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Original Article

The Relationship between SYNTAX Score and Resting/Post-exercise Ankle-Brachial index in Patients with Acute Coronary Syndrome

Akut Koroner Sendromlu Hastalarda SYNTAX Skoru ile Dinlenme/Egzersiz Sonrası Ayak Bileği-Kol İndeksi Arasındaki İlişki

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Highlights

We found that ABI, which is an easily applicable, noninvasive measurement technique in the diagnosis and follow-up of peripheral artery disease, is associated with the prevalence of coronary artery disease in patients with Acute Coronary Syndrome.

Abstract

Background: The aim of this study is to determine the relationship between the complexity of coronary artery disease (CAD), determined by the SYNTAX score, and the resting and post-exercise Ankle-Brachial Index (ABI).
Materials and Methods: Patients who were treated for Acute Coronary Syndrome (ACS) were evaluated in our study. The patients were divided into two groups according to their SYNTAX Score ≤22 or >22. In addition, patients were evaluated in two groups as <30 and ≥30 in the SYNTAX II (PCI) scoring. The measurements of the resting ABI and the post-exercise ABI were done in these patients.**Results**: The mean age of 118 patients was 57.50±11.19 years and 26 (22%) patients were female. In the group with SYNTAX Score>22, lower resting ABI (p <0.001) and post-exercise ABI (p <0.001) were observed, whereas the higher SYNTAX II PCI (p= 0.005) score was found. While lower resting ABI (p<0.001) and post-exercise ABI (p<0.001) were observed in the group with SYNTAX II PCI Score ≥30, TIMI (0.015), GRACE score (0.004) and SYNTAX score (p= 0.001) were higher. As a result of the ROC analysis: resting ABI cut-off value was detected as 0.935 with a sensitivity of 75% and a specificity of 75% [p<0.001; AUC(95% CI)= 0.786 (0.697-0.875)] and post-exercise ABI cut-off value was detected as 0.945 with a sensitivity of 80% and a specificity of 81% to predict SYNTAX score >22 [p <0.001; AUC (95% CI)= 0.836 (0.761-0.912)]. Diabetes mellitus, history of CAD, resting and post-exercise ABI variables were found to be independent predictors of the extent of CAD, expressed as SYNTAX score >22 and SYNTAX II PCI score ≥30.**Conclusion**: In ACS patients, post-exercise ABI measurements have a stronger diagnostic power than resting ABI measurements in predicting CAD complexity. ABI measures at resting and post-exercise are independent predictors of CAD complexity in ACS patients.
Keywords: Acute Coronary Syndrome, Ankle-Brachial Index, Coronary Artery Disease, SYNTAX Score

ÖZ

Amaç: Bu çalışmanın amacı, SYNTAX skoru ile belirlenen koroner arter hastalığı (KAH) yaygınlığı ile istirahat ve egzersiz sonrası Ayak Bileği-Kol İndeksi (ABKİ) arasındaki ilişkiyi belirlemektir.**Materyal ve Metod:** Çalışmamızda Akut Koroner Sendrom (AKS) nedeniyle tedavi edilen hastalar değerlendirildi. Hastalar SYNTAX Skoru ≤22 veya >22 olarak iki gruba ayrıldı. Ayrıca hastalar SYNTAX skoru II (PCI) puanlamasında <30 ve ≥30 olmak üzere iki grup olarak da değerlendirildi. Bu hastalarda istirahat ABKİ ve egzersiz sonrası ABKİ ölçümleri yapıldı.**Bulgular:** Çalışmaya dahil edilen118 hastanın yaş ortalaması 57.50±11.19 yıl ve 26 (%22) hasta kadındı. SYNTAX Skoru > 22 olan grupta daha düşük istirahat ABKİ (p<0.001) ve egzersiz sonrası ABKİ (p<0.001) görülürken, SYNTAX II PCI (p= 0.005) skoru daha yüksek bulundu. SYNTAX II PCI Skoru ≥ 30 olan grupta daha düşük istirahat ABKİ (p<0.001) ve egzersiz sonrası ABKİ (p<0.001) görülürken, TIMI (0.015), GRACE skoru (0.004) ve SYNTAX skoru (p= 0.001) daha yüksek bulundu. SYNTAX skorunu > 22 öngörüsü için yapılan ROC analizi sonucunda: %75 duyarlılık ve %75 özgüllük ile istirahat ABKİ kestirim değeri 0.935 [p<0.001; Eğri Altında kalan Alan (EAA)(95% Güven Aralığı)= 0.786 (0.697-0.875)] ve %80 duyarlılık ve %81 özgüllük ile egzersiz sonrası ABKİ kestirim değeri 0,945 olarak saptandı [p <0.001; EAA (%95 Güven Aralığı)= 0.836 (0.761-0.912)]. Diabetes mellitus, KAH öyküsü, istirahat ve egzersiz sonrası ABKİ değişkenleri SYNTAX skoru >22 ve SYNTAX II PCI skoru ≥ 30 ile ifade edilen KAH yaygınlığının bağımsız öngördürücüleri olarak bulundu.**Sonuç:** AKS hastalarında, egzersiz sonrası ABKİ ölçümleri, KAH yaygınlığını tahmin etmede istirahat ABKİ ölçümlerinden daha güçlü bir tanısal değere sahiptir. İstirahat ve egzersiz sonrası ABKİ ölçümleri, AKS hastalarında KAH yaygınlığının bağımsız öngörücüleridir.**Anahtar Kelimeler:** Akut Koroner Sendrom, Ayak Bileği Kol İndeksi, Koroner Arter Hastalığı, SYNTAX skoru

Introduction

The extensity and complexity of Coronary Artery Diseases (CAD) have improtance in determining the treatment strategy, fully revascularization, follow-up during the hospitalization and for long term adverse cardiac events in the patients with Acute Coronary Syndrome (ACS). Synergy Between PCI With TAXUS and Cardiac Surgery (SYNTAX) Score is one of the most significant scales evaluating the extensity and complexity of the CAD (1, 2). SYNTAX Score is an anatomical scoring system which is projecting the severity of CAD according to the complexity, location and functional feature of the coronary lesion. However, the studies on this subject had been revealed the insufficiency of anatomical evaluation alone in determining the complexity of the CAD and SYNTAX II Score was developed by correlating clinical risk factors. SYNTAX Score can predict short and long term mortality and major cardiac events (MACE) in the patients undergone interventional treatment for CAD. In the present studies, it is stated that SYNTAX II Score have more predictive performance comparing to SYNTAX Score in terms of the prognostic relevence (3).
Ankle-Brachial Index (ABI) is a non-invasive, inexpensive and efficient method for diagnosing peripheral artery disease (PAD) (4). ABI has a good sensitivity and specificity comparing to doppler ultrasonography [sensitivity and specificity of 74.5% and 63.1%] and computed tomography [sensitivity and specificity of 65.5 and 68.8%] for diagnosis of PAD (5). As an indicator for PAD, ABI can be used for predicting the risk of cardiovascular disease (CVD). ABI is an independent risk factor with strong correlation for cardiovascular morbidity and mortality in the atherosclerotic diseases (6, 7). In the literature, it has been shown the relevance between the extensity and complexity of the CAD measured by SYNTAX score and resting ABI (8, 9). However, there is limited information on the effectiveness of such a comparison with SYNTAX II which has been shown to be more correlated with cardiac prognosis by considering clinical factors in addition to anatomical evaluation. Also, the post-exercise ABI has been shown to be more effective for predicting prognosis of ischemic diseases comparing to resting ABI by clinical studies (10, 11).
In our study, it is aimed to do more effective comparison by using the datas of post-exercise ABI, SYNTAX I and II scores. The effect on the power of decision of the afore mentioned scoring systems will be studying by searching the relevance among the complexity of CAD adjusted by the clinical risk factors, ABI at resting and after exercise. Thus, the treatment and follow-up strategies can be determined earlier by predicting the complexity of CAD of the patients with a pracitcal criterion applied at the bedside before diagnostic angiography.

Materials and Methods

The adult patiens subsequently admitted to our clinic with the diagnosis of ACS and executed coronary angiography/angioplasty were included to our prospective study. Ischemic electrophysiological changes in ECG and/or recently occured segmentar wall movement deficiency in left ventricule and/or elevation in troponin levels in addition to anginal complaints related to myocardial infarction were evaluated for the diagnosis of ACS. Exclusion criterias were: (i) clinical phenomenons mimicing ACS with high levels of cardiac biomarkers not originated from trombotic or aterosclerotic events (pulmonaryembolism, tachyarrythmias, coronary vasospasms, slow coronary flow…), (ii) mortality within the first 24 hours after hospitalization, (iii) the history of previous operation for coronary artery by-pass grafting, (iv) the history of previous intervention for revascularization percutanously and/or surgically for peripheral artery disease, (v) any obstacle for the ABI measurement such as: (a) extremity loss for any reason, (b) dialysis fistula in upper extremites, (c) atrial fibrilation, (d) the presence of any diseases preventing vascular compression like scleroderma, CREST syndrome and hypercalcemia, (e) the presence of edema or ulceration on the location of measurement, (f) arm circumferance below 24 cm or above 32 cm, (g) morbid obesity, and (vi) intolerance for ABI measurement. The criterion for terminating the study was failure to reach the adequate number of volunteers to continue the study. The patients were divided into two groups according to their SYNTAX Score ≤22 or >22 and SYNTAX II PCI score <30 or ≥30. The measurements of the resting ABI and the post-exercise ABI were done in these patients. Clinical features and laboratory test results at the admission of all patients were recorded. The study was executed with the permission of the local ethics comittee and by taking the infromed concent form from all of the patients in line with the principles of the Helsinki Declaration (Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Training Research Hospital Clinical Research Ethics Commitee, Reference no:2018-50, Date: 28.05.2018).

The Ankle-Brachial Indeks

The ABI measurements of the patients were done by single vascular operator in seven days during hospitalization. Resting and post-exercise ABI measurements were recorded twice, after hospitalization and after angiography. Mean values of these dual measurements were used in the analsyses.

The resting ABI measurement

Systolic blood pressure were measured from bilateral brachial arteries by using blood pressure cuff and hand held doppler ultrasound(US) device after the patients resting for ten minutes in supine position. Same measurements were done from bilateral posterior tibial or dorsalis pedis artery by covering the cuff around the ankle with hand held doppler US. ABI for each lower extremity was calculated by dividing the lower extremity systolic pressure to the highest brachial pressure obtained from the upper extremities. Calculated low ABI value was used in the analyses. The patients with ABI ≤ 0.9 was defined as PAD, the patients with 0.9 < ABI ≤ 1.4 as normal and ABI > 1.4 as vascular decompressed or vascular calcified (12).

The post-exercise ABI measurement

Active pedal-plantar flexion technique which is an alternative method for exercise treadmill technique for the patients with contraindication or gait disable was executed to measure the post-exercise ABI. To increase the work load and blood flow at the calves, the patients got raised upon the finger tips, stood in balance and stepped on the foot sole again for fifty times subsequently or as much as the patients could do if they can not reach the target repitition number. After the exercise, the patients were taken into the supine position and the ABI was measured. ABI measurement were repeated with an interval of five minutes until the baseline values were observed again. After recording all values for ABI, intra-observer agreements for resting ABI and post-exercise ABI measurements were calculated [Intra-observer agreement: kapa coefficient (ϰ) for resting ABI measurement: 0.82 (p=0.011) (for the vascular operator); kapa coefficient (ϰ) for post-exercise ABI measurement: 0.83 (p=0.014) (for the vascular operator)]

Coronary Angiography

The coronary angiographies were evaluated by two double-blinded invasive cardiologist who had not got any other role in the study design. The consensus was provided by taking the opinion of third double-blinded cardiologist in case of divergency. A stenosis rate of 50% or more in the epicardial arteries with a diameter of 1.5 mm or larger was considered as significant. The complexity of CAD was evaluated with the models of SYNTAX Score I or SYNTAX Score II (13) (http://www.syntaxscore.com). After recording all values for SYNTAX Score (SS) measurements, intra-observer and inter-observer agreements for SS measurements were calculated [Intra-observer agreement: kapa coefficient (ϰ) for SS measurement: 0.85 (p:0.013) (for Cardiologist A) and 0.87 (p: 0.024) (for Cardiologist B); Inter-observer agreement (between Cardiologist A and B): ϰ for SS measurement: 0.84 (p:0.021).

The SYNTAX score I guides operators for percutaneous coronary intervention (PCI) and coronary by-pass graft surgery (CABG) with an anatomical assessment for the management of coronary artery disease. On the other hand, SYNTAX score II evaluates factors such as: age, creatinine clearance, left ventricular ejection fraction, left main coronary involvement, gender, chronic obstructive lung disease and peripheral artery disease in addition to the SYNTAX score I. As a result of the SYNTAX score II calculating, the 4-year mortality of the patients is determined and two separate scores are produced for PCI and CABG. Operators are directed to the intervention with the lowest risk of mortality.

The SYNTAX II PCI score was used to evaluate the study patients by grouping them in the analyzes, since PCI was applied to most of the patients included in the study and it was found to be more compatible with the SYNTAX score.

Definitons

Hypertension was defined as systolic and diastolic arterial blood pressure ≥140 and/or ≥90 mmHg or usage of spesific antihypertensive medication. Diabetes mellitus was defined as the fasting blood glucose level ≥126 mg/dl or post-prandial blood glucose level ≥200 mg/dl or HbA1C level ≥6.5% or usage of spesific antidiabetic medication. Smoking was considered as a definition for the patients with the history of active and regular smoking for six months or more. Chronic renal failure was considered for the patients with glomerular filtration rate (GFR) <60 ml/dk/1.73 m^2. The extensity and complexity of CAD was defined as SS over 22 after diagnostic coronary angiography. GRACE (Global Registery of Acute Coronary Events) risk score was calculated with the KILLIP class, systolic blood pressure, heart rate, age, creatinin (mg/dL) and highly sensitive troponin T levels (>24 ng/L). TIMI score was calculated with age (≥65years) and CAD risk factors (existing coronary artery stenosis over 50%, ST segment deviation in ECG at admission, at least two angina within the past 24 hours, acetylsalicylicacid usage within the past one week, increase in serum cardiac biomarkers). KILLIP class is a system used for classifing and predicting the risk of mortality in patients with acute myocardial infarction. Phyisical examination findings and development of cardiac failure is used to categorize the patients between class I and IV (asymptomatic, existing pulmonary congestion and rals, existing pulmonary edema or cardiogenic shock status).

Statistical Analysis

SPSS version 24.0 (SPSS Inc., Chicago, Illinois, USA) was used for the statistical analysis. Normality of distribution was evaluated with visual (histograms and probability curves) an analitic methods (Kolmogorov-Simirnov's and Shapiro-Wilk tests). Parametric variables were shown as mean ± Standard deviation (SD), non-parametric variables as median and categorical variables as percentage (%). Numeric variables such as the resting and post-exercise ABI values between the groups were analysed with student's T or Mann-Whitney U test and categorical variables with chi-square or Fischer exact test. Correlations between the resting or post-exercise ABI and SYNTAX I or II were studied with pearson or spearman analysis. Logistic regression test was used to determine whether ABI measurements were an independent predictor in identifying ACS patients with a SYNTAX score above 22 and SYNTAX II PCI score ≥30. A p value <0.1 was considered as significant in univariate analysis anda p value <0.05 in multivariate analysis. ROC curve was used to determine the cut-off value of ABI measurements and it was considered as statistical significant if the area under the curve (AUC) larger than 0.5 and a p value <0.005.

Results

118 patients treated and followed up after diagnosis of ACS were included to our study. Of all patients, 92 (78%) were male and 26 (22%) were female. The mean age of the patients was 57.5±11.19 years. All patients divided into two groups according to whether SS calculated after coronary angiography was over 22 or not.32 patients (27.1%) had a SS over 22. In the group with SS>22, statistical significance was observed for higher rate of history of CAD and SBP measurement compared to the group with SS ≤22 (p=0.044 and p=0.048 respectively). All demographics and laboratory results were given inTable 1.

Table 1: Demographicsandlaboratory test results of allpatientsand SYNTAX Scoregroups.

Variables	Allpatients(n=118)	SS≤22 (n=86)	SS>22 (n=32)	*P*
Age (year)	57.50±11.19	56.85±11.39	59.25±10.60	0.302
Male Gender, n (%)	92 (78)	66 (76.7)	26 (81.3)	0.600
Smoking, n (%)	69 (58.5)	46 (53.5)	23 (71.9)	0.072
DM, n (%)	37 (31.4)	23 (26.7)	14 (43.8)	0.077
HT, n (%)	56 (47.5)	39 (45.3)	17 (53.1)	0.452
HL, n (%)	33 (28.0)	24 (27.9)	9 (28.1)	0.981
CAD, n (%)	32 (27.1)	19 (22.1)	13 (40.6)	0.044
COPD, n (%)	5 (4.2)	4 (4.7)	1 (3.1)	1.0
SBP	131.3 ± 20.9	128.9 ± 21.9	137.5 ± 16.6	0.048
DBP	77.8 ± 14.3	77.2 ± 15.8	79.4 ± 9.5	0.467
Heart Rate, beat/m	76.0 ± 12.7	74.8 ± 12.5	79.2 ± 12.9	0.097
Creatinine, mg/dL	0.89 ± 0.22	0.90 ± 0.22	0.85 ± 0.21	0.224
GFR, ml/m/1,73m^2	88.2 ± 22.1	86.7 ± 22.7	92.4 ± 20.1	0.217
Hemoglobin, gr/dL	13.51 ± 1.93	13.55 ± 1.89	13.38 ± 2.05	0.672
Platelet,10^3/uL	261.5 ± 80.0	258.5 ± 76.5	269.4 ± 89.5	0.514
MPV, fL	10.56 ± 1.17	10.61 ± 1.25	10.43 ± 0.89	0.453
RDW,%	13.32 ± 1.41	13.26 ± 1.37	13.49 ± 1.52	0.424
Neutrophyl, 10^3/uL	5.41 ± 1.68	5.55 ± 1.50	5.04 ± 2.09	0.147
Lymphyocyte, 10^3/uL	2.64 ± 1.04	2.67 ± 0.92	2.54 ± 1.31	0.552

SYNTAX: SynergyBetween PCI With TAXUS andCardiacSurgery, DM: DiabetesMellitus, HT:Hypertension, HL: Hyperlipidemia, CAD: CoronaryArteryDisease, COPD: ChronicObstructivePulmonaryDisease, SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure, GFR: GlomerularFiltration Rate.SS: SYNTAX score

ABI and risk scores of the groups were given in Table 2. Lower resting and post-exercise ABI scores and higher SYNTAX II PCI score were found in the group with SS>22 (p<0.001 and p=0.005 respectively). Statistical significance was not observed for other risk scores between the groups. While lower resting ABI (p<0.001) and post-exercise ABI (p<0.001) were observed in the group with SYNTAX II PCI Score ≥30, TIMI (0.015), GRACE score (0.004) and SYNTAX score (p= 0.001) were higher.

Table 2: Values of ABI and risk scores of allpatientsand SYNTAX Scoregroups.

	AllPatients (n=118)	SS ≤22 (n=86)	SS >22 (n=32)	P
Resting ABI	0.98±0.17	1.02± 0.16	0.87±0.12	<0.001
Post-exercise ABI	0.99±0.16	1.04±0.15	0.85±0.12	<0.001
TIMI Score	3.73±1.26	3.72±1.29	3.75±1.19	0.902
GRACE Score	98.77 ± 24.16	97.61 ± 23.57	101.84 ± 25.80	0.401
KILLIP Class	1 (0 - 2)	1 (0 - 2)	1 (0 - 2)	0.629
SYNTAX II PCI	23.2 (18.4 - 31.4)	22.0 (17.1 - 29.4)	28.4 (22.3 - 35.1)	0.005
SYNTAX II CABG	19.3 (13.8 - 25.8)	18.5 (12.0 - 26.3)	21.7 (14.9 - 25.1)	0.484
	AllPatients (n=118)	**SS II (for PCI) <30 (n=74)**	**SS II (for PCI) ≥30 (n=44)**	**P**
Resting ABI	0.98±0.17	1.03 ± 0.14	0.88 ± 0.15	<0.001
Post-exercise ABI	0.99±0.16	1.02 ± 0.17	0.83 ± 0.14	<0.001
TIMI Score	3.73±1.26	3.56 ± 1.14	4.62 ± 1.28	0.015
GRACE Score	98.77 ± 24.16	94.12 ± 20.72	114.25 ± 23.16	0.004
KILLIP Class	1 (0 - 2)	1 (0 - 2)	1 (0 - 2)	0.462
SYNTAX Score I	19.5 (14.7 – 24.3)	19.1 (15.8 – 26.1)	27.6 (21.7 – 34.8)	0.001

ABI: Ankle-BrachialIndeks, SYNTAX: SynergyBetween PCI With TAXUS andCardiacSurgery, GRACE: Global Registry of AcuteCoronaryEvents, TIMI: Thrombolysis in MyocardialInfarction.

It was found that the resting ABI had negative correlation significantly with diastolic blood pressure (p=0.028 and r=-0.202), systolic blood pressure (p<0.001 and r=-0.439), SYNTAX score (p=0.001 and r=-0.312) and SYNTAX II PCI score (p=0.016 andr=-0.222). Also post-exerice ABI was found to be correlated negatively with systolic blood pressure (p<0.001 and r=-0.421), SYNTAX score (p<0.001 and r=-0.513) and SYNTAX II PCI score (p<0.001 and r=-0.322). The negative correlation of SYNTAX score and resting or post-exercise ABI were demonstrated in Figure 1.

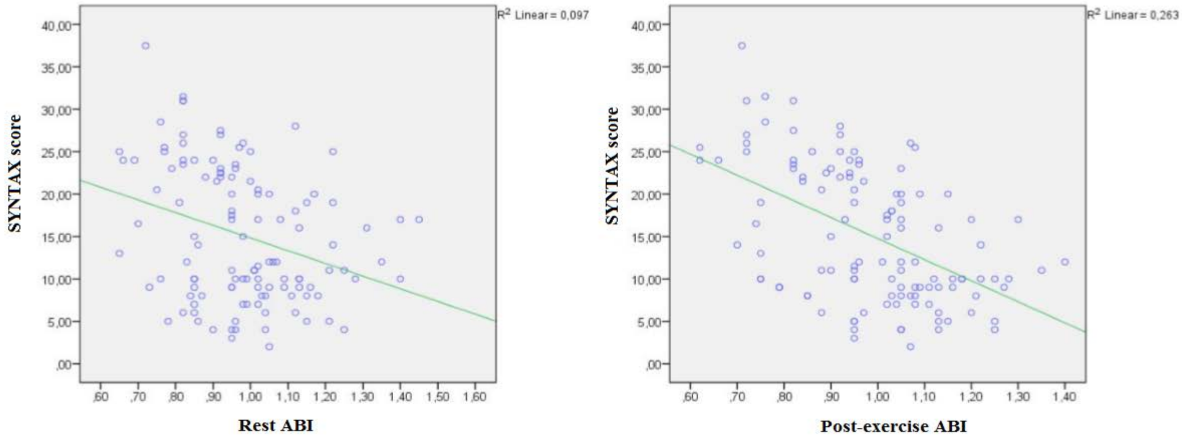

Figure 1: **Graphical presentation of the correlation between SYNTAX Score and resting ABI or post-exercise ABI**

ROC analysis was performed to determine the cut-off values of resting and post-exercise ABI scores in the detection of patients with SS >22. It was observerd that the resting ABI at a value of 0.935 could detect the patients with SS >22 with 75% sensitivity and 75% specificity [p<0.001, AUC (95%CI)= 0.786 (0.697-0.875)]. Also the post-exercise ABI at a value of 0.945 was found to detect the patients with SS >22 with 80% sensitivity and 81% specifity [p<0.001, AUC (95%CI)= 0.836 (0.761-0.912)] (Figure 2).

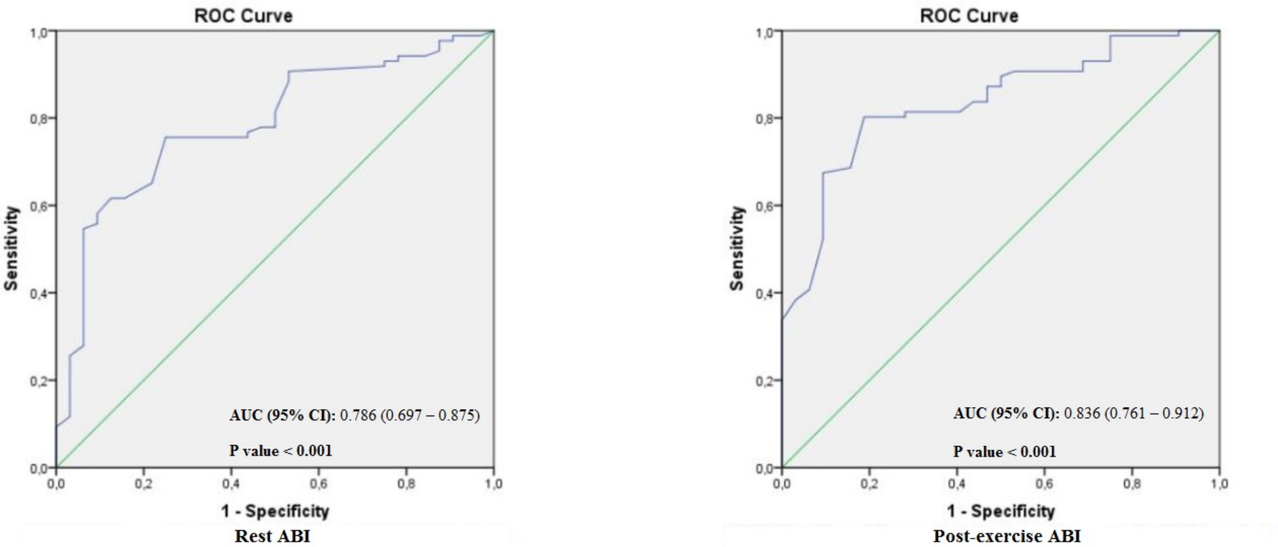

Figure 2: ROC analysis results of resting ABI and post-exercise ABI for SYNTAX Score>22 prediction
AUC: Area Under the Curve, CI: Confidence Interval, ABI: Ankle Brachial Index.

Based on the area under curve (AUC), sensitivity and specificity rates, the post-exercise ABI was considered more superior than the resting ABI in detection of the patients with SS>22.
Univariate logistic regression analysis was performed to determine the variables predicting SS>22 and SYNTAX II PCI score ≥30 in the patients with ACS. Smoking, diabetes mellitus (DM), the history of CAD, hypertension, resting and post-exercise ABI scores were the variables with statistical significance (p=0.075, p=0.08, p=0.047, p=0.052, p<0.001 and p<0.001 respectively) for SS>22. Multivariate regression analysis was performed after a model was built by using these detected variables. Diabetes mellitus [p=0.041, OR (95%CI)= 1.901 (0.691-5.233)], the resting ABI [p<0.001, OR (95%CI) = 2.702 (1.357-7.504)] and the post-

exercise ABI [p<0.001, OR (95%CI)= 2.968 (1.488-7.980)] were determined as independent predictors for SS>22 (Table 3). Age, male gender, GFR, TIMI score, GRACE score, DM, CAD history, rest ABI and post-exercise ABI scores were the variables with statistical significance (p=0.004, p=0.001, p=0.012, p=0.024, p=0.016, p<0.001, p= 0.005, p<0.001 and p<0.001 respectively) for SYNTAX II PCI score ≥30. Multivariate regression analysis was performed after a model was built by using these detected variables. Age [p=0.007, OR (95% CI)= 1.226 (1.028 – 1.402)], male gender [p=0.004, OR (95% CI)= 1.368 (1.206 – 1.544)], GFR [p=0.024, OR (95% CI)= 1.128 (1.066 – 1.296)], GRACE score [p=0.022, OR (95% CI)= 1.188 (1.069 – 1.343)], DM [p=0.001, OR (95% CI)= 1.874 (1.586 – 2.980)], CAD history [p=0.005, OR (95% CI)= 2.428 (1.455 – 4.204)], resting ABI [p<0.001, OR (95% CI)= 2.766 (1.512 – 6.806)] and post-exercise ABI [p<0.001, OR (95% CI)= 2.806 (1.498 – 7.024)] were determined as independent predictors for SYNTAX II PCI score ≥30 (Table 3).

Table 3. **Multivariateregressionanalysisresultsfordeterminingtheindependentpredictorsfordetection of SYNTAX Score>22**

	Univariate		Multivariate	
	OR (95% CI)	**P**	**OR (95% CI)**	**P**
Age	1.020 (0.983 - 1.058)	0.300	-	-
Male Gender	1.313 (0.474 - 3.638)	0.600	-	-
GFR	1.012(0.993-1.033)	0.217	-	-
TIMI Score	1.021(0.738-1.411)	0.901	-	-
GRACE Score	1.007(0.991-1.024)	0.398	-	-
KILLIP Class	1.237(0.521-2.935)	0.630	-	-
Smoking	2.222 (1.922 -5.354)	0.075	1.080 (0.052 - 4.815)	0.214
DM	2.130 (1.914 - 4.965)	0.080	1.901 (1.691 - 5.233)	0.041
CAD	2.413 (1.011 - 5.760)	0.047	2.687 (1.929 - 7.772)	0.068
HT	1.020 (1.000 - 1.040)	0.052	1.004 (0.979 - 1.029)	0.765
Resting ABI	2.844 (1.332 – 7.344)	<0.001	2.702 (1.357 – 7.504)	<0.001
Post-exercise ABI	2.924 (1.461 – 7.904)	<0.001	2.968 (1.488 – 7.980)	<0.001

OR: OddsRatio, CI: ConfidenceInterval, GFR: GlomerularFiltration Rate, TIMI: Thrombolysis in MyocardialInfarction, GRACE: Global Registry of AcuteCoronaryEvents, DM: DiabetesMellitus, HT: Hypertension, ABI: AnkleBrachial Index.

Table 4. **Multivariateregressionanalysisresultsfordeterminingtheindependentpredictorsfordetection of SYNTAX Score II (for PCI) ≥30**

	Univariate		Multivariate	
	OR (95% CI)	**P**	**OR (95% CI)**	**P**
Age	1.232 (1.045 – 1.608)	0.004	1.226 (1.028 – 1.402)	0.007
Male Gender	1.402 (1.006 – 1.860)	0.001	1.368 (1.206 – 1.544)	0.004
GFR	1.108 (1.006 – 1.312)	0.012	1.128 (1.066 – 1.296)	0.024
TIMI Score	1.098 (1.009 – 1.196)	0.024	1.096 (0.968 – 1.202)	0.088
GRACE Score	1.102 (1.044 – 1.284)	0.016	1.188 (1.069 – 1.343)	0.022
KILLIP Class	1.269 (0.945 – 1.962)	0.188	-	-
Smoking	1.986 (0.924 – 4.672)	0.246	-	-
DM	2.084 (1.882 – 3.994)	<0.001	1.874 (1.586 – 2.980)	0.001
CAD	2.406 (1.248 – 4.962)	0.005	2.428 (1.455 – 4.204)	0.005
HT	1.106 (0.902 – 1.342)	0.306	-	-
Resting ABI	2.793 (1.406 – 6.982)	<0.001	2.766 (1.512 – 6.806)	<0.001
Post-exercise ABI	2.892 (1.504 – 6.982)	<0.001	2.806 (1.498 – 7.024)	<0.001

OR: OddsRatio, CI: ConfidenceInterval, GFR: GlomerularFiltration Rate, TIMI: Thrombolysis in MyocardialInfarction, GRACE: Global Registry of AcuteCoronaryEvents, DM: DiabetesMellitus, HT: Hypertension, ABI: AnkleBrachial Index.

Discussion

To summerize our results of the patients with ACS, we observed that i) the CAD extensity can be easily determined by measuring ABI at bedside in the patients with ACS, ii) GRACE, TIMI and KILLIP scoring systems, which are important in the prognostic follow-up in CAD, do not present any significant difference in patients with higher SYNTAX scores, iii) the resting and post-exercise ABI are negatively correlated with blood pressure, SYNTAX score and SYNTAX II PCI score, iv) the post-exercise ABI is superior to the resting ABI in detection of the extensity and complexity of CAD and v) DM, the resting and post-exercise ABI were independent predictors for the CAD extensity.

As the percutaneous invasive interventions has become gold standard method for the treatment world wide, the scoring systems based on specifics of coronary lesions were needed to develope. GENSINI and SYNTAX scores are the methods that shows the extensity of CAD by evaluating the findings of coronary angiography (14). Compared to other scoring systems, SYNTAX scoring system considers the lesion spesifics such as anatomical location, charactheristics, bifurcation or trifurcation features, trombosis and collateral vasculature in more detail. Various studies have stated that higher values of SYNTAX score indicate a higher risk of depression, MACE and mortality (15). Akgun et al showed that SYNTAX score was a independent predictor for MACE and mortality in the period of hospitalization and long term follow-up in their study performed with 2993 patients with STEMI (16).

Although SYNTAX score was firstly defined for stable CAD, recent guidelines have recognised it as available for ACS. Increasing long-term data on morbiditiy and mortality for ACS related to SYNTAX score has led to that score being widely preferred. Suggestions for management and follow-up also differ depending on whether the score calculated below 23, between 23 and 32 or above 32 (17). SYNTAX score is able to provide a prospective risk classification in patients with multiple CAD undergone percutaneous coronary intervention (PCI) and also demonstrates the technical difficulty of PCI (18). Furthermore, SYNTAX score is a guiding tool to determine coronary artery by-pass graft surgery or PCI for the patients with left coronary artery or multiple CAD. High SYNTAX values can predict the unwilling outcomes after PCI in patients undergone revascularization (19, 20). Wykrzykowska et al presented that SYNTAX score is an independent predictor for MACE and mortality in patients with CAD after percutaneous intervention (21). Moreover, SYNTAX score has a role to classify the risks in PCI performed patients with STEMI and is beneficial inproviding an additional risk classification on known MACE risk factors (22, 23). In the patients with high SYNTAX score, poor prognosis and increased MACEs can be explained by the differences on clinical, angiographic and interventional features. To sumup, its prognostic importance and efficacy have been demonstrated in many studies. However, it may delay effective planning of treatment and follow-up in the patients lately performed or not performed angiography due to its complexity of the application, need of multiple calculation process and including of anatomical evaluation. Therefore, a search for more practical method has been going on as an alternative to the SYNTAX score.

Given its prognostic predictive power for the CAD patients, SYNTAX II score is a new and superior to the SYNTAX score and it additionally considers age, left ventricular ejection fraction, glomerular filtration rate, peripheral artery disease, chronical obstructive pulmonary disease and left coronary artery disease (3). In our study, SYNTAX II score was evaluated for the correlation with the resting and post-exercise ABI and it revealed that a negative correlation exists between SYNTAX II score and resting or post-exercise ABI.

Nonaka M et al. reported that the SYNTAX II score was more successful in their study in which they evaluated the mortality and major adverse cardiovascular and cerebrovascular events of their patients after coronary bypass surgery. (3). We did not perform a prognostic follow-up or analysis in our study. According to the design of our study, the relationship between resting and post-exercise ABI indices and the prevalence of coronary artery disease was evaluated. In this context, ABI measurements at rest and after exercise, which were significantly related to the SYNTAX score in our analyzes, were also found to be significantly related to the SYNTAX II PCI score. ABI measurements at rest and after exercise were defined as independent predictors for SYNTAX score >22 and SYNTAX II PCI score ≥30, in which we expressed the prevalence of coronary artery disease.

Determining the mortality and morbidity risks are essential for clinicians after admission of a patient with ACS. Early identification the risks about mortality and morbidity based on objective criterias is important for determining the treatment and management. Various risk scoring systems have been aimed to develope to build a consensus on accurate management. For that purpose, TIMI and GRACE risk scores were defined by using clinical and demographic features of patients and these risk scores have been applying frequently (24, 25). In a study of Hammami et al on 238 patients with ACS, GRACE and TIMI scores were evaluated for the correlation with extensity of CAD measured by SYNTAX score. It was stated that both scoring systems showed a weak correlation with SYNTAX score. It was also revealed that GRACE and TIMI had a medium level predictive value with low rate of specificity and sensitivity but they can not predict the extensity of CAD (26). In our study, it was stated that both scoring systems did not have any role in differentiating the extensity of CAD and did not correlate with CAD extensity defined by SS>22. On the other hand, TIMI and GRACE scores were found to be correlated with the SYNTAX II PCI score. In addition, the GRACE score was found to be an independent predictor of the extent of CAD, expressed as SYNTAX II PCI ≥30.

Cordero et al stated that the pathological ABI is an equivalant to advancedage in terms of mortality and cardiovascular events after ACS. Also, they defined the subgroup of high-risk advanced age who can not be diagnosed as PAD because they do not generally reveal any symptoms after ACS. These results encourages ABI measurement to identify the high-risk patients who would need to be optimized medical interventions and probably have benefit from intense management (27). PAD is also related to significant increase in risk of fatal and nonfatal cardiovascular and cerebrovascular events (28-31). Chang et al studied the correlation between ABI and CAD complexity and extensity in the patients with possibility of CAD performed coronary angiography and angioplasty (32). When compared to the patients with ABI <0.9, the patients with ABI >0.9

had more complex and extend lesions. In another study, the authors reported the indipendent predictive worth of ABI to identify more number of obstructive coronary lesions in the ACS patients (33). In the study of Bertomeu V et al that presents the high prevalence of PAD in patients who had advanced age, smoking habit, diabetus mellitus or the history of cardiovascular event after the age of 40, high cardiovascular complication rates during the hospitalization for ACS were observed in the presence of PAD defined by ABI <0.9 (34). In their study designed with 200 patients over the age of 60 who were treated for ischemic heart disease, Amer et al presented the correlation between CAD complexity and extensity measured by SYNTAX score and ABI (35). In the literature, the relation between SYNTAX score and resting ABI was interpreted in various studies. The results obtained were compatible with our results. However, there have been insufficient data for the correlation between SYNTAX or SYNTAX II score and post-exercise ABI in which low values can be obtained even in patients obtained normal resting ABI measurements. This comparison distinguishes our study from resembling ones. Hyperaemia and other parameters showing an alteration in blood flow after exercise may indicate PAD in patients with hemodinamically in significant atherosclerotic lesions at rest (36). For that reason, it is recommended the post-exercise ABI to be measured in the symptomatic patients having normal resting ABI in order to distinguish arterial claudication and pseudoclaudication (5). Diehm et al evaluated the relation between mortality and cardiovascular event with resting and post-exercise ABI after 5-year follow-up of 6468 patients with advanced age (9). It was observed that the post-exercise ABI was not superior to the resting ABI in terms of more accurate prediction of mortality and cardiovascular event. However, the low sensitivity of ABI cut-off values in that study compromises the reliability of the comparison. In our study, the post-exercise ABI cut-off value for prediction of CAD complexity is 80%. Abnormal post-exercise ABI results are shown to be associated with an increased rate of lower extremity revascularizationin the patients with normal and abnormal resting ABI. Also, when compared to the patients with normal ABI measurements, the patients with abnormal resting or post-exercise ABI measurements was presented to have an increased rate of MACE and all-cause death in the study of Hammad TA et al. In this retrospective study, it is observed that the post-exercise ABI provides clinical and prognostic information beter than normal and abnormal resting ABI (10). The post-exercise ABI measurement has been compared to the resting ABI in various ways by several authors. Nonetheless, the number of studies investigating the correlation with CAD complexity is insufficient in the literature. In our study, the post-exercise ABI is found to be more efficient than the resting ABI in predicting CAD extensity.

Limitation of the study

Relatively lower number of patients and the single-center design of the study are the most important limiting factors of our study. Multi-centered, randomised studies designed with larger patient number are needed for these inferences to be pracitced to the general population. Also, it should be taken into consideration that the KILLIP class III and IV patients who can not tolerate the resting and post-exercise ABI measurements exluded from our study.

Conclusion

The extensity of CAD can be determined with ABI scorings which are able to be applied easily at the bedside in patients admitted to the hospital with the diagnosis of ACS. We found out that the post-exercise ABI is more superior than the resting ABI for determining of the extencity and complexity of CAD (SYNTAX Score >22). ABI at rest and after exercise is associated with the prevalence of CAD, expressed as a SYNTAX score >22 and a SYNTAX II PCI score >30. ABI at rest and after exercise are independent predictors of the prevalence of CAD.

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