International Journal of Advances in Medicine
Khanna M et al. Int J Adv Med. 2020 Jun;7(6):928-935
http://www.ijmedicine.com
pISSN 2349-3925 | eISSN 2349-3933
DOI: http://dx.doi.org/10.18203/2349-3933.ijam20202106

Original Research Article

Role of reciprocal changes in predicting short term prognosis of patients of acute STEMI

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Received: 21 March 2020
Accepted: 20 April 2020

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ABSTRACT

Background: Recent studies indicate that STEMI with reciprocal changes is associated with more myocardial area at risk, larger infarct size and less ejection fraction as compared to STEMI without reciprocal changes. We undertook this study for correlating clinical outcome and complications in patients with and without reciprocal changes in ECG in acute STEMI.
Methods: Eighty patients were divided into two groups of forty each. One having reciprocal changes in ECG and one without reciprocal changes. The KILLIP class of each patient at time of admission was noted. Patients were monitored for development of any complication, Left ventricular ejection fraction (LVEF) and mortality. BNP levels, Trop I levels, Hba1c levels were obtained at time of admission. Echocardiography was done on the second day of the admission.
Results: The patients with reciprocal changes were found to be having a higher KILLIP class on admission. The LVEF of patients with reciprocal changes and who subsequently went on to develop complications was lower than those without reciprocal changes. The number of patients having unsuccessful thrombolysis was significantly higher in the group with reciprocal changes.
Conclusions: There was significant association of reciprocal changes in ECG with higher Hba1c, higher KILLIP class and higher incidence of unsuccessful thrombolysis. Moreover, the sensitivity of other markers of poor clinical outcomes, such as BNP and LVEF increases in patients having reciprocal changes in their ECG. The monitoring in such patients should thus be more intensive.

Keywords: Complications, ECG, KILLIP, Prognosis, Reciprocal changes, STEMI

INTRODUCTION

The global burden of disease study estimates of age-standardized Cardiovascular death (CVD) rate of 272 per 1,00,000 population in India is higher than the global average of 235 per 1,00,000 population.[1]

Patients with Myocardial Infarction (MI) commonly are classified into two groups to facilitate evaluation and management, namely patient with STEMI (ST Elevation MI) and patients with NSTEMI (Non ST Elevation MI).[2]

ST depression in STEMI may be caused by ischaemia in a territory other than the area of infarction termed "ischaemia at a distance" or by reciprocal electrical phenomenon. Such a differentiation cannot be made by electrocardiography or vector cardiography techniques alone. In STEMI, due to myocardial injury, action potentials are slowed, the phase 2 depolarization is delayed in the ischemic region as compared to normal myocardium and hence the vector is directed towards the ischemic injury resulting in true ST segment elevation of the lead. Conversely, a lead oriented towards the

uninjured surface will reflect a depressed ST segment. The depressed ST segments associated with acute myocardial infarction are termed reciprocal changes. There is some controversy about the distinction between reciprocal changes and nearly identical changes reflecting coexisting ischaemia in a vascular bed remote from the infarction that is ischaemia at a distance. It is likely that remote ST depression can be due to either of them, exact mechanism being unknown.[3]

However, recent studies indicate that STEMI with reciprocal changes is associated with more myocardial area at risk, larger infarct size and less ejection fraction as compared to STEMI without reciprocal changes.[4-6]

Hence, we undertook this study for correlating clinical outcomes and complications in patients with and without reciprocal changes in ECG in acute STEMI. The effect of reciprocal changes on laboratory parameters, echocardiographic variables and its implications on various lines of management were also studied.

METHODS

This is a case control study, where eighty patients of acute myocardial infarction with ST segment elevation admitted to the Medicine Department of a teaching tertiary care hospital in Amritsar, Punjab were included. These patients were divided into two groups of forty patients each, Group A having patients of acute ST elevation MI with reciprocal changes in ECG and group B having patients of acute ST elevation MI without reciprocal changes in ECG.

Patients were defined as having acute ST elevation myocardial infarction if they fulfilled the criteria of third universal definition of MI7

A rise in levels of cardiac troponin (with at least one of the value above the 99th percentile upper reference limit (URL)) and at least one of the following:-

- Symptoms of myocardial ischaemia for more than 30 minutes
- New or presumed new ST changes.
- New ST elevation at the J point in two contiguous leads with the following cut points:
    - >0.1 mV in all leads (except V2-V3)
    - In leads V2-V3, the following cut points were applied
        - 0.2 mV in men > 40 years
        - >0.25 mV in men <40 years
        - >0.15 mV in women
    - In right sided leads (V3R and V4R), the threshold for abnormal ST segment elevation at J point was taken as 0.5mm, except in males <30 years in whom it is 1 mm.
    - In posterior leads (V7, V8 and V9), the threshold for abnormal ST segment elevation of J point was taken as 0.5 mm.
- Development of pathological Q waves.
- Echocardiographic evidence of new loss of viable myocardium or new regional wall motion abnormality.

Significant reciprocal changes were defined as 0.5 mm or more of horizontal or down sloping ST segment depression (measured 80ms after J point) in at least 2 leads reflecting the remote non infracting wall.

Patients meeting diagnostic criteria of acute ST elevation MI were subjected to detailed general examination and special attention was given to respiratory system and cardiovascular systems, the KILLIP class of each patient at time of admission was noted.

The extent and duration of persistence of ST depression was also noted. All the cases were looked for development of any complication namely arrhythmias and ectopics, conduction disorder, hypotension with shock, left ventricular failure, left ventricular ejection fraction and mortality.

BNP levels, Trop I levels, Hba1c levels were obtained at time of admission. Echocardiography was done on the second day of the admission.

Exclusion criteria

- Patients having bundle branch block.
- Patients having old MI or a cerebrovascular accident.
- Patients having clinical evidence of valvular or non-coronary cardiac disease.

Authors compared the differences in parameters between the two groups. Detailed statistical analysis was done using SPSS 19.0 version and results were obtained.

The study was conducted from February 2018 till June 2019 after obtaining approval of the hospital ethical committee. An informed consent of the patients or their relatives was also obtained.

RESULTS

Risk factors and complications

Table 1 show that hypertensive patients, if subsequently developed reciprocal changes, had significantly higher chances of developing complications.

Also, for patients who had both diabetes and hypertension, when they developed reciprocal changes in ECG, they had significantly higher chances of developing complications subsequently.

Total 14 out of the 24 (58.33%) diabetics who were having reciprocal changes in the ECG subsequently developed complications. This relation was statistically not significant (X2= 1.172, p= 0.230)

In diabetics not having reciprocal changes in the ECG, 10 out of 18 (55.56%) developed complications. This is also statistically not significant (X2 = 0.051, p= 0.538). Data wise 23 out of 26 (88.46%) of the hypertensive patients having reciprocal changes in the ECG subsequently developed complications. This is statistically significant (X2 = 17.974, p<0.05), 15 out of the 23 (65.22%) patients not having reciprocal changes in the ECG developed complications. This is statistically not significant (x2= 0.251, p= 0.429).

A total of 13 out of 15 (86.67%) patients in the group having reciprocal changes, who had both diabetes and hypertension, subsequently developed complications. This is statistically significant (x2= 4.952, p=0.027), 8 out of the 13 (61.54%) patients in the group without reciprocal changes subsequently developed complications. This was statistically non significant (x2= 0.105, p=0.504), 1 smoker out of the 2 who had reciprocal changes in ECG subsequently developed complications. This is statistically not significant (x2=0.208, p=0.583).

Table 2 shows that mean systolic Blood Pressure in patients having complications was lower. This difference was statistically significant irrespective of the fact whether the patients were having reciprocal ST depressions or not.

The mean systolic BP of the 27 patients having complications (in patients having reciprocal changes) was 101 Hg whereas the mean systolic BP of 13 patients without complications was 133 Hg. This difference is statistically significant (p= 0.04, p<0.05). The mean systolic BP of 23 patients without reciprocal changes in ECG, having complications is 107 Hg whereas in the same group, the mean systolic BP of the 17 patients not having complications is 127 Hg. This difference is also statistically significant (p=0.03).

Table 1: Distribution of patients across various complications.

Type of complication	Group	Total number of patients	Patients with complications	Percentage of patients with complications	p value
Diabetic	With reciprocal ST depression	24	14	58.33	0.230
	Without reciprocal ST depression	18	10	55.56	0.538
Hypertensive	With reciprocal ST depression	26	23	88.46	0.024
	Without reciprocal ST depression	23	15	65.22	0.429
Diabetic and Hypertensive	With reciprocal ST depression	15	13	86.67	0.027
	Without reciprocal ST depression	13	8	61.54	0.504
Smoker	With reciprocal ST depression	2	1	50	0.583
	Without reciprocal ST depression	6	4	66.67	0.489

Table 2: Distribution of mean systolic blood pressure and complications.

	With reciprocal ST depression			Without reciprocal ST depression		
	Number of patients	Mean systolic blood pressure	p value	Number of patients	Mean systolic blood pressure	p value
With complications	27	101	0.004	23	107	0.003
Without complications	13	133		17	127	

As is evident from Table 3 the average KILLIP class for the patients presenting with reciprocal changes was 2.65, whereas it is 1.88 for patients not having reciprocal changes in the ECG. This relationship is statistically

significant (p=0.03). In patients having reciprocal changes, 14 patients were in class IV according to the KILLIP classification, 10 were in class III, 4 were in class II and 12 were in class I. Amongst the patients not having reciprocal changes in their ECG, 4 were in KILLIP class IV, 5 in class III, 13 in class II and 18 in class I.

Table 3: Mean KILLIP.

KILLIP classification	Class I	Class II	Class III	Class IV	Mean KILLIP	p value
With reciprocal ST depression	12	4	10	14	2.65	0.03
Without reciprocal ST depression	18	13	5	4	1.88	

Table 4: Mean BNP and complications.

	With reciprocal ST depression			Without reciprocal ST depression		
	Number of patients	Mean BNP	p value	Number of patients	Mean BNP	p value
With complications	27	772.78	0.016	23	925.79	0.001
Without complications	13	497		17	337.81	

Table 4 show that patients having complications were having significantly higher BNP irrespective of the presence of reciprocal ST changes

In the patients with reciprocal changes who developed complications, the mean BNP was 772 ng/ml whereas it is 497 ng/ml for those who didn't develop complications. This relationship is statistically significant (p=0.016). In the patients without reciprocal changes who developed complications, the mean BNP is 925 ng/ml whereas it is 337 ng/ml for those who didn't develop complications. This relationship is statistically significant (p=0.001).

It is evident from Table 5 that LVEF of patients having reciprocal changes in the ECG, who subsequently went on to develop complications, was significantly lower than those not developing complications. The same was not consistent in the patients not having reciprocal changes. The average LVEF in patients with reciprocal changes in ECG who subsequently developed complications was 29.59% whereas it was 35.15% for the patients who didn't develop complications. This relationship is statistically significant (p=0.039). In patients without reciprocal changes in their ECG who subsequently developed complications, the average LVEF in patients is 33% whereas it is 36% for the patients who didn't develop complications. This difference is statistically non-significant.

Table 6 show that incidence of unsuccessful thrombolysis was significantly higher in patients having reciprocal changes. Total 17 out 40 (42.5%) patients with reciprocal changes underwent PTCA. 20 out of 40 (50%) patients without reciprocal changes underwent PTCA. This relationship is statistically insignificant (p=0.412) , 11 out of 40 patients (27.5%) with reciprocal changes had successful thrombolysis. 16 out of 40 (40%) patients without reciprocal changes had successful thrombolysis. This distribution is statistically insignificant (p=0.111), 12 out of 40 (30%) patients with reciprocal changes had a thrombolysis attempt which was unsuccessful. In the patients not having reciprocal changes in their ECG, only 4 (10%) had an unsuccessful thrombolysis. This relationship is statistically significant (p=0.04).

Table 5: Mean LVEF and complications.

	With reciprocal ST depression			Without reciprocal ST depression		
	Number of patients	Mean EF	p value	Number of patients	Mean EF	p value
With complications	27	29.59	0.03	23	33	0.167
Without complications	13	35.15		17	36	

Table 6: Impact of intervention.

Intervention	PTCA	p value	Successful thrombolysis	p value	Unsuccessful thrombolysis	p value
With reciprocal ST depression	18	0.324	10	0.487	12	0.04
Without reciprocal ST depression	20		16		4	

Table 7: Distribution of complications.

Complications	STEMI patients		
	With reciprocal	Without reciprocal	p value
Atrial fibrillation	2	4	0.338
Death	6	2	0.132
LV apical clot	0	2	0.247
Mitrial regurgitation	0	1	0.500
Pulmonary thromboembolism	0	1	0.500
Cardiogenic shock	16	10	0.074
Sinus bradycardia	1	3	0.120
Supraventricular tachycardia	4	7	0.259
Third degree block	1	1	0.500
Ventricular premature complexes	4	2	0.179
Ventricular tachycardia	2	2	0.692
Total	26	23	0.323

Amongst the patient having reciprocal changes in the ECG, 2 developed AF, whereas amongst those without reciprocal changes, this number was 4 out of the 40 patients in each group. This relationship is statistically insignificant (p=0.338).

Six patients with reciprocal changes ultimately died during the course of treatment. The same number was 2, i.e. the number of patients who died who did not have any reciprocal changes in the ECG. This was statistically insignificant (p=0.132).

Two patients not having reciprocal changes were having apical clot in their left ventricle. None of the patients with reciprocal changes suffered this complication. This relationship is statistically insignificant (p=0.247). One patient not having reciprocal changes in his ECG developed acute MR. None of the patients having reciprocal changes in ECG suffered this complication. This relationship is statistically insignificant (p=0.500).

One patient not having reciprocal changes in his ECG developed PTE. None of the patients having reciprocal changes in ECG suffered this complication. This relationship is statistically insignificant (p=0.500).

Total 16 out of 40 patients (40%) developed cardiogenic shock in patients having reciprocal changes in their ECG. 10 out 40 (25%) patients without reciprocal changes developed cardiogenic shock. This relationship is statistically insignificant (p=0.074). Only 1 patient with reciprocal changes subsequently developed sinus bradycardia. 3 patients without reciprocal changes developed sinus bradycardia. This relationship is statistically insignificant (p=0.120). Total 4 patients with reciprocal changes had SVT during the course of hospital stay. 7 patients without reciprocal changes developed this complication. This relationship is statistically insignificant (p=0.259).

Only 1 patient from each group developed third degree heart block (at presentation). This relationship is statistically insignificant (p=0.500).

Four patients from the group with reciprocal changes had constant VPC's. Only 2 patients without reciprocal changes had this complication. This relationship is statistically insignificant (p= 0.179).

Two patients from each group had Ventricular tachycardia, thus making the incidence of this complication statistically insignificant (p= 0.692).

In totality, 26 out of 40 patients with reciprocal changes subsequently developed complications. Whereas, amongst the patients not having reciprocal changes, only 23 developed complications. This difference is statistically insignificant (p=0.323).

DISCUSSION

This study was undertaken with the objective of finding whether the presence of reciprocal changes in patients of STEMI leads to increased complications. Its correlation with other variables of MI such as Left Ventricular Ejection Fraction (LVEF), Brain Natriuretic Peptide (BNP), KILLIP class and HbA1c was also done. In the era of streptokinase, many studies did point out towards higher risk amongst patients having reciprocal changes but does it still hold true in current era of newer thrombolytic agents and Percutaneous Transluminal Coronary Angioplasty (PTCA) was our main objective. Various studies have independently identified diabetes mellitus as an independent predictor of prognosis of STEMI. The distribution of other risk factors vis a vis, hypertension and smoking was also checked amongst the two groups. The distribution of various risk factors in both the groups was not statistically significant, although the number of diabetics and hypertensives was

marginally higher in the patients having reciprocal changes.

On further analysis it was found that the patients who earlier were hypertensive and then subsequently had STEMI with reciprocal changes in ECG were found to have had more complications than those who were not having reciprocal changes. This finding was also found in patients who had both, diabetes and hypertension. If this subgroup of patients subsequently had reciprocal changes in ECG, they were more prone to develop complications than those who did not develop these changes in the ECG. The mean systolic BP on presentation for patients who subsequently went on to develop complications was lower. It was 101mm Hg for patients having reciprocal changes and 107 mm Hg for patients without reciprocal changes. These differences were statistically significant, that is a low BP at presentation is a predictor for development of subsequent complications irrespective of the fact whether the patient has reciprocal changes in his ECG or not. This is in accordance with a previous study which studied various clinical parameters as a predictor of development of subsequent complications in patients having STEMI.[8]

Amongst the diabetics, the average HbA1c for those having reciprocal changes was 9.59%, whereas it was 7.40% for patients without reciprocal changes. This difference is statistically significant. Thus, it can be commented that patients with poor glycemic control are more likely to develop reciprocal changes in their ECG. This is in accordance with various studies, as poor glycemic control leads to accelerated atherosclerosis which might lead to involvement of arteries at remote non infracting site, ultimately leading to ischemia at a distance. Ghaffari et al had done a similar study and found that the patients with a poorer clinical outcome over 1 year period had a higher HbA1c.[9] The average KILLIP class for patients having reciprocal changes was 2.65, whereas it was 1.88 for patients without reciprocal changes. This difference was statistically significant. Amongst the patients having reciprocal changes, who further went on to develop complications, the average KILLIP class was 3.22. It was 2.04 for patients not having reciprocal changes. This difference again was statistically significant. It can thus be commented that patients having reciprocal changes in ECG have a worse KILLIP class, and worse the KILLIP class, the more is the chance of developing complications, more so in the patients having reciprocal changes.

The average BNP in patients having complications was 772.8 ng/ml, in patients having reciprocal changes and 925 ng/ml in patients not having reciprocal changes. This difference was significant statistically. We also found out that a higher BNP is a predictor of more complications, irrespective of the fact whether the patient has reciprocal changes in his ECG or not, in accordance with various studies done in this matter by Hei et al, Wei et al, etc. who had observed that higher the BNP, worse is the outcome in patients of STEMI.[10-12] Thus, patients having reciprocal changes in their ECG have a higher chance of having a raised BNP level.

The average Left Ventricular Ejection Fraction (LVEF) in patients having reciprocal changes who subsequently developed complications was 29.59%. In patients without reciprocal changes, the average LVEF in patients with complications was found out to be 33%. This difference was statistically significant. This can be simply put as, patients presenting to us with reciprocal changes, if have a lower EF on echocardiography, are more prone to develop complications. In other words, sensitivity of EF in predicting prognosis on echocardiography increases in patients having reciprocal ST depression. Brazinov P et al in their study used a higher KILLIP and lower EF as an overall poor predictor of clinical outcomes and both of these are present in patients with reciprocal changes.[13] A study done using Cardiac Magnetic Resonance imaging by Jia X had found larger area of myocardial injury in patients with reciprocal changes in their ECG.[14]

There were a total of 8 mortalities in our study. Out of these, 6 patients had reciprocal changes and 2 did not have reciprocal changes in their ECG. 5 deaths involved anterior wall, 2 each involving patients having reciprocal changes and patient without reciprocal changes. 2 deaths (with patient having reciprocal changes in ECG) involved the lateral wall and another death happened in patient with changes in the inferior wall.

A relationship was also sought between the impacted wall and eventual complications. In case of patients having reciprocal changes, 78% of patients having infarction in the anterior wall, 50 % of the patients with infarction in antero-lateral wall, 37.5% of patients with changes in inferior wall, and all the patients having changes in the posterior wall went on to develop complications. However, these were statistically insignificant when compared to patients not having reciprocal changes.

When overall complications were considered, 26 out of 40 patients had complications amongst the group having reciprocal changes. About 23 out of 40 patients without reciprocal changes eventually went on to have complications. The marginal high number had no statistical significance. 16 patients with reciprocal changes went on to have cardiogenic shock while this number was only 9 for patients without reciprocal changes. 4 patients with reciprocal changes had Ventricular Premature Complexes (VPC) while this number was only 1 for patients without reciprocal changes. All other individual complications were almost equally distributed. None of this difference was found to be statistically significant on further analysis. These findings are consistent with studies of Hwang et al, who in their study did not find any difference in clinical outcome in both these groups.[15] We also tried to find out whether the management line chosen had a significant outcome on the final clinical picture. We divided the

patients into 3 groups, those who underwent primary Percutaneous Transluminal Coronary Angioplasty (PTCA) those who had a successful thrombolysis and those who had an unsuccessful thrombolysis. It was found out that patients with reciprocal changes in their ECG had a statistically higher incidence of failed thrombolysis. This finding is consistent with the study of Liga et al, who found that on angiography, the patients having reciprocal changes had more 'no flow/ slow flow' phenomena after Percutaneous coronary intervention (PCI).[16] This finding is also consistent with most of the studies which found that patients with reciprocal changes had a higher Area at Risk (AAR) after a STEMI.[4]

On further analysis it was also found out that the patients having a failed thrombolysis also had a statistically higher incidence of complications, in patients having reciprocal changes in their ECG. It can be commented that the patients having reciprocal changes in their ECG have a higher chance of having a failed thrombolysis and this failed thrombolysis in patients having reciprocal changes further leads on to clinical complications. The authors thus recommend that patients having STEMI along with reciprocal changes, be sent to a setup where angioplasty is available if the door to balloon time permits.[17] In other case scenarios, the dose of thrombolytic agents might be higher in such patients.

CONCLUSION

The significant association of reciprocal changes in ECG with higher Hba1c, higher KILLIP class and higher incidence of unsuccessful thrombolysis leads us to the hypothesis that reciprocal changes in the ECG are not merely caused by benign electrical phenomena but represent ischemia at a remote non infracting site. Moreover, the sensitivity of other markers of poor clinical outcomes, such as BNP and LVEF increases in patients having reciprocal changes in their ECG.

The incidence of complications such as death, shock and VPC's are also more in patients having reciprocal changes (although not statistically significant). The monitoring in such patients should thus be more intensive.

From a management point of view, it can also be hypothesized that if reciprocal changes are found in the initial ECG at presentation, primary PTCA leads to significantly less number of future complications. On the basis of the hypothesis of ischemia at a remote non infracting site, it can also be speculated that the modification of doses of thrombolytics (increasing their doses) might lead to decreased complications in such cases.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Khanna M, Mahajan DS. Role of reciprocal changes in predicting short term prognosis of patients of acute STEMI. Int J Adv Med 2020;7:928-35.