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ORIGINAL ARTICLE

Ankle Brachial Index in Relation to Pretest Probability Stratification of Coronary Artery Disease

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ABSTRACT

Background: Globally, coronary artery disease (CAD) continues to be a major cause of morbidity and death. A straightforward, non-invasive diagnostic method mostly used to identify peripheral artery disease (PAD), the ankle-brachial index (ABI) has drawn interest as a possible indicator of systemic atherosclerosis. **Aim:** The goal of this study was to evaluate the prognostic usefulness of ABI for CAD severity was. **Methods**: This cross-sectional study was carried out over a six-month period on a total of 180 patients suspected of having CAD at Cardiology Department - Zagazig University Hospitals. The patients were divided into 3 sub-groups according to pre-test probability into low, intermediate and high. **Results:** The three pre-test probability groups did not differ statistically significantly in terms of left atrial enlargement (LAE), left ventricular ejection fraction (LVEF <50%), or left ventricular end-diastolic dimension (LVEDD). The SYNTAX score and ABI were shown to be significantly correlated negatively (r = -value, P < 0.001). With a P value <0.001 and an AUC of 0.863, the study of the Receiver Operating Characteristic (ROC) curve showed that ABI strongly predicted the severity of CAD. The optimal cut-off value was ≤0.89, yielding 75.76% sensitivity, 85.19% specificity, a positive predictive value (PPV) of 86.2%, and a negative predictive value (NPV) of 74.2%. **Conclusion:** The Ankle-Brachial Index can help with risk stratification and is a useful, easy, and non-invasive indicator of the severity of coronary artery disease especially in high-risk patients.

Keywords: Coronary artery disease; Ankle-Brachial Index ;Pretest Probability

INTRODUCTION

The primary cause of morbidity and death is coronary artery disease, (CAD)[1,2]. Estimating the pre-test probability (PTP) of obstructive CAD is a fundamental step in clinical assessment. The 2019 ESC guidelines for chronic coronary syndrome (CCS) introduced an updated PTP model that provides more accurate estimates compared to the 2013 ESC recommendations and the Modified Diamond-Forrester model [3].The ankle-brachial index (ABI), a non-invasive method for assessing vascular health, is calculated as the ratio of systolic blood pressure in the ankle to that in the arm. Originally proposed for diagnosing peripheral arterial disease (PAD) in the lower extremities [4], ABI has shown high accuracy in predicting the severity of CAD in CCS patients in Egypt [5]. Recent European guidelines recognize ABI as a cardiovascular risk modifier [6]. However, further studies are needed to identify which patient groups may benefit most from incorporating this simple test to enhance clinical probability models. This study uniquely highlights ABI's potential to enhance clinical risk stratification, particularly in the Egyptian population.

Aim of the Work

This study aimed to assess the predictive usefulness of the ankle-brachial index for the degree of coronary artery disease.

METHODS

Participants

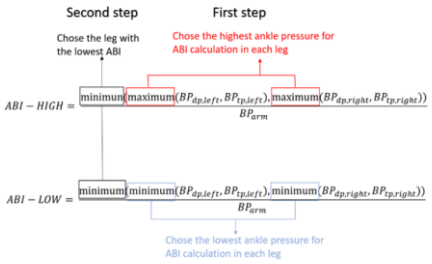
Over the course of six months, 180 patients of both sexes who were at least 18 years old and complaining of chest pain, stable angina, unstable angina, NSTEMI, or STEMI participated in this cross-sectional study. admitted to the Cardiology Department, Zagazig University Hospitals in the duration from March 2024 to March 2025, were randomized into three sub groups according to pre-test probability) into low (n= 14), intermediate (n= 67) and high (n= 99). The classification into low, intermediate, and high PTP groups was based on the 2019 ESC guidelines for chronic coronary syndrome, which define PTP categories according to age, sex, and symptom characteristics. This stratification reflects the estimated likelihood of obstructive CAD and guides subsequent diagnostic steps. The Ethics Committee of Zagazig University's Faculty of Medicine in Egypt gave its approval to the study (IRB # 175/12-March-2024). Every patient provided written informed consent. The Declaration of Helsinki, the World Medical Association's guideline of ethics for research involving human participants, was followed in the conduct of the study. Patients having a diagnosis of coronary artery disease who were at least eighteen years old were included in the trial by thorough clinical evaluation and cardiac evaluation. Exclusion criteria included severe limb ischemia, congenital or valvular heart disease, atrial fibrillation, acute coronary syndrome, chronic kidney disease, ABI ≥ 1.3, significant lower limb edema, refusal to participate, and a pretest probability for CAD <5% based on the 2019 ESC guidelines .A thorough clinical evaluation was performed on each patient, which included a thorough medical history that included information on age, sex, height, weight, and body mass index (BMI), as well as the presenting symptoms and any related comorbidities like diabetes, hypertension, smoking, hyperlipidemia, and other signs of atherosclerotic disease. Blood pressure, heart rate and rhythm, temperature, central venous pressure, respiratory rate, and APACHE II score were among the vital signs that were noted. To evaluate the presence of any murmurs, other sounds, and heart sounds, a comprehensive local cardiac examination was conducted. Tests for liver function (AST and ALT), the laboratory evaluation included a complete blood picture, fasting blood sugar, total cholesterol, triglycerides, LDL, and HDL, as well as renal function (urea and serum creatinine). Each patient's pretest probability (PTP) of coronary artery disease (CAD) was assessed according to the 2023 European Society of Cardiology (ESC) guidelines for the diagnosis and management of chronic coronary syndromes. A typical piece of software (CADENZA, Cardioki Netics, Seattle, WA) was used to determine each patient's pretest chance of having CAD. The accuracy of this software, which is based on the Bayesian theorem, has been confirmed in earlier research.

Patients were categorized into three categories according to the three levels of their coronary artery disease (CAD) pretest probability (PTP): low (<15%), middle (15–85%), and high (>85%). Additionally, patients with a known history of coronary artery disease including previous myocardial infarction, percutaneous coronary intervention, or coronary artery bypass grafting were categorized as having a high pretest probability of CAD [7].

Ankle-brachial index (ABI) Measurement:

Three arteries are used to quantify the ankle-brachial index: the dorsalis pedis and/or posterior tibial artery for the ankle, and the brachial artery for the upper limb. A sphygmomanometer cuff that was at least 40% wider than the circumference of the limb was chosen. The stethoscope picked up a pulse at the arm's brachial artery level. The cuff was gradually deflated at a rate of roughly 1 mmHg/sec after being inflated to about 20 mmHg above the last audible pulse. Records were

kept of the brachial and lower leg systolic pressures. The ABI value was calculated by dividing the brachial artery systolic pressure by the larger pressure of the two ankle arteries **[8]**.Normal ABI ranges from 1.0 - 1.4. ABI was calculated by dividing the highest systolic ankle pressure (either posterior tibial or dorsal pedal) by the highest systolic pressure of both arms. Both limbs were assessed.



(BP = blood pressure, dp = dorsalis pedis artery, tp = tibialis posterior artery).

Cardiovascular Assessment:

In compliance with the 2023 ESC guidelines, all patients received a 12-lead electrocardiogram (ECG) at the time of admission, within 10 minutes of their initial medical interaction [9]. Standard limb leads (I, II, III, aVR, aVL, aVF) and precordial leads (V1–V6) were obtained for all patients. Extra right precordial leads (V3R–V6R) and posterior leads, if required (V7–V9) were acquired to identify right ventricular infarction or posterior wall. Patients were placed in the left lateral decubitus position and a Vivid 4 ultrasound system with a 2 MHz transducer was used to produce a two-dimensional transthoracic echocardiography (2D ECHO) **[9].** The test assessed left ventricular ejection fraction (LVEF), regional wall motion abnormalities (WMA), and valve pathology. Current standard definitions of atherosclerotic risk factors were estimated using the following criteria [10]: The cardiovascular risk factors evaluated in this study included diabetes mellitus, defined as a fasting plasma glucose level ≥126 mg/dl or the use of antidiabetic medications; dyslipidemia, identified by a total cholesterol level ≥200 mg/dl or the use of lipid-lowering agents; and hypertension, defined as a documented history of blood pressure ≥140/90 mmHg or the use of antihypertensive therapy. In addition, current smoking within the three months preceding presentation, as well as a positive family history of coronary artery disease indicated by myocardial infarction or sudden cardiac death in a first-degree relative were also considered.

Cardiovascular scoring:

Coronary angiography was performed for all patients using the Judkins technique. The severity of CAD was subsequently assessed using both the SYNTAX and Gensini scoring systems.

The SYNTAX score[11], Using specialized software, an angiographic tool measuring the quantity, complexity, and location of coronary lesions was computed for every patient. The SYNTAX score was then separated into three tertiles: low (≤16), moderate (16–22), and high (>22).

GENSINI score[12]:

The severity of CAD was determined using the Gensini scoring system, which quantifies the extent of luminal narrowing and assigns a weighted score based on the anatomical location of each coronary artery lesion. Less than 25% narrowing earns one point, 26–50% narrowing earns two, 51–75% narrowing earns four, 76–90% narrowing earns eight, 91–99% narrowing earns sixteen, and complete occlusion earns thirty-two. Each lesion score was multiplied by a weighting factor according to its anatomical location within the coronary circulation: 5 for the left main coronary artery, 2.5 for the proximal segments of the left anterior descending and circumflex arteries, 1.5 for the mid-segment of the left anterior descending artery, 1.0 for the right coronary artery, distal left anterior descending, posterolateral, and obtuse marginal arteries, and 0.5 for other segments. The final Gensini score was calculated by summing the weighted scores from all coronary segments. The Gensini score was separated into three categories: first tier (less than 11 points), second tier (between 11 and 38 points), and third tier (more than 38

points). The number and kind of arterial diseases, such as those affecting the LAD, LCx, and RCA, were recorded.

Statistical analysis

Statistical analysis was performed using SPSS version 27 (IBM©, Chicago, IL, USA). Data normality was evaluated through histograms and the Shapiro-Wilks test. Quantitative parametric variables were expressed as mean ± SD and compared using ANOVA with Tukey's post hoc test, while qualitative variables were presented as frequencies and percentages and analyzed using the Chi-square test. Receiver operating characteristic (ROC) curve analysis was also conducted, with an ideal test curve extending from the lower left to the upper left and then to the upper right corner. The overall diagnostic performance of each test was evaluated using ROC curve analysis. The total test performance is assessed using the AUC; a value of >50% denotes acceptable performance, while a value of almost 100% denotes the best test performance. A two-tailed P value < 0.05 was considered statistically significant.

RESULTS

Age was statistically significantly higher in high pre-test probability than in low pre-test probability and intermediate pre-test probability (P value <0.001). sex was different between low pre-test probability and moderate pre-test probability. Males were significantly higher in high pre-test probability than in (low pre-test probability and intermediate pre-test probability) (P values = 0.003 and <0.001, respectively).The three groups' differences in height, weight, and BMI were not statistically significant (Table 1). The difference in systolic blood pressure between the low pre-test probability and intermediate pre-test probability groups was not statistically significant; however, the high pre-test probability group's systolic blood pressure was statistically significant greater than that of the low and intermediate pre-test probability groups (P values = 0.003 and 0.04, respectively). No statistically significant differences were observed in heart rate or diastolic blood pressure among the three groups. There was no statistically significant difference in the number of vessels impacted or where they were located among the three groups (Table 1).The APACHE II score was higher in the high pre-test probability group compared to both the low and intermediate pre-test probability groups, with a statistically significant difference (P < 0.001). While the difference between the low and intermediate pre-test probability groups was statistically insignificant, a statistically significant reduction in ABI was observed in the high pre-test probability group compared to the low and intermediate pre-test probability groups (P < 0.001). For syntax and gensini scores, the difference between the low and intermediate pre-test probability groups was statistically insignificant, while the high pre-test probability group's scores were statistically significantly higher than those of the low and intermediate pre-test probability groups (P value <0.001) (Table 2).The differences between the three groups in urea, creatinine, cholesterol, LDL, and HDL were not statistically significant as shown in (Table 3). Table 4; showed that the three groups' prior MIs did not differ statistically significantly from one another. Compared to the low pre-test probability and intermediate pre-test probability groups, the high pre-test probability group had ischemic LBBB that was statistically significantly higher (P value = 0.038).The three groups' differences were statistically insignificant for LVE, LVEF <50%, and LAE. The high pre-test probability group had statistically significant higher levels of LVH, WMA, MAC, and AS compared to the low and intermediate pre-test probability groups (P value<0.05). (Table 4).Figure 1; showed that the ABI and syntax score had a negative correlation (r = -0.352, P value <0.001).ABI can significantly predict CAD severity (P value <0.001 and AUC = 0.863 and 95%CI was (0.815- 0.918)) at cut-off

≤0.89with 75.76% and 95%CI (66.4 - 85.2%) sensitivity, 85.19% and 95% CI (89.5 - 98.8%) specificity, 86.2% PPV and 74.2%NPV (Figure 2).

Table 1: Demographic data of the studied patients.

		Low PPT (n=14)	Intermediate PPT (n=67)	High PPT (n=99)	P value	Post hoc
Age (years)		43.1 ± 11.3	58.1 ± 10.8	66.2 ± 12.76	**<0.001***	**P1=<0.001* P2=<0.001* P3=<0.001***
Sex	**Male**	5 (35.71%)	18 (26.87%)	75 (75.76%)	**<0.001***	P1= 0.504 **P2=0.002* P3=<0.001***
	Female	9 (64.29%)	49 (73.13%)	24 (24.24%)		
Weight (kg)		86.6 ± 10.34	89.7 ± 12.65	87.2 ± 11.42	0.762	
Height (cm)		172 ± 7.58	170.6 ± 6.14	170.7 ± 6.18	0.825	
BMI (kg/m^2)		29.4 ± 3.91	30.9 ± 4.82	30 ± 4.16	0.647	
Systolic blood pressure (mmHg)		141.1 ± 26.69	156.1 ± 22.94	166.2 ± 27.87	**0.038***	**P1**=0.125 **P2=0.003* P3=0.04***
Diastolic blood pressure (mmHg)		83.4 ± 6.22	84.4 ± 8.67	87.9 ± 7.07	0.235	
Heart rate (beats/min)		87.8 ± 11.33	96.8 ± 13.56	98.7 ± 16.98	0.095	

Data presented as mean ± (SD) and frequency (%).*:Statistically statistically significant as P value <0.05, P1 :P value between low PPT and intermediate PPT, P2: P value between low PPT and high PPT, P3:P value between intermediate PPT and high PPT.

Table 2: APACHE II score, ABI, syntax score and gensini score of the studied groups.

	Low PPT (n=14)	**Intermediate PPT (n=67)**	**High PPT (n=99)**	**P value**	**Post hoc**
APACHE II score	9.3 ± 1.59	11.7 ± 3.53	22.9 ± 3.79	**0.001***	**P1**=0.053 **P2<0.001* P3<0.001***
ABI	1.1 ± 0.13	1.04 ± 0.13	0.88 ± 0.18	**0.001***	**P1**=0.394 **P2<0.001* P3<0.001***
Syntax score	12.5 ± 4.03	14.6 ± 4.72	26.4 ± 6.13	**0.001***	**P1**=0.384 **P2<0.001* P3<0.001***
Gensini score	41.2 ± 12.23	47.1 ± 12.91	66.7 ± 14.81	**0.001***	**P1**=0.326 **P2<0.001* P3<0.001***

Data presented as mean ± (SD), *: Statistically significant as P value <0.05, P1 :P value between low PPT and intermediate PPT, P2: P value between low PPT and high PPT, P3:P value between intermediate PPT and high PPT.

Table 3: Kidney function and lipid function tests of the studied groups.

	Low PPT (n=14)	**Intermediate PPT (n=67)**	**High PPT (n=99)**	**P value**
Urea (mg/dl)	14.9 ± 5.02	17.7 ± 5.84	18.8 ± 5.6	0.153
Creatinine (mg/dl)	1.01 ± 0.35	1.07 ± 0.32	1.11 ± 0.34	0.745
Cholesterol (mg/dl)	184.3 ± 12.05	189.1 ± 14.75	192.9 ± 14.08	0.248
LDL (mg/dl)	98.5 ± 14.31	106.1 ± 15.98	108.3 ± 18.13	0.247
HDL (mg/dl)	66.6 ± 20.84	68.1 ± 15.19	71.8 ± 15.75	0.718

Data presented as mean ± (SD), LDL: Low-density lipoproteins, HDL: High density lipoprotein .

Table 4: Echocardiography of the studied groups.

	Low PPT (n=18)	Intermediate PPT (n=67)	High PPT (n=99)	P value
Ischemic LBBB	2 (14.29%)	6 (8.96%)	24 (24.24%)	**0.038***
LVE	1 (7.14%)	3 (4.48%)	16 (16.16%)	0.056
LVH	2 (14.29%)	6 (8.96%)	26 (26.26%)	**0.018***
LVEF <50%	0 (0%)	6 (8.96%)	12 (12.12%)	0.344
WMA	1 (7.14%)	1 (1.49%)	18 (18.18%)	**0.003***
LAE	2 (14.29%)	11 (16.42%)	23 (23.23%)	0.480
MAC	1 (7.14%)	5 (7.46%)	25 (25.25%)	**0.007***
AS	2 (14.29%)	4 (5.97%)	25 (25.25%)	**0.005***

Data presented as frequency (%). LVE: Left ventricular enlargement ,LVH: Left ventricular hypertrophy ,LVEF : Left ventricular ejection fraction ,WMA: Wall motion abnormality ,LAE: Left atrial enlargement, MAC: Mitral annular calcification, AS: Aortic sclerosis.

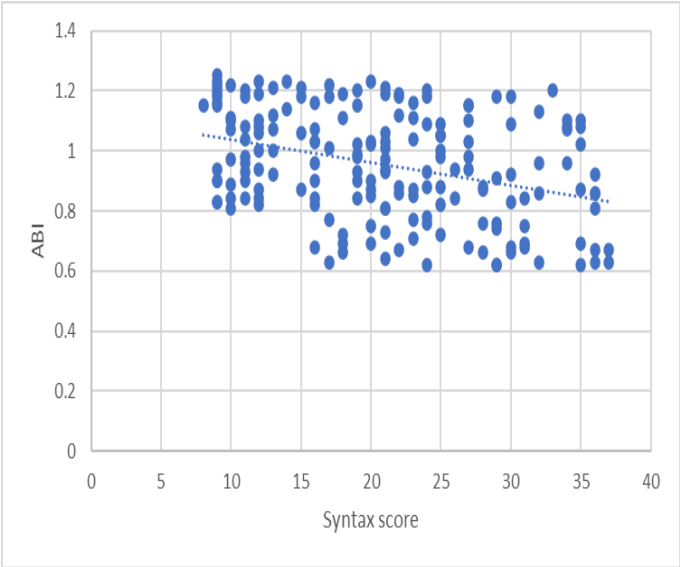


Figure (1): Correlation between syntax score and ABI

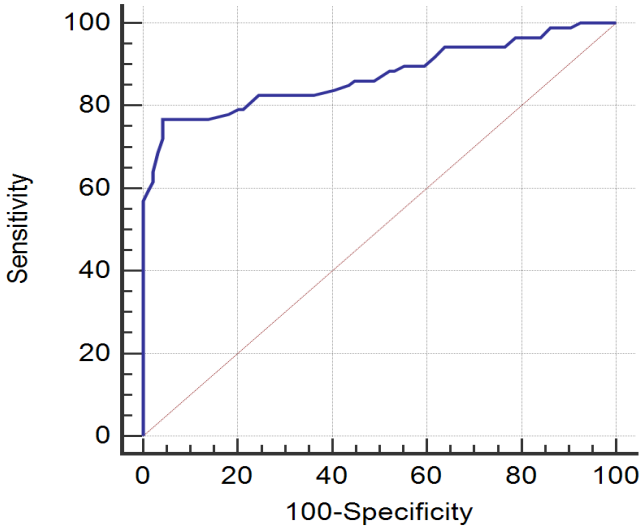


Figure (2): ROC curve of ABI in prediction of CAD severity

DISCUSSION

Our results revealed that age was higher in the high pre-test probability group than in the low and intermediate pre-test probability groups, and statistically substantially lower in the low pre-test probability group than in the intermediate and high pre-test probability groups. The sex differences between the low and moderate pre-test probability groups were not statistically significant. Compared to the low and intermediate pre-test probability groups, there were noticeably more men in the high pre-test probability group. There were no statistically significant variations in height, weight, or body mass index (BMI) between the three groups. According to our research, the high pre-test probability group's age was statistically considerably higher than that of the low and intermediate pre-test probability groups. However, compared to the intermediate and high pre-test probability groups, the age of the low pre-test probability group was statistically considerably lower. The sex differences between the low and moderate pre-test probability groups were not statistically significant [13,14]. Our study was supported by the finding that both males and females had an increased risk of CAD as they age [15]. Additionally, it has been observed that the strongest factor associated with the development of CAD is age [16]. Furthermore, it was noted that cardiovascular disease was more likely to occur in older CAD patients [17].

In contrast to men, who do not benefit from this hormonal advantage, women's estrogen's cardioprotective benefits delay the development and progression of atherosclerosis, particularly before to menopause [18–20]. Furthermore, men may have less favorable lipid profiles and are more prone to smoke and engage in other risky behaviors, which might worsen the advancement of atherosclerotic lesions [21].The three groups in the current investigation did not differ statistically significantly in hypertension, stroke, dyslipidemia, diabetes mellitus (DM), or ischemic heart disease in the family.

According to our research, smoking made atherosclerotic coronary disease patients' CAD worse [22]. Additionally, smoking has been identified as a significant risk factor for CAD [23], contributing to both its severity and the distribution pattern of coronary lesions [24-25].

According to our findings, the systolic blood pressure of the high pre-test probability group was statistically significantly higher than that of the low pre-test probability group and the intermediate pre-test probability group, whereas the two groups' differences were statistically insignificant. The diastolic blood pressure and heart rate did not differ statistically significantly among the three groups. However, it was shown that among those with subclinical atherosclerosis, diastolic blood pressure <60 mmHg was linked to a higher risk of coronary heart disease events and all-cause death [26]. Furthermore, it was showed that in CAD patients, a lower diastolic blood pressure was linked to a higher syntax score [27-28].

The APACHE II score of the high pre-test probability group in this study was greater than that of the low pre-test probability group, and there was no statistically significant difference between the two groups and intermediate pre-test probability groups. In the present study, both the low and intermediate pre-test probability groups revealed lower APACHE II scores compared to the high pre-test probability group; however, the difference between these two groups was not statistically significant. Additionally, it was mentioned in Shiga et al. that the Gensini score can be used to predict the prognosis of CAD patients [29]. Additionally, it was noted in Dadeai et al. that individuals were deemed to have severe CAD if their gensini score was 20 or higher [30]. Additionally, Wang et al., said that in individuals with CAD, Long-term adverse consequences can be independently predicted by the Gensini score [31].

Our findings showed that the three groups did not differ statistically significantly in terms of white blood cells, fasting blood sugar, AST, or ALT. The three groups' differences in urea, creatinine, cholesterol, HDL and LDL, or low-density lipoproteins, did not show statistically significant differences. Similarly, Xia et al. reported no significant relationship between FBG and 90-day outcomes in acute ischemic stroke patients [32]. The same line Inoue et al. found that there was no correlation between the severity or occurrence of CAD and the level of LDL-C [33].The prevalence of prior myocardial infarction did not differ significantly between the three groups in this study. Compared to the low pre-test probability and intermediate pre-test probability groups,

the high pre-test probability group saw a statistically significant increase in ischemic left bundle branch block (LBBB).According to Shen et al. which backed with our findings, the presence of LBBB independently enhanced the likelihood of dying from cardiovascular disease [34].Our results revealed no statistically significant differences among the three groups regarding left ventricular enlargement, left atrial enlargement, or LVEF <50%. However, the high pre-test probability group showed significantly higher rates of AS, mitral annular calcification (MAC), and WMA associated with left ventricular hypertrophy (LVH) compared to both the low and intermediate pre-test probability groups.These findings are in agreement with those of Abd El Azeem et al. [35], who reported that left ventricular hypertrophy (LVH) is linked to an elevated risk of ventricular arrhythmias and cardiovascular mortality. Similarly, Movahed et al. [36] identified LVH as an independent predictor of increased cardiovascular morbidity and mortality. Elsayed et al. also reported an association between AS and the extent and presence of CAD [37]. Milin et al. also noted that AS is more likely to be a marker of CAD or inflammation than a direct cause of death or cardiovascular events, and that CAD patients with AS had an 8.6-fold higher chance of having substantial CAD [38].Our findings showed that ABI has a 75.76% sensitivity, 85.19% specificity, 86.2% PPV, and 74.2% NPV for significantly predicting the severity of CAD (P value<0.001 and AUC = 0.863) at cut-off ≤0.89. In align with our results, Khawaja et al. claimed that ABI might be utilized as a time-saving, non-invasive, and independent predictor of CAD complexity [39].This was supported by Koumelli et al. who shown that ABI and aberrant ABI continued to be important indicators of the severity of CAD [40].

Also, Aykan et al. found that ABI can be used to assess a person's CAD severity with suspected CAD without invasive treatments. Additionally, those with SS>22 were recognized by the ABI at cutoff value <0.9mm with an 82.64 specificity and a 45.28% sensitivity (AUC = 0.689, %95 CI = 0.619-0.763, p<0.001) [41]. Additionally, Kristian et al. discovered that substantial coronary artery stenosis is more common in those with an ABI of less than 0.9. An inverse relationship exists between ABI and the severity of coronary artery stenosis, with lower ABI values indicating more advanced disease. ABI remains a simple, non-invasive, and practical method for assessing the extent of coronary artery stenosis in patients with coronary artery disease [42].This study has a few limitations, such as a limited sample size, the fact that it only involved single center, and unmeasured confounding variables may have influenced the results despite efforts to minimize bias. Future multicenter studies with larger, more diverse cohorts are recommended to validate these findings and explore the integration of ABI into clinical risk models across different populations.

Conclusion

A useful, easy-to-use, and non-invasive measure of coronary artery disease severity, the ankle-brachial index (ABI) can help with risk stratification, particularly in high-risk individuals.

Conflict of interest: The authors declare no conflict of interest.

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