

Corrected QT dispersion improves diagnostic performance of exercise testing in diagnosing coronary artery disease

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تصحيح تشتت QT يحسن الأداء التشخيصي لاختبار التمرين في تشخيص مرض الشريان التاجي

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الخلاصة: لتحديد أفضل مزيج من العوامل الثابتة التي تحسن الأداء التشخيصي لاختبار التمرين، أُجري تصوير الأوعية التاجية واختبار التمرين لـ 112 مريضاً مصابين بالذبحة الصدرية وكان مخطط كهربية القلب لديهم سليماً. وتضمنت المتغيرات المنبئة لمرض الشريان التاجي: العمر أكبر من يساوي 40 عاماً، الجنس الذكري، فرط ضغط الدم، التدخين، نشأة ألم صدري نتيجة لبذل المجهود، انخفاض ضغط الدم الانقباضي أكبر من أو يساوي 10 ملليمتر زئبقي، أو يكون ضغط الدم الانقباضي بعد 3 دقائق من أداء التمرين أعلى من 90% من الذروة، وانخفاض معدل نبض القلب لأقل من 120 نبضة في الدقيقة بعد دقيقة من أداء التمرين، أو ظهور انخفاض في ST بسبب التمرين بعد دقيقة أو أكثر. وأظهر تحليل التحوف اللوجستي العديد المتغيرات أن استخدام أي من انخفاض ST أكثر من أو يساوي ملليمتر واحد أو زيادة QTDC في ذروة التمرين أكثر من 70 ملي ثانية سيحسن بدرجة ملموسة قيمة الحساسية والتنبؤ السلبي للاختبار بدون زيادة ملموسة في النوعية.

ABSTRACT To determine the best combination of parameters that would improve the diagnostic performance of exercise testing, coronary angiography plus exercise testing were done on 112 patients with angina pectoris and normal electrocardiogram. The univariate predictors of coronary artery disease included: age \geq 40 years, male sex, hypertension, smoking, development of exertional chest pain, decrease in systolic blood pressure (BP) \geq 10 mmHg or systolic BP 3 min post-exercise $>$ 90% of peak, heart rate drop $<$ 12 beats/min 1 min post-exercise, exercise-induced ST-segment depression \geq 1 mm. Multivariate logistic regression analysis showed that using either ST depression \geq 1 mm or peak exercise QTDC $>$ 70 ms significantly improved sensitivity and negative predictive value of the test without a significant decrease in specificity.

Amélioration de la performance diagnostique de l'épreuve d'effort aux fins du diagnostic de coronaropathie grâce à la dispersion du QT corrigée

RÉSUMÉ Afin de déterminer la meilleure combinaison de paramètres permettant d'améliorer la performance diagnostique de l'épreuve d'effort, une angiographie coronarienne et une épreuve d'effort ont été pratiquées sur 112 patients présentant un angor et un électrocardiogramme normal. Les facteurs prédictifs univariés de la coronaropathie étaient les suivants : âge supérieur à 40 ans, sexe masculin, hypertension, tabagisme, apparition de douleurs thoraciques à l'effort, baisse de la tension artérielle (TA) systolique supérieure à 10 mmHg ou de la TA systolique trois minutes après l'effort de plus de 90 % de la valeur maximale, chute de la fréquence cardiaque à moins de 12 pulsations/min une minute après l'effort, et dépression du segment ST induite par l'effort de plus de 1 mm. L'analyse de régression logistique multivariée a montré que l'utilisation de la dépression du ST de plus de 1 mm ou de la dispersion du QT corrigée à l'acmé de l'effort de plus de 70 ms améliorerait significativement la sensibilité et la valeur prédictive négative de l'épreuve d'effort, sans baisse sensible de la spécificité.

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Introduction

The exercise electrocardiogram (ECG) is used in the evaluation of symptomatic patients to predict the presence and extent of coronary artery disease (CAD) [1,2]. Although a large number of non-invasive stress testing modalities are currently available, the ECG is still used as standard because it is the least costly of all provocative non-invasive tests [3]. The conventional criterion for designating an exercise test abnormal is demonstration of > 1 mm of slow upsloping or horizontal or downsloping ST-segment. However, when exercise-induced ST-segment change is used as a single criterion for ischaemia, its value is limited by low sensitivity and specificity [1–4]. An alternative to using more expensive tests would be the more efficient use of available low cost data. Several parameters have been studied in a number of reports to improve the sensitivity, specificity and predictive value of the exercise stress test [4–18].

This study was designed to determine the best combination of parameters, clinical and exercise-induced haemodynamic and electrocardiographic, that would improve the capacity of exercise testing in diagnosing CAD with best sensitivity and specificity.

Methods

The study group comprised all 112 patients presenting to our hospital during the period February 2006–October 2006 with typical (definitive) or atypical (probable) angina associated with normal or non-conclusive electrocardiographic changes for the diagnosis of CAD and who gave informed consent to participate in the study. The protocol of the study was fully explained to all participants.

Chest discomfort was classified as follows:

- typical angina (definitive) which meets all the 3 of the following criteria: substernal chest discomfort with characteristic quality and duration; provoked by exertion or emotional stress; and relieved by rest or nitroglycerine;
- atypical angina (probable), which meets 2 of the above 3 criteria; non-cardiac chest discomfort which meets ≤ 1 of the above criteria [19].

Patients were excluded if they had current unstable angina, documented previous myocardial infarction, a prior revascularization procedure, ejection fraction < 50%, valvular or congenital heart disease or haemoglobin level < 8 mg/dL. Patients were also excluded if they were unable to exercise due to a non-cardiac illness, they had an uninterpretable electrocardiogram (ECG) (such as in Wolf–Parkinson–White syndrome or bundle branch block) and they could not achieve > 85% of age-predicted heart rate (HR) during the test without evidence of positivity in their exercise ECG (inadequate test).

Exercise stress test

Before the test the patients had to be free of chest discomfort for at least 1 week, stop anti-anginal, anti-arrhythmic and antipsychotic drugs (each drug according to its half-life), and fasting (with no cigarette smoking) in the previous 3 hours. Standard Bruce protocol was used for all patients [20]. The test was stopped if the target heart rate (HR) was achieved or on the occurrence of any of the following: exertional hypotension, limiting symptoms (chest pain, evidence of poor peripheral perfusion, dyspnoea, fatigue or leg cramps); ST-depression > 3 mm; bundle branch block; or serious arrhythmias (multiform complexes, couplets, triplets, salvos or ventricular tachycardia).

The following variables were measured during the stress test:

- Basic data: resting HR, resting systolic blood pressure (BP), maximum HR

achieved, duration of exercise, peak systolic blood pressure, and chest pain with exertion.

- Abnormal BP response (either systolic BP fails to increase > 130 mmHg or decreases by > 10 mmHg in response to exercise) [5]; systolic BP at 3 minutes post exercise; > 90% of peak exercise systolic BP [6].
- Abnormal HR response (either HR at peak exercise < 100 beats/min [3] or failure of HR to drop > 12 beats at 1 minute post exercise from peak exercise value [7]).
- ST segment changes (measured in ≥ 6 beats) occurring peak exercise and/or during recovery; > 1 mm horizontal or downsloping depression measured 80 ms from the J-point, > 1.5 mm upsloping depression measured 80 ms from the J-point, or > 1 mm elevation in > 2 contiguous leads except aVR [3].
- ST/HR index > 1.6 $\mu\text{V}/\text{beats}/\text{min}$ (measured in the lead with the maximum ST depression, in ≥ 6 beats) as ST depression at peak stress divided by the difference between the peak exercise HR and resting HR [8–10].
- ST/HR slope: a linear regression-based computed measurement [ST depression = dependent variable; HR = independent variable. Both are measured in each lead (excluding aVR, aVL and V_1) at the end of each stage and at peak exercise]. A linear regression analysis is made for each lead: the maximal ST/HR slope is recorded and the highest ST/HR slope with a statistically significant correlation coefficient among all leads is taken as the final result. ST/HR slope $\geq 2.4 \mu\text{V}/\text{beats}/\text{min}$ is considered an indicator of the presence of CAD [9,10].
- Abnormal T-wave response (measured in ≥ 6 beats); increased T-wave amplitude in V_2 > 2.5 mm [11] or T-wave inversion with exercise in V_5 (< 5 mm or ≥ 5 mm) [12].

- Lengthening or no change in P-wave duration in V_2 at peak exercise (measured in ≥ 6 beats) is considered positive, while shortening is considered negative [13].
- Q-wave depth in lead V_5 (measured in > 6 beats). This is considered positive if absent both at rest and at peak exercise, present at rest but with no change with exercise, or present at rest but decreases or disappears with exercise. It is considered negative if absent at rest but appears with exercise, or present at rest and increased by exercise [14].
- Decreased R-wave amplitude > 1 mm [4] or increased ≥ 2 mm [15] at V_5 at peak exercise compared to resting value (measured in ≥ 6 beats) is considered positive.
- QT dispersion (QTD): QT interval was measured manually in as many pericardial and limb leads as possible (≥ 8 leads) after being magnified on a Cannon photocopier ($\times 3$). It is measured from the onset of Q-wave to the end of T-wave. If the end of T-wave is not seen, for example when it is fused with the U-wave or P-wave as in the setting of rapid HR, a straight line is drawn tangential to the down stroke of the T-wave till it meets the base line (identified from level of PR segment) and this is taken as the end of the T-wave. QTD is the difference between the highest and the lowest QT. The test is considered positive if QTD at peak exercise is > 60 ms [16].
- Delta QTD (from rest to peak exercise) > 16 ms. [17].
- Corrected QT dispersion (QTDc) at peak exercise: QT interval (QT) is measured in as many pericardial and limb leads as possible (≥ 8 leads) as mentioned. Corrected QT (QTc) is calculated from Bazett's equation: $QTc = QT / (\sqrt{RR \text{ interval}})$. QTDc is the difference between the highest and the lowest QTc. The test is considered positive if QTDc > 70 ms [16].
- Q-X/QT ratio > 0.5 measured in V_5 in ≥ 6 beats (Q-X measured from the beginning of QRS to crossing of ST) [18].

Coronary angiography

Coronary angiography was carried out within a maximum of 90 days from the exercise test. Multiple views were taken for both the left and right coronary arteries to achieve complete visualization of all coronary segments from ≥ 2 orthogonal planes. The coronary artery was considered diseased if stenosis was $\geq 50\%$ diameter.

Statistical analysis

All data were analysed using SPSS, version 11. Continuous variables were expressed as mean and standard deviation (SD) and discrete variables were presented as frequencies and percentages. Continuous variables were compared between the 2 groups (with and without CAD) using the unpaired Student *t*-test for normally distributed data and the Mann–Whitney U-test for non-normally distributed data. Discrete variables were compared using the chi-squared test with Fisher exact correction. Statistical significance was set at $P < 0.05$.

Variables with a significant difference between the ischaemic and non-ischaemic groups were considered univariate predictors of the presence of CAD. Validation of these variables was tested by computing the sensitivity, specificity and positive and negative predictive values.

The categorical univariate predictors of CAD were entered into multivariate, stepwise, logistic regression analysis to identify independent predictors. Only variables with $P < 0.05$ were eligible to enter the stepwise analysis and be retained in the final model. Validation of the model was also tested using the Holmer–Lemeshow goodness-of-fit statistics across groups of risk. To determine the cut-off point for a positive test according to the above model, a receiver-

operating-characteristic (ROC) curve was plotted for the predicted probability of each case in the study group. Sensitivity, specificity and positive and negative predictive values were compared using the McNemar test.

Results

The mean age of the patients was 46 (SD 9) years. There were 81 (72%) males, 47 (42%) participants with hypertension, 26 (23%) with diabetes, 60 (54%) smokers and 85 (76%) who had had typical chest pain. Based on coronary angiography, significant CAD ($> 50\%$ stenosis) was present in 57 (51%) participants: 21 (19%) had single vessel, 8 (7%) had 2-vessel, 28 (25%) had 3-vessel disease. The remaining 55 participants (49%) did not have significant CAD.

All those with a negative test achieved $\geq 85\%$ of the age-predicted HR with exercise. We were able to measure V_5 variables in 110 (98%) participants; peak exercise QT, QTD, QTc, QTDc was measured in 109 (97%) patients. All missing values were from those in the non-CAD group.

Predictors of CAD

Compared to those without CAD, patients with CAD had higher mean peak exercise QT interval [327 (SD 40) versus 272 (SD 28)] ($P < 0.001$), QTD [61 (SD 21) versus 38 (SD 10)] ($P < 0.001$), QTc interval [485 (SD 36) versus 435 (SD 29)] ($P < 0.001$), QTDc [52 (SD 47) versus 33 (SD 30)] ($P < 0.001$). The univariate predictors of CAD are shown in Table 1.

The statistically significant univariate predictors of CAD were entered into a multivariate, stepwise, logistic regression analysis to determine the best diagnostic model. The independent predictors of CAD were horizontal or downsloping ST depression ≥ 1

Table 1 Univariate predictors of coronary artery disease (CAD)

Predictor	With CAD (n = 57) ^a		No CAD (n = 55) ^a		PPV %	NPV %
	No.	%	No.	%		
Age ≥ 40 years	57	100	24	44	100	75
Male sex	53	93	28***	51	65	87
Hypertension	33	58	14***	25	70	63
Diabetes	18	32	8*	15	67	52
Smoking	40	70	20***	36	67	67
Typical ischaemic chest pain	53	93	32***	58	62	58
Chest pain with exertion	56	98	24***	44	70	94
Abnormal BP response with exercise:	20	35	4***	7	83	53
Peak systolic BP < 130 mmHg	4	7	0	0		
Decrease systolic BP ≥ 10 mmHg	8	14	1*	2	89	52
Systolic BP 3 min post-exercise > 90% peak	16	28	1***	2	94	57
HR at peak exercise < 100 b/m	0	0	0	0		
HR failed to drop ≥ 12 b/m at 1 min post-exercise	16	28	6*	11	73	54
ST-segment shift with exercise:	49	86	24***	44	86	80
≥ 1 mm horizontal or downsloping depression	40	70	5***	9	89	75
≥ 1.5 mm upsloping depression	9	16	15	27		
≥ 1 mm elevation	0		0			
Peak exercise ST/HR index ≥ 1.6 μV/b/m	25	44	16	29		
Peak exercise ST/HR slope ≥ 2.4 μV/b/m	30	53	15**	27	67	59
Increased T amplitude ≥ 2.5 mm in V ₂	33	58	8	15	81	66
T-wave inversion with exercise	1	2	0			
Lengthened or no change in P-wave duration in V ₂	49	86	35***	64	58	71
Decrease or no change in Q-wave depth in V ₅	50	88	39*	71	56	70
R amplitude in V5 increase ≥ 2 mm or decrease ≥ 1 mm	45	79	20***	36	69	73
Peak exercise QTD > 60 ms	37	65	4***	7	90	71
Delta QTD rest to peak exercise ≥ 16 mm	26	46	10**	18	72	58
Peak exercise QTDC > 70 ms	45	80	4***	7	92	80
Peak exercise Q-X/QT ratio in V ₅ > 0.5	28	49	16*	29	64	56
Axis shift with exercise	2	4	1	2		
Transient bundle branch block with exercise	0	0	1	2		
Exercise-induced ventricular ectopics	12	21	4	7		

*P < 0.05; **P < 0.01; ***P < 0.001.

^a% within the group with CAD is equivalent to sensitivity while % within the group with no CAD is equivalent to 1 - specificity.

HR = heart rate; b/m, beats per minute; BP = blood pressure; QT = QT interval; QTD = QT dispersion; QTDC = corrected QT dispersion; PPV, positive predictive value; NPV = negative predictive value.

mm and peak exercise QTDC > 70 ms (Table 2).

The Holmer–Lemeshow goodness-of-fit statistic across groups of risk was not statistically significant ($P = 0.89$) indicating little departure from a perfect fit. The area under the ROC curve for the predicted probability of each case in the study group from this multivariate model was 0.94. The cut-off point of the

predicted probability for a positive test according to the above model was obtained from the ROC curve. The cut-off point of the predicted probability of the model was 0.39 with the best sensitivity (93%) and specificity (85%) (Table 3). The predicted probability from the above model was computed from the following equation:

$$Probability = \frac{e^{\alpha + B_1 X_1 + B_2 X_2}}{1 + e^{\alpha + B_1 X_1 + B_2 X_2}}$$

where, α is the constant (intercept) of the regression model, B is the B coefficient of the variables, X is the value of the variable (0 when absent, 1 when present).

This predicted probability ≥ 0.39 can be achieved when ≥ 1 variables in

Table 2 Multivariate stepwise logistic regression analysis for prediction of coronary artery disease (CAD)

Variable	β coefficient (SE)	OR (95% CI)	P-value
ST depression ≥ 1 mm ^a	3.3 (0.8)	27.3 (6.2–60.2)	< 0.001
Peak exercise QTDC > 70 ms	3.8 (0.7)	43.6 (10.3–84.9)	< 0.001
Constant	-9.6 (1.7)	-	< 0.001

^aHorizontal or downsloping.

QTDC = corrected QT dispersion; SE = standard error; OR = odds ratio; CI = confidence interval.

the equation are positive. So, according to the above model, the presence of horizontal or downsloping ST depression ≥ 1 mm and/or peak exercise QTDC > 70 ms is an indication of a positive test.

To study the additive effect of both independent variables in the model, 3 logistic regression models were created, 1 for each independent variable alone and 1 using either or both variables as an indication of a positive test. The discriminative ability of the 3 models was compared by computing the area under the ROC curve for each. Sensitivity, specificity, positive and negative predictive values were computed for each and compared to those of ST depression to make a simple numerical comparison (Table 4). Adding peak exercise QTDC > 70 ms to horizontal or downsloping ST depression ≥ 1 mm in the diagnosis of CAD during the interpretation of the exercise test significantly improved the sensitivity (70% to 93%; $P < 0.001$) and the negative predictive value of the test (75% to 92%; $P < 0.01$) with no significant decrease in the specificity.

The validity indices were higher for the peak exercise QTDC compared to ST depression but the differences were not statistically significant.

The additive effect of the independent variables in the model was re-tested in the detection of single vessel disease as well as multi-vessel disease (Table 4). ST depression had a lower sensitivity in single vessel (57%) than in multi-vessel disease (78%; $P < 0.01$), with specificity 91% for both. Similarly, peak exercise QTDC had sensitivity 81% for single

and 78% for multi-vessel, with specificity 92% for both. The diagnostic accuracy was even better than ST depression in single vessel disease, as indicated from the greater area under the ROC curve (0.87 versus 0.74) and higher sensitivity (81% versus 57%; $P < 0.001$). Although the specificity and predictive values were higher, the differences were not statistically significant. In single vessel disease, adding peak exercise QTDC to ST depression offered advantages over QTDC alone. In multi-vessel disease the diagnostic accuracy of the test improved (area under ROC curve 0.97, which is higher than either alone). The sensitivity and negative predictive value in multi-vessel disease increased significantly to 100% with no significant decrease in specificity.

Discussion

The exercise test has a reported sensitivity of 50%–70% and specificity of 70%–90% using conventional ST depression criteria with exercise [3]. In a meta-analysis, mean sensitivity was 68% (range 23%–100%) and mean specificity 77% (range 17%–100%) [1]. In our study, sensitivity was 86% and specificity

44%. This relatively high sensitivity is attributed to the use of 50% angiographic stenosis as a reference standard for the presence of CAD and measurement of ST depression at peak exercise and/or during recovery, which improves test sensitivity. Recovery-onset ST depression has been reported to represent about 30% of ischaemic ECG response with exercise [21].

Another explanation could be referral bias as the participants included patients with typical and probable ischaemic chest pain. Referral bias was reported to be the most important factor increasing sensitivity and decreasing specificity [2]. This referral bias is ethically unavoidable as coronary angiography could not be done for patients with atypical, likely non-ischaemic, chest pain and negative exercise test. Horizontal or downsloping ST depression > 1 mm had a significantly lower sensitivity (70%) and a higher specificity (91%). Sansoy Watson and Beller similarly reported that adding upsloping ST-segment depression increased sensitivity at the expense of specificity and a significant decrease in the positive predictive value of the test [22]. Also, in a more recent report, both rapid and slow upsloping ST depression were found to be associated with very low likelihood of CAD compared to horizontal or downsloping ST depression [23]. Similar to previous reports [1,2], we found that in single vessel disease, ST depression had a lower sensitivity than in multi-vessel disease, with a similar specificity.

Normally, the QT interval (corrected for HR) shortens with exercise [24].

Table 3 Sensitivity and specificity of the predicted model at different predicted probabilities

Positive if predicted probability \geq :	Sensitivity	Specificity
0.00	1.00	0.00
0.39	0.93	0.85
0.74	0.79	0.92
0.89	0.57	1.00
1.00	0.00	1.00

Table 4 Validity of the additive effect of the 2 variables in the logistic regression model for the detection of coronary artery disease (CAD), single vessel disease (SVD) and multi-vessel disease(MVD)

Measure	Horizontal or downsloping ST depression ≥ 1 mm	Peak exercise QTDC > 70 ms	Either or both positive
Detection of CAD			
Area under ROC curve (SE)	0.80 (0.04)	0.86 (0.04)	0.94 (0.02)
Sensitivity (%)	70	80	93***
Specificity (%)	91	92	85
PPV (%)	89	92	87
NPV (%)	75	80	92***
Detection of SVD			
Area under ROC curve (SE)	0.74 (0.07)	0.87 (0.06)	0.88 (0.06)
Sensitivity (%)	57	81***	81***
Specificity (%)	91	92	85
PPV (%)	71	81	68
NPV (%)	85	92	92
Detection of MVD			
Area under ROC curve (SE)	0.84 (0.05)	0.85 (0.05)	0.97 (0.02)
Sensitivity (%)	78	78	100***
Specificity (%)	91	92	85
PPV (%)	85	86	82
NPV (%)	86	86	100***

*** $P < 0.001$ (compared with ST depression).

ROC = receiver operating characteristics; PPV = positive predictive value; NPV = negative predictive value; QTDC = corrected QT dispersion; SE = standard error.

Some investigators have found that this interval fails to shorten, or lengthens, when ischaemia is present [18,25]. They have also reported a higher Q-X/QT ratio in CAD patients with no additive value to ST segment criteria in terms of sensitivity and specificity [18,25]. QT interval difference with age and sex is not thought to affect its usefulness in exercise ECG. This is based on previous findings that sex differences in QT disappear at HR ≥ 110 beats/min, whereas age differences are smaller but are present throughout exercise, with no significant age–sex interaction [26]. Moreover, QTD, QTDC and/or their differences between rest and peak exercise have emerged as useful additional diagnostic criteria in the interpretation of the exercise test, irrespective of sex [16,17,26,27].

Exercise QTD > 60 ms has been found to be a clinically useful indicator of significant coronary stenosis

independent of sex or the presence or absence of significant exercise-induced ST-segment depression [26] and in patients who do not have exercise-induced chest pain or significant ST-segment depression [27]. It has been reported in a study on female patients to have a significantly higher sensitivity and specificity for the diagnosis of CAD compared with 1-mm ST-segment depression. When a QTD > 60 ms was added to ST-segment depression as a condition for a positive test, the specificity increased to 100% [16]. Also, it has been reported to have a greater sensitivity and specificity than ST depression in the detection of restenosis after percutaneous coronary angioplasty at ≥ 50 ms [28]. Adding QTD ≥ 60 ms to ST depression improved the diagnostic value of the exercise test in diagnosing restenosis after percutaneous coronary angioplasty [29]. A rise of QTD with exercise ≥ 16 mm was another predictor of CAD [17]. Exercise QTDC of > 70

ms significantly increased the sensitivity of exercise testing for CAD; in addition, combining with ST-segment depression gave a specificity of 100%. Both QTD and QTDC were measurable with an acceptable reproducibility [16]. Similarly Ozdemir et al., in a study of a series of female patients, have reported that QTDC with a different cut-off point of a positive test (> 60 ms) had a greater sensitivity and specificity than ST-depression [30].

In our study, peak exercise QTD > 60 ms, delta QTD rest to peak exercise ≥ 16 mm, QTDC > 70 ms and Q-X/QT ratio in $V_5 > 0.5$ were significantly higher in CAD patients. Q-X/QT ratio in $V_5 > 0.5$ had the lowest sensitivity and specificity. The other 3 parameters had high specificity but differed in sensitivity, high for QTDC > 70 ms and low for QTD > 60 ms and delta QTD.

Peak exercise QTDC and horizontal or downsloping ST depression were the

only variables found to be independent predictors of CAD in multivariate analysis. The validity indices, despite being higher for peak exercise QTDC compared to ST depression, were not statistically significant. The diagnostic accuracy of QTDC was even better than ST depression in single vessel disease, as indicated by the greater area under

the ROC curve and better sensitivity. We showed that using either variable as a marker of a positive exercise test significantly improved the sensitivity and negative predictive value of the test without a significant decrease in the specificity.

In conclusion, clinical and exercise-induced haemodynamic and ECG

changes could provide additional information that could increase the ability of the exercise test to diagnose CAD. Using either horizontal or downsloping ST depression ≥ 1 mm or QTDC peak exercise > 70 ms as a marker of a positive exercise test significantly improves the diagnostic value of the test.

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