (n,%)	MACEs		P	OR	CI 95%
	Presence	Absence			
Presence	2 (10,5)	28 (68,3)	<0,001	18,31	3,67-91,23
Absence	17 (89,5)	13 (31,7)			

Table 4. Bivariate Analysis on MACEs in 30 Days after STEMI Treated with Alteplase

Variables	MACEs (+) n (%)	MACEs (-) n (%)	<i>p</i>	OR (CI 95%)
SBP <100 mmHg	2 (10,5)	1 (2,4)	0,233	4,71 (0,40-55,45)
EF < 40%	9 (47,4)	4 (9,8)	0,001	8,32 (2,11-32,74)
Smoker	16 (84,2)	23 (56,1)	0,034	4,17 (1,05-16,57)
Anterior STEMI	15 (78,9)	20 (48,8)	0,027	3,94 (1,11-13,90)
Cretinine > 1,97 mg/dl	12 (63,2)	13 (31,7)	0,022	3,69 (1,18-11,55)
Drugs compliance	6 (31,6)	29 (70,7)	0,004	5,23 (1,61-17,01)
QRS Fragmentation	13 (68,4)	10 (24,4)	0,001	6,71 (2,02-22,33)
Resolution in STSD	2 (10,5)	31 (75,6)	<0,001	26,35 (5,16-134,40)
Resolution in STE	6 (31,6)	34 (82,9)	<0,001	10,5 (2,97-37,24)

Table 5. Multivariate Analysis on MACEs in 30 Days after STEMI Treated with Alteplase Analysis

Variables	OR	CI (95%)	<i>p</i>
Resolution on STSD	11,47	1,14 – 115,10	0,038
Drug compliance	10,63	1,33 – 84,67	0,026
Creatinine	9,92	1,30 – 75,73	0,027
Resolution on STE	5,79	0,80 – 41,98	0,083
Ejection Fraction	6,05	0,75 – 48,56	0,090
Smoker	11,25	0,90 – 140,01	0,060

Figure 1. Graphic Comparison of MACEs in 30 Days after STEMI treated with Alteplase, with and without Resolution in Reciprocal STSD

References

1. Arso IA. Kejadian Kardiovaskular Mayor Pada Penderita Infark Miokard Akut Dengan Elevasi Segment ST (IMAEST) Yang Dilakukan Terapi Fibrinolitik Dibanding Intervensi Koroner Perkutan (IKP) Primer Selama Perawatan Di Rumah Sakit. Tesis Profesi Ilmu Penyakit Jantung dan Pembuluh Darah FK UGM. 2012.
2. Perhimpunan Dokter Spesialis Kardiovaskular Indonesia. *Pedoman Tatalaksana Sindrom Koroner Akut*. Edisi Ketiga. Centra Communications. 2014.
3. Steg G, James SK, Atar D, et al. (2012). ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. *European Heart Journal*, 2012, 1-51.
4. Sarahazti MF. Global Longitudinal Strain (GLS) ventrikel kiri sebagai prediktor kejadian kardiovaskular mayor dalam 30 hari setelah infark miokard akut elevasi segmen ST di Rumah Sakit Haji Adam Malik Medan. Tesis Profesi Ilmu Penyakit Jantung dan Pembuluh Darah FK USU. 2017.
5. Birnbaum, Y., & Drew, B. J. (2003). The electrocardiogram in ST elevation acute myocardial infarction: correlation with coronary anatomy and prognosis. *Postgraduate Medical Journal*, 79(935), 490–504. [doi:10.1136/pmj.79.935.490](https://doi.org/10.1136/pmj.79.935.490).
6. Zimetbaum, P. J., & Josephson, M. E. (2003). Use of Electrocardiogram in Acute Myocardial Infarction. *The New England Journal of Medicine*, 348(10), 933–940. [doi:10.1056/NEJMr022700](https://doi.org/10.1056/NEJMr022700).
7. The Lancet. Reciprocal Changes Accompanying Acute Myocardial Infarction. *Lancet*, •••, (1986). 1370–1371.
8. Noriega, F. J., Jorge, E., Arzamendi, D., & Cinca, J. (2013). Mechanism and diagnostic potential of reciprocal ECG changes induced by acute coronary artery occlusion in pigs. *Journal of Heart Rhythm*, 10(6), 883–890. [doi:10.1016/j.hrthm.2013.02.022](https://doi.org/10.1016/j.hrthm.2013.02.022).
9. Ferguson, D. W., Pandian, N., Kioschos, J. M., Marcus, M. L., & White, C. W. (1984). Angiographic evidence that reciprocal ST-segment depression during acute myocardial infarction does not indicate remote ischemia: Analysis of 23 patient. *The American Journal of Cardiology*, 53(1), 55–62. [doi:10.1016/0002-9149\(84\)90683-0](https://doi.org/10.1016/0002-9149(84)90683-0).
10. Katz, R., Conroy, R. M., Robinson, K., & Mulcahy, R. (1986). The aetiology and prognostic implications of reciprocal electrocardiographic changes in acute myocardial infarction. *British Heart Journal*, 55(5), 423–427. [doi:10.1136/hrt.55.5.423](https://doi.org/10.1136/hrt.55.5.423).
11. Rude, R. E., Croft, C. H., & Willerson, J. T. (1983). “Reciprocal” anterior ST depression early in the course of transmural inferior myocardial infarction: an ECG finding of uncertain clinical significance. *International Journal of Cardiology*, 4(1), 80–85. [doi:10.1016/0167-5273\(83\)90219-X](https://doi.org/10.1016/0167-5273(83)90219-X).
12. Berger, P. B., & Ryan, T. J. (1990). Inferior myocardial infarction: high-risk subgroups. *Circulation*, 81(2), 401–411. [doi:10.1161/01.CIR.81.2.401](https://doi.org/10.1161/01.CIR.81.2.401).
13. Jennings, K., Reid, D. S., & Julian, D. G. (1983). “Reciprocal” depression of ST segment in acute myocardial infarction. *British Medical Journal*, 287(6393), 634–637. [doi:10.1136/bmj.287.6393.634](https://doi.org/10.1136/bmj.287.6393.634).
14. Gelman, J. S., & Saltrup, A. (1982). Pericardial ST depression in patients with inferior infarction: clinical implications. *British Heart Journal*, 7, 133–139.
15. Herlitz, J., & Hjalmarson, H. (1987). Occurrence of Anterior ST depression in Inferior Myocardial Infarction and relation to clinical outcome. *Clinical Cardiology*, 10(9), 529–534. [doi:10.1002/clc.4960100914](https://doi.org/10.1002/clc.4960100914).
16. Hasdai, D., Sclarovsky, S., Solodky, A., Sulkes, J., Strasberg, B., & Birnbaum, Y. (1994). Prognostic significance of maximal pericardial ST segment depression in right (V1-V3) versus left (V4-V6) leads in patients with inferior wall acute myocardial infarction. *The American Journal of Cardiology*, 74(11), 1081–1084. [doi:10.1016/0002-9149\(94\)90455-3](https://doi.org/10.1016/0002-9149(94)90455-3).
17. Forfar, J. C. (1989). Reciprocal ST segment changes in acute myocardial infarction: informative or incidental? *The Quarterly Journal of Medicine*, 72, 763–765.
18. Stevenson, R. N., Ranjadayalan, K., Umachandran, V., & Timmis, A. D. (1993). Significance of reciprocal ST depression in acute myocardial infarction: a study of 258 patients treated by thrombolysis. *British Heart Journal*, 69(3), 211–214. [doi:10.1136/hrt.69.3.211](https://doi.org/10.1136/hrt.69.3.211).
19. Buller, C. E., Fu, Y., Mahaffey, K. W., Todaro, T. G., Adams, P., Westerhout, C. M., & Armstrong, P. W. (2008). ST-Segment Recovery and Outcome After Primary Percutaneous Coronary Intervention for ST-Elevation Myocardial Infarction. *Circulation*, 118(13), 1335–1346. [doi:10.1161/CIRCULATIONAHA.108.767772](https://doi.org/10.1161/CIRCULATIONAHA.108.767772).

20. Suganti J. Perbandingan Kejadian Klinis Kardiovaskular Mayor Selama Perawatan di Rumah Sakit Pada Penderita Infark Miokard Akut Elevasi Segment ST Inferior dengan dan Tanpa Depresi Segment ST Perikordial di Rumah Sakit Haji Adam Malik Medan. Tesis Magister Ilmu Penyakit Jantung dan Pembuluh Darah FK USU. 2016.
21. Wong, C. K., Gao, W., & White, H. D. (2015). Resolution of ST depression after fibrinolysis can be more important than resolution of ST elevation for many patients with inferior STEMIs. *International Journal of Cardiology*, 182, 232–234. [doi:10.1016/j.ijcard.2014.12.117](https://doi.org/10.1016/j.ijcard.2014.12.117).
22. Antman, E. M. “ST-Segment Elevation Myocardial: Pathology, Pathophysiology and Clinical Features”. In: Braunwald E, Bonow RO, Mann DL, Zipes DP, Libby P, eds. *Braunwald’s Heart Disease: A textbook of Cardiovascular Medicine*. 9th ed. Philadelphia: Elsevier; 2012:1087-1111.
23. De Lemos, J. A., & Braunwald, E. (2001). ST segment resolution as a tool for assessing the efficacy of reperfusion therapy. *Journal of the American College of Cardiology*, 38(5), 1283–1294. [doi:10.1016/S0735-1097\(01\)01550-9](https://doi.org/10.1016/S0735-1097(01)01550-9).
24. Angeja, B. G., Gunda, M., Murphy, S. A., (2002). TIMI myocardial perfusion grade and ST segment resolution: association with infarct size as assessed by single photon emission computed tomography. *Circulation*, 105(3), 282–285. [doi:10.1161/hc0302.103588](https://doi.org/10.1161/hc0302.103588).
25. Hathaway, W. R., Peterson, E. D., Wagner, G. S., (1998). Prognostic Significance of the Initial Electrocardiogram in Patients With Acute Myocardial Infarction. *Journal of the American Medical Association*, 279(5), 387–391. [doi:10.1001/jama.279.5.387](https://doi.org/10.1001/jama.279.5.387).
26. Peterson, E. D., Hathaway, W. R., Zabel, K. M., Pieper, K. S., Granger, C. B., Wagner, G. S., & Califf, R. M. (1996). Prognostic significance of pericordial ST Segment depression during inferior myocardial infarction in the thrombolytic era: results in 16,521 patients. *Journal of the American College of Cardiology*, 28(2), 305–312. [doi:10.1016/0735-1097\(96\)00133-7](https://doi.org/10.1016/0735-1097(96)00133-7).
27. Birnbaum, Y., Kloner, R. A., Sclarovsky, S., Cannon, C. P., McCabe, C. H., Davis, V. G., & Braunwald, E. (1996, August). Distortion of the Terminal Portion of the QRS on the Admission Electrocardiogram in Acute Myocardial Infarction and Correlation With Infarct Size and Long-Term Prognosis (Thrombolysis In Myocardial Infarction 4 Trial)**This study was supported in part by a grant from SmithKline Beecham, Philadelphia, Pennsylvania. *The American Journal of Cardiology*, 78(4), 396–403. [doi:10.1016/S0002-9149\(96\)00326-8](https://doi.org/10.1016/S0002-9149(96)00326-8).
28. Shah, A., Wagner, G. S., Califf, R. M., Boineau, R. E., Green, C. L., Wildermann, N. M., & Krucoff, M. W. (1997). Comparative prognostic significance of simultaneous versus independent resolution of ST segment depression relative to ST segment elevation during acute myocardial infarction. *Journal of the American College of Cardiology*, 30(6), 1478–1483. [doi:10.1016/S0735-1097\(97\)00331-8](https://doi.org/10.1016/S0735-1097(97)00331-8).
29. Becker, R. C., Burns, M., Gore, J. M., (1998). Becker, R. C., Burns, M., Gore, J. M., Spencer, F. A., Ball, S. P., French, W., & Rogers, W. J. (1998, May). Early assessment and in-hospital management of patients with acute myocardial infarction at increased risk for adverse outcomes: A nationwide perspective of current clinical practice. *American Heart Journal*, 135(5), 786–796. [doi:10.1016/S0002-8703\(98\)70036-5](https://doi.org/10.1016/S0002-8703(98)70036-5).
30. Tjandrawidjaja, M. C., Fu, Y., Westerhout, C. M., White, H. D., Todaro, T. G., Van de Werf, F., & Armstrong, P. W. (2010). Resolution of ST-segment depression: a new prognostic marker in ST-segment elevation myocardial infarction. *European Heart Journal*, 31(5), 573–581. [doi:10.1093/eurheartj/ehp494](https://doi.org/10.1093/eurheartj/ehp494).
31. Wong, C. K., Gao, W., & White, H. D. (2015). Resolution of ST depression after fibrinolysis can be more important than resolution of ST elevation for many patients with inferior STEMIs. *International Journal of Cardiology*, 182, 232–234. [doi:10.1016/j.ijcard.2014.12.117](https://doi.org/10.1016/j.ijcard.2014.12.117).
32. Reinstadler, S. J., Baum, A., Rommel, K. P., (2015). ST-Segment depression resolution predicts infarct size and reperfusion injury in ST-elevation myocardial infarction. *British Medical Journal*, •••, 1–7.
