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COMPARISON OF R WAVE AMPLITUDE CHANGES VERSUS ST-SEGMENT DEPRESSION IN STRESS TESTING ELECTROCARDIOGRAM AMONG ISCHEMIC HEART DISEASE PATIENTS

By

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ABSTRACT

Background: R-wave changes might be helpful in accurate diagnosis of coronary artery disease with exercise testing in combination with ST segment changes as ∆RST index and might be superior to the traditional ST segment depression only.

Objective: To further clarify R-wave amplitude (RWA) changes during exercise stress test (EST) among established IHD patients.

Patients and methods: The study enrolled 50 subjects - aged from above 35 to below 65 years old of both sexes, known to be ischemic by a previous angiography, divided into two main groups: Group I (control group): 15 subjects with normal coronaries (lesion < 30 % stenosis), and Group II (IHD group): 35 patients with stable ischemic heart disease which were subdivided according to previous coronary angiography results (lesion >70 % stenosis).The study was conducted at the Department of Cardiovascular Medicine and its Out-patient Clinic, Al-Hussein University Hospital during the period from September 2019 to March 2021.

∆RST index was formed from algebraic summation of RWA difference between (rest and immediate recovery) plus ST segment depression in mile meters.

Results: ∆RST index was more useful in detection of coronary artery disease with higher sensitivity and specify among chronic ischemic patients than RWA difference or ST segment depression alone. When cutoff ≥ -1.65 cardiac ischemia could be predicted with a sensitivity rate of 98.93%, a specificity rate of 96.00%, a positive predictive value of 96.3 %, and a negative predictive value of 98%. RWA at a cut-off point of -1.2 was sensitive 95.02% and specific 94.0 % , a positive predictive value of 95.7%, and a negative predictive value of 96.6%. ST segment depression at a cut-off point of ≥ 0.45 was sensitive 77.1% and specific 80%, a positive predictive value of 78.4%, and a negative predictive value of 60.3%.

Conclusion: ∆RST index was more useful in detection of coronary artery disease with higher sensitivity and specify among chronic ischemic patients than RWA difference or ST segment depression alone.

Keywords: Ischemic heart disease, R-wave amplitude, Exercise stress test, ST-Segment.

INTRODUCTION

Coronary artery disease (CAD) is considered a leading cause of morbidity and mortality in the world, and its incidence has been gradually increasing. CAD is a progressive inflammatory disease in which atherosclerosis plays a major role in its etiology *(Mehta et al., 2015).*

Atherosclerosis progresses, especially if left untreated, symptoms may occur. They are most likely to occur during exercise or emotional stress, when the demand for the oxygen carried by the blood increases *(O'Gara et al., 2013).*

The exercise stress test (EST) is performed routinely in cardiology and commonly used for evaluation of prognosis and as a gateway to other imaging modalities. Stand-alone testing for CAD diagnosis is reserved for patients with intermediate risk for CAD and should be ordered with a careful understanding of the limitations of the test for this purpose. The advantages of exercise electrocardiographic testing are its ability to assess a variety of prognostic markers, most importantly functional capacity, which is a powerful predictor of mortality, widespread availability, safety, ease of administration, and relatively low cost. EST is conducted while monitoring the dynamic electrocardiogram changes (ECG), ventilatory threshold, blood pressure (BP), heart rate (HR), oxygen consumption, general patient self-reported effort (e.g., by a Borg Scale test) and physical appearance—including chest pain and dyspnea *(Greenslade et al., 2015).*

Exercise stress testing can be accomplished by either treadmill or cycle ergometer, although treadmills are predominantly used. There are several standard treadmill protocols that can be customized for patients to reach the endpoint of 85% to 100% maximum predicted heart rate. Among them, the Bruce protocol and modified Bruce are most popular. These protocols consist of 3-minute stages with incremental increases in speed and incline *(Macintyre et al., 2013).*

Horizontal or down sloping ST depression greater than or equal to 1 mm for at least 60–80 ms is commonly considered a positive stress test. However, the capacity of a stress test to localize ischemia based on leads demonstrating ischemic changes is poor. Patients with equivocal (up sloping) or non-diagnostic stress test results may be recommended for radionuclide myocardial perfusion image (MPI) or echocardiographic stress testing before a final decision regarding coronary angiography is made *(Skyler et al., 2017).*

Many factors affect the R-wave amplitude response to exercise. R-wave amplitude typically increases from rest to submaximal exercise, then decreases to a minimum at maximal exercise. If a patient were limited by objective signs or subjective symptoms, R-wave amplitude would increase from rest to such an end point. Such patients may be demonstrating a normal R-wave response but are classified as abnormal because of a submaximal effort. Exercise induced changes in R-wave amplitude have no independent predictive power but are associated with CAD because such patients are often sub maximally tested, and an R-wave decrease normally occurs at maximal exercise *(Mittleman et al., 2011).*

The aim of the present study was to clarify R-wave amplitude (RWA) changes during exercise stress test (EST) among established IHD patients.

PATIENTS AND METHODS

This prospective cohort study on cases conducted at the Department of Cardiovascular Medicine and its Out-patient Clinic, Al-Hussein University Hospital during the period from September 2019 to March 2021. The study enrolled 50 subjects aged from above 35 to below 65 years old of both sexes, known to be ischemic on grounds of previous angiography, divided into two main groups as follows:

Group I (control group): Fifteen subjects with normal coronaries according to coronary angiography (lesion < 30 % stenosis).

Group II (IHD group): Thirty five patients with stable ischemic heart disease which are subdivided according to previous coronary angiography results (lesion >70 % stenosis).

Inclusion Criteria: Controlled blood sugar, blood pressure, normal hepatic, renal functions, and previously documented ischemic heart patients on grounds of angiography.

Exclusion Criteria: Patients ages >65ys & <35ys, other causes of coronary ischemia such as congenital coronaries malformations, recent acute MI (within 2ds), and valvular heart diseases.

All the patients underwent detailed clinical evaluation that included:

1. **Complete history taking:** Full history was taken from the patients regarding the age, sex and risk factors of CAD including: smoking, hypertension, diabetes mellitus, dyslipidemia and family history of atherosclerosis.
2. **General and cardiac examination:** Vital signs (blood pressure, pulse, chest examination), and heart examination (normal heart sounds, abnormal heart sounds).
3. **Resting 12-lead ECG by Philips TC20 electrocardiograph machine:**

All of the patients in this study underwent resting sitting and if ECG has QRS 120 milliseconds, LBBB, LVH, WPW pattern, Paced rhythm, Pericarditis resting ST depression > 1mm, it will be excluded from the start. The ECG was recorded at a paper speed of 25mm/second at a calibration of 1 mv equals 10 mm. ST segment deviation was measured 60 - 80 milliseconds from the J point, using the TP segment as isoelectric line unless tachycardia caused fusion of the T and P waves, in which case the PR segment was used.

4. **Stress ECG (EST): by GE CASE V6.73 machine using Modified Bruce protocol:**

The submaximal treadmill stress test was terminated at least 70% to 85 % maximal age predicted heart rate as a target end point.

Twelve leads (Mason- Likar lead placement) ECG were monitored continuously and recorded in the sitting position (control) and in the standing position immediately after exercise. The R wave control measurement was taken in the sitting position for comparison with ST changes.

- **ST-segment deviation analysis:**

ST-segment deviation was measured relative to the end of the PR segment because the T (U)–P segment during exercise was difficult or impossible to measure when HR were fast. Three or more consecutive beats in the same lead with a stable baseline in any lead (other than aVR) compared with the resting trace.

ST depression > 1 mm (0.1mV) below the resting level 60-80 msec from the J point if horizontal or downsloping and > 1.5 mm (0.15 mV) if upsloping during exercise or immediate recovery period, was defined as positive test (ischemic).

- **R wave amplitude (RWA) analysis:**

R wave amplitude was measured from the isoelectric line to the peak of the R wave in mm for an average of 6 consecutive beats. The average value was used in the study so the respiratory variation, if any, was minimized. R wave amplitude (RWA) changes were measured in the control (Rest) and in the immediate post exercise period (Immediate Recovery). An increase or no change in R wave was taken as evidence of an abnormal response, while a decrease in the R wave was a normal response.

5. **Coronary angiogram** using the standard Judkins technique from right to left anterior oblique projections with cranial and caudal angulations. The culprit artery was determined from angiographic characteristics of occlusion (occlusion due to thrombus formation or ulceration with decreased contrast density).

Statistical methods:

The collected data were coded, processed and analyzed using the SPSS (Statistical Package for the Social Sciences) version 22 for Windows® (IBM SPSS Inc, Chicago, IL, USA). Data are expressed as mean ± standard deviation (SD or number (percent). Comparison between categorical data [number (%)] in the two studied groups was performed using Chi square test. Comparison between mean values of different variables in the two studied groups was performed using unpaired t test or Mann-Whitney U test. Receiver operating curve (ROC) was used to calculate the diagnostic indices of EST. P value less than or equal to 0.05 was considered significant.

RESULTS

Patients in Group one included 9 males 60 % and 6 females 40% with a mean age of 47.5 ± 8.8. Group two included 27 males 77 % and 8 females 23% with a mean aged 51.4 ± 9.6. There was no statistical difference between both groups as regards the gender and the age distribution of the patients. There were no differences between both groups regarding the presence of hypertension, heart rate, diabetes mellitus, dyslipidemia, family history, body mass index and smoking.

ΔRST and RWA were statistically significantly different between the ischemic group and the control group and the changes in ST segment was non-significant **(Table 1)**.

Table (1): Demographic data, examination, lipid profile and stress ECG findings regarding studied groups

Parameters \ Groups		IHD (n=35) Mean ± SD	Control (n=15) Mean ± SD	P-value
Age		51.4 ± 9.6	47.5 ± 8.8	>0.05
Gender	Male	27 (77%)	9 (60%)	>0.05
	Female	8 (23%)	6 (40%)	
Smoking	Yes	19 (54%)	10 (66%)	>0.05
	No	16 (46%)	5 (34%)	
FH - IHD	Yes	15 (43%)	9 (60%)	>0.05
	No	20 (57%)	6 (40%)	
MAP		91.9 ± 9.4	92.9 ± 10.9	>0.05
HR		79.4 ± 11.9	80.5 ± 11.0	>0.05
RBS		7.5 ± 1.9	6.5 ± 1.9	>0.05
BMI		30.8 ± 4.0	29.4 ± 3.7	>0.05
LDL		5.8 ± 0.9	3.9 ± 0.8	<0.001
HDL		1.0 ± 0.3	1.1 ± 0.3	>0.05
TGs		4.7 ± 1.3	2.8 ± 0.6	<0.001
RWA Rest		10.1 ± 3.8	11.5 ± 4.5	>0.05
RWA Recovery		10.7 ± 5.2	9.3 ± 5.5	>0.05
RWA Diff		0.6 ± 2.6	-34.2 ± 2.6	0.007
ST Seg.Dep		1.3 ± 0.8	0.9 ± 0.5	>0.05
ΔRST		1.8 ± 3.0	-8.3 ± 2.9	0.001

ΔRST was index more useful in detection of coronary artery disease with higher sensitivity and specify among chronic ischemic patients than RWA difference or ST segment depression alone. Particularly when cutoff ≥ -1.65 cardiac ischemia could be predicted with a sensitivity rate of 98.93%, a specificity rate of 96.00%, a positive predictive value of 96.3 %, and a negative predictive value of 98%. RWA at a cut-off point of ≥ -1.2 was sensitive 95.02% and specific 94.0 %, a positive predictive value of 95.7%, and a negative predictive value of 96.6%. ST segment depression at a cut-off point of ≥ 0.45 was sensitive 77.1% and specific 80%, a positive predictive value of 78.4%, and a negative predictive value of 60.3% **(Table 2)**.

Table (2): Diagnostic indices of stress ECG using ROC curve in the two studied groups

	AUC	P value	Cut off	Sensitivity	Specificity	PPV	NPV
RWA Diff	0.69	0.031*	≥ -1.2	95.02%	94.0%	95.7%	96.6%
ΔRST Index	0.74	0.008*	≥ -1.65	98.93%	96.00%	96.3%	98%
ST Seg Dep	0.612	0.212	≥ 0.45	77.1%	80%	78.4%	60.3%

AUC: Area under a Curve, p value: Probability value
NPV: Negative predictive value, PPV: Positive predictive value

Table (3): Detection of coronary artery disease

Values / Parameters	Sensitivity	Specificity	+ve predictive value	-ve predictive value
ΔRST ≥- 1.6	98.93%	96%	96.3%	98%
RWA ≥- 1.2	95.02%	94%	95.7%	96.6%
ST segment depression > 0.45	77.1%	80%	78.4%	60.3%

DISCUSSION

Insignificant difference of ST segment depression in both groups might be related to the submaximal test. In patients with stable CAD who has done submaximal exercise or cannot exceed 85% of their target HR. The RWA is a valuable diagnostic test for ischemia than ST segment changes.

Glazier et al. (2013) correlated ST segment changes and ischemia demonstrated by thallium-20 I imaging and showed that the standard ST segment criteria may not correlate as well with ischemia as previously thought in patients with anterior myocardial infarction, the analysis was repeated after patients with anterior myocardial infarction were excluded. This procedure did not change the results significantly.

Deshpande and Birnbaum (2014) demonstrated R wave changes to be helpful in diagnosing coronary artery disease with exercise testing. R wave changes were shown to be sensitive independently and, in combination with

ST segment changes to be superior to ST segment changes alone.

Fifty subjects were enrolled to our study, 72% were males and 28% were females with age ranging from above 35 to below 65 years old.

Increases in the R wave amplitude of the electrocardiogram during exercise or no change have been reported to indicate left ventricular dysfunction or coronary artery obstruction, or both, while decreases have been found consistent with normal left ventricular function. The physiologic mechanism for these changes, once thought to be related to changes in heart volume and the Brody effect, has more recently been suggested to be increased intramyocardial conduction secondary to ischemia, change in contractility or simply changes in heart rate and axis *(Deshpande and Birnbaum, 2014)*.

In our study, when using more complex statistical analysis, ΔRST index was more useful in detection of coronary artery disease with higher sensitivity and specify among chronic ischemic patients than RWA difference or ST segment depression alone. Particularly when cutoff ≥ -1.65 cardiac ischemia could be predicted with a sensitivity rate of 98.93%, a specificity rate of 96.00%, a positive predictive value of 96.3 %, and a negative predictive value of 98%.

RWA at a cut-off point of ≥ -1.2 was sensitive 95.02% and specific 94.0 % , a positive predictive value of 95.7%, and a negative predictive value of 96.6%. ST segment depression at a cut-off point of ≥ 0.45 was sensitive 77.1% and specific 80%, a positive predictive value of 78.4%, and a negative predictive value of 60.3%.

Smith et al. (2012) found similar results but with lower sensitivity of 63% and a specificity of 79% for R wave criteria compared with 48% and 59%, respectively for ST segment criteria alone, and reported that an increase or no change in R wave amplitude in lead CMs immediately after exercise was suggestive of severe coronary artery disease and ischemic left ventricular dysfunction, whereas a decrease in R wave amplitude was considered a normal response occurring in patients without coronary artery disease.

Harrigan and Brady (2011) clarified the usefulness of R-wave changes during stress testing in the diagnosis of CAD. They studied two groups of patients by means of electrocardiographic (ECG) treadmill testing and coronary arteriography found that R-wave amplitude changes measured from rest to peak exercise are not useful in the diagnosis of coronary artery disease. However, changes in amplitude measured from preexercise to immediately postexercise are a specific and fairly sensitive indicator of coronary artery disease.

Klein et al. (2015) revealed evidence of CAD in 62.5% (one vessel disease in 12.5%, two vessel disease in 20%, and three vessel disease in 30%) of patients. QRS indices of individual lead S of Q, R, and S wave show statistically significant difference in lead II, III, AVF, and V5. Athens score (aVF+V5) ≤ 5mm was highly significant and most sensitive (92%) and specific (80%) followed by QRS score of leads combination II+III (<5mm) being 88% sensitive and 80% specific for diagnosis of CAD.

Comparison of Athens QRS score and coronary angiography revealed that it was 100% sensitive for detection of two and three vessel disease and only 40% sensitive for detection of single vessel disease. Alternative QRS score (II+III) showed sensitivity of 100% for three-vessel disease, 87.5% for two-vessel disease, and 40% for single vessel disease. They concluded that exercise-induced depolarization abnormality is a useful index not only for diagnosis but also for assessing severity of CAD. However, a larger study especially including those cases with resting depolarization abnormality, e.g., left ventricular hypertrophy (LVH), left bundle branch block (LBBB) might bring out a possible utility of incorporating this parameter in assessing provocable myocardial ischemia when conventional ST-T analysis is not rewarding.

Patel et al. (2010) compared R wave indices of amplitude and ST segment criteria with angiographically determined coronary artery disease. Using R wave criteria, the sensitivity of exercise testing was 52% and specificity 63%, compared with 88 and 72%, respectively, using ST segment criteria. No significant correlation was found between the extent of angiographically determined coronary artery disease and R wave changes.

Smith et al. (2012) demonstrated left ventricular function to be related to R wave amplitude at rest and to its change during exercise. *Antzelevitch et al. (2015)* did not find R wave changes during exercise to have a definite physiologic explanation or clinical value.

That cardiac enlargement secondary to congestive heart failure may cause a decrease in R wave amplitude also contradicts the Brody hypothesis. Correlations of the R wave to systolic volume and left ventricular ejection fraction suggest an association with contractility. Changes in axis shifts have also been shown to alter R wave amplitude; this shift of the QRS axis as well as that of the ST segment vector toward the right and posteriorly occur normally during exercise *(Barnhill et al., 2012).*

CONCLUSION

ΔRST index was more useful in detection of coronary artery disease with higher sensitivity and specify among chronic ischemic patients than RWA difference or ST segment depression alone.

There were variations in age, gender, smoking, family history, hypertension, heart rate, sugar level, BMI and lipid profile between two groups. However, these differences did not reach a statistical significance.

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تقيم إرتفاع موجة أر مقارنة بانخفاض قطعة اس–تى باستخدام رسم القلب بالمجهود بين مرضى قصور الشريان التاجى

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خلفيـــة البحـــث: قـــد تكـــون تغييـــرات الموجـــة ار مفيـــدة فـــي التشـــخيص الـــدقيق لمـــرض الشـــريان التـــاجي بـــالتزامن مـــع تغيـــرات قطعـــة اس تـــي وذلـــك كمعامـــل ار اس تـــي, وقـــد تكـــون أفضـــل مـــن الانخفـــاض التقليـــدي لقطعـــة اس تـــي فقـــط أثنـــاء إختبـــار رســـم القلـــب بالمجهود

الهـــدف مـــن البحـــث: توضـــيح مـــدى فائـــدة تغييـــرات ارتفـــاع الموجـــة ار أثنـــاء إختبـــار رسم القلب بالمجهود في زيادة دقة تشخيص قصور الشريان التاجى.

المرضـــي وطـــرق البحـــث: أجريـــت الدراســـة الحاليـــة علـــى 50 شخصـــاً قـــدموا إلـــى قســـم أمـــراض القلـــب فـــي مستشـــفي الحســـين الجـــامعي خـــلال الفتـــرة مـــن ســـبتمبر 2019 إلـــى مـــارس 2021. وقـــد تـــم تقســـيم مجتمـــع الدراســـة إلـــى مجمـــوعتين: المجموعـــة الأولـــى وقـــد إشـــتملت 15 حالـــة مـــن الأشـــخاص الأصـــحاء كمجموعـــة ضـــابطة, والمجموعـــة الثانيـــة 35 حالـــة مـــن مرضـــي قصـــور الشـــريان التـــاجي. وقـــد خضـــع الجميـــع لتســـجيل التـــاريخ المرضـــي المفصـــل للحـــالات والفحـــص الأكلينيكـــى الكامـــل ورســـم القلـــب العادي وبالمجهود وقسطرة الشرايين التاجية.

نتـــائج البحـــث: لا توجـــد فـــروق ذات دلالـــة إحصـــائية بـــين المجمـــوعتين فيمـــا يتعلـــق بـــالنوع، والعمـــر والتـــدخين والتـــاريخ العـــائلي لقصـــور الشـــريين التاجيـــة ونســـبة الســـكرفي الـــدم ومعـــدل ضـــربات القلـــب، وإرتفـــاع ضـــغط الـــدم، وخلـــل شـــحميات الـــدم. وقـــد وجـــدت الدراســـة الحاليـــة أن مـــن الممكـــن زيـــادة دقـــة رســـم القلـــب بـــالمجهود فـــي تشـــخيص قصـــور الشـــريين التاجيـــة باضـــافة معامـــل اراس تـــي او باســـتخدام التغيـــرت في موجة ار مقابل الطريقة التقليدية باستخدام انخفاض قطعة اس تي فقط.

الاســـتنتاج: معامـــل اراس تـــي او التغيـــرت فـــي موجـــة ار لهـــا أهميـــة فـــي زيـــادة دقـــة جهـــاز رســـم القلـــب بـــالمجهود فـــي تشـــخيص قصـــور الشـــريين التاجيـــة مقابـــل الطريقـــة التقليدية بإستخدام إنخفاض قطعة اس تي فقط.

الكلمـــات الدالـــة: قصـــور الشـــرايين التاجيـــة، رســـم القلـــب بـــالمجهود، معامـــل ار اس تـــي، التغيرات في موجة ار.