Correlation Between Ankle Brachial Index and SYNTAX Score to Predict Severity of Coronary Artery Disease

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Abstract: Background: Atherosclerosis is a progressive disease affecting large and medium-sized arteries causing luminal stenosis. It is a systemic illness, so presence of peripheral artery disease (PAD) is considered a strong predictor of cardiovascular events, which occurs around 5-7% annually. Patients with PAD in one vascular bed had a 35% chance to have the disease in at least one other territory, and 50% had cerebrovascular or cardiovascular events. Ankle brachial index (ABI) is a simple bedside tool with high specificity and sensitivity for the diagnosis of PAD. SYNTAX score is a well validated tool to predict complexity of coronary artery disease (CAD). In this study, we aimed to correlate between ABI and SYNTAX score as a marker of severity of CAD. **Methods:** This study was designed as a prospective single-center cross-sectional study. It included 152 patients referred for coronary angiography in our tertiary center. Patients with objective evidence of myocardial ischemia were enrolled. All candidates were subjected to thorough history taking with an emphasis on risk factors for CAD. A precise physical examination targeting signs of PAD was conducted. Routine preprocedural ECG and blood tests were drawn. ABI was measured for the entire studied cohort before coronary angiography. SYNTAX score 1 was calculated using the online SYNATAX calculator for all patients once coronary anatomy was defined. **Results:** The age of our study population ranged from 33 to 80 years (Mean 58.74±8.99). Males represented 75.7% of the studied patients. The most prevalent risk factor was hypertension, then diabetes mellitus, and smoking ,respectively. ABI ranged from 0.73–1.2 with mean 1.00±0.08. Fifteen patients (9.9%) had a low ABI of <0.9. ABI showed significant negative correlation with age and smoking. SYNTAX score ranged from 0–51 with Mean 11.57±12.07 with significant positive correlation with age and smoking. We studied the correlation between SYNTAX score and ABI among the total number of cases and we found a highly significant negative correlation between ABI and SYNTAX score with a P-value of 0.0001. Results were tested by logistic regression model for relation between low ABI and high SYNTAX score after adjustment of other co-variants which revealed that an ABI <0.9 is an independent predictor of SYNTAX score >33. **Conclusion:** ABI can be used as a useful predictor for CAD complexity assessed by SYNTAX Score.

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Key words: ABI, SYNTAX, peripheral arterial disease (PAD), coronary artery disease (CAD)

Introduction

Atherosclerosis is a disease of the large and medium-sized arteries resulting in luminal stenosis, resulting from accumulation of lipids and fibrosis between the arterial intima and its media. It is a multifocal, immune-inflammatory disease of muscular arteries provoked by lipids. Endothelial cells, leukocytes, and intimal smooth muscle cells are the major tools in progress of this disease, resulting in plaque formation, vascular remodeling, luminal narrowing and turbulence of blood flow.[1]

Ischemic heart disease (IHD) is a condition of imbalance between myocardial oxygen supply and demand, commonly caused by coronary atherosclerosis, resulting in myocardial hypoxia and ischemia, ranging from stable coronary artery disease to acute coronary syndromes with dramatic increase in cardiovascular mortality.[2]

Atherosclerosis of the non-coronary vessels is named as PAD. Owing to the fact that atherosclerosis is a systemic illness; patients with PAD had a two to three-fold increase in the occurrence of angina compared with age-matched controls. Risk of cardiovascular death increases with asymptomatic PAD and surprisingly the risk may not differ from symptomatic PAD.

PAD is an iconic marker of extensive atherosclerosis and high cardiovascular risk. Patients with claudication have a 30% 5-year mortality risk with an additional 20% suffering a nonfatal MI or stroke. In a published case series of PAD patients, 60% to 80% had significant obstruction in at least one vessel on angiography and up to 25% of them will have significant internal carotid artery stenosis.[3-7]

ABI is a non-invasive bedside tool with appreciable specificity and sensitivity for the diagnosis of PAD. Because of the well-established relationship between PAD and CAD, a low ABI is associated with higher rates of cardiovascular morbidity and mortality (for each decrement of 0.1 in ABI, mortality increases about 13%).[8-10]

The SYNTAX score is an anatomical risk score to assess complexity of CAD taking into account features such as bifurcations, total occlusions, thrombus, calcification and small vessels. Each coronary lesion with a greater than 50% luminal obstruction lumen in vessels ≥1.5 mm are separately scored and summated to provide the overall SYNTAX score.[11]

Patients with PAD who underwent cardiac catheterization had more severe and calcified lesions, suggesting a more aggressive form of atherosclerosis. Based on this fact, we hypothesized that low ABI even in asymptomatic PAD can be a useful tool to predict the complexity of CAD.[12,13]

Aim of work:

To correlate between ankle brachia index and Syntax score as a predictor of severity of coronary artery disease.

Methods

Study population

The study is a prospective, single-center, cross-sectional study. It included 152 consecutive patients referred for elective coronary angiography with objective evidence of CAD (stress ECG, pharmacological stress test or CT coronary angiography). Patients known to have PAD were excluded. Written and informed consent was achieved from the studied cohort.

Methodology

Detailed history, precise examination emphasis on arterial blood pressure, peripheral pulsations and signs of PAD, laboratory samples (electrolytes, thyroid profile) to rule out reversible causes were done. Trans-thoracic echocardiogram was conducted at the first patient appointment to identify the presence of structural heart disease, and less frequently post-procedurally to exclude short term complications. ABI was measured before coronary angiog¬raphy.

Study limitations

Single center study and relatively small study size.

Limb pressure measurement protocol for the determination of the ABI with the Doppler method[14-18]:

- Patient should be at rest 5 to 10 min in the supine position, relaxed, with supported elbows and heels, in a room with suitable temperature (19°C-22°C/66°F-72°F).
- Smoking is prohibited 2 hours before measurements.

Table 1. Classification of ABI results.

>1.4	High (non-compressible vessels)
1–1.4	Normal
0.91–0.99	Border Line
<0.9	Low

- The cuff size should be suitable with a width of at least 40% of the limb circumference (Class I; Level of Evidence B).
- In case of distal bypass, the use of pressure calf should be avoided (risk of bypass thrombosis) (Class III harm; Level of Evidence C).
- Any open lesion with risk of contamination should be covered with an impermeable cloth (Class I; Level of Evidence C).
- The patient should stay calm during the pressure measurement. If the patient is unable to move his/her limbs (eg, tremor), other methods should be considered.
- The ankle cuff should be placed just above the malleoli with the straight wrapping method (Class I; Level of Evidence B).
- The Doppler method should be used to measure the SBP in each arm and each ankle for the determination of the ABI (Class I; Level of Evidence A).
- An 8- to 10-MHz Doppler probe is used. Doppler lubricant should be applied over the sensor.
- After the Doppler device is turned on, the probe should be placed in the area of interest at a 45° to 60° angulations. The probe should be manipulated gently until achieving a clear signal.
- The cuff should be inflated progressively up to 20 mm Hg beyond the level of flow signal disappearance and then deflated slowly to detect the pressure level of flow signal reappearance. The maximum inflation is 300 mm Hg; if the flow is still detected, the cuff should be deflated rapidly to avoid pain.
- Brachial artery flow during the arm pressure measurement should be done by Doppler.
- The first measurement should be repeated at the end of the sequence and both results averaged to overcome the white coat effect, except if the difference between the 2 measurements of the first arm exceeds 10 mm Hg. In that case, the first measurement should be neglected and only the second measurement should be considered.
- If repeated measurements of four limbs are required, the measurements should be repeated in the reverse order of the first.

Recommendations for the calculation of the ABI[19-22]:

- The ABI of each leg should be calculated by dividing the higher of the posterior tibial artery (PT) or dorsalis pedis (DP) pressure by the higher of the right or left arm SBP (Class I; Level of Evidence A).
- ABI results should be classified into 4 groups: (Class I; Level of Evidence: B) as shown below in **Table 1**.

Recommendations for the use and interpretation of the ABI[23-26]:

- An ABI below 0.90 should be considered the cut off value for confirming the diagnosis of lower-extremity PAD (Class I; Level of Evidence A).
- An ABI decline exceeding >0.15 over time can be valuable to detect significant disease progression (Class IIa; Level of Evidence B).
- Subjects with an ABI <0.90 or >1.40 are considered at tremendous risk of cardiovascular morbidity and mortality independently of the presence of symptoms of PAD and other cardiovascular risk factors (Class I; Level of Evidence A).
- Patients with an ABI between 0.91 and 1.00 are considered "borderline". (Class IIa; Level of Evidence A).

Coronary angiography was performed for all studied population via either trans-femoral or trans-radial approach and analyzed separately by 2 experienced operators. SYNTAX score was calculated using an online calculator (http://www.syntaxscore.com).

Syntax Score:

Each coronary lesion with a Stenosis ≥50% in vessels ≥1.5 mm must be documented. Each lesion can involve one or more diseased segments. If serial lesions are less than 3 vessel reference diameters apart, they should be scored as one lesion. However, stenoses at a greater distance from each other (more than 3 vessel reference diameters), are defined as separate lesions.[27-29]

The algorithm consists of twelve main questions. They can be divided in two groups:

The first three questions determine the dominance, the total number of lesions and the vessel segments involved per lesion and they appear once. The maximum allowed number of lesions is twelve and each lesion is marked by a number, 1 to 12. The lesions will be scored in the numerical order inserted in question 3. Each lesion can involve more than a single segment. In this case each vessel segment involved contributes to the lesion scoring. There is no limit in the number of segments involved per lesion.

The last nine questions are concerned with adverse lesion properties and are repeated for each lesion:

The first question is that related to total occlusion. If a total occlusion is scored, data must be passed to detailed sub-questions. The last of these sub-questions refers to the presence or absence of side branches and their size. If there are no side branches or if their diameter is <1.5 mm then the questions related to the trifurcation and bifurcation lesions will be automatically skipped since vessels <1.5 mm are not considered sizable enough for percutaneous or surgical intervention. If side branches with diameter 1.5 mm are involved then the lesion is considered as both total occlusion and bifurcation lesion and the algorithm will continue with all the questions. The same is the case for non-occlusive lesions.

All questions can be answered by "yes" or "no" except those related to the lesion type regarding bifurcation or trifurcation. The last question of the algorithm, diffuse disease/small vessels, is the only question that is non-lesion-specific as it is related to vessel anatomy regardless of the stenotic lesion.

A peculiar characteristic of the SYNTAX score is that it is lesion based. For every lesion a separate score is calculated. The total SYNTAX score is calculated from the summation of these individual scorings. After finishing data entry into the algorithm, a report is automatically generated summarizing all the adverse characteristics, and the individual scoring of each lesion together with the total SYNTAX score.[27-29]

Statistics

Data were analyzed using SPSS version 21 for Windows and graphics by MS Excel. Categorical data were expressed as frequencies and percentages, while continuous data were expressed as mean ± SD or median. Comparison between categorical variables was done using Chi square or Fisher's exact test as appropriate. Comparison between continuous variables was done using t-test or Mann-Whitney test according to normality of distribution.

Results

This study was conducted on 152 patients referred for elective coronary angiography in our center; ABI was calculated routinely before proceeding to catheterization laboratory. Mean age of the studied cohort was 58±8 years with male predominance, comprising 75% of studied subjects. The most prevailing risk factor was hypertension (63.2%) followed by diabetes mellitus (43.4%), smoking (26.3%), and dyslipidemia (8.6%) respectively.

Ankle brachial index ranged from 0.73–1.2 with mean 1.00±0.08. Fifteen patients (9.9%) had a low ABI <0.9, 40 patients (26.3%) had a borderline ABI = 0.91-0.99 and 97 patients (63.8%) had a normal ABI = 1-1.4. None of the enrolled patients had an ABI >1.4, as shown in **Table 2**.

Table 2. Number of patients in each ABI group.

ABI	(<0.9)	(0.91-0.99)	(1-1.4)
Number of patients	15	40	97

SYNTAX score ranged from 0–51 with Mean 11.57 ± 12.07. SYNTAX score of 0 was found in 39 patients (25.7%), 87 patients (57.2%) had a low SNTAX score of 1-22, 13 patients (8.55%) had an intermediate SYNTAX score (23-33), and 13 patients (8.55%) had a high SYNTAX score (>33), as shown in **Table 3**.

Table 3. Number of patients in each SYNTAX score group.

SYNTAX score	0	1-22	23-33	>33
Number of patients	39	87	13	13

Regarding correlation between demographic factors and ABI, only age and smoking showed highly significant negative correlation with ABI.

Table 4. Relation between ABI and demographic factors.

		ABI (<0.9)	ABI (0.91–0.99)	ABI (1–1.4)	One Way ANOVA test	
					F/X2*	P-value
Age	Mean ± SD	64.93 ± 5.35	61.10 ± 7.71	56.81 ± 9.31	7.815	0.0001
	Range	57 – 75	47 – 80	33 – 76		
Sex	Females	1 (6.7%)	7 (17.5%)	29 (29.9%)	5.187	0.075*
	Males	14 (93.3%)	33 (82.5%)	68 (70.1%)		

Table 5. Relation between ABI groups and risk factors.

		ABI		Independent t-test	
		Mean ± SD	Range	t/F*	P-value
Hypertension	Negative	1.01 ± 0.08	0.85 – 1.18	-0.945	0.346
	Positive	0.99 ± 0.09	0.73 – 1.2		
Diabetes Mellitus	Negative	1 ± 0.08	0.73 – 1.2	0.049	0.961
	Positive	1 ± 0.08	0.82 – 1.18		
Dyslipidemia	Negative	1 ± 0.08	0.73 – 1.2	-0.009	0.992
	Positive	1 ± 0.1	0.86 – 1.18		
Smoking	Non smoker	1.02 ± 0.08	0.82 – 1.2	3.901	0.022*
	Smoker	0.97 ± 0.09	0.73 – 1.15		
	Ex-smoker	0.99 ± 0.08	0.83 – 1.18		

Male gender and smoking were the only demographic parameters that showed significant positive correlation with coronary SYNTAX score.

Table 6. Relation between SYNTAX score and demographic data.

		SYNTAX score		Independent t-test	
		Mean ± SD	Range	t/F*	P-value
Hypertension	Negative	11.48 ± 12.75	0 – 51	0.068	0.946
	Positive	11.62 ± 11.72	0 – 41		
Diabetes Mellitus	Negative	10.98 ± 12.10	0 – 51	0.683	0.496
	Positive	12.33 ± 12.08	0 – 48		
Dyslipidemia	Negative	11.41 ± 12.27	0 – 51	0.518	0.605
	Positive	13.23 ± 9.99	0 – 40		
Smoking	Non smoker	9.11 ± 11.24	0 – 51	3.842	0.024*
	Smoker	15.59 ± 12.41	0 – 48		
	Ex-smoker	11.90 ± 12.31	0 – 39		

We studied the correlation between SYNTAX score and ABI among the total number of cases and we found a highly significant negative correlation between ABI and SYNTAX score with a *P*-value of 0.0001.

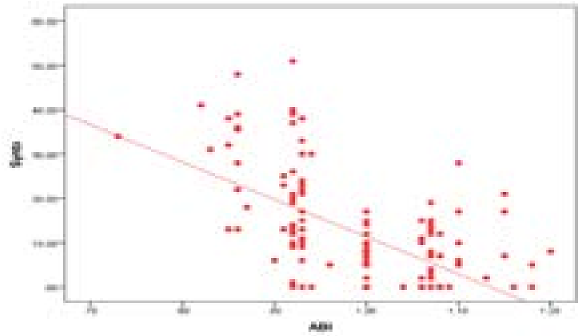

Figure 1. Relation between ABI and SYNTAX score.

Regarding distribution of SYNTAX score in each ABI group, we found that SYNTAX score in patients with ABI <0.9 ranged from 6-48 (mean 28.97 ± 12.03), it ranged from 0-51 in patients with borderline ABI (0.91-0.99) with mean 19.30 ± 12.53, and in patients with normal ABI it ranged from 0-28 with mean 5.69 ± 6.09. Based on these results, a highly significant negative correlation was found between SYNTAX score and ABI with *P*-value 0.0001.

Table 7. Relation between SYNTAX score and ABI subgroups.

SYNTAX	ABI (<0.9)	ABI (0.91 - 0.99)	ABI (1 - 1.4)	One Way ANOVA test	
				F	P-value
Mean ± SD	28.97 ± 12.03	19.30 ± 12.53	5.69 ± 6.09	65.395	0.0001
Range	6 – 48	0 – 51	0 – 28		

Table 8. Individual value of Syntax score among patients with low ABI <0.9.

Group with low ABI <0.9 (15 patients)	
ABI	Syntax
0.85	13
0.86	22
0.82	31
0.83	41
0.73	36
0.86	48
0.89	6
0.86	13
0.87	18
0.85	35
0.86	37
0.85	39
0.83	32
0.84	34
0.86	28

Results were tested by logistic regression model for relation between low ABI and high SYNTAX score after adjustment of other co-variants which revealed that ABI <0.9 is an independent predictor of SYNTAX score >33 (OR=16.25; CI:4.57–37.7; *P*<0.001).

Discussion

Atherosclerosis is a systemic progressive disease with no geographical limits; it can affect the peripheral arterial tree as well as cerebral, coronary, and retinal vessels. Patients with atherosclerosis tend to have multiple co-existent risk factors including male gender, aging, diabetes mellitus, smoking, hypertension and dyslipidemia, and it is highly predicted to detect coronary atherosclerosis in patients with peripheral arterial atherosclerotic disease even in a silent presentation.

Assessment of lower extremity peripheral arterial disease can be easily done through bedside examination using simple and rapid methods such as ABI. This is in contrary to coronary atherosclerosis that dictates invasive evaluation of coronary artery disease through angiography. In this study we aimed to correlate the values of ABI to severity of coronary atherosclerosis using a measurable tool which is the SYNTAX score, aiming to use peripheral arterial atherosclerosis as mirror image of severity of coronary artery disease.

In this study we recruited 152 consecutive patients referred to our center for elective coronary angiogram. Bedside ABI was calculated for all patients before proceeding to the catheterization laboratory after which SYNTAX score was calculated.

In our study, we found a highly significant negative correlation between SYNTAX score and ABI values—the lower the ABI, the higher is the SYNTAX score—signifying more complex coronary anatomy. After applying a logistic regression model and adjustment of all co-variants, we detected that ABI <0.9 is an independent predictor of SYNTAX score >33 (OR=16.25; CI=4.57–37.7; *P*<0.001).

These results go hand in hand with results from Aykan et al, who concluded that ABI was significantly correlated with SYNTAX score (r=0.650, *P*<0.001) and was found to be an independent predictor of SYNTAX score. ABI <0.9 identified patients with a SYNTAX score >22 with a sensitivity of 45.28% and a specificity of 82.64% (AUC=0.689, 95% CI=0.619-0.763, *P*<0.001). In the study conducted by Falcão et al, 204 elderly patients referred for elective coronary angiography were studied. They found that an ABI of <0.9 was strongly associated with the presence of CAD (OR=2.43; CI=1.47–4.03; *P*=0.0001). Median SYNTAX score was significantly higher in patients with ABI <0.9 (*P*=0.001), which is concordant with our results. However, the study population included more elderly subjects with female predominance.[12,30]

The main concept was studied by Korkmaz et al but in a more specific group of subjects with acute coronary syndrome. Their study showed that patients with ABI <0.9 had a higher SYNTAX score, compared with patients with ABI of 1.0–1.09 (17.8±9.1 vs 12.5±5.9; *P*=0.001). Ikeda et al studied the same postulation but in a specific ethnic group. They studied 496 Asian patients, with a mean age of 69.2±11.4 years, and compared ABI against SYNTAX score. They reported that patients with low ABI (<0.9) had a significantly higher SYNTAX score than patients with ABI ≥0.9 (*P*<0.0001).[31,32]

Hashizume et al enrolled 1468 patients who underwent percutaneous coronary intervention and had their ABI measured. The SYNTAX score was significantly higher in patients with the low ABI group (13.9±9.8 vs 13.2±9.6 vs 11.8±8.1, *P*=0.010). ABI value was an independent negative predictor (ABI per 0.1, OR 0.870, 95% CI 0.788-0.961, *P*=0.006) of coronary artery lesion complexity (the SYNTAX score ≥22). It differs from our study by the large number of recruited elderly subjects.[33]

In our study, age showed significant negative correlation with ABI (*P*-value 0.0001), matching what stated by Sebastianski et al with (*P*-value 0.001) and Ikeda et al with (*P*-value 0.03). Also, smoking showed significant negative correlation with ABI (*P*-value 0.022), which is concordant with Sebastianski et al with (*P*-value 0.012).[13,32]

We concluded that ABI has a highly significant negative correlation with SYNTAX score (*P*-value 0.0001) after adjustment of other co-variants. Moreover, patients with low ABI (<0.9) had 16 times the risk of having complex coronary anatomy indicated by high SYNTAX score (>33) compared with patients with normal ABI.

Conclusion

Ankle brachial index can be used as independent predictor of coronary artery disease complexity. ■

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Disclosure

The authors have completed and returned the ICMJE Form for Disclosure of Potential Conflicts of Interest. The authors report no financial relationships or conflicts of interest regarding the content herein.

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