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ANKLE BRACHIAL INDEX AS A PREDICTOR OF CORONARY ARTERY DISEASE COMPLEXITY

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Abstract:
Background: Coronary artery disease and peripheral arterial disease shares common risk factors for etiopathogenesis. Present study is designed to find out relationship between ankle brachial index (ABI) and syntax score.
Methods: Total 152 consecutive patients of stable coronary artery disease in whom angiography was indicated were taken for the study. ABI measurement was performed using a portable ultrasound doppler before coronary angiography and syntax score was calculated by using online syntax score calculator. Statistical analysis was done by SPSS V18 software.
Results: Our study has 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) has 16 times risk of having complex coronary anatomy indicated by high syntax score (>33) compared with patients with normal ABI
Conclusions: Ankle Brachial Index might be used as an independent predictor of coronary artery disease complexity.
Keywords: ABI, syntax score, peripheral arterial disease, ankle brachial index

Introduction

Atherosclerosis is a disease of the large and medium-sized arteries causing luminal narrowing (focal or diffuse). This occurs as a result of the accumulation of lipid and fibrous material between the intimal and medial layers of the vessel. Atherosclerosis of the non-cardiac vessels is defined as peripheral artery disease (PAD).[1]

Because atherosclerosis is a systemic disease, presence of PAD is considered a strong predictor of cardiovascular events which is 5-7% annually. In the AGATHA study, patients with PAD in one vascular bed had a 35% chance of having disease in at least one other territory, and 50% had cerebrovascular or coronary heart disease. There was a 2-3% nonfatal myocardial infarction rate, and a twofold to threefold increase in the occurrence of angina compared with age-matched controls. Risk of cardiovascular mortality increases with asymptomatic PAD and surprisingly the risk may not differ from symptomatic PAD.[2]

Ankle brachial index (ABI), is a simple and non-invasive tool with high specificity and sensitivity for the diagnosis of PAD. Because of the well-established relationship between PAD and coronary artery disease (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%).[1,3]

It has been found that patients with PAD who had undergone cardiac catheterization had more extensive and calcified lesions, suggesting a more aggressive form of atherosclerosis. This study is to investigate the correlation between ankle brachial index and the complexity of CAD.

PATIENTS AND METHODS

The study was designed as a prospective single center cross-sectional study conducted at Ain shams university hospitals. The study included 152 patients referred for coronary angiography in the time period from July 2015 till December 2015.

Patients

Inclusion criteria:

Indication for coronary angiography (CA) for coronary artery disease according to ESC 2014 revascularization guidelines.

Exclusion criteria:

Patient's refusal.

Known PAD.

Contraindication for CA e.g. (active bleeding, coagulopathy, active infection, etc.).

Inability to measure blood pressure in a limb for any reason.

Methods

Factors studied:

All cases were analyzed thoroughly as regards:

- **History:** Emphasized on the presence of cardiovascular risk factors, (diabetes mellitus, hypertension, smoking, dyslipidemia, family history of premature CAD), cardiac symptoms, PAD symptoms, presence of exclusion criteria and history of any cardiac or vascular condition.

- **Complete physical examination:** Emphasized on arterial blood pressure, the presence of any sign of other peripheral arterial disease (lost peripheral pulses, carotid bruits…etc.).

- **Laboratory investigations:** Included complete blood count, serum creatinine, prothrombin time, INR, partial thromboplastin time and random blood sugar.

- **Measurement of Ankle Brachial index:** Ankle Brachial Index (ABI) was measured **before** coronary angiography. After patient had rest for at least 5 minutes in a supine position, measurement was performed using a portable ultrasound Doppler with cuff inflators with appropriate size. Systolic blood pressure measurements of the brachial, posterior tibial, and dorsalis pedis arteries was taken on both sides of the limb. Ankle brachial index was calculated as the ratio between the lowest ankle systolic pressure and the highest brachial systolic pressure. Ankle brachial index was determined for each leg, and the lowest value was considered for analysis.

- **Coronary angiography:** It was performed using conventional techniques and was analyzed by two experienced interventional cardiologists.

- **Coronary scoring:** SYNTAX score was calculated using an online calculator (http://www.syntaxscore.com).A SYNTAX score of 0 indicates no measurable coronary disease, while a score 1 indicates the presence of CAD, with CAD complexity increasing as the SYNTAX score increases.

- **Statistical Analysis:** Data were expressed as mean value ± SD for continuous variables, and as percentages for categorical variables. In this study, statistical significance was established as follows:

p>0.05 insignificant
p≤0.05 significant
p≤0.01 highly significant

Comparisons between continuous variables were performed using the paired t-test, unpaired t test or Mann-Whitney U test. For comparisons of categorical variables, frequency tables and chi-square analyses were used.

All analyses of the present study were done using the **SPSS V18 software.**

The hypothesis that the row and column variables are independent, without indicating strength or direction of the relationship. Pearson chi-square and likelihood-ratio chi-square. Fisher's exact test and Yates' corrected chi-square are computed for 2x2 tables.

RESULTS

This study included 152 patients who underwent coronary angiography at Ain Shams University hospitals in the time period from July 2015 till December 2015. They all had their ABI measured before the coronary angiography to find out whether or not it might be a predictor of Coronary artery disease complexity.

Baseline data:

Socio-demographic data:

The age of our study population ranged from 33 to 80 years (Mean 58.74 ± 8.99). Males represented 75.7% of the study population. **Table (1)**

Risk Factors:

The most prevalent risk factor was Hypertension affecting 96 patients (63.2%). Regarding Smoking, 40 patients were smokers (26.3%), 41 were ex-smokers (27%) and 71 were non-smokers (46.7%). 66 patients had DM (43.4%), while history of dyslipidemia was found only in 13 patients (8.6%). **Table (2), Figure (1) & Figure (2)**

Laboratory data:

Serum creatinine ranged from 0.4 – 8.7 with mean 1.05 ± 0.69, while INR ranged from 0.8 – 2.3 with mean 1.09 ± 0.18. **Table (3)**

Ankle brachial index:

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. **Table (4) & Table (5)**

SYNTAX score:

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). **Table (6) & Table (7)**

i. Correlations with Ankle brachial index:

Ankle brachial index with socio-demographic data:

Age showed highly significant negative correlation with ABI with P-value 0.0001. **Table (8) & Figure (1)**

Ankle brachial index with risk factors:

Among risk factors, only Smoking showed significant negative correlation with ABI when studied with total number of cases with P-value 0.022. **Table (1) & Figure (2)**

Regarding distribution of risk factors in each ABI group, no significant correlation was found between ABI groups and risk factors. **Table (2)**

Ankle brachial index with Laboratory investigations:

None of laboratory investigations showed significant correlation with ABI. **Table (3)**

ii. Correlations with SYNTAX score:

SYNTAX score with socio-demographic data:

Male gender showed positive correlation with SYNTAX score with P-value 0.009. **Table (12) &Table (13) & Figure (5)**

SYNTAX score with risk factors:

Smoking was the only risk factor that showed positive significant correlation with SYNTAX score with P-value 0.024. **Table (4) & Figure (6)**

SYNTAX score with Laboratory findings:

No laboratory findings showed significant correlation with SYNTAX score. **Table (15)**

Correlation between SYNTAX score and Ankle brachial index:

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 P-value 0.0001. **Table (16) & Figure (7)**

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 (17) & Figure (8)

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). Table (18)**

ABI and SYNTAX score after adjustment of other co-variants (age, gender, Hypertension, DM, smoking and dyslipidemia) revealed highly significant negative correlation between ABI and SYNTAX score (P 0.0001). **Table (19)**

These results goes hand by hand with ***Aykan et al*** who concluded that ABI was significantly correlated with SYNTAX score (r = 0.650, p< 0.001) and was found to be independent predictors of SYNTAX score. ABI<0.9mm identified patients with 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). [85]

Falcão et al. have also studied the correlation between ABI and SYNTAX score in 204 patients older than 65 years old who were undergoing elective coronary angiography for ischemic coronary disease. They found that patients with 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, study population included elderly with female predominance. [4]

Korkmaz et al. after evaluating 150 patients with Acute coronary syndromes, irrespective of age, 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 versus 12.5±5.9; *P*, 0.001). [20]

This correlation was also concluded by ***Ikeda et al.*** who selected 496 Asian coronary angiography 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 significantly higher SYNTAX score than patients with ABI ≥0.9 (P<0.0001). [21]

In ***2014, Naoto et al.*** enrolled 1468 patients who underwent percutaneous coronary intervention and had their ABI measured. The SYNTAX score was significantly higher in patients with low ABI group (13.9±9.8 vs. 13.2±9.6 vs. 11.8±8.1, p=.010). ABI value was independent negative predictor (ABI per 0.1, OR 0.870, 95%CI 0.788-0.961, p=.006) of coronary artery lesion complexity (the SYNTAX score≥ 22). It differs also from our study that it included elderly patients. [22]

In our study, Age showed significant positive correlation with ABI (P-value 0.0001). The same results were found in ***Sebastianski et al.*** [5] with (P-value 0.001) and in **Ikeda et al** [23] with (P-value 0.03)

Also, Smoking showed significant positive correlation with ABI (P-value 0.022), which is concordant with ***Sebastianski et al.*** [5] with (P-value 0.012) in current smokers.

DISCUSSION

The main aim of our study was to find out whether ABI can predict CAD complexity or not by investigating the correlation between ABI and SYNTAX score. So, we measured ABI in 152 consecutive patients before CA and calculated their SYNTAX score following CA.

Our study has 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) has 16 times risk of having complex coronary anatomy indicated by high SYNTAX score (>33) compared with patients with normal ABI.

Moreover, we found a correlation between ABI and age, the more the age the less the ABI (P 0.0001), also ABI was found to correlate with smoking (P 0.022).

This study has also found a correlation between SYNTAX score and smoking (P 0.024). SYNTAX score was higher in males (P 0.009).

Limitations:

Single center study.

Relatively small study population.

Table 1: Socio-demographic data

Age (years)	
Range	33-80
Mean±SD	58.74 ± 8.99
Gender N (%)	
Male	115 (75.7)
Female	37 (24.3)

Table 2: Distribution of risk factors:

Hypertension N (%)	
Negative	56 (36.8)
Positive	96 (63.2)
Smoking N (%)	
Non smokers	71 (46.7)
Ex-Smokers	41 (27)
Smokers	40 (26.3)
Diabetes Mellitus N (%)	
Negative	86 (56.6)
Positive	66 (43.4)
Dyslipidemia	
Negative	139 (91.4)
Positive	13 (8.6)

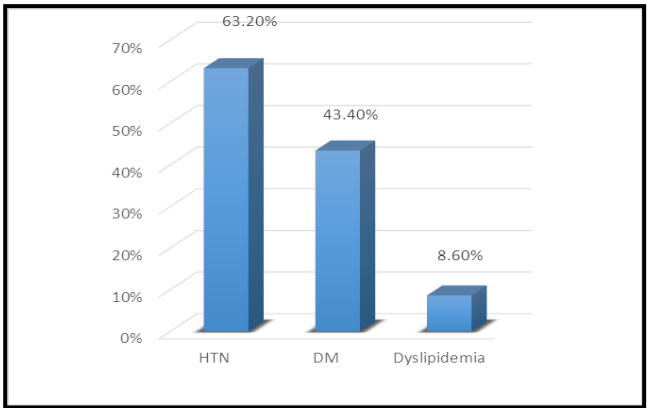

Figure 1: Risk factors studied.

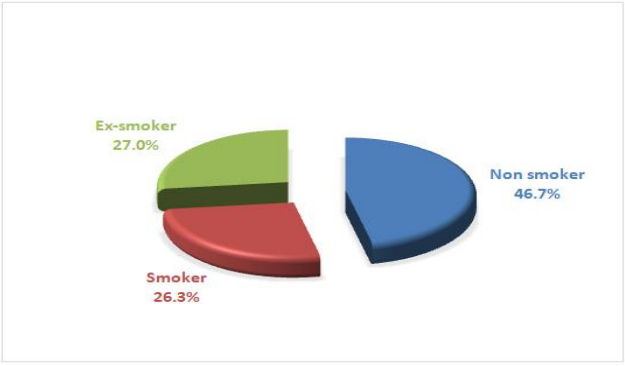

Figure 2: Distribution of Smoking.

Table 3: Laboratory Findings:

	Mean ± SD	Range
Serum Creatinine	1.05 ± 0.69	0.4 – 8.7
INR	1.09 ± 0.18	0.8-2.3

Table 4: ABI Mean & range:

	Mean ± SD	Range
ABI	1.00 ± 0.08	0.73 – 1.2

Table 5: Number of Patients in each ABI group:

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

Table 6: SYNTAX score mean & range

	Mean ± SD	Range
SYNTAX score	11.57 ± 12.07	0 – 51

Table 7: Number of Patients in each SYNTAX score group:

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

Table 8: Relation between ABI groups and socio-demographic data:

		ABI (< 0.9)	**ABI (0.91 - 0.99)**	**ABI (1 - 1.4)**	**One Way ANOVA test**	
					F/X^2*	**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%)		

*: Chi-square test

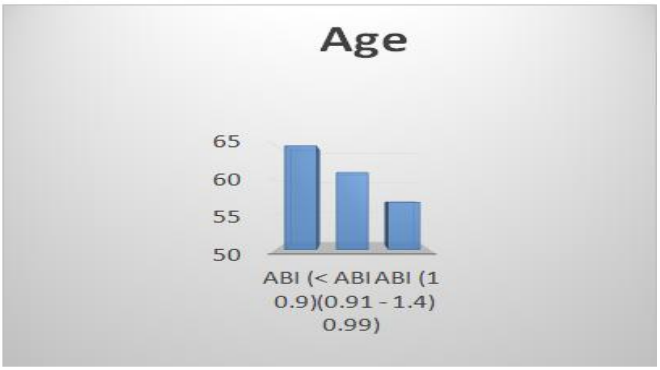

Figure 3: Age in different ABI groups.

Table 5: Relation between ABI in total cases 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		

*: One Way ANOVA test

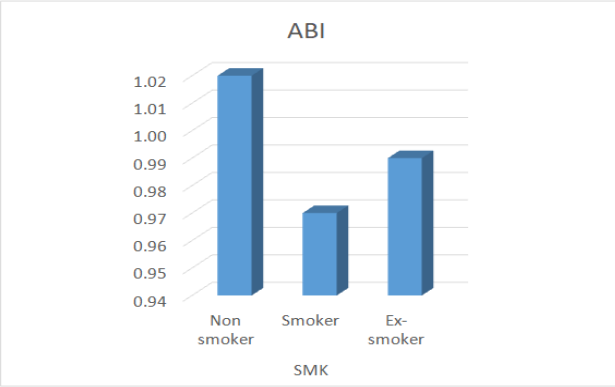

Figure 4: Relation between ABI and Smoking.

Table 6: Relation between ABI groups and risk factors:

		ABI (< 0.9)		ABI (0.91 - 0.99)		ABI (1 - 1.4)		Chi-square test	
		No.	%	No.	%	No.	%	X^2	P-value
Hypertension	Negative	6	40.0%	9	22.5%	41	42.3%	4.828	0.089
	Positive	9	60.0%	31	77.5%	56	57.7%		
Diabetes mellitus	Negative	8	53.3%	22	55.0%	56	57.7%	0.157	0.924
	Positive	7	46.7%	18	45.0%	41	42.3%		
Dyslipidemia	Negative	13	86.7%	37	92.5%	89	91.8%	0.507	0.776
	Positive	2	13.3%	3	7.5%	8	8.2%		
Smoking	Non smoker	4	26.7%	15	37.5%	52	53.6%	7.007	0.136
	Smoker	7	46.7%	12	30.0%	21	21.6%		
	Ex-smoker	4	26.7%	13	32.5%	24	24.7%		

Table 11: ABI groups and Laboratory results:

		ABI (< 0.9)	ABI (0.91 - 0.99)	ABI (1 - 1.4)	One Way ANOVA test	
					F	P-value
Serum creatinine	Mean ± SD	1.14 ± 0.48	1.17 ± 1.23	0.98 ± 0.28	1.171	0.313
	Range	0.7 – 2.6	0.6 – 8.7	0.4 – 2.3		
INR	Mean ± SD	1.17 ± 0.34	1.07 ± 0.12	1.08 ± 0.16	2.049	0.132
	Range	1 – 2.3	0.9 – 1.4	– 1.9		

Table 12: Relation between SYNTAX score and Age:

	SYNTAX score	
	r	P-value
Age	0.067	0.411

Table 13: Relation between SYNTAX score and Sex:

		SYNTAX score		Independent t-test	
		Mean ± SD	Range	t/F*	P-value
Sex	Females	7.11 ± 9.83	0 – 51	2.635	0.009
	Males	13.00 ± 12.41	0 – 48		

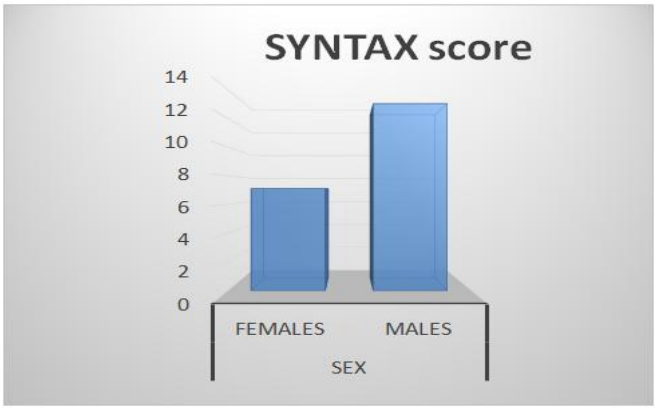

Figure 5: Relation between SYNTAX score and Sex.

Table 7: Relation between SYNTAX score and risk factors:

		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		
Dyslipemia	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		

*: One Way ANOVA test

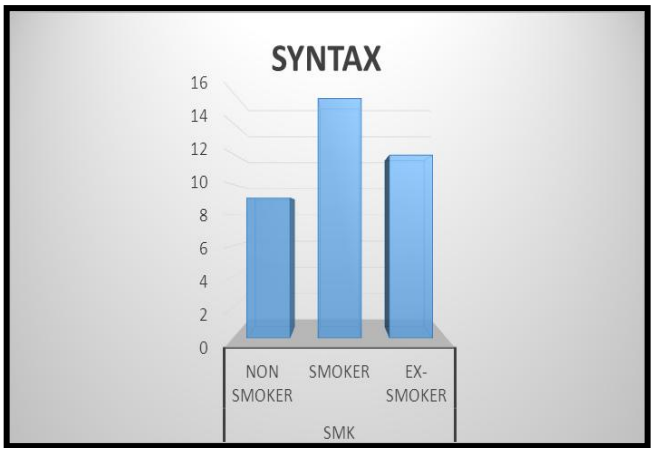

Figure 6: Relation between SYNTAX score and Smoking

Table 15: SYNTAX score and Laboratory results:

	SYNTAX score	
	r	P-value
Serum creatinine	0.137	0.093
INR	-0.146	0.073

Table 16: Correlation between ABI and SYNTAX score:

ABI	SYNTAX score	
	R	P-value
	-0.528	0.0001

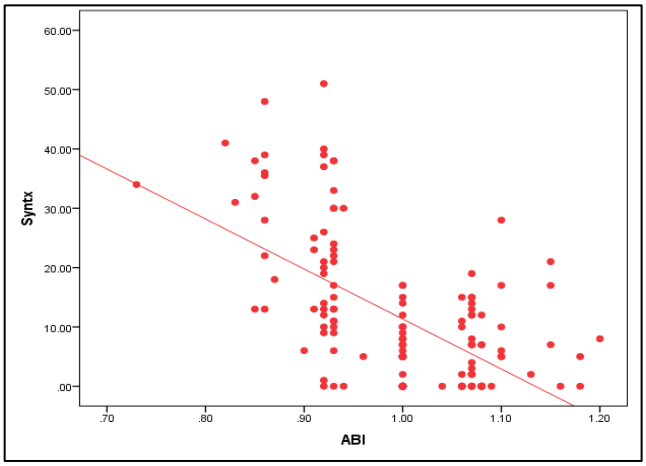

Figure 7: Relation between ABI and SYNTAX score

Table 17: Relation between ABI and SYNTAX score:

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 18: Logistic regression for the relation between ABI and SYNTAX score

Variable	Coefficient	Std. Error	P	OR	95% CI
ABI	-28.3610	6.9463	<0.001	16.25	4.57 – 37.7
Constant	24.3182				

Table 19: Partial correlation between syntax score and ABI

	Syntax score	
	r	p-value
ABI	-.571	0.0001

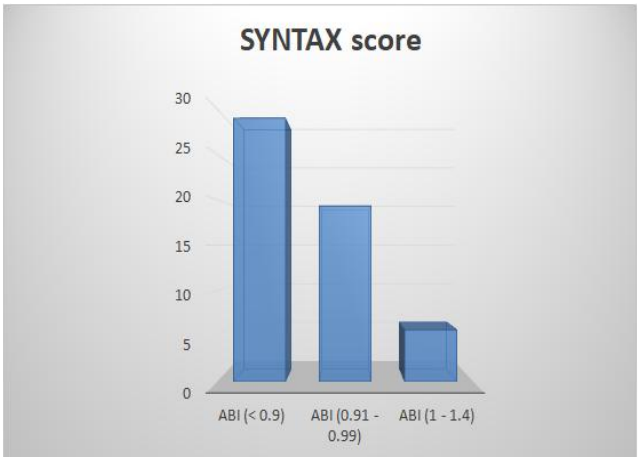

Figure 8: SYNTAX score in different ABI groups

Conclusion:

ABI might be used as an independent predictor of CAD complexity.

Recommendations:

Prospective validation of results by multi-Centre study with larger study population.

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