ARCHIVES OF THE TURKISH SOCIETY OF CARDIOLOGY

Official journal of the TURKISH SOCIETY OF CARDIOLOGY

Is There a Relationship Between Metabolic Equivalence and the SYNTAX Score as Strong Prognostic Markers?

Güçlü Prognostik Belirteçler Olan Metabolik Eşdeğer ve SYNTAX Skoru Arasında Bir İlişki Var Mıdır?

ORIGINAL ARTICLE
KLİNİK ÇALIŞMA

ABSTRACT

Objective: The metabolic equivalent (MET) and Synergy between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery (SYNTAX) score are two parameters with known cardiovascular prognostic significance. In this study, we aimed to investigate the direct relationship between MET and SYNTAX score in patients with chronic coronary syndrome (CCS).

Method: This retrospective study included 200 patients over 18 years of age who underwent coronary angiography and had a positive exercise electrocardiography test result. Patients were divided into two groups: Group 1 with a low SYNTAX score and Group 2 with a medium-high SYNTAX score. MET values were then compared between these groups.

Results: Baseline demographic characteristics and laboratory values were similar between the groups. The mean MET values in the low and medium-high SYNTAX score groups were 9.36 ± 2.38 and 8.78 ± 2.43, respectively. No statistical difference was observed (P = 0.086). Additionally, there was no statistical difference between the two groups in terms of MET values being 10 ≤ or 10 > (P = 0.172).

Conclusion: The main conclusion of our study is that there is no correlation between the SYNTAX score and functional MET value in CCS.

Keywords: Chronic coronary syndrome, metabolic equivalent, SYNTAX score

ÖZET

Amaç: Metabolik eşdeğer (MET) ve SYNTAX skoru kardiyovasküler prognostik önemi bilinen iki parametredir. Bu çalışmada, kronik koroner sendrom (KKS) hastalarında MET ile SYNTAX skorunun doğrudan ilişkiyi araştırmayı amaçladık.

Yöntem: Bu retrospektif çalışmaya koroner anjiyografi yapılan ve pozitif egzersiz elektrokardiyografi testi sonucu olan 18 yaş üstü 200 hasta dahil edildi. Hastalar iki gruba ayrıldı: Düşük SYNTAX skoru olan Grup 1 ve orta-yüksek SYNTAX skoru olan Grup 2. Ardından bu gruplar arasında MET değerleri karşılaştırıldı.

Bulgular: Hastaların bazal demografik özellikleri ve laboratuvar değerleri benzerdi. Düşük ve orta-yüksek SYNTAX skoru gruplarında ortalama MET değeri sırasıyla 9,36 ± 2,38 ve 8,78 ± 2,43 olarak saptandı. İstatiksel farklılık izlenmedi (P = 0,086). Ayrıca, MET değerlerinin 10 ≤ veya 10 > olması açısından yapılan değerlendirmede her iki grup arasında istatistiksel fark saptanmadı (P = 0,172).

Sonuç: Çalışmamızda saptadığımız temel sonuç, KKS'de SYNTAX skoru ile fonksiyonel MET değeri arasında ilişki olmadığıdır.

Anahtar Kelimeler: Kronik koroner sendrom, metabolik eşdeğer, SYNTAX skoru

Gökhan Ergün[1]
Halime Tanrıverdi[1]
Erkan Demirci[1]
Yasemin Doğan[1]
Yücel Yılmaz[1]
Şaban Keleşoğlu[2]
Ziya Şimşek[1]
Selami Demirelli[1]

[1]*Department of Cardiology, University of Health Sciences, Kayseri City Training and Research Hospital, Kayseri, Türkiye*
[2]*Department of Cardiology, Erciyes University Faculty of Medicine, Kayseri, Türkiye*

Corresponding author:
Gökhan Ergün
✉ 2015.drergun@gmail.com

Received: August 02, 2023
Accepted: September 28, 2023

Cite this article as: Ergün G, Tanrıverdi H, Demirci E, et al. Is there a relationship between metabolic equivalence and the syntax score as strong prognostic markers? *Turk Kardiyol Dern Ars.* 2024;52(2):110-115.

DOI:10.5543/tkda.2023.20745

The exercise electrocardiography test (EET) is a test that is frequently requested for patients presenting at the cardiology polyclinic with symptoms such as chest pain and dyspnea. EET is used as an adjunct to other tests, particularly in diagnosing chronic coronary syndrome (CCS), determining functional capacity, and/or predicting cardiovascular prognosis. Many parameters can be determined during the EET. The most frequently used of these are maximum heart rate, maximum blood pressure, maximum ST depression, the Duke treadmill score (DTS), and post-exercise heart rate recovery time (HRRT). Some of these parameters have been associated with the severity of coronary artery disease (CAD), and some have prognostic importance. In a previous study, a significant relationship was found between DTS and the SYNergy between percutaneous coronary intervention (PCI) with TAXUS and Cardiac Surgery (SYNTAX) score, concluding that DTS is an important prognostic tool.[1] Another study suggested that DTS alone was a useful marker in cases with suspected severe coronary artery narrowing.[2] Research involving post-exercise HRRT identified a relationship between post-exercise HRRT and the presence of CAD,[3] and a reduced post-exercise HRRT in stable CAD was associated with a high SYNTAX score.[4]

Another parameter measured in EET is the metabolic equivalent (MET), which is a marker of functional capacity. One MET is defined as the amount of oxygen consumption in a resting condition, averaging 3.5 ml O_2/kg/min for an adult.[5] In a review published in 2021, an increase of 1 unit in the MET value was associated with a lower risk of all-cause mortality in patients with CAD.[6] Additionally, a MET value of 10 is important in EET and is often used as a threshold in studies. A study found that patients achieving ≥ 10 MET in EET had a very low prevalence of inducible ischemia and excellent prognoses.[7]

The SYNTAX score, first introduced in 2005, objectively evaluates the extent and severity of CAD.[8] A previous study has shown that higher SYNTAX scores are associated with higher rates of major cardiovascular events in patients with diabetes and stable ischemic heart disease.[9]

There are two primary reasons for planning this study. First, considering the association of EET parameters such as HRRT and DTS with the SYNTAX score, it is plausible that the MET value is also associated with the SYNTAX score. Second, since a high MET value indicates good cardiovascular prognosis and a high SYNTAX score suggests poor cardiovascular prognosis, there may be a correlation between these two parameters. Therefore, this study was planned with the hypothesis that there could be a negative correlation between the SYNTAX score and the MET value. The MET value was hypothesized to be a potential tool for estimating the SYNTAX score before coronary angiography. As there are no studies in the literature demonstrating a relationship between the SYNTAX score and the MET value, this study aims to make a significant contribution to the literature by being the first to investigate a direct relationship between these two parameters.

ABBREVIATIONS

ACC/AHA	American College of Cardiology/American Heart Association
AUC	Area under the curve
CABG	Coronary arterial bypass graft
CAD	Coronary artery disease
CCS	Chronic coronary syndrome
CTO	Chronic total occlusion
ECG	Electrocardiogram
EET	Exercise electrocardiography test
FSSQFR	Functional SYNTAX score based on quantitative flow rate
HRRT	Heart rate recovery time
MET	Metabolic equivalent
PCI	Percutaneous coronary intervention
SYNTAX	Synergy between percutaneous coronary intervention with TAXUS and cardiac surgery

Materials and Methods

This retrospective study included patients aged 18 years and older who presented at the Cardiology Polyclinic and underwent coronary angiography due to suspected CCS. Patients were excluded from the study if they had acute coronary syndrome, a history of bypass surgery, known chronic renal, liver, or cardiac failure, bundle branch block and ST-T alteration on baseline electrocardiogram (ECG), a history of malignancy, known asthma/chronic obstructive pulmonary disease, a history of inflammatory or rheumatological disease, or the presence of an active infection. A retrospective evaluation was conducted on the records of patients diagnosed with major CAD (> 50% narrowing in the epicardial arteries) following coronary angiography (CAG), and 200 consecutive patients with a positive EET result prior to CAG were included in the study.

The EET was performed on all patients following the modified Bruce protocol. Before the exercise test, resting heart rate, blood pressure, and a 12-lead ECG were recorded in both supine and upright positions. Heart rate, blood pressure, and ECG were then recorded at every minute of the exercise. The ECG recordings obtained were evaluated according to the American College of Cardiology/American Heart Association (ACC/AHA) guidelines.[10] In the exercise electrocardiography evaluation, patients exhibiting > 1 mm horizontal or downsloping ST depression 60-80 milliseconds (msn) from the J point, or those with typical angina or angina-equivalent symptoms were considered to have a positive EET. The EET results of all the patients were evaluated by two experienced cardiology specialists, and those with a positive EET were selected for MET value recording.

Selective coronary angiography was performed on all patients using the Judkins technique in multiple projections. The SYNTAX scores of patients with vessel diameters > 1.5 mm were calculated through the website syntaxscore.org. The CAG results of all patients were evaluated by two experienced cardiology specialists.

For laboratory tests, blood samples were taken from all patients after 12 hours of fasting before the angiography. A comprehensive metabolic panel and full blood count evaluation were performed for each patient.

Patients were divided into two groups based on their SYNTAX scores: low SYNTAX score (≤ 22) and moderate-high SYNTAX score (≥ 23). The MET values were then compared between these two groups. With 10 METs established as the threshold for ischemia,[11] patients were further categorized into two groups based on their MET values: those below 10 and those above 10. Comparisons were then made between these groups.

The study was conducted in strict compliance with the principles of the Declaration of Helsinki. Approval was granted by the Kayseri City Training and Research Hospital Clinical Research Ethics Committee (Approval Number: 788, Date: 31.01.2023).

Statistical Analysis

Data from the study were analyzed using IBM Statistical Package for the Social Sciences (SPSS) Statistics Standard

Table 1. Comparison of Basic Clinical, Demographic Characteristics, and Laboratory Values

	Group 1 n = 156	Group 2 n = 44	*P*
Age	58.68 ± 8.59	59.16 ± 10.02	0.753
Sex, M/F, n (%)	36 (81.8)/120 (76.9)	8 (18.2)/36 (23.1)	0.489
BMI	29.47 ± 4.05	28.7 ± 3.57	0.266
HT, n (%)	64 (41)	12 (27.2)	0.097
DM, n (%)	52 (33.3)	16 (36.3)	0.708
HL, n (%)	38 (24.3)	13 (29.5)	0.486
CAD, n (%)	40 (25.6)	6 (13.6)	0.095
Glucose (mg/dL)	143.44 ± 69.32	151.68 ± 76.45	0.351
GFR (mL/min/1.73 m^2)	90.3 ± 13.67	86.05 ± 16.02	0.243
LDL (mg/dL)	122.19 ± 36.53	134.86 ± 41.71	0.064
TG (mg/dL)	203.33 ± 97.49	222.8 ± 98.16	0.160
HDL (mg/dL)	41.74 ± 13.77	39.91 ± 10.58	0.548
White Blood Cell (/mL)	7,706.28 ± 2,111.41	7,774.09 ± 1,727.19	0.756
Hemoglobin (g/L)	14.94 ± 1.54	15 ± 1.44	0.907
Platelet (10^3/mL)	258.19 ± 70.51	268.14 ± 74.18	0.411

Group 1: Low SYNTAX score (≤ 22), Group 2: Medium-high SYNTAX score (≥ 23).
BMI, Body Mass Index; CAD, Coronary Artery Disease; DM, Diabetes Mellitus; F, Female; GFR, Glomerular Filtration Rate; HDL, High-Density Lipoprotein; HL, Hyperlipidemia; HT, Hypertension; LDL, Low-Density Lipoprotein; M, Male; SYNTAX, SYNergy between PCI with TAXUS and Cardiac Surgery; TG, Triglyceride.

Table 2. Comparison of Coronary Angiographic Results

	Group 1 n = 156	Group 2 n = 44	*P*
SYNTAX Score	9.62 ± 6.07	34.06 ± 8.56	**0.001**
CTO n (%)	22 (14.1)	29 (65.9)	**0.001**
PCI n (%)	95 (60.8)	10 (22.7)	**0.001**
CABG n (%)	20 (12.8)	29 (65.9)	**0.001**

Group 1: Low SYNTAX score (≤ 22), Group 2: Medium-high SYNTAX score (≥ 23).
CABG, Coronary Arterial Bypass Graft; CTO, Chronic Total Occlusion; PCI, Percutaneous Coronary Intervention; SYNTAX, SYNergy between PCI with TAXUS and Cardiac Surgery.

Concurrent User v26 software (IBM Corp., Armonk, NY, USA) and MedCalc® Statistical Software version 19.6 (MedCalc Software Ltd, Ostend, Belgium). Descriptive statistics were presented as mean ± standard deviation values or as number (n) and percentage (%). Categorical variables were compared using Pearson's Chi-square analysis. Regarding the preconditions of the parametric tests, variance homogeneity was assessed using the Levene test. The conformity of the data to normal distribution was examined with the Shapiro-Wilk test. To evaluate the differences between the two groups, the Student's t-test was used when parametric assumptions were met, and the Mann-Whitney U test was applied otherwise. The performance of the MET score in predicting the SYNTAX group was analyzed using Receiver Operating Characteristic (ROC) curve analysis. A p-value of < 0.05 was accepted as statistically significant.

Table 3. Comparison of MET Values

	Group 1 n = 156	Group 2 n = 44	*P*
MET	9.36 ± 2.38	8.78 ± 2.43	0.086
MET < 10, n (%)	74 (47.4)	26 (59.1)	0.172
MET ≥ 10, n (%)	82 (52.6)	18 (40.9)	

Group 1: Low SYNTAX score (≤ 22), Group 2: Medium-high SYNTAX score (≥ 23).
MET, Metabolic Equivalent; SYNTAX, SYNergy between PCI with TAXUS and Cardiac Surgery.

Results

The demographic characteristics and laboratory values of the patients are presented in Table 1. No significant differences were observed between the groups regarding age, gender, body mass index, and known chronic diseases. The laboratory values of both groups were found to be similar.

The mean SYNTAX scores are presented in Table 2, along with the patients for whom the decision was made for percutaneous coronary intervention (PCI) or coronary arterial bypass graft (CABG) following coronary angiography and the identification of chronic total occlusion (CTO). As anticipated, a higher percentage of patients with CTO and a decision for CABG was observed in the group with a moderate-high SYNTAX score (P = 0.001). The mean SYNTAX score was 9.62 ± 6.07 in the low SYNTAX score group and 34.06 ± 8.56 in the moderate-high group (P = 0.001). Statistically, PCI was more common in the low SYNTAX score group than in the moderate-high group (P = 0.001). Additionally, a significantly higher percentage of

Table 4. Evaluation of the Performance of MET Score in Predicting SYNTAX Groups by ROC Curve Analysis

	AUC (95.0% CI)	*P*	Cut-off	Sensitivity (95.0% CI)	Specificity (95.0% CI)
MET	0.585 (0.513-0.654)	0.088	≤ 7.6	43.2 (28.3-59.0)	76.2 (68.8-82.7)

AUC, Area Under the ROC Curve; MET, Metabolic Equivalent.

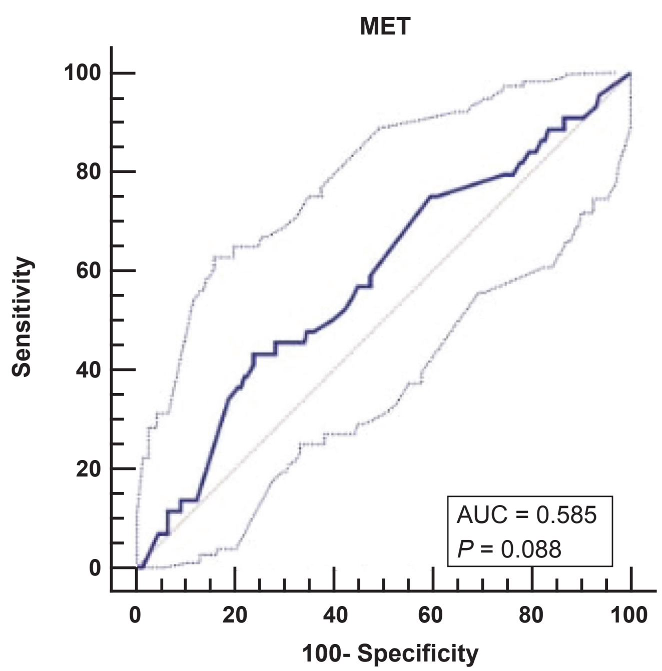

Figure 1. ROC curves of MET in predicting SYNTAX Score.

patients in the low SYNTAX score group were chosen for medical observation with no intervention (*P* = 0.001).

Correlations between the MET values and the SYNTAX groups are depicted in Table 3. The mean MET values were similar in both groups; 9.36 ± 2.38 in the low SYNTAX score group and 8.78 ± 2.43 in the moderate-high SYNTAX score group (*P* = 0.086). No statistically significant difference was found between the two groups when evaluating according to MET values of ≤ 10 or > 10 (*P* = 0.172). The performance of the MET score in predicting SYNTAX groups is illustrated through ROC curve analysis in Table 4 and Figure 1. The Area Under the Curve (AUC) was not statistically significant (*P* = 0.088). The optimum cut-off value for the MET was determined to be ≤ 7.6, with a sensitivity of 43.2% and specificity of 76.2%.

Discussion

The most significant finding of this study was the lack of correlation between the SYNTAX score, a marker of coronary artery anatomic severity in CCS, and the MET value, a marker of functional capacity.

The MET value, an important parameter detected in EET, is a reliable indicator of cardiovascular prognosis. A 2020 study found that higher MET values were a reliable indicator of lower mortality across all exercise protocols.[12] Additionally, Fitzgerald et al.[13] emphasized that a high exercise capacity (more than 13 METs) indicates a good prognosis, even in the presence of ECG changes during exercise testing. Another important aspect of MET is its cut-off value. In studies utilizing MET values, 10 METs have been emphasized as the threshold. Bourque et al.[11] observed that patients reaching a functional capacity of ≥ 10 METs had a very low probability of ischemia, as determined by myocardial perfusion scintigraphy in patients with ≥ 10% of the left ventricle affected. Furthermore, two separate studies have demonstrated that a MET value of ≥ 10 is a good prognostic marker.[7,14]

The SYNTAX score, developed to anatomically evaluate the extent and severity of CAD in patients, is used in decision-making for both PCI and CABG and is a significant marker for cardiovascular prognosis. In a 10-year follow-up study, the SYNTAX score was shown to have predictive value for major adverse cardiac or cerebrovascular events following left main coronary intervention.[15] According to the SYNTAX score, patients are categorized into three groups: low (SYNTAX score ≤ 22), intermediate (SYNTAX score 23-32), and high risk (SYNTAX score ≥ 33). As the SYNTAX score increases, so does the severity of coronary artery disease, and these risk groups become important in deciding on CABG or PCI. Wang et al.[16] found the SYNTAX score to be valuable in predicting 1-year prognosis in coronary heart disease patients undergoing PCI, with major adverse cardiac events being 8.1% in the low-risk group, 11.7% in the intermediate-risk group, and 14.5% in the high-risk group. These findings collectively indicate that the SYNTAX score is an effective prognostic marker.

To date, studies have yielded varied results regarding the relationship between functional capacity and the severity of coronary narrowing, and this relationship has not been clearly established. A literature review revealed no studies showing a direct relationship between the SYNTAX score and MET value. However, one study did investigate the association between the SYNTAX score and functional capacity, finding a correlation between an increase in exercise capacity and a decrease in the functional SYNTAX score in patients with revascularized stable CAD post-PCI.[17] In that study, the change in exercise capacity was defined as an increase of ≥ 10% in exercise duration, and the MET value was not utilized. Another study investigating the relationship between coronary narrowing severity and MET did not use the SYNTAX score. In that study, the diameter of the coronary artery lumen was used to evaluate the severity of coronary narrowing, and a decrease in MET value was found to be a strong marker of restenosis.[18]

Although previous studies have not directly correlated the SYNTAX score with the MET value, a negative correlation has been observed between functional capacity and the severity of coronary artery narrowing. The aim of the current study was to investigate the direct relationship between the SYNTAX score and the MET value. The data obtained showed that although the MET value was higher in the low SYNTAX score group than in the other group, the difference was not statistically significant. Additionally, while the rate of patients with < 10 MET in the moderate-high SYNTAX score group was higher than in the other group, this difference was not statistically significant. In the visual and computerized evaluations of another previously published study, no strong correlation was found between exercise duration and lesion severity, expressed as a percentage.[19] These findings support the results of the current study.

The hypothesis suggesting a relationship between the MET value and the SYNTAX score, whose prognostic importance has been established in previous studies, could not be substantiated. Two possible explanations are considered for this outcome.

Firstly, the potential inadequacy of the SYNTAX score in accurately identifying high-risk patients and its limitations in prognosis might have contributed to the absence of a correlation with the MET value. While the SYNTAX score is an anatomical marker of CAD severity, it does not reflect functional narrowing. A study showed that risk stratification and prognostic assessment were significantly enhanced with the Functional SYNTAX Score based on Quantitative Flow Rate (FSSQFR), a combination of anatomical and physiological assessment, compared to the SYNTAX score alone. After calculating the FSSQFR, 16% of patients were reclassified from the high-risk group to a lower-risk group, according to the SYNTAX score. Consequently, the decision for the type of revascularization changed in some cases. For instance, 6% of patients initially recommended for coronary artery bypass grafting based on the SYNTAX score alone were shifted to PCI following FSSQFR calculation.[20]

The second explanation is that factors other than coronary anatomy could influence the determination of the MET value. A low MET value might not be solely explained by coronary anatomy. A previous study highlighted that functional capacity of the patient could be affected by various factors, including the patient's compliance with exercise test equipment, the selection of an appropriate exercise protocol, the patient's educational level, and environmental factors during the test.[21] Therefore, a low MET value may not necessarily indicate a higher SYNTAX score.

Consequently, the lack of a relationship between the MET value and the SYNTAX score, both recognized as strong prognostic markers, may be attributed to the limited prognostic value of the SYNTAX score alone or inaccurate determination of the MET value due to factors unrelated to coronary disease.

Limitations

This study had some limitations, the most notable being its retrospective nature and that it was conducted at a single center. Another limitation was the non-utilization of the SYNTAX II score. The SYNTAX II score is a scoring system that incorporates clinical conditions such as ejection fraction and creatinine clearance into the original SYNTAX score. A previous study demonstrated that the SYNTAX II score offers better predictive capability than the SYNTAX score alone for major adverse cardiovascular events, death, and cardiac death.[22] The retrospective design of our study restricted access to some clinical data, thereby precluding the use of the SYNTAX II score. To more definitively establish the relationship between MET and the SYNTAX score, there is a need for further multicenter, prospective studies with larger populations that include clinical risk factors.

Conclusion

The primary outcome of this study was the determination that there is no correlation between the SYNTAX score and the MET value in patients with CCS.

Ethics Committee Approval: Ethics committee approval was obtained from Kayseri City Research Ethics Training and Research Hospital Clinical Board (Approval Number: 788, Date: 31.01.2023).

Informed Consent: Informed consent was not obtained due to the retrospective nature of the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – G.E., H.T., E.D., Y.D., Y.Y., Ş.K., Z.Ş., S.D.; Design – G.E., H.T., E.D., Y.D., Y.Y., Ş.K., Z.Ş., S.D.; Supervision – G.E., H.T., E.D., Y.D., Y.Y., Ş.K., Z.Ş., S.D.; Data Collection and/or Processing - G.E., H.T., E.D., Y.D., Y.Y., Ş.K., Z.Ş., S.D.; Analysis and/or Interpretation – G.E., H.T., E.D., Y.D., Y.Y., Ş.K., Z.Ş., S.D.; Literature Review – G.E., H.T., E.D., Y.D., Y.Y., Ş.K., Z.Ş., S.D.; Writing – G.E., H.T., E.D., Y.D., Y.Y., Ş.K., Z.Ş., S.D.; Critical Review – G.E., H.T., E.D., Y.D., Y.Y., Ş.K., Z.Ş., S.D.

Conflict of Interest: The authors have no conflicts of interest to declare.

Funding: The authors declared that this study received no financial support.

References

1. Asad M, Khadim R, Iqbal T, et al. Role of Duke treadmill score in assessing the severity of coronary artery disease in patients presenting with angina. *Pak Armed Forces Med J.* 2018;68(Suppl-1):147-152.
2. Dzenkeviciute V, Sapoka V, Kasiulevicius V, et al. Value of Duke treadmill score in predicting coronary artery lesion and the need for revascularisation. *Kardiol Pol*. 2017;75(5):439-444. [CrossRef]
3. Akyüz A, Alpsoy S, Akkoyun DC, Değirmenci H, Güler N. Heart rate recovery may predict the presence of coronary artery disease. *Anadolu Kardiyol Derg*. 2014;14(4):351-356. [CrossRef]
4. Volkan Emren S, Gediz RB, Şenöz O, et al. Decreased heart rate recovery may predict a high SYNTAX score in patients with stable coronary artery disease. *Bosn J Basic Med Sci.* 2019;19(1):109-115. [CrossRef]
5. Bruce RA, Kusumi F, Hosmer D. Maximal oxygen intake and nomographic assessment of functional aerobic impairment in cardiovascular disease. *Am Heart J*. 1973;85(4):546-562. [CrossRef]
6. Ezzatvar Y, Izquierdo M, Núñez J, Calatayud J, Ramírez-Vélez R, García-Hermoso A. Cardiorespiratory fitness measured with cardiopulmonary exercise testing and mortality in patients with cardiovascular disease: A systematic review and meta-analysis. *J Sport Health Sci*. 2021;10(6):609-619. [CrossRef]
7. Bourque JM, Beller GA. Value of Exercise ECG for Risk Stratification in Suspected or Known CAD in the Era of Advanced Imaging Technologies. *JACC Cardiovasc Imaging*. 2015;8(11):1309-1321. [CrossRef]
8. Sianos G, Morel MA, Kappetein AP, et al. The SYNTAX Score: an angiographic tool grading the complexity of coronary artery disease. *EuroIntervention*. 2005;1(2):219-227.
9. Ikeno F, Brooks MM, Nakagawa K, et al.; BARI-2D Study Group. SYNTAX Score and Long-Term Outcomes: The BARI-2D Trial. *J Am Coll Cardiol*. 2017;69(4):395-403. [CrossRef]
10. Fletcher GF, Ades PA, Kligfield P, et al.; American Heart Association Exercise, Cardiac Rehabilitation, and Prevention Committee of the Council on Clinical Cardiology, Council on Nutrition, Physical Activity

and Metabolism, Council on Cardiovascular and Stroke Nursing, and Council on Epidemiology and Prevention. Exercise standards for testing and training: a scientific statement from the American Heart Association. *Circulation*. 2013;128(8):873-934. [CrossRef]
11. Bourque JM, Holland BH, Watson DD, Beller GA. Achieving an exercise workload of > or = 10 metabolic equivalents predicts a very low risk of inducible ischemia: does myocardial perfusion imaging have a role? *J Am Coll Cardiol*. 2009;54(6):538-545. [CrossRef]
12. Harb SC, Bhat P, Cremer PC, et al. Prognostic Value of Functional Capacity in Different Exercise Protocols. *J Am Heart Assoc*. 2020;9(13):e015986. [CrossRef]
13. Fitzgerald BT, Smith E, Scalia GM. What are the prognostic implications and factors relating to exercise induced electrocardiographic ST segment changes in the setting of a non-ischemic stress echocardiogram? *Int J Cardiol.* 2022;364:157-161. [CrossRef]
14. Beri N, Dang P, Bhat A, Venugopal S, Amsterdam EA. Usefulness of Excellent Functional Capacity in Men and Women With Ischemic Exercise Electrocardiography to Predict a Negative Stress Imaging Test and Very Low Late Mortality. *Am J Cardiol.* 2019;124(5):661-665. [CrossRef]
15. Lee J, Ahn JM, Kim JH, et al.; on the behalf of the PRECOMBAT Investigators. Prognostic Effect of the SYNTAX Score on 10-Year Outcomes After Left Main Coronary Artery Revascularization in a Randomized Population: Insights From the Extended PRECOMBAT Trial. *J Am Heart Assoc*. 2021;10(14):e020359. [CrossRef]
16. Wang J, Guan CD, Yuan JS, Gao RL, Xu B, Qiao SB. Prognostic value of SYNTAX score on 1 year outcome in patients underwent percutaneous coronary intervention. *Zhonghua Xin Xue Guan Bing Za Zhi.* 2018;46(4):267-273. Chinese.
17. Lee SH, Choi KH, Lee JM, et al. Residual functional SYNTAX score by quantitative flow ratio and improvement of exercise capacity after revascularization. *Catheter Cardiovasc Interv*. 2021;97(4):E454-E466.
18. Jørgensen B, Simonsen S, Endresen K, Forfang K, Egeland T, Thaulow E. Physiologic response to gain and loss in coronary minimal luminal diameter in patients treated with coronary angioplasty: prediction of restenosis on the basis of exercise capacity. *Am Heart J*. 2000;139(3):482-490. [CrossRef]
19. Folland ED, Vogel RA, Hartigan P, et al. Relation between coronary artery stenosis assessed by visual, caliper, and computer methods and exercise capacity in patients with single-vessel coronary artery disease. The Veterans Affairs ACME Investigators. *Circulation*. 1994;89(5):2005-2014. [CrossRef]
20. Zhang R, Song C, Guan C, et al. Prognostic Value of Quantitative Flow Ratio Based Functional SYNTAX Score in Patients With Left Main or Multivessel Coronary Artery Disease. *Circ Cardiovasc Interv*. 2020;13(10):e009155. [CrossRef]
21. Arena R, Myers J, Williams MA, et al.; American Heart Association Committee on Exercise, Rehabilitation, and Prevention of the Council on Clinical Cardiology; American Heart Association Council on Cardiovascular Nursing. Assessment of functional capacity in clinical and research settings: a scientific statement from the American Heart Association Committee on Exercise, Rehabilitation, and Prevention of the Council on Clinical Cardiology and the Council on Cardiovascular Nursing. *Circulation*. 2007;116(3):329-343. [CrossRef]
22. Yanes Bowden GJ, Bosa Ojeda F, Jiménez Sosa A, et al. Prognostic value of SYNTAX score and SYNTAX score II in an 'all-comers' population treated with angoplasty. *Coron Artery Dis*. 2021;32(3):231-240. [CrossRef]