University Heart Journal
Vol. 17, No. 1, January 2021

ORIGINAL ARTICLES

Correlation between Abnormal Signal-Averaged ECG and Left Ventricular Ejection Fraction in Patients of Acute Myocardial Infarction within Seven Days of Sustaining the Infarction.

MOHAMMAD ABDUL MALEK[1], SAYED ASIF IQBAL[1], A F M SHAMSUL HAQUE[1], SAYEDA ALEYA SULTANA[1], MD WALIUR RAHMAN[1], MD. MUKHLESUR RAHMAN[2]

[1]Cardiology Department, Combined Military Hospital (CMH), Dhaka Cantonment, Bangladesh, [2]Cardiology Department, University Cardiac Center, Bangabandhu Sheikh Mujib Medical University (BSMMU)

Address of Correspondence: Dr (Col) Abdul Malek. Consultant Cardiologist, Combined Military Hospital, Dhaka Cantonment, Bangladesh. E mail: malek100932@gmail.com

Abrstact:

Objective: This study sought to evaluate the correlation of left ventricular ejection fraction (LVEF) with Signal – Average Electrocardiogram (SAECG) in patient with acute myocardial infarction. Background: Post MI risk stratification is still a debatable issue. Appropriate investigation to ascertain the patient at risk of sudden cardiac death is sometimes difficult. Abnormalities in the SAECG have been determined to be independent predictors of risk of developing ventricular arrhythmias in patients convalescing from myocardial infarction. Correlation of LVEF with SAECG will identify the small group of patient at risk of fatal arrhythmia. Method: This observational study was carried out in the cardiology center, Combined Military Hospital, Dhaka cantonment during the period of January 2010 to January 2011. Patient with first acute myocardial infarction within 7 days of sustaining acute myocardial infarction were included in the study. All three parameters of SAECG (Total QRS duration, Low Amplitude Signal (LAS) under 40µvolt, Root - mean -square (RMS) voltage of last 40 msec) were recorded, and basing on the results, patients were grouped into normal or abnormal SAECG. Result: A total of 106 patients of acute MI were studied. Mean age of the patients were 54(SD±10.5) years (range 34 to 90 years). Only 13(12%) patients were female with male to female ratio of 7.15:1. 32% patients were thrombolysed & abnormal SAECG was more in patients who were thrombolysed (p value<0.05) but logistic regression analysis showed no significant association. Smoking had significant association with abnormal SAECG by univariate analysis (p value<0.05) but logistic regression analysis showed no significant association with smoking and sex (p value >0.05). 46% patients had inferior/infero-posterior myocardial infarction. Abnormal SAECG was more among patients with inferior MI (p <0.05). Mean LVEF was 45.81% (SD±9.68). Correlation of LV function was assessed by both Pearson's correlation and Ç2 test but no significant association was seen. Logistic regression analysis showed the similar result. Conclusion: In our study, no correlation was found between abnormal signal-averaged ECG and left ventricular ejection fraction following acute myocardial infarction. Further large, multi center study with more selective variables is required to find out any association of SAECG and LV ejection fraction.

Keywords: Myocardial infarction; Sudden death; Signal-averaged electrocardiogram; Ventricular late potentials; Ventricular tachycardia

University Heart Journal 2021; 17(1): 3-9

Introduction:

Despite significant reduction in cardiovascular mortality during the past 30 years, cardiovascular disease still remains the single largest categorical cause of natural death. Approximately 50% of all cardiac deaths result from serious arrhythmias.[1] Individuals with ischemic heart disease, particularly those with a history of myocardial infarction (MI) represent a large proportion of those at risk for sudden cardiac death (SCD). Most SCDs are caused by acute fatal arrhythmias—ventricular tachycardia/fibrillation (VT/VF). Most have coronary artery disease and left ventricular dysfunction.[2] Prediction of patient groups at increased risk of developing spontaneous VT and VF has been evaluated using Electrophysiologic study (EPS),[3] signal averaging of the surface ECG,[4] and assessment of left ventricular function.[5] Due to large

Received: 05 July 2020 **Accepted:** 15 November 2020

number of these patients and high cost of implantable cardioverter-defibrillator (ICD) implantation, selection of eligible patients is very important.

Signal Averaged Electrocardiography (SAECG) is a very specialized type of surface ECG which involves computerized analysis of small segments of a standard ECG in order to detect abnormalities, termed Ventricular Late Potentials (VLP) that would be otherwise obscured by skeletal muscle and electrical noise.[6] The goal of these signal-averaged ECG techniques is to detect occult derangements of ventricular activation, or late potentials, present during sinus rhythm that appears to be a hallmark for sudden ventricular arrhythmias. The aim of our study was to evaluate the relationship between abnormal SAECG and left ventricular ejection fraction in patients of acute myocardial infarction within 7 days of sustaining infarction.

Material and Methods:

Between January 2010 to January 2011, a total of 106 consecutive patients with acute MI admitted to Combined Military Hospital, Dhaka Cantonment, Bangladesh, were prospectively enrolled in the study. Inclusion criteria were "Patient with first acute myocardial infarction within 7 days of sustaining acute myocardial infarction and clinically stable". Joint ESC/ACCF/AHA/WHF TASK FORCE for Redefinition of Myocardial Infarction[7] was followed for Criteria for acute myocardial infarction. Exclusion criteria were: Current arrhythmia, Bundle branch block, Previous myocardial infarction, Intraventricular conduction delay, Cardiomyopathy, Past documented ventricular arrhythmia, Stage 4 heart failure. LVEF was measured by Simpson's method and divided into four groups according to the severity of LV function.

All relevant investigations were done routinely. S Troponin I was repeated after 12 hours if 1st sample of Troponin was found negative. S Troponin I level ≥1.0 ngm/ml was considered as abnormal in our study.

A signal-averaged ECG was obtained 7 days within hospitalization. The patients were not receiving antiarrhythmic drugs, except the beta-blocking agents. The signal-averaged ECG was recorded with standard bipolar orthogonal X, Y and Z leads. The averaged QRS complexes were filtered with bidirectional high pass filters at 40Hz. After filtering, the total QRS duration was determined by computer algorithm.[5,8] Three parameters have been identified to describe late potentials: Filtered QRS duration (QRSd), Root - mean -square voltage of the terminal 40 msec of the QRS complex (RMS40) and the duration of the low amplitude signal (LAS) >40 mV. Representative criteria for abnormal SAECG were defined as being present if two of the following criteria were met: QRSd > 114 msec, RMS 40 < 20 mV and LAS >38 msec.

Result:

A total one hundred and six patients fulfilling the inclusion criteria were finally included in the study. Basing on the result of Signal Averaged ECG, patients were divided into two groups: normal SAECG and abnormal SAECG. All relevant data's were compared with the result of SAECG. Characteristic of the study subjects are mentioned here (Table 1).

Table-I

Characteristics of the study patients (n 106)

Characteristics	Minimum	Maximum	Mean (± SD)
Clinical			
Age (years)	54 (10.5)	34	90
Body Mass Index (kg/m2)	23.8 (3.1)	18	32
Pulse (beat/min)	77 (15.5)	50	116
Blood pressure (mm Hg)			
Systolic	110 (16.8)	80	170
Diastolic	69 (9.1)	50	90
Day of examination (day)	4 (1.6)	1	7
Investigations			
S Troponin I (ngm/ml)	41 (49)	1.1	180
Peak creatine kinase UI/L)	84 (83)	10	480
Random Blood sugar (mol/L)	8.6 (3.7)	3.4	23.7
Lipid profile (mg/dl)			
Total Cholesterol	228 (25)	102	370
LDL-C	125 (33)	52	197
TG	176 (82)	56	412
HDL-C	38 (9)	20	67
Serum Creatinine (mg/dl)	1.2 (0.4)	0.6	4.7
LVEF (%)	45.7 (9.6)	25	70

Mean age of the patients are 54±10.5 years (range 34 to 90 years). 88% of the total patients were within 35 years to 65 years. Only 7% patients had age less than 40 years. Among the 106 patients, 93(88%) patients were male and only 13(12%) were female with male to female ratio 7.15:1. There is no statistically significant difference between male and female patients (p >0.05). Incidence of SAECG was compared in both sex and in different age group and found not significant (p>0.05).

The following quantitative signal - averaged ECG variables were calculated by computer then visually inspected &edited: QRSd,RMS40 and LAS >40. 60 (57%) patients (Table 2) had abnormal total QRS duration and RMS voltage criteria was found abnormal in 11(10%) patients.

In this study, six important cardiovascular risk factors (Diabetes mellitus, Hypertension, Family history, Smoking, Dyslipidemia) were assessed. Mean BMI was 23.8(SD±3.11) kg/m2. 51(48.1%) patients had history of Diabetes mellitus and only 15(14.1%) patients had positive family history of ischemic heart disease. Others minor risk factors were not considered during analysis. Univariate analysis shows significant association of smoking with abnormal SAECG (p <0.05)(Table 3). Among 106 patients 3% patients had no risk factors and another 3% patients had 5 five risk factors. There is no significant association with number of risk factors with abnormal SAECG (p value >0.05).

Table-II

Parameters related to Signal-averaged ECG (n 106)

Category		Mean (±SD)	Minimum	Maximum	Abnormaln (%)	Abnormal SAECGn (%)
SAECG	Total QRS duration (m sec)	115.09(18.12)	69	169	60 (57)	54(51)
	LAS under 40 µ volt	34.43(15.46)	6	95	49 (46)	
	RMS voltage last 40 m sec	76.95(70.60)	8	358	11(10)	

Table-III

Risk factors affecting SAECG

Characters	Yes/No	SAECG		p Value
		Normaln (%)	Abnormaln (%)	
Diabetes Mellitus	yes	26(52)	24(48)	>0.05*
	No	25(46)	30(54)	
Hypertension	yes	23(52)	21(48)	>0.05*
	No	29(47)	33(53)	
Family history	yes	7(48)	8(52)	>0.05*
	No	45(49)	46(51)	
Smoking	yes	18(37)	30(63)	<0.05**
	No	34(59)	24(41)	
Dyslipidemia	yes	23(51)	22(49)	>0.05*
	No	29(47)	32(53)	
Obesity	yes	17(57)	13(43)	>0.05*
	No	35(46)	41(54)	

Chi-Square tests were employed to analyze the data.

* = Not significant.** = Significant

At presentation, patients were classified into three groups: 1) Anterior 2) Inferior/Infero-posterior 3) others which included Non STE myocardial infarction. Number of patients with Inferior MI (43%) was more than that of Anterior MI (32%) (Fig 1). Significant association was observed between type of myocardial infarction at presentation with SAECG ($p < 0.05$) (Table 4).

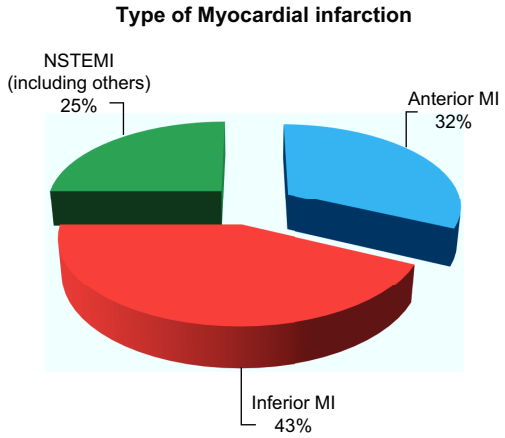

Fig.-1: *Type of Myocardial Infarction*

Table-IV

Association of different types of myocardial infarction with SAECG

Type of myocardial infarction	SAECG n (%)		p value
	Normal	Abnormal	<0.05*
Anterior MI	19(56)	15(44)	
Inferior/ infero-posterior MI	19(41)	27(59)	
Others	14(54)	12(46)	

Chi-Square tests were employed to analyze the data
* = Not significant

When patient became fully stable and those who fulfilled inclusion criteria, Left ventricular ejection fraction and Signal-Averaged Electrocardiogram (SAECG) was carried out.

Depending on the severity of LVEF, patients were categorized into four groups (Fig 2). Mean LVEF was 45.81 %(SD±9.68). Minimum LVEF was 25%. Out of 106 patients 54 (50.94%) had abnormal SAECG(Table 2).

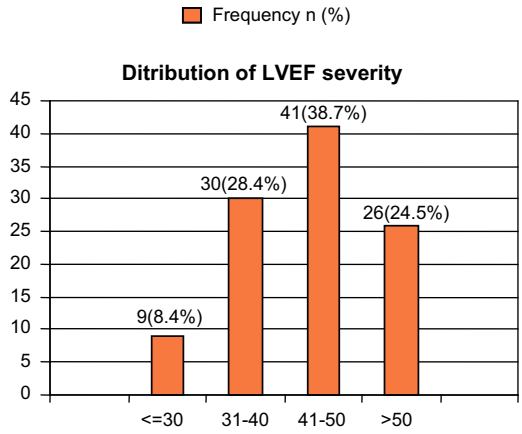

Fig.-2: *Distribution of LVEF severity*

Each group of patients with different LV function was compared with SAECG. No significant association was found between severity of LV function and SAECG (p value>0.05) (Table 5). Mean value of LVEF was compared with mean value of three different parameter of SAECG. Simple Pearson's correlation was done and found no significant association ($p > 0.05$).

Table-V

Association of LVEF with SAECG

LVEF Severity (%)	SAECGn (%)		p value
	Normal	Abnormal	
<= 30	4(44)	5(56)	>0.05*
31-40	17(57)	13(43)	
41-50	23(56)	18(44)	
>50	8(31)	18(69)	

Chi-Square tests were employed to analyze the data
* Not significant

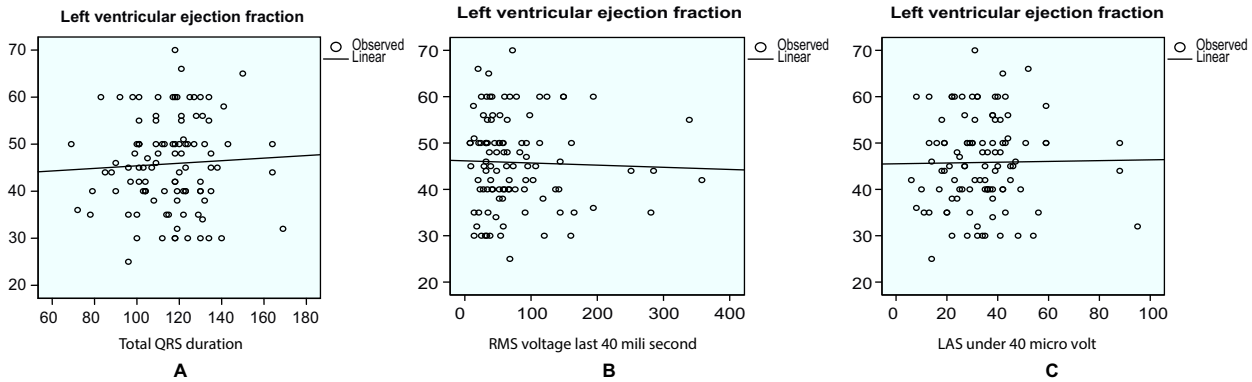

Fig.-3: *(a) Plot of relation between LVEF with total QRS duration, (b) Plot of relation of LVEF with RMS voltage of SAECG, (c) Plot of relation of LVEF with LAS under 40 micro volt of SAECG*

Table-VI

Result of multiple logistic regression analysis where SAECG is dependant variable, LVEF and other variables are independent.

Variables	Beta co-efficient	S.E.	Sig.	Odd ratio	95% C.I
age	0.042	.024	.075	1.043	0.996 -1.092
LVEF	0.019	.036	.601	1.019	0.950 -1.093
Troponin I	0.004	.005	.396	1.004	0.994 -1.014
DM	-0.029	.473	.951	.971	0.384-2.457
HTN	0.212	.499	.671	1.236	0.465-3.287
Smoking	0.713	.526	.175	2.041	0.728-5.725
Family history	0.767	.791	.332	2.153	0.457-10.149
Dyslipidemia	-0.516	.500	.302	.597	0.224-1.589
BMI	1.169	.557	.036*	3.219	1.079-9.598
RWMA					
RWMA_cat(1)	-2.499	1.511	.098	.082	0.004-1.586
RWMA_cat(2)	-1.432	1.319	.278	.239	0.018-3.171
RWMA_cat(3)	-2.569	1.592	.106	.077	0.003-1.734
RWMA_cat(4)	-1.789	1.510	.236	.167	0.009-3.225
sex	1.528	.770	.047*	4.610	1.019-20.846
Thrombolysis performed	1.3	.651	0.08	2.31	0.752- 8.342

* = Significant

Multiple logistic regression analysis was done after initial univariate analysis of the study subjects. Here SAECG was considered as dependant variable. LVEF & other factors were treated as independent variable. During univariate analysis smoking and type of MI were found to have significant association but multiple logistic regression analysis showed significant association with obesity ($p<0.05$, odd ratio 3.2 , CI 1.07 to 9.5) and sex. ($p<0.05$, odd ratio 2.3, CI 1.01 to 20.8) (table 6).

Discussion:

Improved approaches are needed for identifying those patients at highest risk for subsequent major arrhythmic event (MAE). EF<40% is the strongest predictor of arrhythmic events in post MI patients with sensitivity of 100%.[9] However, specificity of EF<40% is low (54%) and this limits ICD case selection based on low ejection fraction alone.[6] The same result was obtained in several studies.[10,11] SAECG is also significantly related to arrhythmic events but they seem to have lesser predicting power than EF<40%.

To our knowledge after thorough Google search, this is the first study which described the correlation of SAECG with LVEF. Earlier studies were considered mainly on predictive outcome for risk stratification. In our study no significant correlation was found between severity of LV dysfunction and abnormal SAECG (p value >0.05). Study only revealed correlation between SAECG and LVEF in single occasion. Univariate analysis was done first, then considering the influence of multiple factors on SAECG, logistic regression analysis also done which showed similar result between SAECG and LVEF.

A staged application of noninvasive tests followed by the use of EPS was done by James J. Bailey et al[12] (2001). With this approach, the first step was the performance of both SAECG and LVEF. If the two tests were both negative or both positive, further testing would not be done, as the two-year probability of a major arrhythmic event (MAE) would be very low in the former situation (2.2%), and high enough in the latter situation (38.7%) to warrant consideration of ICD implantation.

Majid Haghjoo et al (2007)[13] designed a logistic model based on EF and then another model constructed based on EF plus SAECG and HRV. The two models were compared using likelihood ratio test and observed that the additional value of SAECG and HRV on EF<40% is marginally significant (P=0.036). Presences of late potentials and abnormal HRV have been correlated with the inducibility of VT and their prognostic value in post MI patients have also been established in previous studies.[14] This study was not prospective nor did they evaluate consecutive series of patients with myocardial infarction. In another study,[15] it was seen that depressed baroreflex sensitivity is a superior predictor arrhythmic risk compared with any other variables.

The relation between the prevalence of late potentials and the site of the myocardial infarction is still controversial. In

our study, incidence of abnormal SAECG is more in patients with inferior than anterior myocardial infarction (43% vs. 32%). Univariate analysis shows significant association ($p < 0.05$) but multiple logistic regression analysis revealed that association is not significant ($p > 0.05$). In a previous study[16] which support the similar result. This finding may be related to the fact that the inferoposterior segment of the left ventricle is the last to be depolarized relative to the anteroseptal or anterior wall. Thereby, regional slow fractionated activity may be hidden within QRS complex in the anterior myocardial infarction.[17]

In our study with univariate analysis, age and sex has no significant association with SAECG ($p > 0.05$) but logistic regression analysis shows weak relation with sex (p value <0.05, Odd ratio 4.61, CI 1.01 to 20.84). This is probably due to small number of study subjects. Malik M et al[18] showed significant correlations between age, sex and the SAECG in MI patients. Even, factors such as sex, age, and MI location significantly affect the SAECG; adjustments of SAECG criteria for these factors do not improve the overall sensitivity and specificity for predicting arrhythmic events after MI.[19]

In this study, multiple logistic regression analysis showed significant positive correlation with obesity (p value <0.05, odd ratio 3.21 & CI 1.07 to 9.6). Atul P et al,[20] (2000) described those obese patients with BMI of >30 kg/m^2 had significantly more abnormalities on SAECG (4.6% vs. 55%). Atul P et al, (2000) also showed some effect of Diabetes mellitus and hypertension on SAECG. Leonid M. Kozer et al (2000) also states that Diabetes mellitus is an independent predictor of the variability of late potentials ($P < .0001$).[21]

In our study abnormal Signal – averaged ECG was more in patients who were thrombolysed. Univariate analysis showed significant association (p value >0.05) but logistic regression analysis showed no significant association(p value >0.05, Odd ratio 2.3, CI .752 to 8.342). This study differ with other studies.[22] The early studies of the pre-thrombolytic era consistently found that an abnormal SAECG indicated a significantly increased risk of sudden death, ventricular fibrillation, or sustained ventricular tachycardia.[21, 22] Axel Bauer1 et al,[23] in their study have shown that the presence of ventricular LPs is of little value for predicting cardiac death and serious arrhythmic events in post-infarction patient populations receiving modern reperfusion therapy. Later studies of the thrombolytic era do not find such a clear association.

Conclusion:

Combination of abnormal signal-averaged ECG result and low ejection fraction can provide a higher predictive accuracy for serious arrhythmic event during post infarction period. However, in our study no correlation was found between abnormal signal-averaged ECG and left ventricular ejection fraction following acute myocardial infarction. Although univariate analysis showed significant association of SAECG with smoking, site of myocardial infarction and thrombolysis but logistic regression analysis showed weak correlation of SAECG with obesity and sex. Further large, multi center study with more selective variables is required to find out any association of SAECG and LV ejection fraction.

References:

1. Myerburg RJ, Castellanos A. 2001. Cardiac arrest and sudden cardiac death. In: Braunwald E, Zipes DP, Libby P, editors. Heart Disease- A Textbook of Cardiovascular Medicine. Philadelphia, PA: Saunders, 890–931.
2. Richards DA, Denniss AR. Assessment, significance and mechanism of ventricular electrical instability after myocardial infarction. Heart Lung Circ, 2007;16:149–55.
3. Cooper MJ, Hunt LJ, Richards DA, Denniss AR, Uther JB, Ross DL. Effect of repetition of extra stimuli on sensitivity and reproducibility of mode of induction of ventricular tachycardia by programmed stimulation. J Am Coll Cardiol, 1988;1:1260-67.
4. Denniss AR, Ross DL, Uther JB. Reproducibility of measurements of ventricular activation time using the signal-averaged Frank vectorcardiogram. Am J Cardiol,1986; 10:156–60.
5. Richards DA, Byth K, Ross DL, Uther JB. What is the best predictor of spontaneous ventricular tachycardia and sudden death after myocardial infarction? Circulation,1991; 83:756–63.
6. Imran Majeed, Muhammad Alamgir Khan, Muhammad Mazhar Hussain, Muhammad Aslam. High Resolution Electrocardiography.Pak J Physiol,2005; 1: 1-2.
7. Kristian Thygesen, Joseph S. Alpert, Harvey D. White, on behalf of the Joint ESC/ACCF/AHA/WHF Task Force for the Redefinition of Myocardial Infarction: Expert Consensus Document. Circulation, 2007;116:2634-53
8. Cain ME, Anderson JL, Arnsdorf MF, Jay W. Mason, Melvin M. Scheinman, Albert L. Waldo, et al. Signal-averaged electrocardiography. ACC Expert Consensus Document. J Am Col Cardiol. 1996; 27(1):238-49.
9. Robert J. Burns, Raymond J. Gibbons, Qilong Yi, Robin S. Roberts, Todd D. Miller, Gary L. Schaer. Ventricular ejection fraction, end-systolic volume index and infarct size to six-month mortality after hospital discharge following myocardial infarction treated by thrombolysis. J Am Coll Cardiol, 2002 ; 39:30-36
10. Buxton AE, Lee KL, Fisher JD, Arke. J Osephson, Eric N. P Rystowsky, Gail Hafley et al. A randomized study of the prevention of sudden death in patients with coronary artery disease. N Engl J Med. 1999; 341:1882-90

11. Bigger JT, Jr, Fleiss JL, Kleiger R. The relationships among ventricular arrhythmias, left ventricular dysfunction, and mortality in the 2 years after myocardial infarction. Circulation, 1984;69:250-58.

12. James J. Bailey, Alan S. Berson, Harry Handelsman & Morrison Hodges. Utility of Current Risk Stratification Tests for Predicting Major Arrhythmic Events after Myocardial Infarction. J Am Coll Cardiol, 2001;38:1902-11.

13. Majid Haghjoo, Reza Kiani, Amir Farjam Fazelifar, Abolfath Alizadeh, Zahra Emkanjoo, and Mohammad Ali Sadr-Ameli. Early Risk stratification for Arrhythmic death in Patients with ST-Elevation Myocardial Infarction. Indian Pacing Electrophysiol J. 2007;7(1):19–25

14. Kanovsky MS, Falcone RA, Dresden CA, et al. Identification of patients with ventricular tachycardia after myocardial infarction: signal-averaged electrocardiogram, Holter monitoring, and cardiac catheterization. Circulation, 1984; 70:264-70.

15. T G Farrell, 0 Odemuyiwa, Y Bashir, T R Cripps, M Malik, D E Ward et al..Prognostic value of baroreflex sensitivity testing after acute myocardial infarction. Br Heart J, 1992; 67: 129-37

16. Lutz Reinhardt, Markku Makijarv, Thomas Fetsch, Juha Montonen, Gilbert Sierra, Antoni Martinez, Toivo Katila et al.. Predictive value of wavelet correlation functions of Signal-Averaged ECG in patients after Anterior versus Inferior myocardial infarction. J Am Coll Cardiol, 1996;27:53-9.

17. Hood MA, Pogwizd SM, Peirick J, Cain ME. Contribution of myocardium responsible for ventricular tachycardia to abnormalities detected by analysis of signal-averaged ECGs. Circulation, 1992; 86:1888-901

18. Malik M, Odemuyiwa O, Poloniecki J, Kulakowski P, Farrel T, Stauton A, Camm AJ. Age-related normal values of the signal averaged-electrocardiographic variables after acute myocardial infarction. Am J Cardiol. 1991;68:440-45.

19. Pierre Savard, Jean-Lucien Rouleau, John Ferguson, Nicole Poitras, Patrick Morel, Richard F. Davies, et al. Risk stratification after myocardial infarction using signal-averaged electrocardiographic criteria adjusted for sex, age, and myocardial infarction location. Circulation, 1997;96: 202-13.

20. Atul P. Lalani, Balavenkatesh Kanna, Joseph John, Kevin J. Ferrick, Michael S. Huber and Lawrence E. Shapiro. Abnormal Signal-Averaged Electrocardiogram (SAECG) in Obesity. Obesity Research, 2000;8:20-28.

21. Leonid M. Kozer, Kuruvilla M. Cheriparambil, David R. Schifter, Barry I. Saul, and Chatla V.R Reddy. Clinical significance of variability of ventricular late potentials detected before discharge in patients after myocardial infarction. Am Heart J, 2000;139(2):134-41.

22. Lomama E, Helft G, Persoz A, Vacheron A. Relation between successful late coronary angioplasty of an occluded, infarction-related artery and lower prevalence of ventricular late potentials. Coron Artery Dis, 1998;9:125-29.

23. Axel Bauer, Przemyslaw Guzik, Petra Barthel, Raphael Schneider1, Kurt Ulm,Mari A et al..Reduced prognostic power of ventricular late potentials in post-infarction patients of the reperfusion era. European Heart Journal, 2005;26(8): 755-61.