

## Computerised Stress - Test: Usual or New Derivative Electrocardiographic Variables

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### Introduction

Evaluation of electrocardiographic ST-segment response to exercise has been the most widely used laboratory method for the assessment of ischemic heart disease (IHD) for half a century. The availability, accessibility, and relatively simple technological requirements of exercise electrocardiology make it useful tool, but the limitations of standard test criteria are well recognised. Sensitivity for the detection of coronary disease is poor, particularly when only modest coronary obstruction is present, and test responses are often indeterminate in the presence of upsloping ST-segment depression. Contemporary medical literature has evolved the perception that the exercise electrocardiogram (ECG) cannot be improved and that attempting to improve it is presumptuous. This perception is wrong, but the exercise electrocardiogram is in need of rehabilitation [1]. There is a little reason why the test performance should be constrained by empirically derived criteria that have been based on visual estimation of ST-segment depression since mid-century. We need development of new criteria with improved sensitivity and specificity and it is reasonable to expect that in future diagnostic cardiology we will use in practice some new parameters of computerised exercise test. These new approaches include heart rate adjustment to ST depression (ST/HR index), quantification of non-ST-segment exercise findings, such as QRS duration, QRS scores based on measurement of amplitudes, axis change, as well as algorithms based on workload adjustment of ST depression [2, 3, 4]. QT or JT dispersion alone or in combination with ST depression is associated with ischaemia in heart muscle [5]. It seems reasonable to join two separate variables of repolarisation which both are closely related with ischaemia in heart muscle: JT interval shortens more in healthy people comparing with those with coronary heart disease and the shortest value of JT interval in healthy people at the maximum load is 160 seconds [6]. G.Jaruševičius in his study [7] analysed new complex parameter of ventricular repolarisation ST and JT product. In above study ST and JT product seemed to be more sensitive and specific than ST depression greater than 0,1mV, but it was analysed in male population predominantly. The aim of our study was to evaluate ventricular repolarisation variables - JT, JTa, JTc, JT

dispersion, JTa dispersion, ST and JT product - in female population (with IHD and healthy ones) and to compare their sensitivity, specificity with common stress-test variable - ST depression greater than 0,1 mV. Exercise stress-test is a mean for separating patients with highest risk for cardiovascular events – those with three vessel disease. On the other hand we need to confirm a man is healthy one and presence of ST depression at the peak of exercise makes the test of little value. It is clear that we must find more features of exercise test to state there is no cardiac disease in examined population.

### Methods

**Patients:** 90 female patients hospitalized in Kaunas medical university hospital with high risk unstable angina pectoris (chest pain, admission ECG changes or elevated troponin-I level) after 2-3 days period of stabilisation underwent coronary artery angiography and symptom limited or submaximal stress test. For control group we selected 35 women which were confirmed healthy (without cardiac disease and risk factors, normotensive, normal plasma cholesterol level).

**Stress test:** The bicycle exercise test has been performed and test variables were calculated by means of ECG system "Kaunas-Krūvis. Twelve ECG leads of 10 sec duration were recorded simultaneously every minute until 5 minutes after the end of load. Ventricular repolarisation variables - JT, JTa, JTc,  $\Sigma$ ST (sum of ST depression in 12 leads), JT dispersion, JTa dispersion, ST and JT product - were computed and analyzed before the load, at the maximum load and at the recovery (first, third and fifth minute after the end of exercise). All calculations were made by means of ECG system before analysis excluding by observer all ECG recordings with multiple artifacts. ST-segment level was measured 40 ms after J point in all 12 leads. The sum of ST depression in all 12 leads was calculated. A mean of JT interval of every series of cardiocycles was computed. JT dispersion – a difference between shortest and longest JT interval in every series was measured only in chest leads, because accuracy of measurement in limb leads was insufficient. The same way JTa dispersion was calculated. For detection of T wave offset tangent method was used. Schematic model of measurement of JT, JTa and Te intervals is represented in

Fig. 1. For calculation of JT and ST product we used algorithm introduced in computerized system. JT and ST product was calculated according formula:

$ST \times JT = \sum ST(JT-160)$ , where JT – duration of averaged 12 lead ECG JT interval in milliseconds (ms)  $ST \times JT - ST$  and JT product in mVms,  $\sum ST$  – sum of ST segment depression in all 12 leads.  $ST \times JT$  was calculated in every phase of veloergometry: at rest, at the peak of exercise and at the first, the third and the fifth minute of recovery period.

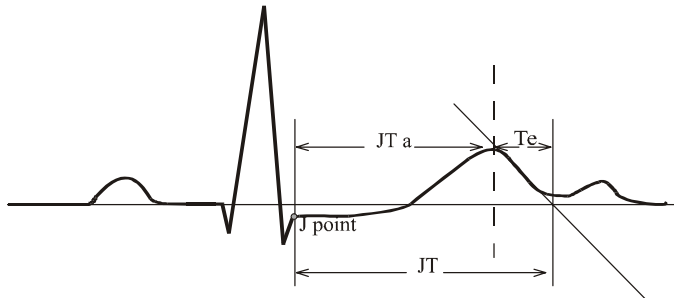


Fig. 1. Schematic measurement of JTa, JT, Te intervals: tangent method with a tangent to the steepest point of descending limb of the T wave

**Coronary angiography:** All women with IHD have undergone coronarangiography for evaluating women with coronary artery stenoses. Coronary arteries were evaluated in multiple projections. Coronary stenoses were quantified visually and with help of calipers. A luminal narrowing  $\geq 70\%$  was considered as significant if it was present in one or two main coronary vessels. In 3-vessel disease group limits for lumen narrowing were not so strict (1 or 2 vessels with 70% and 1 vessel 50-70% narrowing), because we couldn't find in 3-vessel group enough female patients who could exercise.

**Statistical analysis:** Results were expressed as the mean  $\pm$  SD. A  $\chi^2$  test was used to compare categorical variables. Correlation power between variables and IHD was expressed by Pearson correlation coefficient ( $r_p$ ). Two-way ANOVA was used for multical comparisons. Definitions of test sensitivity and specificity conform to standart use. Partitions of variables were used to compare sensitivity and specificity for IHD and for three-vessel disease. Because sensitivity and specificity of a test are dependent of a partition value chosen for test positivity, test accuracy was compared with the use of ROC curve analysis. The independant predictive power of variables for presence of IHD and three-vessel disease was determined with logistic regression analysis. For all comparisons, a value of  $p < 0,05$  was required for rejection of null hypothesis.

## Results

According results of coronarangiography women with IHD were distributed to groups: 33 patients without coronary artery stenoses, 32 patients with one or two stenoses and 23 patients with three-vessel disease.

Women with IHD were more obese comparing with healthy ones, 30% of women with IHD were with previous MI. There was significant age difference between healthy women and IHD group. All healthy women have achieved

submaximal target heart rate comparing with 73% in IHD group.

Table 1. Common test characteristics

Charact eristics	Unit	Healthy n=35	IHD n=90	p
Age	years	45,1 $\pm$ 2,9	62,8 $\pm$ 7,4	<0,0001
BMI	kg/m <sup>2</sup>	24,46 $\pm$ 3,80	29,08 $\pm$ 3,91	<0,0001
Max load	W	104,3 $\pm$ 17,7	76,9 $\pm$ 19,9	<0,0001
HR at rest	bpm	78,9 $\pm$ 11,0	75,3 $\pm$ 14,1	NS
HRmax	bpm	155,5 $\pm$ 10,3	125,1 $\pm$ 19,9	<0,0001

BMI- body mass index, max- maximum, HR-heart rate, bmp- beats per minute.

At the rest there was a difference in JT and JTa duration between healthy women and women with three-vessel disease ( $p < 0,05$ ). In all groups JT and JTa decreased at the maximum of load comparing with JT before load ( $p < 0,0001$ ). At the maximum load statistically significant difference of JT duration has occurred between women with 1-2 coronary artery stenoses and those with 3-vessel disease ( $p < 0,05$ ), but during all test periods there was no difference between patients without coronary artery stenoses and those with 1-2 artery stenoses. JTa was shorter in healthy women comparing with those with IHD during maximum load, but there was no difference between groups at rest.

Variables having the best correlation with ischemic heart disease are shown in the table 1.  $ST \times JT$  at the maximum load ( $ST \times JT_{max}$ ) has strongest correlation with IHD. Other variables, which showed significant correlation were:  $ST \times JT$  at the first minute of recovery, heart rate at the peak of exercise,  $ST \times JT$  at the third minute of recovery. Usual diagnostic index – ST depression  $> 0,1$ mV has weaker correlation.

Table2. Correlation between stress ECG variables and IHD

Variable	$\chi^2$	p	$r_p$
$ST \times JT$ max	74,4	0,0001	0,61
$ST \times JT$ 1min	64,8	0,0001	0,58
HR at the max	59,6	0,0001	0,57
$ST \times JT$ 3min	50,2	0,0001	0,53
JT max	42,8	0,0001	0,5
$ST \times JT$ 5min	41,6	0,0001	0,5
$\Sigma ST$ 1min	35,3	0,0001	0,47
$\Sigma ST$ 0	32,3	0,0001	0,45
$ST \times JT$ 0	32,4	0,0001	0,45
JT 1min	32,6	0,0001	0,45
$\Sigma ST$ max	25,8	0,0001	0,41
$ST \downarrow > 0,1$ mV	25,3	0,0001	0,41

max-maximum load, 1min(3min, 5min) – at first (third or fifth) minute after exercise, 0-before load,  $ST \downarrow$  -ST depression.

Variables having the best correlation with three-vessel disease are presented in the table 3. The strongest correlation with three-vessel disease had JTD max,  $ST \times JT$

max, heart rate at the peak of exercise, JTa dispersion at the first minute of recovery.

**Table 3.** Correlation between stress ECG variables and three-vessel disease

Variable	$\chi^2$	p	$r_p$
JT D max	19,84	0,0001	0,42
ST×JTmax	14,94	0,0001	0,38
HR max	13,41	0,001	0,36
JTa D 1min	12,86	0,001	0,35
ST×JT 1min	8,44	0,01	0,29
JTa D 3min	7,83	0,01	0,28
JT D 3min	7,48	0,01	0,28
ST ↓ >0,1 mV	5,51	0,05	0,24

HR - heart rate, max-maximum load, 1min(3min, 5min) – at first (third or fifth) minute after exercise, 0-before load, ST↓ -ST depression.

ST ↓ >0,1 mV was not sensitive enough for detecting IHD (table 4). Inability to develop heart rate at the peak of exercise and ST×JTmax were more sensitive and specific.

**Table 4.** Sensitivity and specificity of stress ECG variables for detecting IHD.

Variable	Partition	Sensitivity	Specificity
ST×JTmax	>10,3 mV·ms	88	94
HR max	<140kpm	79	97
JT D max	>18,5 ms	76	63
JTa D 1min	>75,5 ms	50	89
ST×JT 1min	>10,5 mV·ms	86	91
Σ ST max	>0,47 mV	59	91
JT max	>190 ms	73	91
ST ↓ >0,1 mV	>0,1mV	53	86

Partitions with sign “>” – the value is more, partitions with sign “<”- the value is little.

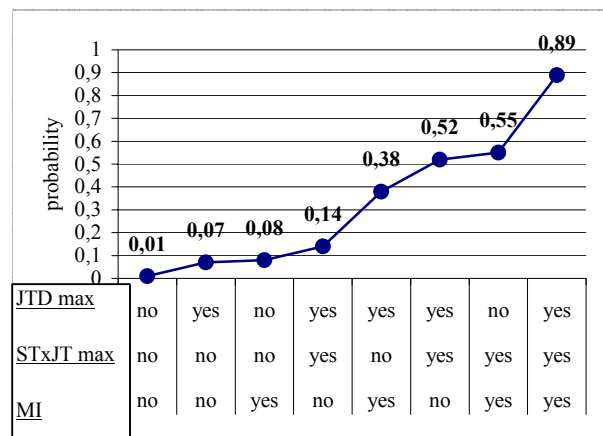
The best partition for detecting IHD was ST×JT<sub>max</sub> >10,3 mVms, but for detecting three-vessel disease the partition was higher: ST×JT<sub>max</sub> > 22mVms. It with 87% sensitivity and 60% specificity predicted three-vessel disease in women ( table 5 ).

**Table 5.** Sensitivity and specificity of stress ECG variables for detecting three-vessel disease

Variable	Partition	Sensitivity	Specificity
JT D max	>33ms	74	78
ST×JTmax	>22mVms	87	60
HR max	<130 bpm	91	52
JTa D 1min	>110ms	52	85
ST×JT 1min	>18mVms	91	42
JTa D 3min	>57,48ms	91	40
JT D 3min	>46,42ms	70	58
Σ ST max	>0,59mV	61	63
JT 5 min	>251ms	91	37
ST ↓ >0,1 mV	>0,1mV	61	49

Partitions with sign “>” – the value is more, partitions with sign “<”- the value is little.

Prognosis of three-vessel in women with unstable angina pectoris is represented in Fig.2.



**Fig. 2.** Prognosis of three-vessel in women with unstable angina pectoris: if the woman has no previous MI and stress-exercise variables at the peak of exercise ST×JT≤22 mVms and JT dispersion ≤33 ms, probability of three-vessel disease is 0,01. If ST×JTmax>22 mVms and JTD>33 ms and woman with previous MI, probability of three-vessel disease increases up to 0,89

## Discussion

This study demonstrates that that the majority of computerised stress ECG variables are more specific and sensitive for diagnosing IHD in women and on other hand their sensitivity and specificity isn't significant diagnosing one or two coronary artery stenoses. ST and JT product in our study had the best correlation with ischaemic heart disease among other analysed variables and correlation of that more complex variable with ICH is better than of his components (JT, ΣST) alone. ST× JTmax < 17 mVms for healthy population [7] differs from ours, but in that study male population was examined predominantly and in our opinion greater values are associated with higher heart rate achieved. JTmax in our study has stronger correlation with IHD than ΣST, which correlation with IHD at the peak of exercise was similar with conventional variable - ST ↓ > 0,1mV. JT max was more sensitive and specific than ST ↓ > 0,1mV too, but the best partition of JT interval in our study confirming the woman is healthy, was JTmax < 190 ms. Only two healthy women achieved the shortest JT (160 ms).

JT dispersion in our study isn't among most informative variables detecting ICH in women, but it is strongly correlated with three-vessel disease. It seems reasonable because JT dispersion is a variable which depends on degree of repolarisation abnormality – greater values of QT or JT dispersion indicate greater repolarisation pathology which is common in three-vessel disease. On another hand there are difficulties associated with the measurement of JT dispersion [8]. Errors may occur when stress electrocardiograms have even rare artifacts, but alone artifacts have little influence when measuring JT interval in our study, because it is averaged from the series. In the last decade cardiological literature has been flooded by articles reporting QT and JT dispersion in practically every cardiac syndrome and disease. However, voices of concern about the validity of concept and methodology of the measurement were raised

repeatedly. Today, after the decade of the “QT dispersion era” we can state that group differences of only few milliseconds even when statistically significant should always be interpreted with caution and, similarly, the lack of a difference in QT or JT dispersion values does not prove the absence of the involvement of myocardial repolarisation [8]. Technology is clearly too crude to depict minor repolarisation changes.

**Study limitations.** One of undesirable facts that might have influence on our results was age difference between healthy women and those with IHD. Problems have occurred when we tried to confirm that women older than sixty are healthy and without risk factors. Other study limitation was relatively small number of patients.

## Conclusions

Sensitivity and specificity of stress test variable – STxJT at the peak of exercise - is greater comparing with ST depression greater than 0,1 mV.

These independent variables are significant in IHD prognosis in women: STxJT at the peak of exercise, STxJT at the 1<sup>st</sup> min of recovery, STxJT at the 5<sup>th</sup> min of recovery, JT dispersion at the peak of exercise.

The most accurate predictors of three-vessel disease are JT dispersion at the peak of exercise, STxJT at the peak of exercise and the fact of previous MI.

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**Z. Bertašienė, J. Blužas, J. Braždžionytė, A. Vainoras, R. Žaliūnas. Kompiuterizuotas fizinio krūvio mėginys: pirmenybė įprastiniams ar naujiems išvestiniams krūvio elektrokardiogramos rodmenims // Elektronika ir elektrotechnika. – Kaunas: Technologija, 2004. – Nr. 3(52). – P. 63-66.**

Norėdami nustatyti rodmenis, leidžiančius tiksliau prognozuoti išeminę širdies ligą (IŠL) bei vainikinių arterijų susiaurėjimus, 35 sveikoms moterims bei 90 IŠL sergančių moterų, gydytų Kauno medicinos universiteto Kardiologijos klinikoje, atlikome veloergometrinių mėginių kompiuterizuota sistema „Kaunas-Krūvis“. Nustatėme, kad kompiuteriu apskaičiuojamas rodmuo „ST ir JT sandauga“ labiau susijęs su IŠL bei 3-jų vainikinių arterijų stenozėmis, negu įprastai vertinamas ST segmento nusileidimas didesnis už 0,1 mV. ST ir JT sandaugos maksimalaus krūvio metu reikšmė didesnė už 10,3 mVms 88 proc. jautrumu ir 94 proc. specifiskumu nustato IŠL moterims. trijų pagrindinių vainikinių kraujagyslių stenozes tiksliausiai nurodo ST ir JT sandauga ir JT dispersija maksimalaus krūvio metu bei klinikinis rodmuo – anksčiau persirgta miokardo infarktas. Il.2, bibl. 8 (anglų kalba; santraukos lietuvių, anglų ir rusų k.).

**Z. Bertašienė, J. Blužas, J. Braždžionytė, A. Vainoras, R. Žaliūnas. Computerised Stress -Test: Usual or New Derivative Electrocardiographic Variables // Electronics and Electrical Engineering. – Kaunas: Technologija, 2004. – No. 3(52). – P. 63-66.**

For better prediction ischemic heart disease (IHD) and coronary artery stenoses 35 healthy women and 90 women with IHD hospitalised at Kaunas medical university hospital undergone veloergometry by means of computerised system “Kaunas-Krūvis”. Calculated variable - ST and JT product at the maximum load - has stronger correlation with IHD and three-vessel disease than routine variable – ST depression greater than 0,1 mV. The value of ST and JT product at the peak of exercise >10,3 mVms with 88% sensitivity and 94% specificity predicts IHD in women. The most accurate predictors of three-vessel disease in women with IHD were ST and JT product and JT dispersion at the peak of exercise, and the fact of previous MI. Ill. 2, bibl. 8 (in English; summaries in Lithuanian, English and Russian).

**З. Берташене, Ю. Блужас, Ю. Бражджоните, А. Вайнорас, Р. Жалюнас. Компьютерное велоэргометрическое исследование: преимущество обычным или новым производным показателям электрокардиограммы при физической нагрузке // Электроника и электротехника. – Каунас. Технологія, 2004. – № 3(52). – С. 63-66.**

Для наиболее точного прогнозирования ишемической болезни сердца (ИБС), проведён анализ данных компьютеризированной велоэргометрической пробы двух групп женщин – 35 здоровых и 90 больных ИБС. Корреляционная связь показателя (произведения ST и JT) вычисленного при помощи компьютерной программы с ИБС лучше чем обычного показателя – ST спуска более чем 0,1 см. Произведение ST и JT больше чем 10,3 с 88% чувствительностью и 94% специфичностью

позволяет определить ИБС. Для диагностики сужений в трёх коронарных артериях самыми информативными показателями являются: произведение ST и JT и дисперсия интервала JT при максимальной нагрузке и факт раньше перенесённого инфаркта миокарда. Ил. 2, библ. 8 (на английском языке; рефераты на английском, литовском и русском яз.).