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The Effect of Reperfusion on Repolarization Index (T Peak – T end Interval) on the Surface Electrocardiogram in Patients With St- Segment Elevation Myocardial Infarction and its Prognostic Significance

KEYWORDS: Primary PTCA, ST segment elevation myocardial infarction, thrombolysis, T peak-T end interval

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ABSTRACT *Objectives: To determine the effect of reperfusion on TpTe interval in patients with STEMI.*

Method: Patients with new onset STEMI treated with reperfusion therapy were included. TpTe interval was measured and patients were followed up at 30 days. Major adverse cardiac events were noted.

Results: Two hundred and sixteen patients who underwent primary PCI, thrombolysis and rescue PCI were included. The reduction in TpTe interval following reperfusion in all the treatment arms was statistically significant. TpTe interval difference (pre - post) was found to be significantly associated with duration of chest pain at presentation. Pre TpTe interval of more than 100 ms was associated with an increased risk of ventricular arrhythmias. However, it did not predict mortality or heart failure at 30 days.

Conclusion: In patients with STEMI undergoing reperfusion, the TpTe interval significantly reduced subsequent to reperfusion therapy. Pre TpTe interval predicted the risk of arrhythmias at 30 days.

INTRODUCTION

The modern "reperfusion era" of coronary care was introduced by intra-venous fibrinolysis, and with increased use of aspirin supplemented by development of primary percutaneous coronary intervention, the case fatality rate of ST elevation myocardial infarction (STEMI) has reduced significantly.(1,2) However, it continues to be a major public health problem in the industrialized world and is slated to rise in the low and middle-income countries.(3)where CVD tends to strike those in their prime working years. Since resources for managing CVD are limited, it is important that interventions be guided by cost-effectiveness results for low- and middle-income countries. Despite the burden, cost-effective strategies exist at the population and individual levels for reducing CVD. Integral to all personal intervention strategies is an adequate assessment of the underlying risk of disease.","DOI":"10.1377/hlthaff.26.1.13","ISSN":"1544-5208","note":"PMID: 17211010 \nPMCID: PMC2365905","journalAbbreviation": "Health Aff (Millwood

The primary aim of treatment of STEMI is to salvage the myocardium by opening the infarct related artery In this context, reperfusion by primary percutaneous coronary intervention (primary PCI) has become the gold standard of treatment.(4) However, reperfusion by thrombolysis is still common in developing countries.

One of the important long term goals of reperfusion strategy is to prevent sudden cardiac death which is most often related to ventricular arrhythmias. Patients with abnormal repolarization have been shown to have an increased risk of sudden death.(5) Repolarization of the myocardium is dependent on its perfusion.(6) Towards this end, electrophysiological characterizations of post-STEMI patients by the indices of repolarization on the surface electrocardiogram (ECG) have shown clinical promise for the prediction of death and malignant arrhythmias. In the standard 12 lead ECG, the interval from the peak (Tp) to the end (Te) of the T wave (TpTe) has been proposed to represent repolarization dispersion in the heart.(7)midmyocardium and subendocardium. Whether these differences are present in vivo and are relevant to humans has been the subject of controversy. Our objectives were (1

OBJECTIVES

- To analyze prospectively, in patients with STEMI undergoing reperfusion therapy, the effect of reperfusion on the Tpeak-Tend interval on the surface 12 lead Electrocardiogram.
- To study the association of major adverse cardiac events with the above repolarization index.

METHODOLOGY

This was a prospective, observational, single-centre study conducted in the cardiology department of a tertiary care referral hospital in India. The study was approved by the institutional review board (IRB Min.No.8291 dated 16/4/2013). All consecutive patients with STEMI who gave informed consent to participate in the study were included. Patients with new onset left bundle branch block (LBBB), right bundle branch block (qRBBB), primary ventricular tachycardia, atrial fibrillation, prior myocardial infarction and those who required temporary venous pacing and had uninterpretable ECG recordings due to noise were excluded.

Two hundred and sixty two patients in the age group of 18 -80 years, with STEMI who underwent reperfusion between June 2013 and December 2013 were recruited. Forty six patients were excluded. The final study population included 216 patients whose baseline demographic characteristics, history of cardiovascular morbidities, clinical risk factors, and mode of treatment and laboratory results were acquired. World Health Organization criteria were used to diagnose STEMI; which was essentially established

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by history of typical chest pain, diagnostic electrocardiographic changes, and serial elevation of cardiac enzymes. The method of reperfusion was left to the discretion of the clinician. It was either primary PCI or thrombolysis (with Streptokinase). Patients who had persistent chest pain and/or poor ST segment resolution in the ECG after lysis underwent rescue PCI.

ECGs (in 50 mm/sec speed and 20 mm/mV gain) were taken before and after reperfusion (90 minutes after thrombolysis and after the patient reached the ward after primary PCI). TpTe intervals were evaluated in the non-infarct leads (with ST deviation < 0.5 mV at the J point in the pre-perfusion ECG) to avoid difficulties in assessing T wave markers. The intervals between Q onset and T-wave peak (QTp) and T wave end (QTe) were manually measured by cardiologists who were blinded to the mode of reperfusion (to overcome observer bias). The TpTe interval is defined as the difference between the QTe and QTp intervals and the averages of TpTe calculated in the various leads were taken.

Data entry was done using Epidata and exported to SPSS (v 18.0 Chicago: SPSS Inc) for analysis. Descriptive statistics were tabulated using the SPSS software. The chi-square test was used for comparison of categorical variables. Odds ratios (OR) and 95% confidence intervals (CI) were calculated and a p value <0.05 was considered statistically significant. Continuous variable were handled with Mann-Whitney u test and Kruskal-Wallis tests.

RESULTS

The baseline characteristics of the patients studied are presented in Table 1.

Table 1 Baseline characteristics of the study group

Patient characteristics	Type of intervention			Significance (p value)
	Primary PCI (113)	Lysis (57)	Rescue PCI (46)	
Mean age in years (SD)	55.1 2.5)	58.8 (9.6)	49.3 (11.8)	<0.001*
Males (%)	95 (84.1)	46 (80.7)	42 (91.3)	0.318
Chest pain at presentation (%)	108 (95.6)	55 (96.5)	46 (100)	0.357
Mean duration of presenting complaints in hours (SD)	7.83 (7.44)	5.05 (3.67)	5.24 (3.88)	<0.001*
Pre-existing comorbidities				
Diabetes Mellitus (%)	49 (43.4)	23 (40.4)	11 (23.9)	0.069
Hypertension (%)	45 (39.8)	18 (31.6)	16 (34.8)	0.551
Smoking (%)	47 (41.6)	26 (45.6)	27 (58.7)	0.145
Dyslipidemia (%)	4 (3.5)	4 (7.0)	0	0.171
Family history of Coronary Artery Disease (%)	6 (5.3)	0	0	0
Killip class at presentation (%)				
I	91 (80.5)	38 (66.7)	42 (91.3)	0.021#
II	17 (15.0)	10 (17.5)	2 (4.3)	
III	1 (0.9)	5 (8.8)	1 (2.2)	
IV	4 (3.5)	4 (7.0)	1 (2.2)	
ECG - site of infarction (%)				
Anterior	67 (59.3)	33 (57.9)	25 (54.3)	0.849
Inferior	46 (40.7)	(42.1)	21 (45.7)	

*One way ANOVA; # Chi-Square test

Note: Hypertension was defined JNC 7 guidelines. Dyslipidemia was defined by ATP III guidelines. JNC=Joint national committee, ATP III = Adult Treatment Panel III, PCI – Percutaneous coronary intervention, ECG –Electrocardiogram, SD Standard Deviation

The study group included 216 patients, of which 183 were males (85%). The most common age groups that presented with STEMI were between 51-60 years followed by 41-50 and 61-70 years. Majority of patients presented in Killip class I (79.2%) while 7.6% of patients presented in Killip class III and IV. One hundred and thirteen (52%) patients underwent primary PCI, 46 (21%) rescue PCI and 57 (27%) underwent thrombolysis alone with streptokinase. There were significant differences with respect to distribution of age, duration of chest pain and Killip class at presentation among the 3 intervention groups (Table 1).

Effect of reperfusion on TpTe interval

There was a significant reduction in duration of repolarization following reperfusion as noted by reduction in TpTe interval in the three intervention groups (primary PCI, lysis and rescue PCI) with p values of < 0.001, 0.001 & 0.005.

Table 2 Pre and post TpTe correlation in the intervention groups - Paired Samples Statistics

Intervention	Percentile			p value	Mean+/-SD	
	25th	50th	75th		Pre	Post
Primary PCI (n=113)	80	84	100	<0.001*	88.49(15.23)	74.93(13.61)
Lysis (n=56)	80	82	98	<0.001*	86.89(14.14)	72.76(16.76)
Rescue PCI (n=46)	80	86	100	<0.001*	91.53(14.13)	72.86(12.99)

**p<0.05, sign test;* PCI= percutaneous coronary intervention

The mean baseline pre TpTe intervals were 88.49, 86.49 and 91.53 ms among the three intervention groups and the differences in mean pre TpTe intervals between the groups was not statistically significant (p>0.05). The mean post TpTe intervals were 74.93, 72,76 and 72.86 ms in the primary PCI, lysis and rescue PCI groups and the reduction within groups were statistically significant (p values of 0.0001, 0.0001 and 0.004 respectively). After adjusting for other risk factors, duration of chest pain at presentation was significantly associated with the change in TpTe intervals pre and post intervention.

Major adverse cardiac events (MACE) at 30 days and association with TpTe interval

There were a total of 11 (5.1%) deaths at 30 day follow up. Of these patients, 8 (3.7%) had heart failure and 3 (1.4%) had ventricular arrhythmias. Ventricular arrhythmias was higher among the patients with Pre TpTe interval above 100 ms (6.7% Versus. 0.5%) which was statistically significant with an odds ratio of 13.21 (95% CI 1.16 – 150.57 , p value>0.05)

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Table 3 Association between pre TpTe and 30 day mortality, heart failure and arrhythmia

		Upto 100 (ms)	101(ms) and above	Odds ratio	95% Confidence Interval		P value
30 day mortality	Yes	9(4.8%)	2(6.7%)	1.405	0.288	6.842	0.674
	No	177(95.2%)	28(93.3%)				
30 day heart failure	Yes	6(3.2%)	2(6.7%)	2.143	0.412	11.148	0.365
	No	180(96.8%)	28(93.3%)				
30 day arrhythmias	Yes	1(0.5%)	2(6.7%)	13.214	1.160	150.571	0.038 *
	No	185(99.5%)	28(93.3%)				

Univariate logistic regression,* statistically significant p<0.05

The 30 day mortality was higher among the patients with pre TpTe interval above 100 ms (6.7% Versus. 4.8%, p value>0.05) and the thirty day heart failure was higher among the patients with pre TpTe interval more than 100 ms (6.7% Versus. 3.2%) (Table 3). However, these were not statistically significant (p>0.05).

DISCUSSION

The ΔTpTe (pre TpTe interval - post TpTe interval) was reduced in all the intervention groups, and was statistically significant in all the groups. This was similar to the study by LIN Xiao-ming et al, where the TpTe interval was significantly reduced after PCI in patients with severe coronary artery stenosis.(9) In contrast, a study by Christian Haarmark et al found that the, TpTe interval was prolonged after primary PCI in the survivor group but decreased in patients who died during follow up, with a hazard ratio of 10.5.(8)respectively. Tpeak-Tend interval was measured in leads with limited ST-segment deviation. The primary end point was all-cause mortality during 22 +/- 7 months (mean +/- SD

The present study has shown that the different reperfusion strategies did not confer any advantage with respect to change in TpTe interval. To the best of our knowledge, there are no previous studies that have assessed pre and post TpTe interval in thrombolysed patients.

On a multi-variate regression analysis, duration of symptom at presentation showed significant associations with ΔTpTe while other clinical parameters such as age, gender, pre-existing co-morbidities, site of infarction as determined by ECG, extent of coronary artery disease (single versus multi-vessel disease) were not associated with ΔTpTe. Our findings were similar to Christian Haarmark et al, in that they also did not find correlation between TpTe and culprit vessel or LV ejection fraction.(8)respectively. Tpeak-Tend interval was measured in leads with limited ST-segment deviation. The primary end point was all-cause mortality during 22 +/- 7 months (mean +/- SD However, in the study by Lin Xiao-ming et al, TpTe interval was found to correlate with the extent and severity of coronary artery disease.(9)

TPTE interval and Major Adverse Cardiac Effects

Considering the healthy population has a TpTe interval of <100 ms (10), we used this as cut off for comparison of 30-day mortality, heart failure and arrhythmias to demarcate two groups of patients with STEMI pre- intervention. Though there was a trend for increased number of deaths (OR – 1.41, 95% CI – 0.29 – 6.84) and heart failure (OR- 2.14, 95% CI – 0.41 – 11.15) in the group of patients with higher pre TpTe interval (> 100 ms), this was not statistically significant (p>0.05). This is in contrast with the study done by Haarmark et al, where the pre primary PCI TpTe interval predicted all-cause mortality. (8) respectively. Tpeak-Tend interval was measured in leads with limited ST-segment deviation. The primary end point was all-cause mortality during 22 +/- 7 months (mean +/- SDThe post PCI TpTe was similar among survivors and non-survivors. The inference was that the temporary arrhythmic substrate caused by STEMI was resolved by reperfusion. However, with recurrent ischemic episodes, the substrate reappeared and caused the increased TpTe in nonsurvivors. Zabel et al also assessed post PCI TpTe interval in STEMI and found no significant difference in those who died.(11)the 12-lead ECG was optically scanned and digitized for analysis of QTD (QTmax-QTmin

The association between pre- TpTe interval of >100 ms and 30 day mortality was found to be significant in this study. It portended a 16% increase in the risk of arrhythmia in the study group. This was again in agreement with other studies which showed that increased TpTe interval was associated with an increase in arrhythmias in patients with coronary artery disease and post acute coronary syndrome. (12–14)

CONCLUSION

Pre TpTe interval more than 100 ms may be used to predict risk of arrhythmias at 30 days in patients who have suffered ST-segment elevation Myocardial Infarction. There was statistically significant reduction of TpTe interval in all intervention groups at 90 minutes (primary PCI, thrombolysis or rescue PCI). However, pre TpTe interval cannot be used to predict 30 day mortality or heart failure.

Reference :

1. Anderson, J. L., Adams, C. D., Antman, E. M., Bridges, C. R., Califf, R. M., Casey, D. E., Jr, … Society for Academic Emergency Medicine. (2007). ACC/AHA 2007 guidelines for the management of patients with unstable angina/non-ST-Elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines for the Management of Patients With Unstable Angina/Non-ST-Elevation Myocardial Infarction) developed in collaboration with the American College of Emergency Physicians, the Society for Cardiovascular Angiography and Interventions, and the Society of Thoracic Surgeons endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation and the Society for Academic Emergency Medicine. *Journal of the American College of Cardiology*, *50*(7), e1–e157. http://doi.org/10.1016/j.jacc.2007.02.013
2. Antman, E. M., Anbe, D. T., Armstrong, P. W., Bates, E. R., Green, L. A., Hand, M., … Canadian Cardiovascular Society. (2004). ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1999 Guidelines for the Management of Patients with Acute Myocardial Infarction). *Circulation*, *110*(9), e82–292.
3. Brodie, B. R., Stuckey, T. D., Hansen, C., VerSteeg, D. S., Muncy, D. B., Moore, S., … Downey, W. E. (2005). Relation between electrocardiographic ST-segment resolution and early and late outcomes after primary percutaneous coronary intervention for acute myocardial infarction. *The American Journal of Cardiology*, *95*(3), 343–348. http://doi.org/10.1016/j.amjcard.2004.09.031
4. Gaziano, T. A. (2007). Reducing the growing burden of cardiovascular disease in the developing world. *Health Affairs (Project Hope)*, *26*(1), 13–24. http://doi.org/10.1377/hlthaff.26.1.13

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5. Haarmark, C., Hansen, P. R., Vedel-Larsen, E., Pedersen, S. H., Graff, C., Andersen, M. P., … Kanters, J. K. (2009). The prognostic value of the Tpeak-Tend interval in patients undergoing primary percutaneous coronary intervention for ST-segment elevation myocardial infarction. *Journal of Electrocardiology*, *42*(6), 555–560. http://doi.org/10.1016/j.jelectrocard.2009.06.009
6. Lin, X., Yang, X., Liu, H., & Lai, Y. (2010). [Relationship between Tpeak-Tend interval and coronary artery stenosis and effects of percutaneous transluminal coronary angioplasty on Tpeak-Tend]. *Nan fang yi ke da xue xue bao = Journal of Southern Medical University*, *30*(8), 1877–1879.
7. Lloyd-Jones, D., Adams, R., Carnethon, M., De Simone, G., Ferguson, T. B., Flegal, K., … American Heart Association Statistics Committee and Stroke Statistics Subcommittee. (2009). Heart disease and stroke statistics--2009 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation*, *119*(3), 480–486. http://doi.org/10.1161/CIRCULATIONAHA.108.191259
8. Lubinski, A., Kornacewicz-Jach, Z., Wnuk-Wojnar, A. M., Adamus, J., Kempa, M., Królak, T., … Swiatecka, G. (2000). The terminal portion of the T wave: a new electrocardiographic marker of risk of ventricular arrhythmias. *Pacing and Clinical Electrophysiology: PACE*, *23*(11 Pt 2), 1957–1959.
9. Morrow, D. A. (2010). Cardiovascular risk prediction in patients with stable and unstable coronary heart disease. *Circulation*, *121*(24), 2681–2691. http://doi.org/10.1161/CIRCULATIONAHA.109.852749
10. O'Donnell, J., Knoebel, S. B., Lovelace, D. E., & McHenry, P. L. (1981). Computer quantitation of Q-T and terminal T wave (aT-eT) intervals during exercise: methodology and results in normal men. *The American Journal of Cardiology*, *47*(5), 1168–1172.
11. Oikarinen, L., Viitasalo, M., Korhonen, P., Väänänen, H., Hänninen, H., Montonen, J., … Toivonen, L. (2001). Postmyocardial infarction patients susceptible to ventricular tachycardia show increased T wave dispersion independent of delayed ventricular conduction. *Journal of Cardiovascular Electrophysiology*, *12*(10), 1115–1120.
12. Taggart, P., Sutton, P. M., Opthof, T., Coronel, R., Trimlett, R., Pugsley, W., & Kallis, P. (2001). Transmural repolarisation in the left ventricle in humans during normoxia and ischaemia. *Cardiovascular Research*, *50*(3), 454–462.
13. Watanabe, N., Kobayashi, Y., Tanno, K., Miyoshi, F., Asano, T., Kawamura, M., … Katagiri, T. (2004). Transmural dispersion of repolarization and ventricular tachyarrhythmias. *Journal of Electrocardiology*, *37*(3), 191–200.
14. Zabel, M., Klingenheben, T., Franz, M. R., & Hohnloser, S. H. (1998). Assessment of QT dispersion for prediction of mortality or arrhythmic events after myocardial infarction: results of a prospective, long-term follow-up study. *Circulation*, *97*(25), 2543–2550.