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Relationship Between Exercise Electrocardiography Findings and Cardiovascular Events and the Extent of Coronary Artery Disease: What is New?

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Abstract

Objectives: The exercise treadmill test (ETT) is commonly used in cardiology practice. Detection of the severity of coronary artery disease (CAD) by the surrogates of ETT is of great importance to guide the management plan. Here, we aimed to identify the best ETT surrogates to detect the extent of CAD and major adverse cardiovascular events (MACE) during follow-up.

Materials and Methods: This retrospective study included patients with positive ETT results for coronary ischemia who underwent invasive coronary angiography after the index ETT. The following surrogates of ETT were used in the study for the analyses: exercise duration; maximum workload achieved in METS; rate-pressure product (RPP) at rest, at peak, and at 3rd minute in the recovery; number of leads with ST deviation; and Duke treadmill score (DTS). Patients were classified into low-risk, intermediate-risk, and high-risk groups according to the SYNTAX score. The ETT findings of the groups were compared.

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Results: The study included 48 patients: low-risk group: 24 (50%); intermediate-risk group: 10 (21%); and high-risk group: 14 (21%). The average age was 50±8 years. DTS, peak RPP, recovery RPP, and number of leads with ST deviation were significantly different between the high-risk group and the other groups. These variables were well correlated with the SYNTAX score, presence of the left main coronary artery (LMCA) lesion, and development of MACE at follow-up.

Conclusion: DTS, peak RPP, recovery RPP, and number of leads with ST deviation are well correlated with the extent of CAD, presence of LMCA lesions, and development of MACE at follow-up.

Keywords: Coronary artery disease, exercise treadmill test, Duke treadmill score, rate-pressure product, SYNTAX score

Introduction

Chest pain or its equivalent is the most frequently occurring cardiac symptom[1]. Evaluation in an emergency or office setting is performed with the help of non-invasive stress modalities such as the exercise treadmill test (ETT), stress echocardiography, and myocardial perfusion scintigraphy[1,2].

The ETT is the most commonly used and first-step diagnostic tool in the assessment of chest pain or other cardiac symptoms in patients with low to intermediate 10-year cardiovascular risk[3]. Because of its low cost and widespread availability, ETT is commonly recommended for patients presenting with interpretable baseline electrocardiography (ECG) findings in the evaluation of chest pain or other cardiac symptoms[4]. However, its sensitivity and specificity are limited (67% and 71%, respectively) depending on the target population[1,4-6].

Improper interpretation of ETT may result in the underestimation of underlying coronary artery disease (CAD) or ignoring warning findings that may lead to false-negative results for coronary ischemia[7]. Thus, the detection of such warning findings in ETT may help guide physicians.

Although the sensitivity and specificity of the ETT vary according to the population in concern and the clinical setting in which the ETT is performed, its value in the long-term survival of patients with regard to the development of new cardiovascular events has not been studied sufficiently. Additionally, surrogates that may reflect coronary artery anatomy and long-term survival have not been studied in detail in the literature.

Duration of the ETT, the maximum workload achieved in metabolic equivalents (METs), heart rate at peak exercise and the third minute in recovery, percentage of the maximum heart rate achieved as per age-predicted target heart rate, blood pressure readings at peak exercise and the third minute in recovery, number of leads with ST deviation in positive ETT, Duke treadmill score, maximum ST deviation in millimeter in patients with positive ETT, ST deviation developed at peak exercise or recovery in patients with positive ETT, number of leads with ST deviation in positive ETT may be mentioned among these potential ETT surrogates. The establishment of such studies can improve the quality of care in institutions and can guide physicians in respect to the proper interpretation of this test in the evaluation of cardiac patients. Detecting such abnormal surrogates during ETT may help physicians take early action to achieve close follow-up or intervention.

Here, we aimed to identify the best ETT surrogates to detect the extent of CAD and major adverse cardiovascular events (MACE) during follow-up.

Materials and Methods

This was a retrospective; non-invasive study that included patients aged between 18 and 65 years who underwent ETT between March 2015 and February 2020 in the cardiology department due to CAD assessment due to chest pain, dyspnea, and palpitation evaluation. The study included patients who were ETT positive for coronary ischemia. All patients underwent invasive coronary angiography within six months following the index ETT. The study protocol was approved by Hamad Medical Corporation Ethical and Institutional (approval no.: MRC-01-21-279 date: 23.03.2021).

Any patient who was not able to complete ETT due to orthopedic reasons was excluded. Additionally, patients with previously diagnosed CAD, history of cardiac surgery, acute coronary syndrome before ETT, renal disease (glomerular filtration rate less than 90 mL/minute), elevated hepatic transaminase levels (more than 3 times from the upper normal limit) at baseline, concomitant moderate or severe valvular disease, wall motion abnormalities on echocardiographic examination, malignancy, hemoglobin level 10 gm/dL, and active infection at the time of ETT were excluded. Additionally, patients with a left ventricle ejection fraction (LVEF) of 50%, hypertrophic cardiomyopathy, congenital heart disease, and moderate or severe valvulopathy were not included. Additionally, patients with non-interpretable baseline ECG findings, such as left bundle-branch block, baseline ST depression, and pre-excitation were not enrolled in the study.

Age, gender, and body mass index (BMI) of each subject were recorded. BMI was calculated using a formula (weight in kg divided by square of height in meters). Concomitant morbidities, such as hypertension (the last 3 blood pressure measurements >140/90 mmHg or treatment with antihypertensive medication within the last 6 months) and diabetes mellitus (any patient under oral anti-glycemic drugs or insulin treatment or HbA1c over 7.0%), were recorded.

The presence of other cardiovascular risk factors was determined according to the following criteria: positive family history of CAD (presence of CAD in first-degree family members, male <55 years, or female <65 years), and cigarette smoking (current cigarette smoker or using tobacco products in the last 2 years).

Blood hemoglobin, creatinine, HbA1c, thyroid-stimulating hormone values, and fasting lipid profile [total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL)] at the time of ETT were obtained.

Transthoracic echocardiographic examinations (TTE) of the patients were performed on the same day as the index ETT. TTE images of all patients were reviewed, and all measurements related to interventricular septum thickness at diastole (IVSd), posterior wall thickness at diastole, left atrium (LA) volume index, LVEF, mitral flow E/mitral annulus lateral e' ratio, and grade of the left ventricle diastolic dysfunction were obtained as per the recommendations of the American Society of Echocardiography[8].

Baseline ECG data for all patients were obtained before ETT was performed to exclude patients with non-interpretable baseline ECG. All ETTs were performed as per the Bruce protocol in the same non-invasive laboratory of the same health center by the same staff who were blinded to the study protocol. ETT was considered abnormal in the development of exertional hypotension, malignant ventricular arrhythmias, or limiting chest pain during ETT. Additionally, an abnormal exercise ST response was defined as follows: 1 mm of horizontal or down-sloping ST deviation depression (80 ms after J point) or 1 mm of ST segment elevation in leads without pathological Q waves (excluding aVR lead)[2].

The following surrogates of ETT were used in the study for the analyses: duration of the exercise; maximum workload achieved in METS; heart rate at rest, at peak exercise, and at the third minute in recovery; percentage of the maximum heart rate achieved as per age-predicted target heart rate; blood pressure readings at rest, at peak exercise, and at the third minute in recovery; number of leads with ST deviation of more than 0.5 mm except lead aVR; presence of cardiac symptoms.

Statistical Analysis

The data analyses were performed by using version 20 SPSS analysis program (Statistical Package for Social Sciences-SPSS, Inc., Chicago, lllinois) for Windows. The distribution of data was assessed using the Kolmogorov-

Smirnov test. Age, BMI, hemoglobin, creatinine, LDL, HDL, ETT duration, ETT workload in METs, maximum ST segment during ETT, rate-pressure product (RPP), Duke treadmill score (DTS), SYNTAX score, LVEF, and left ventricle end-diastolic diameter (LVEDD) values were normally distributed. Normally distributed continuous variables are presented as mean ± standard deviation, whereas non-normally distributed variables are expressed as median (interquartile range). Categorical data are presented as counts and percentages.

The Mann-Whitney U and Kruskal-Wallis tests were used to compare the difference of the groups with respect to non-normally distributed variables, whereas Student's t-test and ANOVA were used for normally distributed variables. The chi-square test was used to analyze the relationships among categorical variables of the groups if all cells had an expected frequency of >25. In the 2x2 contingency tables; the Yates (Continuity Correction) test was used when one or more of the cells had an expected frequency of 5-25, the Fisher's exact test was used when one or more of the cells had an expected frequency of 5 or less. Furthermore, in the R X C contingency tables, Fisher-Freeman-Halton test was preferred over chi-square test when one or more of the cells had an expected frequency of 5 or less. Pearson or Spearman correlations were used to perform correlation analyses as per homogenity of the variables. P values below 0.05 was considered statistically significant.

Results

The study included 48 patients who satisfied the inclusion criteria. Of them, 5 (10.4%) patients were female. The number of patients in each group was as follows: low-risk group, 24 patients (50%); intermediate-risk group, 10 patients (21%); and high-risk group, 14 patients (21%). The average age of the study population was 50±8 years.

In comparison of the groups, there were no significant differences in age, sex, BMI, presence of diabetes mellitus, hypertension, smoking status, or family history of premature CAD (for all comparisons p>0.05) (Table 1). All laboratory results used in the study were not statistically significant in the groups (for all comparisons p>0.05) (Table 1).

Table 1. Demographic and laboratory findings of the groups classified as per SYNTAX score

	Low-risk group (n=24)	Intermediate-risk group (n=10)	High-risk group (n=14)	p-value
Age (year)	49±6	52±9	51±11	0.528
Sex (female, %)	3 (12.5)	1 (10.0)	1 (7.1)	0.867
BMI	26.5 (6.75)	27.5 (4.3)	26.0 (6.0)	0.985
DM (%)	9 (37.5)	6 (60.0)	8 (57.1)	0.346
HTN (%)	8 (33.3)	5 (50.0)	9 (64.0)	0.170
Smoking status (%)				
Smoker	18 (75.0)	9 (90.0)	11 (78.6)	
Ex-smoker	5 (20.8)	1 (10.0)	3 (21.4)	0.703
Non-smoker	1 (4.2)	0 (0.0)	0 (0.0)	
Family history of premature CAD (%)	6 (25.0)	2 (20.0)	4 (28.6)	0.892
Hgb (gr/dL)	14.2±1.5	14.1±1.9	14.0±0.8	0.849
Creatinine (mg/dL)	78±15	87±20	86±15	0.242
HbA1c (%)	5.9 (1.0)	6.5 (2.2)	6.1 (2.3)	0.418
TSH (mIU/mL)	1.32 (1.02)	1.08 (1.04)	1.31 (2.58)	0.318
Total cholesterol (mmol/L)	3.45 (2.23)	2.90 (3.89)	3.80 (2.82)	0.626
LDL (mmol/L)	2.42±1.17	2.28±1.65	2.26±0.94	0.911
HDL (mmol/L)	1.11±0.27	1.07±0.34	0.92±0.31	0.163

BMI: Body mass index, DM: Diabetes mellitus, HTN: Hypertension, Hgb: Hemoglobin, CAD: Coronary artery disease, TSH: Thyroid-stimulating hormone, LDL: Low-density lipoprotein, HDL: High-density lipoprotein

The echocardiographic examination results of the groups were similar in respect to LVEF, LVEDD, IVSd at diastole, posterior wall thickness at diastole, LA diameter, LA volume index, and mitral annulus E/e' ratio (p>0.05 for all comparisons) (Table 2). Although ETT duration, ETT workload, RPP at rest, and angina development during ETT were similar overall groups; percentage of maximum heart rate achieved, RPP at peak and recovery, maximum ST deviation, number of leads with ST deviation, and DTS differed significantly between the groups (Table 2).

The coronary angiographic findings of the groups were expressed in Table 3. The high-risk group received significantly more surgical revascularization compared with the other groups (p<0.001). The low-risk group received more percutaneous coronary intervention than the other groups (p<0.001). Although the number of MACE events was higher in the high-risk group, the difference was not statistically significant (p=0.100). Follow-up durations were similar between the groups (p=0.876).

The average percentage of maximum heart rate achieved by the high-risk group (81±10 bpm) was significantly lower than that of the low-risk group (89±10 bpm) (p=0.021) and the intermediate-risk group (90±10 bpm) (p=0.034). The high-risk group achieved significantly less RPP at peak exercise compared with the low-risk group (p<0.001) and intermediate-risk group (p<0.001). A similar relationship was found between the high-risk group versus the low-risk group (p<0.001) and the high-risk group versus the intermediate-risk group (p=0.016) concerning RPP at recovery.

Although a higher ST deviation was observed in the high-risk group compared with the intermediate group, it did not reach the level of statistical significance (p=0.178). However, a higher maximum ST deviation was observed in the high-risk group compared with the low-risk group (p<0.001). The high-risk group developed a higher number of leads with ST deviation than the low-risk group (p<0.001) however higher number of leads with ST

Table 2. The findings of echocardiographic examination and ETT among the groups

	Low-risk group (n=24)	Intermediate-risk group (n=10)	High-risk group (n=14)	p-value
LVEF (%)	59±3	58±3	57±4	0.355
LVEDD (mm)	47±3	46±6	48±3	0.501
IVSd (mm)	10 (2)	9 (4)	10 (3)	0.679
PWd (mm)	9 (3)	9 (3)	10 (3)	0.081
LA diameter (mm)	35 (7)	34 (11)	36 (3)	0.842
LA volume index (mL/m^2)	25.5 (10.6)	18.0 (10.8)	24.6 (7.1)	0.308
Mitral lateral annulus E/e' ratio	7.0 (2.2)	9.0 (3.9)	8.0 (2.7)	0.394
ETT duration (minute)	7.2±2.4	7.4±2.5	5.6±2.3	0.092
ETT workload (MET)	8.9±2.4	9.1±2.3	7.6±2.1	0.171
Percentage of the maximum heart rate as a function of age-predicted target heart rate (%)	89±10	90±10	81±10	0.035
RPP at rest (bpm*mmHg)	9679±2121	11046±2367	10109±1731	0.225
RPP at peak (bpm*mmHg)	26920±4726	26568±3711	18483±4576	0.000
RPP upon recovery (bpm*mmHg)	15483±2579	14289±2538	11678±2314	0.000
Angina during ETT (%)	15 (62.5)	5 (50.0)	8 (57.1)	0.792
Maximum ST deviation during ETT (mm)	1.63±1.28	2.40±1.28	3.01±0.86	0.004
Number of leads with ST deviation	5.5 (4.0)	7.0 (4.0)	9.0 (3.0)	0.001
Duke treadmill score (points)	-3.7±6.8	-8.2±5.2	-13.3±6.4	0.000

ETT: Exercise treadmill test, LA: Left atrium, LVEF: Left ventricle ejection fraction, LVEDD: Left ventricle end-diastolic diameter, IVSd: Interventricular septum thickness at diastole, PWd: Posterior wall thickness at diastole, RPP: Rate-pressure product, MET: Metabolic equivalent deviation was significant in respect to the low-risk group (p=0.177). DTS was significantly lower in the high-risk group than in the intermediate-risk group (p=0.047) and low-risk group (p<0.001).

In the correlation analyses, the SYNTAX score was found to be significantly correlated with DKS (r=-0.576, p<0.001), the number of leads with ST deviation (r=0.585, p<0.001), the maximum ST deviation (r=0.467, p<0.005), the percentage of maximum heart rate achieved (r=-0.371, p<0.01), RPP at peak (r=-0.491, p<0.001), and RPP at recovery (r=-0.438, p<0.005) respectively.

The study population was re-grouped as follows: the first group (normal or non-obstructive CAD); the second group [obstructive CAD without left main coronary artery (LMCA) disease], and third group (obstructive CAD with LMCA disease). The third group had statistically significantly lower DKS (p=0.002), higher SYNTAX score (p<0.001), lower ETT duration (p=0.025), lower RPP at peak (p=0.007), lower RPP at recovery (p=0.043), and higher number of leads with ST deviation compared with the second group (p=0.011) (Table 4).

Patients who developed MACE at follow-up had significantly lower DKS (-14.5±8.9 vs -6.4±6.9, p=0.012) and lower RPP at peak (19495±6895 bpm*mmHg vs 25085±5405 bpm*mmHg, p=0.026) compared with patients without MACE at follow-up.

There were 35 patients with obstructive CAD underwent revascularization either by percutaneous or surgical revascularization after the index ETT. Eight patients with obstructive CAD did not receive revascularization. There was no statistical difference between patients with obstructive coronary disease who underwent medical treatment (n=8) and patients with obstructive coronary disease undergone revascularization (n=35) in terms of SYNTAX score, DKS, ETT duration, RPP at peak, RPP at recovery, and number of leads with ST deviation or number of MACE events at follow-up (one event in medical treatment group and 5 events in revascularization group).

Discussion

In this retrospective single-center study, we sought to identify ETT parameters that were correlated with the extent of CAD and development of MACE at follow-up. SYNTAX score, DKS, ETT duration, RPP at peak, RPP at recovery, and number of leads with ST deviation were

Table 3. Coronary angiographic findings, follow-up durations, and treatment modalities of the patients were expressed as appropriate in each group

	Low-risk group (n=24)	Intermediate-risk group (n=10)	High-risk group (n=14)	p-value
CAG result (%)				
Normal	3 (12.5)	0 (0.0)	0 (0.0)	
Non-obstructive CAD	2 (8.3)	0 (0.0)	0 (0.0)	
SVD	9 (37.5)	2 (20.0)	0 (0.0)	
2VD	7 (29.2)	4 (40.0)	0 (0.0)	0.000
3VD	3 (12.5)	2 (20.0)	4 (28.6)	
LMCA disease	0 (0.0)	0 (0.0)	2 (14.3)	
LMCA with SVD	0 (0.0)	0 (0.0)	0 (0.0)	
LMCA with 2VD	0 (0.0)	2 (20.0)	2 (14.3)	
LMCA with 3VD	0 (0.0)	0 (0.0)	6 (42.9)	
SYNTAX score (points)	7.3±5.2	19.1±1.4	28.7±4.8	0.000
Treatment method (%)				
Medical treatment	9 (37.5)	2 (20.0)	2 (14.3)	
PCI	15 (62.5)	3 (30.0)	2 (14.3)	0.000
CABG	0 (0.0)	5 (50.0)	10 (71.4)	
MACE at follow-up (%)	1 (4.2)	1 (10.0)	4 (28.6)	0.100
Follow-up duration (month)	51 (37)	46 (44)	31 (58)	0.876

CAD: Coronary artery disease CABG: Coronary artery bypass grafting, CAG: Coronary angiography, SVD: Single-vessel disease, 2VD: Two-vessel disease, 3VD: Three-vessel disease, LMCA: Left main coronary artery, MACE: Major adverse cardiovascular event, PCI: Percutaneous coronary intervention

Table 4. Comparison of study parameters among the groups classified as per CAD type

	Non-obstructive coronary arteries (n=5)	Obstructive CAD without LMCA disease (n=31)	Obstructive CAD with LMCA disease (n=12)	p-value
SYNTAX score (points)	1.8±4.0	13.7±7.9	27.6±6.0	0.000
ETT duration (minute)	7.7±1.6	7.2±2.5	5.3±2.2	0.047
ETT workload (MET)	9.2±1.5	8.9±2.4	7.3±2.0	0.081
Percentage of the maximum heart rate as a function of age-predicted target heart rate (%)	93±14	87±10	83±9	0.143
RPP at peak (bpm*mmHg)	30389±3700	25107±5292	20020±5040	0.001
RPP upon recovery (bpm*mmHg)	16386±1983	14318±3185	12682±1834	0.048
Maximum ST deviation during ETT (mm)	1.80±1.60	2.00±1.36	2.85±0.78	0.121
Number of leads with ST	7.0 (6.0)	7.0 (4.0)	8.5 (3.0)	0.033
Duke treadmill score (points)	-4.5±8.2	-5.65±6.5	-13.2±7.4	0.006
MACE at follow-up (%)	0 (0.0)	2 (6.5)	4 (33.3)	0.100
Follow-up duration (month)	55 (19)	42 (39)	31 (52)	0.608

CAD: Coronary artery disease, ETT: Exercise treadmill test, LMCA: Left main coronary artery, MACE: Major adverse cardiovascular event, MET: Metabolic equivalent, RPP: Rate-pressure product

found to be significantly different in patients with severe CAD, such as those with higher SYNTAX scores or those with significant LMCA disease.

The ETT is a widely used initial diagnostic tool for assessing cardiac complaints, such as chest pain, dyspnea, palpitation, or syncope. Sensitivity and specificity change according to the population concerned[9,10]. We also used ETT as an initial diagnostic tool to rule out obstructive CAD. It is particularly valuable and recommended for intermediate-risk patients to assess CAD[10,12]. Our study population also included middle-aged adults. The number of female patients is less compared to the literature due to the immigrant-based, male-dominant sociodemographic structure of the country. It may be considered not to include female patients in the study. However, we included all patients meeting the inclusion criteria to reflect our practice at our tertiary center as much as possible. Thus, it should be kept in mind that the clinical applicability of the study to female patients is limited.

The study population included only patients without a previous cardiac history and those without structural heart disease. Thus echocardiographic findings of the groups were similar. As is well known, longer ETT duration and higher ETT workload are associated with good prognosis among patients with CAD[11-13]. In our study, these parameters were statistically similar among the groups classified according to the SYNTAX score. Thus, other ETT parameters that differ significantly in the high-risk group can be assumed to be high-risk indicators. For example, RPP at peak and recovery were found to be lower in the high-risk group than in the others. These parameters have not been investigated in the literature.

The DTS is a well-known indicator of risk assessment, and it is widely used to triage patients with ETT exhibiting coronary ischemia[14,15]. DKS helps institutions develop their strategies for triaging patients to same-day admission, early outpatient appointments, or elective appointments, etc. In our study, DKS was also well correlated with the SYNTAX score, and the score was significantly higher in the high-risk group than in the other groups.

The amplitude of maximum ST deviation during ETT calculation is a part of the formula for calculating DKS[15]. Considering the similar frequencies of angina and ETT durations across the groups, the high-risk group was expected to have significantly more ST deviation. Additionally, our study detected a new parameter that may indicate CAD severity. This is the number of leads with ST deviation. As the severity of CAD increased, the number of leads with ST deviation increased. Although the location of ST deviation on ECG tracings does not imply the location of the lesion, the number of leads with ST deviation may indicate more global ischemia in cases of extensive obstructive CAD.

In a study by Whitman and Jenkins[16] peak RPP was found to be correlated with the development of cardiovascular events with a mean follow-up of 5.3±2.6 years. However, they did not confirm their findings with the CAD status of the subjects. Additionally, they included patients regardless of their previous CAD status. As a result, the number of MACEs at follow-up was sufficient to perform multivariate analysis and further correlation analyses. In our study, we also found that the RPP peak was significantly lower in patients who developed MACE at a follow-up period of 45 (38) months. The follow-up duration and composition of the study population did not allow to produce a higher number of MACEs at follow-up, which is necessary for advanced statistical analyses. RPP at peak was significantly higher among high-risk patients, and was well correlated with the SYNTAX score.

A novel finding in the literature, we showed that RPP at the third minute of the recovery phase was also statistically higher in high-risk patients and was well correlated with the SYNTAX score.

Detection of an LMCA lesion in patients with cardiac symptoms during ETT is of great importance to guide and expedite the treatment plan of the patients[17]. In the literature, previous studies have mostly focused on electrocardiographic changes, especially lead aVR[17,18]. In our study, we excluded the aVR to determine the importance of deviations over other leads. For this purpose, the patients were re-grouped as having obstructive CAD without LMCA and obstructive CAD with LMCA disease. We found that patients with LMCA had significantly lower DKS, ETT duration, peak RPP, recovery RPP, and a higher number of leads with ST deviation. All these parameters imply the effect of global ischemia caused by LMCA-related ischemia. Large-scale studies are needed to determine threshold ETT parameter levels for detecting LMCA lesions or warning levels for indicating the presence of LMCA lesions.

Study Limitations

This study has some limitations to be considered. First, it was a single-center study, reflecting the experience of only one center. Second, the study population was not large enough, but the relations were very strong and stronger in the case of a large-scale population. Third, the achievement of the age-predicted maximum heart rate was subject to the efforts of the patient, and this effort cannot be fully controlled. Thus, there may be an element of subjectivity between the groups that cannot be avoided. Lastly, the exact cutoff values of the ETT parameters have not been validated in large-scale studies, which is a major limitation of ETT studies. This fact is also valid for our study.

Conclusion

In conclusion, surrogates of ETTs, such as DTS, RPP at peak, RPP at recovery, and number of leads with ST deviation, are well correlated with the extent of CAD, presence of LMCA lesions, and development of MACE at follow-up. Large-scale prospective studies are needed to determine cut-off values for these parameters to imply the severity of CAD and/or the presence of LMCA lesions.

Ethics

Ethics Committee Approval: The study protocol was approved by Hamad Medical Corporation Ethical and Institutional (approval no.: MRC-01-21-279 date: 23.03.2021).

Informed Consent: This retrospective study included patients with positive ETT results for coronary ischemia who underwent invasive coronary angiography after the index ETT.

Authorship Contributions

Surgical and Medical Practices: Ede H, Ahmed HSS, Mahfouz AS, Bedardeen UK, Manoher G, Raja SA, Choyimadathil A, Al Okka LS, Damodharan PP, Al-Hashemi MA, Al-Qahtani AAR, Asaad NA, Concept: Ede H, Ahmed HSS, Mahfouz AS, Bedardeen UK, Manoher G, Raja SA, Choyimadathil A, Al Okka LS, Damodharan PP, Design: Ede H, Ahmed HSS, Mahfouz AS, Bedardeen UK, Manoher G, Raja SA, Choyimadathil A, Al Okka LS, Damodharan PP, Data Collection and/or Processing: Ede H, Ahmed HSS, Mahfouz AS, Bedardeen UK, Manoher G, Raja SA, Choyimadathil A, Al Okka LS, Damodharan PP, Al-Hashemi MA, Al-Qahtani AAR, Asaad NA, Analysis and/or Interpretation: Ede H, Ahmed HSS, Mahfouz AS, Bedardeen UK, Manoher G, Raja SA, Choyimadathil A, Al Okka LS, Damodharan PP, Al-Hashemi MA, Al-Qahtani AAR, Asaad NA, Literature Search: Ede H, Ahmed HSS, Mahfouz AS, Bedardeen UK, Manoher G, Raja SA, Choyimadathil A, Al Okka LS, Damodharan PP, Al-Hashemi MA, Al-Qahtani AAR, Asaad NA, Writing: Ede H, Ahmed HSS, Mahfouz AS, Bedardeen UK, Manoher G, Raja SA, Choyimadathil A, Al Okka LS, Damodharan PP, Al-Hashemi MA, Al-Qahtani AAR, Asaad NA.

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