Exercise induced ST segment elevation in aVR more than 2 mm to differentiate between left main and three vessel disease in patients with Duke score ≤-11

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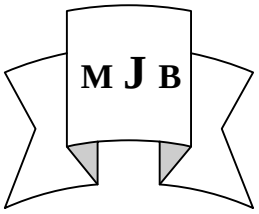

Abstract

Back ground : This study evaluated the ability of exercise induced ST segment elevation in aVR in patients with Duke treadmill score ≤ -11 to predict left main stem disease and three vessel disease and to investigate the ability of ST segment elevation in aVR more than 2 mm to differentiate between left main stem and three vessel disease.

Methods :66 patients with Duke score ≤ -11 were divided into three groups. group 1 included 16 patients with no ST elevation in aVR, group 2 included 21 patients with ST elevation less than 2 mm and group 3 included 29 patients with ST elevation more than 2 mm, coronary angiography was done and results were correlated with ST elevation in aVR

Results : 70% of patients with ST segment elevation in aVR had either left main stem or 3 vessel disease. Exercise induced ST elevation in aVR had sensitivity of 95% and specificity of 32% in predicting left main disease, while exercise induced ST elevation in aVR more than 2 mm had sensitivity of 89% and specificity 74% in predicting left main disease.

Conclusion : Eercise induced ST segment elevation in aVR in patients with Duke score ≤-11 is sensitive but not specific for both left main and three vessel disease while ST segment elevation in aVR of more than 2 mm is both sensitive and specific for left main but not for three vessel disease

ارتفاع مستوى ST في جزء aVR لأكثر من 2 ملم للتفريق بين الشريان الرئيسي الأيسر و ثلاثة أوعية دموية متضايقة للمرضى الذين لديهم نسبة ديوك اقل من -11

الخلاصة

الأهداف : أنجزت هذه الدراسة لمعرفة مقدرة ارتفاع مستوى ST في جزء aVR من التخطيط إثناء فحص الإجهـــاد لتحديـــد المرضى المصابين بتضييق الشريان الرئيسي الأيسر أو ثلاثة أوعية دموية في القلب لدى المرضى الذين مستوى ديوك لديهم اقل من -11 و لمعرفة مقدرة مستوى ارتفاع ST أكثر من 2 ملم للتفريق بين المرضى المصابين بتضييق الشريان الأيسر الرئيسي أو ثلاثة أوعية دموية قلبية .

الطرائق : شملت هذه الدراسة 66 مريضا (لديهم مستوى ديوك اقل من 11) وقسموا إلى ثلاثة مجاميع ، المجموعة الأولى شملت 16 مريضا ليس لديهم ارتفاع في مستوى ST و المجموعة الثانية شملت 21 مريضا لديهم ارتفاع في مستوى ST اقل من 2 ملم و المجموعة الثالثة 29 شملت مريضا لديهم ارتفاع في مستوى ST أكثر من 2ملم .

النتائج : 70% من المرضى الذين لديهم ارتفاع في مستوى ST في جزء aVR لديهم إما الشريان الأيسر الرئيسي أو ثلاثة أوعية دموية قلبية متضايقة. فحص الإجهاد المسبب لارتفاع مستوى ST في جزء aVR لديه حساسية بنسبة 95% وخصوصية بنسبة 32% للتنبؤ بتضييق الشريان الأيسر الرئيسي في حين فحص الإجهاد المسبب لارتفاع مستوى ST في جزء aVR لأكثر من 2 ملم لديه حساسية بنسبة 89% وخصوصية بنسبة 74% للتنبؤ بتضييق الشريان الأيسر الرئيسي المريض .

الاستنتاج : هذه الدراسة أظهرت إن فحص الإجهاد المسبب لارتفاع مستوى ST في جزء aVR هو حساس لكن ليس متخصص للتنبؤ بتضييق الشريان الرئيسي الأيسر المريض أو ثلاثة أوعية دموية قلبية متضايقة ولكن فحص الإجهاد المسبب لارتفاع مستوى

ST لأكثر من 2 ملم هو ليس فقط حساس ولكن أيضا متخصص للتنبؤ بتضايق الشريان الرئيسي الأيسر للمرضى الذين نسبة ديوك لديهم اقل من - 11 .

Introduction

The exercise treadmill is used in the evaluation of symptomatic patients to predict the presence and extent of coronary artery disease and the short and the long term prognosis [1,2] . Although a large number of non invasive stress testing modalities are currently available , the exercise ECG is still used as a standard for comparsion with other clinical and testing risk markers , it is also the least costly of all provocative non invasive tests .

Although the exercise electrocardiogram has been extensively studied in numerous reports there are limited data regarding the significance of exercise induced ST segment changes in aVR to detect myocardial ischemia[3-6]

It has been postulated that ST elevation in aVR in patients with stable angina is highly predictive of left main or three vessel disease [7] with out mentioning the degree of ST segment elevation.

The present study was undertaken to investigate the ability of exercise induced ST elevation in aVR for the detection of severe coronary artery disease including left main stem or three vessel disease and the ability of degree of ST segment elevation in aVR to predict left main coronary artery disease .

Patients and Method

The study was conducted in Merjan teaching hospital between January 2009 to June 2010 including 66 patients age 29-82 mean 57 ± 8, 49 males and 17 females.

According to Bruce protocol exercise test was carried out, resting heart rate , blood pressure , and 12 lead ECG was recorded ,a 12- lead electrocardiographic tracing was observed continuously,blood pressure was measured by arm-cuff sphy gmomametor during the last 30 seconds of each work stage,
test was terminated when patient got limiting chest pain , severe fatigue, dyspnea, or severe ventricular arrhythmias , the test also was terminated if patient got maximum ST depression 3mm or greater , systolic blood pressure more than 230 mm Hg or diastolic blood pressure more than 130 mm Hg or the patient reached the target heart rate.

An exercise test result was considered positive if there was horizontal or down sloping ST segment depression of at least 1mm at 60 ms after J point or an up sloping ST segment depression $\geq$ 1.5 mm at 80 ms after the J point [8].

Duke tread mill score was calculated for every patient as described by Mark and coauthors as duration of exercise in minutes – (5 X maximum ST deviation in milli meters)- (4 X tread mill anginal index). The tread mill anginal index was taken as 0 after no angina, 1 for non limiting angina and 2 for exercise limiting angina[9] .The score typically ranges from -25 to +15 , these values correspond to low risk (with score of $\geq$+5) , moderate risk (with a score ranging from -10 to+4) and high risk (with a score of $\leq$-11).

All medications that may interfere with the exercise test results was discontinued at least five half-lives before the exercise testing .

Patients with left or right bundle branch block, left or right ventricular hypertrophy, preexcitation, prior myocardial infarction, coronary

angioplasty or aortocoronary by pass surgery and valvular heart disease were excluded from the study.

ST segment in lead aVR was accepted as elevation if the elevation was ≥ 0.5 mm from isoelectric line at 60 ms after J point .Intraobserver and interobserver mean percent error (absolute difference between two observations divided by the mean and expressed in percent) was determined in 21 randomly selected study participants and were less than 4% and 5% respectively.

Out of 82 patients with high risk according to Duke score 66 patients underwent coronary angiography with in 3 months of exercise test and were included in the study ,they were divided into 3 groups, group 1 including patients with no ST elevation in aVR, group 2 including patients with ST elevation of less than 2 mm in aVR and group 3 including patients with ST elevation in aVR of more than 2 mm.

Coronary angiography was done by percutaneous (Judkins) technique. Significant coronary artery disease was diagnosed when there was diameter narrowing of ≥ 70% in the lumen of coronary artery except left main coronary artery where diameter narrowing ≥ 50% was considered significant (the patient was considered to have LM disease even if there was single, two or three vessel disease with LM diseased vessel) . Catheterization laboratory investigators were unaware of the results of exercise test.

Statistical analysis

The varaibles were presented as means ± SD as proportions for categorical data. Analysis of variance (ANOVA) test was used to determine the significant level of difference in various variables of ST segment elevation . P value less than 0.05 was considered significant.

Results

There was 16 patients in group 1(no ST segment elevation in aVR), 21 patients in group 2 (ST segment elevation in aVR less than 2 mm mean 1.5 ± 0.4mm), and 29 patients in group 3 (ST segment in aVR more than 2 mm mean 2.4 ± 0.3mm)

The clinical characteristics of the study population are presented in table 1.

Table 1 The clinical characteristics of the study population

Variable	Group 1 No. 16	Group 2 No. 21	Group 3 No. 29	P value
Age	57 ± 7	58 ± 7	57 ± 6	**N.S**
Male	12 (75%)	16 (76%)	20 (72%)	**N.S**
Diabetes mellitus	7 (44%)	10 (48%)	14 (48%)	**N.S**
Hypertension	9 (56%)	10 (48%)	15 (52%)	**N.S**
Smoker	7 (44%)	11 (52%)	16 (55%)	**N.S**

Demographic variables and major cardiovascular risk factors were similar between patients groups (p >0.05)

The exercise parameters in studied groups are shown in table 2.

Table 2 exercise parameters in patient's groups

Variable	Group 1 No. 16	Group 2 No. 21	Group 3 No. 29	P value
Exercise duration (in minutes)	6 ± 1.3	5 ± 1.1	5 ± 1.2	**N.S**
Maximum systolic blood pressure	170 ± 10	168 ± 11	165 ± 9	**N.S**
Incidence of angina	7 (43%)	12 (57%)	17 (59%)	**N.S**
Duke treadmill score	-15 ± -2	-15 ± -2	-17 ± -2	**N.S**

The exercise parameters were similar between patient's groups.

The results of angiographic finding of patients with ST segment elevation in aVR and patients with out ST segment elevation in aVR are shown in table 3 .

Table 3 Results of angiography in patients with and without ST elevation

	No ST segment elevation in aVR(Group 1) No. 16	ST segment elevation in aVR (Group 2 and Group 3) No. 50	P value
LM CA	1 (6%)	18 (36%)	**0.0222**
3 vessel disease	3 (19%)	17 (34%)	**0.2483**
2 vessel disease	5 (31%)	5 (10%)	**0.039`**
1 vessel disease	7 (44%)	10 (20%)	**0.0586**

negative predictive value of 93% in detecting LM disease and had sensitivity of 85% ,specificity of 28% , positive predictive value of 34 % and negative predictive value of 81 % in detecting three vessel disease.

Out of 50 patients with ST elevation in aVR there were 29 patients with ST elevation more than 2 mm and the angio graphic finding in patients with ST elevation more than 2 mm are presented in table 4.

This table shows that out of 50 patients with ST segment elevation in aVR 35 (70%) patients had either left main disease or three vessel disease while 25% of patients (4 out of 16 patients) with out ST segment elevation in aVR had either left main stem or three vessel disease

This study showed that exercise induced ST elevation in aVR had sensitivity of 95 % , specificity of 32 % positive predictive value 36 % , and

Table 4 Angiographic finding of study population with respect to ST segment elevation in lead aVR more than 2 mm

	No ST segment elevation in aVR more than 2mm(Group 1and group2) No. 37	STsegment elevation in aVR more than 2mm(Group 3) No. 29	P value
LM CA	2 (6%)	17 (59%)	**0.0001**
3 vessel disease	16 (43%)	4 (13.7%)	**0.0098**
2 vessel disease	6 (16%)	4 (13.7%)	**0.7852**
1 vessel disease	13 (35%)	4 (13.7%)	**0.0491**

The finding of ST elevation in aVR more than 2mm had sensitivity of 89 % , specificity of 74% positive predictive value 59 % and negative predictive value of 95 % for detecting LM disease and sensitivity of 20 % specificity of 46%, positive predictive value 14% and negative predictive value 57% for detecting three vessel disease.

Discussion

Exercise induced ST depression although the most common and accepted criterion for detecting coronary artery disease is unable to discriminate the significantly narrowed coronary vessel [2].

Exercise induced ST segment elevation is less frequent than depression but it's presence has been attributed to ventricular wall motion abnormalities[11,15] ventricular aneurysm[10,12] and ischemia due to either coronary vaso spasm or severe proximal coronary stenosis [11,13]. Bruce et al [14] studying 350 ambulatory patients with coronary heart disease postulated ventricular dysfunction and poor prognosis in patients with exercise induced ST segment elevation.

Lead aVR has not only been under evaluated for the detection of coronary artery disease during exercise testing but surprisingly has been selectively ignored in pervious reports [3,5]

In Mason's modified 12 lead system, arm electrodes are placed in the infraclavicular fossae and leg electrodes mid way between the rib margin and iliac spine [15],different lead placement during standard ECG recording and exercise testing ECG recording might possibly raise some concern about the interpretation and comparison of evidence demonstrated in these two setting, however as the final pathophysiological mechanism involves a common pathway resulting in raised left ventricular end diastolic pressure either in demand ischemia (i.e exercise testing) or supply ischemia (i.e acute coronary syndrome) the ECG finding reflecting as ST segment elevation in aVR may also be similar in both sitting[16].

The ability to discriminate among various coronary artery patterns may influence early management decision, thus the ability to identify left main coronary artery disease is important [17].

Some studies reported that ST segment elevation in lead aVR could predict LM disease in patients with acute coronary syndrome [18,19].

Zhan Znong-Qum et al mentioned that ST segment elevation in aVR has been associated with left main or 3 vessel disease (with out mentioning the degree of ST elevation) and with adverse out come [20,21].

Yamaji showed that ST elevation in aVR more than 0.5 mv present in 88% of patients with acute LM obstruction with out mentioning three vessel disease or the degree of ST elevation [22].

Kosuge et al [23] found that ST elevation greater than 0.5 mm in lead aVR is strongest predictor of LMCA or 3 vessel disease in patients with acute coronary syndromes superior to presence of ST depression in other leads with sensitivity of 78%, specificity of 86%, positive predictive value 57%, negative predictive value 95%.

M. Tuna Katercibasi et al showed that exercise induced ST segment elevation in aVR is sensitive 92% but not specific (48.6%) electrocardiographic finding of significant LM coronary artery disease in patients with Duke treadmill score $\leq$-11 , with out taking in consideration the degree of ST segment elevation[24].

Some of the reports took other criteria to increase specificity for detecting LM disease in patients with ST elevation in aVR like ST elevation in aVR with less elevation in V1 as predictor of total or sub total left main stem obstruction in patients with acute coronary syndrome [22] .

This study showed that increased specificity for detection of LM disease can be achieved when we take ST segment elevation of more than 2 mm in aVR in patients with Duke score less than -11. So finding of ST segment elevation in aVR should attract attention toward left main stem or three vessel disease (high sensitivity with low specificity)and finding of ST segment elevation more than 2 mm gives high sensitivity with specificity for LM coronary disease rather than 3 vessel disease.

Nikus and Sclarosky stated that ST segment depression specifically in V_4-V_5 induces reciprocal ST segment elevationin lead aVR since aVR is electrically opposite to these leads [25] although this statment seems to be correct but is not the only explanation for ST segment elevation in aVR as mentionted above for ST elevation in aVR can occur with out ST segment depression in chest leads [26].

Yamaji et al [22] suggested that acute LM obstruction causes ischemia to the basal part of the septum through disturbance of the major septal branch flow which could account for lead aVR ST segment elevation.

Lead aVR is orientated to ward the cavity behaving as pseudo-intra cavitary lead and consequently detects inter ventricular amplitudes of the left ventricle. Transmural anterior wall ischemia during maximum exercise testing may result in ST elevation in lead V_1 and possibly aVR [27].

Another explanation for ST segment elevation in aVR in LM stenosis may be that ST segment elevation in lead aVR reflects endocardial ischemia because this lead faces the cavity of the left ventricle[28] further more ischemia due to LM stenosis may lead to increase in left ventricular end diastolic pressure. The result of this raised left ventricular end diastolic pressure is sub endocardial ischemia which may be reflected as ST depression in the precordial lead and ST esgment elevation in aVR. [29]

So according to these as far as ischemia is more and degree of obstruction is more one expect that degree of ST elevation will be more in LM disease.

Engelen et al [30] reported that lead aVR ST segment elevation is observed in acute obstruction of the left anterior descending artery proximal to the major septal branch but not in acute LAD obstruction distal to the major branch. They concluded that lead aVR ST segment elevation associated with proximal LAD obstruction is caused by transmural ischemia of the basal part of the septum. This led to assume that acute LMCA obstruction also cause lead aVR ST segment elevation through disturbance of major septal branch blood flow that is interruption of LAD blood flow, since not all patients with three vessel disease get involvement of proximal LAD so the incidence of ST elevation in aVR in these patients is less although they can get it through causing sub endocardial ischemia even in absence of proximal diseased LAD.

Since L.M disease is more able to cause transmural ischemia of the basal part of septum and more able to cause endocardial ischemia thus it is more able to cause more degree of ST elevation in aVR.

Conclusion and Recommendation

1- Lead aVR needs not to be ignored
2- Exercise induced ST segment elevation in aVR Should attract attention to LM or 3 vessel disease and its elevation of more than 2 mm should attract attention to LM disease in patients with Duke score ≤-11

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