FREQUENCY OF LATE VENTRICULAR POTENTIALS AS A PRECURSOR OF COMPLEX VENTRICULAR ARRHYTHMIAS IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION.

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ABSTRACT:

INTRODUCTION: Studies on Late Ventricular potentials (LVPs) in subjects of myocardial infarction (MI) were mostly done before the time period when reperfusion techniques were introduced. Controversial results were reported in the studies which were conducted to probe the effects of thrombolysis on Late Ventricular Potentials (LVPs) & incidence of complex ventricular arrhythmias. The predictive significance of late ventricular potentials (LVPs) depends on early thrombolysis so that complete coronary blood flow can be achieved.

AIMS & OBJECTIVE: The objective of the study was to determine the frequency of late ventricular potentials as a precursor of complex ventricular arrhythmias in patients with acute myocardial infarction.

MATERIAL & METHODS: This comparative prospective study was conducted at Cardiology department of Mayo Hospital, Lahore. Patients who presented with Myocardial Infarction(MI), diagnosed by history, ECG, enzymes were subjected to late potential analysis by Signal Averaged Electrocardiography (SAECG).Patients were divided in to two groups, group-A patients were thrombolysed with Streptokinase (SK+) and group-B patients were not thrombolysed with Streptokinase (SK-). Each group had 66 patients.

Patients were followed for a total duration of 6 months. Patients were asked to visit the hospital after specified intervals. The occurrence of LVP was recorded within 1st month (30 days) before any interventional treatment (percutaneous coronary intervention/coronary artery bypass grafting), 90 days and 180 days after acute myocardial infarction. Left ventricular ejection fraction (LVEF) was determined by transthoracic echocardiography within 15 to 20 days after the occurrence of ST elevation myocardial infarction (STEMI). Complex ventricular arrhythmias were detected by 12 lead standard ECG and by 24 hours Holter monitoring after 30 days, 90 days & 180 days of MI. All episodes of fatal or nonfatal arrhythmic events, re-infarction and revascularization procedure were carefully recorded.

RESULTS: Late ventricular potentials were seen in 8 (12.12%) patients who were given SK (group A) and in 14(21.21%) patients who were not given SK (group B). Stratification of ejection fraction showed that patients with ejection fraction less than 40% , late ventricular potentials were seen in 2 patients of group A and none of the patients in group B developed late ventricular potentials. However patients whose ejection fraction was more than 40%, late ventricular potentials were seen in 6 patients of group A and in 14 patients of group B.

However no statistically significant association was seen between thrombolytic status of patients with late ventricular potentials stratified on the basis of ejection fraction. Although R on T phenomena which can be an initiating factor for development of ventricular arrhythmias was observed in 7 patients (5.3%) out of 132, only 1 patient (0.75 %) was suspected to have sudden cardiac death due to fatal ventricular arrhythmias. This patient had anterior wall MI and was not thrombolysed with streptokinase (group B). His ejection fraction was 42 % and late ventricular potentials were recorded on signal averaged ECG. 4 patients (3.03 %) were observed to have non sustained ventricular tachycardia but no episodes of sustained ventricular arrhythmias or sudden cardiac death were reported in these patients. 3 (75%) out of 4 patients had inferior wall MI who did not received thrombolysis with streptokinase (group B) with ejection fraction > 40 % and late ventricular potentials were recorded . 1 (25%) out of 4 patient had anterior wall MI, belonged to group B , ejection fraction >40% and late ventricular potentials were present.

According to our study patients of group B had high frequency of late ventricular potentials. However patients with ejection fraction >40% from group B showed higher frequency of late ventricular potential as compared to patients of group A. Thrombolysis was main determinant of late ventricular potentials. i.e. Group A : 12.12% vs. Group B:21.21% with p-value=0.161 showing no strong association between ejection fraction and occurrence of late ventricular potentials.

CONCLUSION: *Late ventricular potentials were more common in patients who did not receive thrombolytic treatment.*

KEY WORDS: *Late ventricular potentials, signal averaged electrocardiogram, myocardial infarction, ventricular tachycardia.*

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INTRODUCTION:

Myocardial infarction reflects to be part of a spectrum known as Acute coronary syndrome (ACS). The ACS continuum includes Unstable angina (UA), Non ST segment elevation acute coronary syndrome (NSTE-ACS) and ST segment elevation myocardial infarction (STEMI) representing myocardial ischemia or injury. Patients suffering from ischemia might or might not have ST segment or T wave changes on the electrocardiogram (ECG). ST segment elevations on the ECG indicates continuing transmural injury of myocardium. If instant reperfusion therapy is not given, large number of subjects with STEMI develop Q waves, which indicates deceased area of myocardium that has suffered from irreparable impairment and death. Patients with no ST segment elevations are diagnosed to have either NSTEMI or unstable angina, and this can be distinguished by the presence of raised cardiac enzymes in the blood. In both of these conditions, ECG changes (ST segment depression, T wave changes) may or may not be present.

Systolic or diastolic dysfunction may be caused by MI and there are bigger chances for developing arrhythmias & other complications. Patients who do not receive thrombolysis and are prone to develop late ventricular potentials on signal averaged ECG which is a substrate for ventricular arrhythmias. Thrombolytic treatment & stenting (primary PCI) have greatly influenced the major treatment of acute MI, since by using above mentioned techniques early after the onset of ischemia, myocardium can be rescued.[1-4] The objective of the study was to determine the frequency of late ventricular potentials as a precursor of complex ventricular arrhythmias in patients with acute myocardial infarction.

MATERIAL AND METHODS:

This comparative, prospective study was conducted

at Cardiology department of Mayo Hospital Lahore. In this study 132 patients were included and 66 patients were enrolled in each group. All the patients selected for the study were informed about the study and a written informed consent was taken. Patients were admitted in cardiology department and recruited in the consecutively 6 defined months to our study. Patients who presented with Myocardial Infarction(MI), diagnosed by history, ECG, enzymes were subjected to late potential analysis by Signal Averaged Electrocardiography (SAECG). SAECG using Frank xyz leads with cutoff value as total QRS duration >120 m sec, high frequency low amplitude duration >38 m sec, root mean square <20 mV were recorded between 7 to 10 day. SAECG was considered positive by standard late potential criteria when the filtered vector QRS duration was >114 msec and either the root mean square voltage of the terminal 40 msec of the altered QRS was <20 micro V or the low amplitude signal of the terminal filtered QRS was >38 msec, Streptokinase (SK) was given to 66 patients (Group A) while SK was not given to other 66 patients (Group B).

Patients with typical chest pain lasting greater than 30 minutes, ECG features of acute MI (STEMI),ST elevation greater than 1mm in limb leads in > or equal to two consecutive leads, ST elevation greater than 2mm in chest leads in > or equal to two consecutive leads, patient thrombolysed with streptokinase and patients not thrombolysed with streptokinase were included. Patients were excluded from the study considering the following reasons, absence of informed consent, cardiogenic shock, rhythm other than sinus origin, bundle branch blocks, Intra ventricular conduction abnormalities on the electrocardiogram, use of class I and III antiarrhythmic drugs, transthoracic echocardiographic analysis of congenital and acquired heart disorders, patients with primary cardiomyopathy, patients with other illness (e.g. Chronic kidney disease, Chronic liver disease etc.), patients with mechanical MI complications (consequence of reperfusion therapy),new disturbances of supraventricular heart rhythm.

Both of these subgroups are further subdivided into: patients with EF less than 40 % and with late potentials, patients with EF less than 40 % and without late potentials. Patients with EF more than 40 % and with late potentials and Patients with EF more than 40 % and without late potentials.

Patients were followed for total duration of 6 months. Patients were asked to visit the hospital after specified intervals. These specified intervals were: For late ventricular potentials (LVP) the occurrence of LVP was recorded at following intervals. Within 30 days before any other interventional procedure (PCI/CABG), 90 days and 180 days.

Left ventricular ejection fraction (LVEF) was determined by transthoracic echocardiography within 15 to 20 days after the occurrence of STEMI.

Complex ventricular arrhythmias were detected by standard ECG and by 24 hours Holter monitoring in the: 1st month (30 days).3rd month (90 days) and 6th month (180 days).All episodes of fatal and nonfatal arrhythmic events, re-infarction and revascularization procedure were carefully recorded. Following parameters checked were on every visit: Vitals (pulse, B.P, temperature, ECG, high resolution ECG / SAECG, serum electrolytes (Sodium, Potassium, Calcium, magnesium), holter monitoring, HbA1c (if pt. was diabetic), renal & liver function tests and complete blood count.

Patients were followed through trans-telephonic contact. Complete residential addresses and phone numbers were recorded so that patient can be followed easily. Information about the deceased patients were obtained from their family members.

Data entry & analysis was done by the usage of SPSS 23. Quantitative variables were offered with the help of mean ± SD. Qualitative variables were offered by using frequency tables & appropriate graphics. Data was stratified on the basis of streptokinase (given or not) and ejection fraction. Chi-Square test was used to see the association between onset of late ventricular potential in patients who received and who did not receive SK. A p-value < 0.05 at given level of alpha (x) was taken as significant.

RESULTS:

Mean age in years of patients in SK+ and SK- was 51.33±8.18 and 51.37±7.82 years. No significance in mean age was seen in both groups. (Table 1)

In SK+ group there were 41 male and 25 female patients were included while in SK- group there were 44 male and 22 female patients were included. (Table 2)

Mean height of patients in SK+ and SK- group was 163.97±6.97cm and 165.30±7.98 cm while mean weight of patients in both groups was 83.21±13.21 kg and 83.12±17.80 kg respectively. (Table 3)

As per BMI criteria in SK+ group 6 patients BMI

was normal, 10 were overweight and 50 patients were obese while in SK- group 4 patients BMI was normal, 16 were overweight and 46 were obese. (Table 4, 4.1)

In SK+ 58% patients in SK- 30% patients were hypertensive. In SK+ group 42% patients were diabetic and 36% were smokers while among SK- patients 33% were diabetic and 64% smokers.

(Table 5)

There were 56 patients who presented with inferior wall MI followed by Antero-septal wall MI (38 patients), antero-lateral wall MI (28 patients) (Table 6), Infero-posterior wall MI (10 patients) respectively. Although majority of the patients had inferior wall MI but no statistically significant association was seen between study groups and type of MI.

Table-1: Age distribution of patients		
	Group A	Group B
Number of patients	66	66
Mean age (Years)	51.33	51.37
SD	8.188	7.82
Min	40	39
Max	70	69
t- Test = 0.0287, p-value = 0.9771		

Table-2: Gender distribution of patients			
	Group A	Group B	Total
Male	41(62.1%)	44(66.7%)	85
Female	25(37.9%)	22(33.3%)	47
Total	66	66	132

Table-3: Descriptive statistic for Height & Weight				
	Height (cm)		Weight (kg)	
	Group A	Group B	Group A	Group B
Number of patients	66	66	66	66
Mean	163.97	165.30	83.21	83.12
SD	6.975	7.983	13.217	17.807
Min	149	150	50	55
Max	174	182	103	150

Table-4: Descriptive statistic for body mass index		
	BMI (kg/m^2)	
	Group A	Group B
Number of patients	66	66
Mean	30.92	30.34
SD	4.42	5.38
Min	20.03	19.48
Max	36.49	47.33

Table-4.1: Body mass index status of patients			
BMI status	Group A	Group B	Total
Normal Weight	06	04	10
Over Wight	10	16	26
Obese	50	46	96
Total	66	66	132

Table-5: Medical History of patients				
Medical History of Patients	Group A		Group B	
History of previous MI	0/66	0%	0/66	0%
Revascularization	0/66	0%	0/66	0%
Hypertension	38/66	58%	20/66	30%
Supraventricular arrhythmias	0/66	0%	0/66	0%
Ventricular arrhythmias	0/66	0%	0/66	0%
Atrioventricular conduction defect	0/66	0%	0/66	0%
Palpitations	0/66	0%	0/66	0%
Dizziness	0/66	0%	0/66	0%
Syncope	0/66	0%	0/66	0%
Coronary bypass surgery	0/66	0%	0/66	0%
Transient ischemic attack or stroke	0/66	0%	0/66	0%
Intermittent claudication	0/66	0%	0/66	0%
Diabetes mellitus	28/66	42%	22/66	33%
COPD	0/66	0%	0/66	0%
Smoking	24/66	36%	42/66	64%

Table-6: Type of Myocardial Infarction			
Type of MI	Group A	Group B	Total
Anterolateral wall MI	18(27.27%)	10(15.15%)	28
Anteroseptal wall MI	20(30.30%)	18(27.27%)	38
Inferior wall MI	26(39.39%)	30(45.45%)	56
Inferoposterior wall MI	2(3.03%)	8(12.12%)	10
Total	**66**	**66**	**132**
Chi-Square Test= 6.277, p-value= 0.098			

Table-7: Descriptive statistic for Ejection Fraction		
	Ejection Fraction (%)	
	Group A	Group B
Number of patients	66	66
Mean	44.06	42.85
SD	7.93	6.24

Mean ejection fraction of patients in SK+ group was 44.06±7.93 %and in SK- group 42.85±6.24 %. (Table 7)

In SK+ group 8 patients and in SK- group 14 patients had late ventricular potentials. Although patients in SK- group had higher frequency of late

Table-8: Frequency distribution for late potential in study groups			
	Late Ventricular Potential		Total
	Group A	Group B	
Positive	8(12%)	14(21%)	22
Negative	58(88%)	52(79%)	110
Total	66	66	132
Chi-Square Test=1.964		P -value = 0.161	

Table-9: Frequency distribution for late potential in study Stratified for Ejection fraction				
Ejection Fraction	Late Ventricular Potential	Group A	Group B	p-value
<40%	Positive	2	0	0.296
	Negative	14	8	
>40%	Positive	6	14	0.105
	Negative	44	44	

potentials but no statistically significant difference was observed between the two groups. i.e. p-value=0.161

Patients whose ejection fraction was <40%, 2 patients in SK+ and none of the patients in SK-group had late potentials (Table 8). While patients whose ejection fraction was >40% among them 6 patients in SK+ and 14 patients in SK- group had late potential. No statistical significant effect of ejection fraction on occurrence of LVPs was observed. (Table 9)

DISCUSSION:

Signal-averaged ECG (SAECG) gives an average of multiple QRS complexes, reducing the level of noise which interferes with the intermittent ECG signal, so that signals at the microvolt level that are normally hidden within noise are revealed. [5]

These high frequency and low amplitude signals of the ventricles at the terminal part of QRS complex are named as late ventricular potentials (LVPs) and signifies a delay in conduction in the ailing myocardium, as a result of reduced conduction of the impulse, and are possible physical substrate for reentry ventricular tachycardias.[6]

Mostly those patients are considered to be at risk who previously had ischemic episodes. The inhibition of these serious malignant arrhythmias is made possible by the correct detection of LVPs.

The typical ECG signal has amplitude of the order of a few microvolt which encloses maximum data at frequencies lower than 100 Hz. LVPs, if exist, are considered non-stationary & non-Gaussian signals with an amplitude between 1 & 20 Mv. [7]

In our study late ventricular potentials were seen in 8 (12.12%) patients who were given SK (group A) and in 14 (21.21%) patients who were not given SK (group B). Stratification of ejection fraction showed that patients with ejection fraction <40, late ventricular potentials were seen in 2 subjects of group A & none of the patients in group B developed late ventricular potentials. However patients whose ejection fraction was >40 among them late ventricular potentials were seen in 6 patients of group A and in 14 patients of group B. However no statistically significant association was seen between thrombolytic status of patients with late ventricular potentials stratified on the basis of ejection fraction. Only 1 patient (0.75 %) is suspected to have abrupt cardiac death because of fatal ventricular arrhythmias. This patient had anterior wall MI and was not thrombolysed with streptokinase (group B). His ejection fraction was 42 % and late ventricular potentials were present. 4 patients (3.03 %) were observed to have non sustained ventricular tachycardia but no episodes of sustained ventricular arrhythmias (VF/VT) or

sudden cardiac death were reported in these patients. 3 (75%) out of 4 patients had inferior wall MI , not thrombolysed with streptokinase (group B) , ejection fraction > 40 % and late ventricular potentials were present . 1 (25%) out of 4 patient had anterior wall MI, belonged to group B , ejection fraction >40% and late ventricular potentials were present.

According to our study frequency of late ventricular potential was higher in patients who were not thrombolysed as compared to that of patients who were thrombolysed i.e. Late ventricular potential [SK+: 12.12% vs. SK-:21.21%] but results remained same when studied just after myocardial infarction or few months later.

Late potentials are considered to be strong predictors of arrhythmic episodes after MI[8]. If the progression of an arrhythmogenic substrate is prevented, improvement in prognosis has been seen in the form of low incidence of LVPs in subjects with prompt reperfusion as compared to patients treated conservatively having high percentage of late potentials and associated arrhythmic episodes and abrupt cardiac death.[9]

In the modern era, the most important problem in the field of cardiology is abrupt cardiac death. Ventricular arrhythmias in the form of ventricular tachycardia and ventricular fibrillation causes more than 50% of these deaths. For about twenty years, ventricular late potentials (LVP) are known to be the probable cause of serious ventricular arrhythmias.[10] No statistical significance was reported by Swiatowiec et al10 in ventricular arrhythmia assessment but there was significant association with late ventricular potential occurrence in all groups.Ventricular arrhythmias are very much common early after commencement of acute myocardial infarction. There are multiple factors responsible for the occurrence of ventricular arrhythmias which includes electrolyte imbalance (hypokalemia, hypomagnesemia), continuous ischemia, hemodynamic instability, metabolic abnormalities (acidosis, hypoxia), re-entry phenomena, and increased automaticity.

Volosin et al[11] as well assessed the time period of development of LVPs after MI. It has been found by them that in reperfusion cases the occurrence of LVPs was associated with the manifestation of Q waves & was not dependent of infarct location and highest levels of CK (creatinine kinase). Sometimes late ventricular potentials were present only in the initial period after myocardial infarction. Areas of transiently delayed myocardial activation that resolve with the curing of infarct may be represented by these.

Gang et al study[12] supported the fact that there is high frequency of late ventricular potential among patients who were not thrombolysed.

Riccio et al[13] results also support the findings of our study by showing high frequency of late potential in patients who were not thrombolysed.

In a study done by M.U.Rabbani[14] it has been shown that the outcome of thrombolysis on occurrence of late ventricular potentials is not very much significant in patients of inferior wall MI i.e higher number of patients with inferior wall MI had positive late ventricular potentials even if they were thrombolysed as compared to patients with anterior wall MI (thrombolytic group)

In a study by Levent CAN[15], it was shown that after thrombolytic treatment the occurrence of late ventricular potentials   was decreased in patients having reciprocal changes on ECG as compared to patients with no reciprocal changes on ECG.

The goal of thrombolytic therapy is to open an occluded coronary artery. By doing this infarct size is also reduced and prognosis is improved. Results after thrombolytic therapy depends upon the fact that how early the patient reached to hospital after onset of myocardial infarction and early administration of thrombolytic agent, degree of patency of occluded artery and the area of myocardial infarction. Though, it is not known that better prognostic results after thrombolysis are due to reduced arrhythmic events or decreased mortality rate.[16,17]

According to a study done by Ritchie et al, a reduction in infarct size of about 15% was observed in patients who were thrombolysed with streptokinase as compared to patients who were taken as controls in which reduction in infarct size was observed to be 19%.[18]

Study done by Bass et al revealed improved ejection fraction in thrombolysed group of patients as compared to patients who were not thrombolysed. Group which was given anistreplase for thrombolysis showed higher LV ejection fraction (53%) while non-thrombolytic group patients had lower LVEF (47%).[19]

In the study conducted by GISSI, it was found that those patients who were treated with streptokinase had no difference in ejection fraction from those who were treated conservatively when examined before discharge from hospital.[20]

The association between arrhythmias and occurrence of LVPs after acute MI along with

low frequency of late ventricular potentials after successful thrombolytic therapy gives an idea that if the formation of an arrythmogenic substrate is avoided then better prognostic results can be obtained.[21,22]

 Factors responsible for the generation of LVPs during the development of MI are not very much clear. Many possible mechanisms have been proposed by Gang et al that may be the possible cause of decreased frequency of late ventricular potentials in patients who have been successfully reperfused.[12] It was suggested that the decreased frequency of LVPs might be due to reperfusion, as reperfusion reduces ischemia, permits very fast removal of toxic materials of anaerobic metabolism, causes contraction-band necrosis to occur, permits the reappearance of many plasma ingredients to the area where ischemia occurs, causes the production of oxygen free radicals and may increases the hemorrhage within the area of infarct.[12]

It seems that high resolution electrocardiography could be used as a commanding tool for identification of an arrhythmogenic substrate following acute MI in a patient who has been thrombolysed. Future studies by the usage of this new technique should support to explain whether in subjects with comparable grades of left ventricular damage, consequence is poorer in individuals with late potentials or not.[22]

CONCLUSION:

Late ventricular potentials were more common in patients who did not receive thrombolytic treatment. We can say that late ventricular potentials have significant role in the assessment of risk for the occurrence of complex ventricular arrhythmias in patients of acute MI. Thus more studies are required to prove the same.

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