DOI: 10.7860/JCDR/2023/63982.18325

Original Article

Internal Medicine Section

Significance of Rate-pressure Product and Duke Treadmill Score in Predicting Disease Severity in Patients with Coronary Artery Disease: A Cross-sectional Study

EV SHAVEEN[1], K JAYAPRAKASH[2], V SUDHAKUMARY[3], SURESH MADHAVAN[4], CICY BASTIAN[5], VL JAYAPRAKASH[6]

ABSTRACT

Introduction: Exercise electrocardiography is a well-established and cost-effective investigation for evaluating Coronary Artery Disease (CAD). The Rate-pressure Product (RPP), which is the product of maximal Systolic Blood Pressure (SBP) and peak Heart Rate (HR) during exercise, is a widely accepted parameter reflecting cardiac work and evaluating ventricular function. The use of Duke Treadmill Score (DTS) improves the diagnostic accuracy of exercise-induced ST-segment depression and has been observed to provide independent prognostic information. It has been shown that DTS provides information about the complexity of coronary artery lesions assessed by invasive coronary artery testing.

Aim: To determine the significance of RPP and DTS in predicting the severity and complexity of angiographic lesions in patients with Stable Ischemic Heart Disease (SIHD) and a positive Treadmill Test (TMT).

Materials and Methods: This study involved 100 consecutive patients with a positive TMT but no prior history of Acute Coronary Syndrome (ACS) who underwent coronary angiography at Government Medical College, Kottayam, Kerala, India, between March 2018 and March 2019 after obtaining ethical clearance from the Institutional Review Board. The DTS and RPP were calculated for these patients. All patients then underwent coronary angiography, and their SYNTAX scores were calculated. Correlation analysis was performed to assess the relationship between DTS, RPP, and SYNTAX score using Spearman's correlation coefficient. The Kruskall-Wallis test was used to compare risk factors among groups.

Results: A total of 100 patients were evaluated, ranging in age from 40 to 74 years with an average age of 57 years. The average SYNTAX score was 15, ranging from 2 to 56. The average Duke TMT score was -5.2, ranging from 6 to -22. There was a significant negative correlation between DTS and angiographic severity determined by SYNTAX score (r=-0.702, p=0.001). The average RPP was 22174, ranging from 14000 to 37620. The study showed a significant negative correlation between RPP and SYNTAX score (r=-0.201, p=0.04). Diabetic patients had a significantly higher SYNTAX score compared to non-diabetics (r=-0.602, p=0.013). Additionally, a significant negative correlation was observed between the Metabolic Equivalents (METs) attained, duration of exercise, and the SYNTAX score.

Conclusion: DTS and RPP derived from the exercise treadmill test have a significant negative correlation with the severity and complexity of CAD as determined by the SYNTAX score in coronary angiography.

Keywords: Stable ischaemic heart disease, SYNTAX score, Tread mill test

INTRODUCTION

Exercise testing is widely used for the diagnosis of CAD and to assess disease severity and prognosis. The increasing use of cardiac imaging procedures has resulted in a marked increase in healthcare expenditures for CAD assessment [1,2]. Exercise Electrocardiogram (ECG) remains the least expensive investigation for diagnosing patients with suspected CAD [1]. Using the standard diagnostic criteria, the exercise ECG test has a sensitivity of 68% and specificity of 77% [3]. However, its sensitivity and specificity are limited compared to other exercise-based diagnostic tests such as Stress Echocardiography or exercise thallium-201 myocardial perfusion imaging. To improve the sensitivity and specificity of the exercise ECG test, various scoring systems have been introduced. The Duke Treadmill Score (DTS) [4,5] is a widely validated index used to enhance the diagnostic accuracy of the exercise ECG test. It has been observed that assessing DTS provides additional information about the complexity of CAD before invasive investigations such as coronary angiography. Similarly, the Rate-pressure Product (RPP) has been recognised as another parameter for predicting disease severity [6]. RPP is calculated by multiplying SBP and peak HR and correlates well with myocardial oxygen consumption. Previous studies have shown that a higher RPP is associated with less significant CAD [7,8], good ventricular function, and a non-ischemic status [9].

The SYNTAX (Synergy between PCI with Taxus and Cardiac Surgery) score was developed as part of the SYNTAX trial to objectively quantify the severity and extent of CAD [10]. Each significant lesion (defined as a diameter stenosis of >50% in vessels with a minimum diameter of 1.5 mm) is visually assessed in the angiogram and analysed according to the American College of Cardiology/American Heart Association lesion classification system. Each coronary artery segment is given a score based on lesion morphology and complexity. The scores of individual lesions are summed to derive the final score. The derived score was categorised into three groups as evaluated in the SYNTAX trial (low: 0 to 22, intermediate: 23 to 32, high: >32) [10,11].

The aim of the present study was to determine the significance of RPP and DTS in predicting the severity and complexity of coronary artery stenosis in patients with SIHD and a positive TMT and to define cut-off points for identifying complex coronary anatomy through non-invasive evaluation. If there is a significant correlation between DTS and RPP with the SYNTAX score in the present study, it may be possible to predict the severity of angiographic lesions in patients with stable CAD noninvasively based on these parameters.

MATERIALS AND METHODS

This was a cross-sectional study conducted from March 2018 to March 2019 in the Department of Cardiology, Government Medical College, Kottayam, Kerala, India. Ethical clearance was obtained from the Institutional Review Board with approval number 64/2018 dated 30-10-2018.

Sample size estimation: was done using the formula: Sample size for proportions=(Z^2*P*Q)/d^2. Using the values at a 95% confidence level, a sample size of 94 was obtained, which was rounded off to one hundred (100).

Inclusion criteria: Patients with exertional angina or exertional dyspnoea with a positive TMT undergoing coronary angiography from March 2018 in the Cardiology Department of a tertiary-level academic healthcare institution were included in the study.

Exclusion criteria: Patients with previous ST elevation Myocardial Infarction, Non-ST Elevation Acute Coronary Syndrome (NSTE ACS), coronary artery bypass graft, previous Percutaneous Transluminal Coronary Angioplasty (PTCA), or valvular heart disease were excluded from the study.

Procedure

After obtaining informed consent, patients were evaluated clinically. Baseline investigations including 2D echo were performed. These patients were then subjected to a Treadmill test using the Bruce protocol [5]. The functional capacity of the patients in terms of Metabolic Equivalents (METs) attained during the exercise stress test was recorded [12]. DTS and RPP were calculated in those patients with a positive TMT. DTS was calculated using the following equation: DTS=exercise time-(5×ST deviation)-(4×exercise angina index). The exercise angina index was expressed in terms of the severity of angina during the test:

- 0- no angina;
- 1- non-limiting angina;
- 2- exercise-limiting angina.

The DTS was grouped into low-risk (with a score of ≥ +5), moderate-risk (with scores ranging from -10 to +4), and high-risk (with a score of ≤ -11) categories [5]. The RPP was calculated by multiplying the maximum HR with the maximum SBP [13].

Patients with a positive TMT then underwent coronary angiographic study. Coronary angiography was performed through a radial approach. Femoral access was chosen when the radial approach was not feasible due to technical reasons. A coronary lesion was considered significant when the stenosis of the left main coronary artery was ≥50%. For the other coronary arteries, stenosis ≥70% was considered significant.

The overall SYNTAX score was calculated by scoring each coronary lesion independently based on pre-determined lesion features in arteries with a caliber of 1.5 mm and 50% diameter stenosis. Patients were divided based on SYNTAX scores:

- Low (≤22),
- Intermediate (≥23 to 32),
- High (≥ 33) [10].

The DTS, RPP, and SYNTAX score were evaluated and correlated among all the patients.

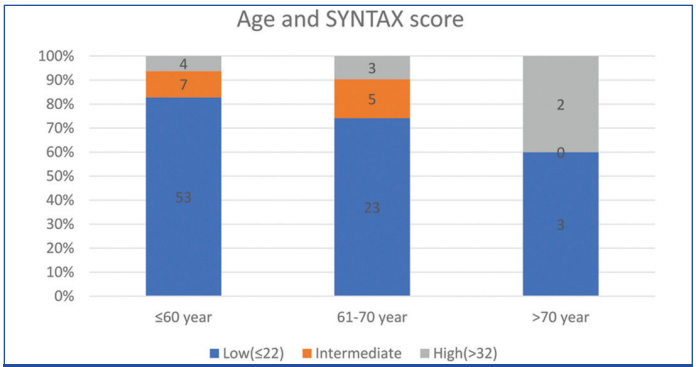
STATISTICAL ANALYSIS

Statistical analysis was performed using IBM Statistical Package for Social Sciences (SPSS) version 18.0. Continuous and normally distributed variables were presented as mean±Standard Deviation (SD). Spearman's correlation analysis was used to assess the correlation between DTS and the SYNTAX score, RPP and the SYNTAX score. A p-value ≤0.05 was considered statistically significant.

RESULTS

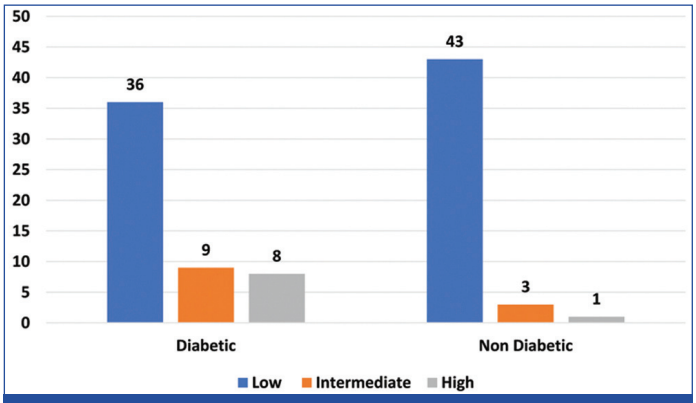
One hundred patients were evaluated. The age of these patients ranged from 40 to 74 with an average age of 57 years. Most of the patients presented with effort angina as the predominant symptom. Another common presenting symptom was dyspnoea on exertion. Sixty-one patients (61%) were males, and 39 (39%) were females. The most common risk factor associated was hypertension. A total of 57 patients were hypertensive, and 53 were diabetic. Dyslipidemia was found in 10 patients. Thirty-nine patients were smokers, and 31 patients consumed alcohol.

One patient had CKD, and three patients were diagnosed with hypothyroidism. Two patients had a history of CVA. Three patients had baseline regional wall motion abnormality, and one patient had left ventricular dysfunction. The average SYNTAX score was 15 and ranged from 2 to 56. The average Duke TMT score of the patients was -5.2 and ranged from 6 to -22. Most patients below 60 years had a low SYNTAX score (n=53, 82%). In the age group between 61-70 years, proportionately more patients belonged to the intermediate or high SYNTAX score (n=8, 25.8%), and in patients aged more than 70 years, 40% (n=2) had a high SYNTAX score; however, the difference was not statistically significant (p=0.459) [Table/Fig-1].



[Table/Fig-1]: Effect of age group on SYNTAX score.

In diabetic patients, the SYNTAX score was significantly higher compared to non-diabetics (r=-0.602, p=0.013) [Table/Fig-2]. There was no significant influence of sex category on the SYNTAX score in the study population (p=0.837). No significant difference was observed in the anatomical complexity of the stenosis assessed by the SYNTAX score between patients with and without hypertension (p=0.137). Smoking and alcoholism did not significantly influence the SYNTAX score (p=0.128 and 0.176).



[Table/Fig-2]: Effect of diabetes on Syntax score.

There was a significant negative correlation between DTS and angiographic severity assessed by the SYNTAX score (r=-0.702, p=0.001). The high-risk DTS group and the medium-risk group had a higher SYNTAX score, 44.4% and 55.6%, respectively, whereas none of the low-risk DTS group had a high SYNTAX score [Table/Fig-3,4]. It was observed that patients with a DTS score of one or more had a lower chance of having a SYNTAX score of more than 22 (p=0.03). There was a significant negative correlation

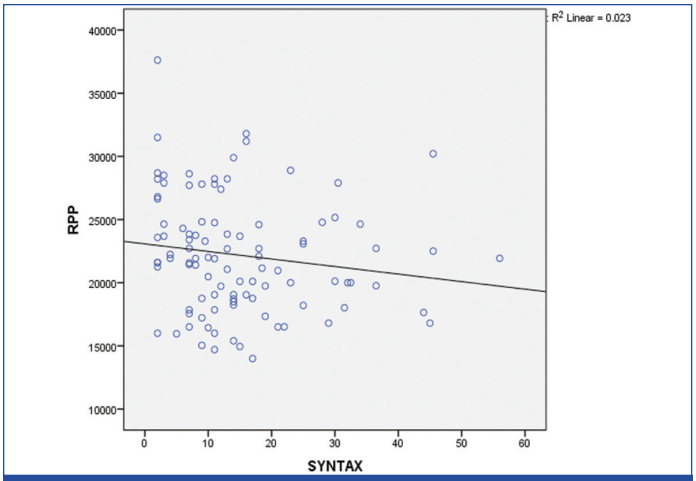
between RPP and the SYNTAX score (R=-0.201, p=0.04) [Table/Fig-5,6]. Additionally, the Spearman correlation showed a significant negative correlation between exercise duration and the SYNTAX score (R=-0.387, p=0.02) [Table/Fig-7], as well as between METs achieved and the SYNTAX score (R=-0.287, p=0.01).

			Syntax score class			Total	p-value
			Low	Intermediate	High		
DTS class	Low risk group	Count	2	0	0	2	0.001
		% Within syntax score class	2.5%	0.0%	0.0%	2.0%	
	Medium risk group	Count	64	8	5	77	
		% Within syntax score class	81.0%	66.7%	55.6%	77.0%	
	High-risk group	Count	13	4	4	21	
		% Within syntax score class	16.5%	33.3%	44.4%	21.0%	
Total		Count	79	12	9	100	
		% Within syntax score class	100.0%	100.0%	100.0%	100.0%	

[Table/Fig-3]: DTS Class- Syntax Score class cross tabulation.

DTS	Syntax		p-value
	Less than 22	22 or more	
0 or less	59 (75.6%)	21 (95.5%)	0.03
1 or more	19 (24.4%)	1 (4.5%)	

[Table/Fig-4]: Relation between DTS and SYNTAX Score.

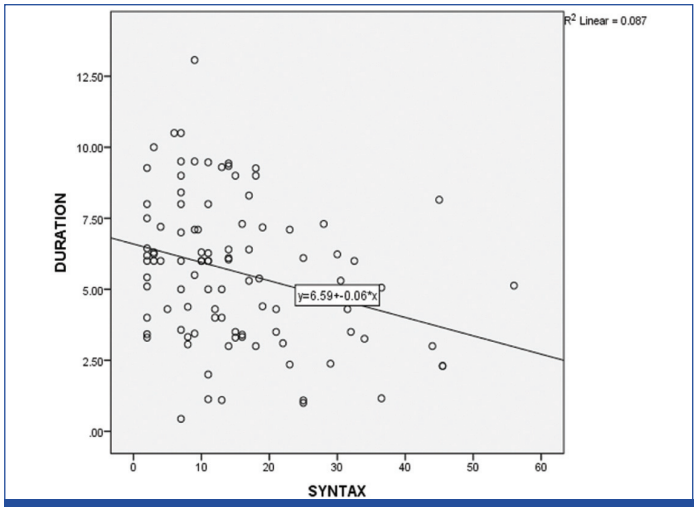


[Table/Fig-5]: Correlation between SYNTAX score and Rate Pressure Product (RPP).

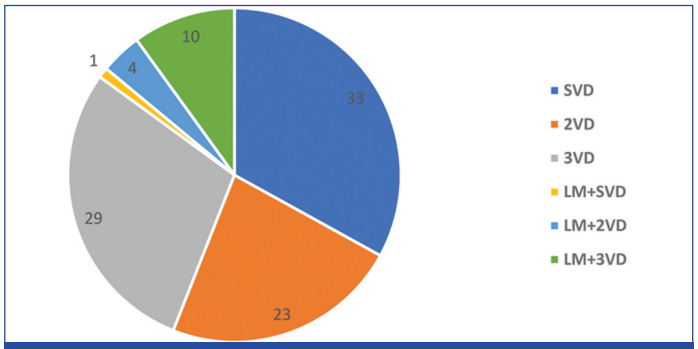
			RPP	SYNTAX
Spearman's rho	RPP	Correlation coefficient	1.000	-0.201*
		Sig. (2-tailed)	-	0.045
		N	100	100
	SYNTAX	Correlation coefficient	-0.201*	1.000
		Sig. (2-tailed)	0.045	-
		N	100	100

[Table/Fig-6]: Rate Pressure Product (RPP)-SYNTAX score Correlations.
*Correlation is significant at the 0.05 level (2-tailed)

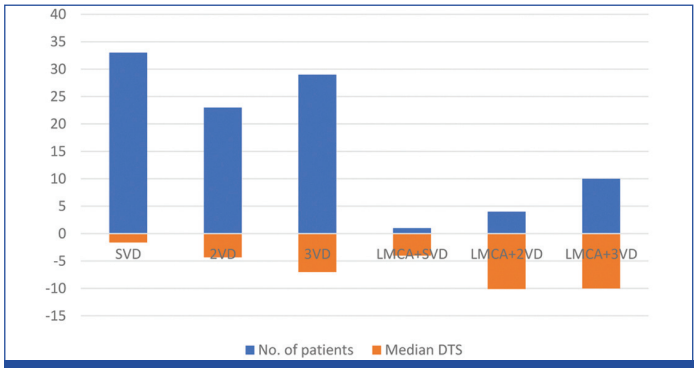
In the study population, 33% had single vessel disease, 29% had three vessel disease, 23% had double vessel disease, and 15% had left main CAD, either alone or with disease in other vessels [Table/Fig-8]. The median RPP was highest among patients with single vessel disease and lowest in patients with left main coronary artery stenosis with three vessel disease. DTS was lowest in patients with left main coronary artery stenosis associated with either double or triple vessel disease. DTS was highest in patients with single vessel disease [Table/Fig-9].



[Table/Fig-7]: Correlation between exercise duration and SYNTAX score.



[Table/Fig-8]: Pattern of coronary artery involvement.
SVD: Single vessel disease; 2VD: Two vessel disease, 3VD: Three vessel disease; LM: Left main coronary artery



[Table/Fig-9]: Coronary artery involvement and median Duke tread mill score.
SVD: Single vessel disease; 2VD: Two vessel disease; 3VD: Three vessel disease; LMCA: Left main coronary artery

DISCUSSION

The present study analysed the significance of RPP and DTS in predicting significant angiographic lesions in patients with stable CAD and a positive TMT. There was a significant negative correlation between DTS and angiographic severity assessed by the SYNTAX score (r=-0.702, p=0.001). The high-risk DTS group and the medium-risk group had a higher SYNTAX score compared to the low-risk group, 44.4% and 55.6%, respectively. This is in line with the study by Dzenkeviciute V et al., which showed a significant negative correlation between DTS and significant coronary artery stenosis using the SYNTAX score (r=-0.181, p=0.005) [4]. Shaw LJ et al., observed that 83% of high-risk DTS patients had 2-vessel or 3-vessel or left main coronary disease [14]. Low-risk patients had

no significant coronary stenosis (60%) or had single vessel coronary disease (16%).

The present study was able to find a negative correlation between RPP and the SYNTAX score (r=-0.201, p=0.04). A similar correlation was observed in the study conducted by Fornitano LD and Godoy MF [15]. They divided patients into two groups: those who achieved RPP above 30,000 (Group-A) and those below that (Group-B). Significant coronary artery involvement was observed in 48.7% of patients in Group-B compared to 24% in Group-A (Fisher-exact test; p=0.0034; Odds Ratio 0.3327).

Exercise capacity measured in METs has a strong correlation with future cardiovascular events, with higher workloads predicting improved survival rates [12]. Exercise capacity above 10 METs was associated with low mortality, even in patients with significant CAD [12]. In addition to the primary objective, the study also found a negative correlation between the METs attained, duration of exercise, and the SYNTAX score. In another study involving 122,007 consecutive patients undergoing exercise stress testing, patients with the highest functional capacity were associated with the lowest risk-adjusted all-cause mortality [16].

The present study was able to demonstrate that patients with diabetes had more severe CAD as assessed by the SYNTAX Score. Earlier studies have suggested that the overall prevalence and prognosis of CAD in diabetes are high [17]. The severity of CAD was found to be high in diabetes when compared to the non-diabetic population [18]. In a study by Srinivasan MP et al., it was observed that patients with diabetes of more than five years had more severe disease than non-diabetics [19]. Findings from the study by Shaw LJ et al., demonstrated angiographically more severe disease in diabetic patients than in non-diabetic controls [14].

Limitation(s)

Selection bias in cases as it was a single-center study and it may not reflect the trend in the community. Larger multicenter community-based studies are needed. Although a negative correlation was obtained between RPP and the SYNTAX score, a specific cut-off value above which the absolute risk increased could not be defined. Larger multicenter community-based studies in the future may overcome these limitations.

CONCLUSION(S)

The exercise ECG test is a useful and cost-effective investigation for the evaluation of CAD, and the diagnostic value may be enhanced by analysing the DTS and RPP. The study demonstrated a negative correlation between DTS, RPP, and the complexity of coronary anatomy assessed by the SYNTAX score. Diabetic patients had more severe CAD with a significantly high SYNTAX score compared to the non-diabetic population. There was also a negative correlation between exercise duration, METs achieved, and the SYNTAX score in coronary angiogram.

REFERENCES

[1] Vaidya GN, Application of exercise ECG stress test in the current high cost modern-era healthcare system, Indian Heart J. 2017;69(4):551-55.
[2] Lauer MS. Elements of danger-the case of medical imaging. N Engl J Med. 2009;361(9):841-43.
[3] Pais P, Treadmill stress tests should not be part of "routine health check package", Indian Heart J. 2018;70(6):934-36.
[4] Dzenkeviciute V, Sapoka V, Kasiulevicius V, Rinkuniene E, Steponeniene R, Einikyte R, et al. Value of Duke treadmill score in predicting coronary artery lesion and the need for revascularisation. Kardiologia Polska. 2017;75(5):439-44.
[5] Wolk MJ, Bailey SR, Doherty JU, Douglas PS, Hendel RC, Kramer CM, et al. ACCF/AHA/ASE/ASNC/HFSA/HRS/SCAI/SCCT/SCMR/STS 2013 multimodality appropriate use criteria for the detection and risk assessment of stable ischemic heart disease: A report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, American Heart Association, American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Failure Society of America, Heart Rhythm Society, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, Society for Cardiovascular Magnetic Resonance, and Society of Thoracic Surgeons. J Am Coll Cardiol. 2014;63(4):380-406.
[6] El-Dosouky II, Abomandour HG. Rate pressure product and severely impaired systolic function in heart failure patients. Clinical & Experimental Cardiology. 2019;10(5). https://www.longdom.org/open-access/rate-pressure-product-and-severely-impaired-systolic-function-in-heart-failure-patients-heart-failure-and-severe-systoli-52623.html.
[7] Jiang ZH, Aierken A, Wu TT, Zheng YY, Ma YT, Xie X, Rate pressure product as a novel predictor of long-term adverse outcomes in patients after percutaneous coronary intervention: a retrospective cohort study. BMJ Open. 2023;13(4):e067951.
[8] Whitman M, Jenkins C, Sabapathy S, Adams L. Comparison of heart rate blood pressure product versus age-predicted maximum heart rate as predictors of cardiovascular events during exercise stress echocardiography. Am J Cardiol. 2019;124(4):528-33.
[9] Whitman M, Jenkins C, Rate pressure product, age predicted maximum heart rate or heart rate reserve. Which one better predicts cardiovascular events following exercise stress echocardiography? Am J Cardiovasc Dis. 2021;11(4):450-57
[10] Sianos G, More MA, Kappetein AP, Morice MC, Colombo A, Dawkins K, et al. The SYNTAX score: An angiographic tool grading the complexity of coronary artery disease. EuroIntervention. 2005;1(2):219-27.
[11] Serruys PW, Morice MC, Kappetein AP, Colombo A, Holmes DR, Mack MJ, et al. SYNTAX Investigators. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. N Engl J Med. 2009;360(10):961-72.
[12] Kharabsheh SM, Al-Sugair A, Al-Buraiki J, Al-Farhan J. Overview of exercise stress testing. Ann Saudi Med. 2006;26(1):01-06.
[13] Stoschitzky K, Blood pressure, heart rate, or the rate pressure product: what is the best predictor of clinical outcome? European Heart Journal Open. 2022;2(5):oeac063. 01-02.
[14] Shaw LJ, Peterson ED, Shaw LK, Kesler KL, DeLong ER, Harrell FE, et al. Use of a prognostic treadmill score in identifying diagnostic coronary disease subgroups. Circulation. 1998;98(16):1622-30.
[15] Fornitano LD, Godoy MF. Increased rate-pressure product as predictor for the absence of significant obstructive coronary artery disease in patients with positive exercise test. Arq Bras Cardiol. 2006;86(2):138-44.
[16] Mandsager K, Harb S, Cremer P, Phelan D, Nissen SE, Jaber W. Association of cardiorespiratory fitness with long-term mortality among adults undergoing exercise treadmill testing. JAMA Netw Open. 2018;1(6):e183605.
[17] Aronson D, Edelman ER. Coronary artery disease and diabetes mellitus. Cardiol Clin. 2014;32(3):439-55.
[18] Sponder M, Fritzer-Szekeres M, Marculescu R, Litschauer B, Strametz-Juranek J. A new coronary artery disease grading system correlates with numerous routine parameters that were associated with atherosclerosis: a grading system for coronary artery disease severity. Vasc Health Risk Manag. 2014;10:641-47.
[19] Srinivasan MP, Kamath PK, Bhat NM, Pai ND, Bhat RU, Shah TD, et al. Severity of coronary artery disease in type 2 diabetes mellitus: Does the timing matter? Indian Heart J. 2016;68(2):158-63.

PARTICULARS OF CONTRIBUTORS:
1. Consultant Cardiologist, Department of Cardiology, Sree Narayana Institute of Medical Science, Chalakka, Kuthiathode, Kerala, India.
2. Additional Professor, Department of Cardiology, Government Medical College, Ernakulam, Kerala, India.
3. Associate Professor, Department of Cardiology, Government Medical College, Kottayam, Kerala, India.
4. Additional Professor, Department of Cardiology, Government Medical College, Kottayam, Kerala, India.
5. Professor, Department of Cardiology, Government Medical College, Ernakulam, Kerala, India.
6. Professor, Department of Cardiology, Government Medical College, Kottayam, Kerala, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. K Jayaprakash,
"Sreelekshmi", Arattukadavu Road, Gandhinagar, P.O. Kottayam-686008, Kerala, India.
E-mail: jayaprakashkpillai@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Mar 18, 2023
- Manual Googling: May 24, 2023
- iThenticate Software: Jul 31, 2023 (15%)

ETYMOLOGY: Author Origin

EMENDATIONS: 10

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Mar 09, 2023**
Date of Peer Review: **Apr 27, 2023**
Date of Acceptance: **Aug 03, 2023**
Date of Publishing: **Sep 01, 2023**