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# Ambulatory Arterial Stiffness Index is Associated with the Presence and Severity of Coronary Artery Disease

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## Abstract

**Objective** To evaluate the relationship between the ambulatory arterial stiffness index (AASI) and the degree of coronary stenosis, and assess its predictive value for the presence and severity of coronary artery disease (CAD).

**Materials and methods** In total, 619 consecutive patients who presented with exertional anginal symptoms and/or acute coronary syndrome between January 2021 and December 2022 underwent elective non-urgent CAG with no emergency conditions and performed 24-h ambulatory blood pressure monitoring (ABPM) were included in this study and were divided into the control group ( $n=68$ ) and CAD group ( $n=551$ ) according to the angiography results. Ambulatory Arterial Stiffness Index (AASI) is obtained from the 24-h ABPM recordings, defined as 1 minus the regression slope of diastolic blood pressure on systolic blood pressure values. CAD complexity was determined by the Gensini score (GS). The patients with CAD were stratified according to the tertiles of the Gensini score ( $GS < 24$  versus  $GS > 48$ ), and  $GS > 48$  is considered severe coronary artery disease. To explore the relationship between AASI and the severity of CAD, Spearman correlation analysis was conducted. Logistic regression analysis was then performed to determine the influence of AASI on CAD as well as severe CAD. Moreover, a Receiver Operating Characteristic (ROC) curve was constructed to assess the predictive value of AASI for CAD and severe CAD.

**Results** The CAD group had a substantially higher median AASI than the control group [0.47 (0.4, 0.58) vs. 0.32 (0.24, 0.41),  $P < 0.001$ ]. There was a positive correlation between AASI and Gensini score. Compared to controls, patients in low-, medium-, and high-GS had significantly higher levels of AASI in a rising trend ( $P < 0.001$ ). Logistic regression demonstrated that AASI was an independent contributor to CAD and severe CAD. The area under the curve (AUC) for AASI in predicting CAD was 0.806 ( $P < 0.001$ ), and for predicting high-GS CAD was 0.663 ( $P < 0.001$ ).

**Conclusion** AASI was associated with CAD and the severity of coronary stenosis and demonstrated predictive potential for both CAD and severe CAD.

**Keywords** Ambulatory arterial stiffness index (AASI), Coronary artery disease (CAD), Gensini score, Ambulatory blood pressure monitoring (ABPM)

## 1 Introduction

Coronary artery disease (CAD) is a prevalent cardiovascular disorder that arises due to a combination of genetic predisposition and environmental factors. It ranks among the leading causes of mortality worldwide [1]. However, the initial symptoms of CAD frequently exhibit atypical characteristics, which can result in underdiagnosis. Although coronary angiography (CAG) is a reliable

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method for assessing the severity, location, and extent of coronary artery lesions, its clinical utility is limited due to its complex nature, invasive nature, and associated high costs [2]. In addition, other diagnostic modalities, such as coronary computed tomography angiography, stress echocardiography, or single-photon emission computed tomography, often offer limited information or have drawbacks, including limited availability, high costs, complex protocols, and radiation exposure. Consequently, there is a pressing necessity to explore novel indicators that can effectively identify individuals with CAD, particularly those at high risk.

Ambulatory arterial stiffness index (AASI) is a measure used to evaluate arterial function, assessing arterial elasticity by calculating the variations in systolic blood pressure (SBP) and diastolic blood pressure (DBP) [3]. AASI has been shown to positively correlate with increased cardiovascular mortality and incidence, indicating its predictive value in assessing the occurrence and prognosis of ischaemic cardiovascular disease [4, 5]. It has been observed that AASI is higher in coronary artery disease patients compared to non-coronary artery disease patients [6]. This finding was also observed in the clinical data analysis of patients with combined hypertension and coronary artery disease, particularly in those with essential hypertension and hyperhomocysteinemia [7]. However, to our knowledge, there is conflicting evidence regarding the relationship between AASI and the severity of coronary artery disease [8, 9]. The clinical applicability of AASI remains a subject of debate. Therefore, in this study, we aim to investigate the relationship between AASI and Gensini score, as well as the value in predicting CAD risk and severity.

## 2 Materials and Methods

### 2.1 Study Design and Subjects

This retrospective study was conducted in a single center at the second hospital affiliated with Zhengzhou University. 892 patients presented with exertional anginal symptoms and/or acute coronary syndrome between January 2021 and December 2022 underwent elective non-urgent CAG with no emergency conditions and performed 24-h ambulatory blood pressure monitoring. Individuals with previously or recently discovered left ventricular systolic ejection fraction of less than 30%, had atrial fibrillation, pacemaker, valvular heart disease, autoimmune disease, infectious disease, renal failure, hepatic failure, or malignancy were excluded. Finally, 619 patients participated in this study.

The study protocol was approved by the ethics committee of the second affiliated hospital of Zhengzhou University and conformed to the principles of the Declaration

of Helsinki. Informed consent was obtained from all participants.

### 2.2 Anthropometric and Biochemical Measurements

Trained clinicians collected clinical data including patients' demographics, medical history, and laboratory tests from the medical records.

The patient's anthropometric measures and biochemical variables were recorded at admission. Body mass index (BMI) was calculated by measuring all patients' height and weight according to the formula for weight/height<sup>2</sup> (kg/m<sup>2</sup>). All patients were required to fast the previous night before peripheral venous blood samples were collected for fasting blood glucose (FBG), total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), blood lipids, liver and kidney function, and laboratory indicators related to other function using an Olympus AU270 biochemistry analyzer (Olympus, Tokyo, Japan). Type 2 diabetes mellitus (T2DM) was defined as follows: FBG  $\geq 7.0$  mM, 2-h PBG  $\geq 11.1$  mM, and/or HbA1c  $\geq 6.5\%$  of the subjects who are using glucose-controlling medicines [10]. Hypertension was defined as having an untreated average systolic blood pressure (SBP) of  $\geq 140$  mm Hg or diastolic blood pressure (DBP) of  $\geq 90$  mm Hg, based on three measurements taken on at least two separate days. Individuals with SBP/DBP levels below 140/90 mm Hg were still considered to have hypertension if they had a prior diagnosis of hypertension documented and were currently receiving antihypertensive treatment. For ambulatory blood pressure monitoring (ABPM), the thresholds for defining hypertension were as follows: a 24-h average blood pressure (BP) of  $\geq 130/80$  mm Hg, a daytime average BP of  $\geq 135/85$  mm Hg, or a nighttime average BP of  $\geq 120/70$  mm Hg [11].

### 2.3 24-h ABPM and AASI

Twenty-four-hour ambulatory blood pressure monitoring (ABPM) was conducted using the MGY-ABP1 (MEI-GAOYI, Beijing, China), a non-invasive instrument for ambulatory blood pressure measurement. An automated oscillometric cuff was placed on the non-dominant arm. BP readings were taken at 30-min intervals throughout the day and night. A minimum of 80% of the total readings was considered valid for analysis. Additionally, to ensure the reliability of the records, at least 14 measurements during the daytime period or at least 7 measurements during the night or rest period were required.

The ambulatory arterial stiffness index (AASI) is calculated as 1 minus the regression slope of diastolic blood pressure on systolic blood pressure values derived from

the 24-h ABPM recordings [12]. AASI was obtained as follows:

$$\text{AASI} = 1 - \text{slope (diastolic BP/systolic BP)}$$

Night-time/daytime dip was calculated by the formula, [(mean BP of daytime – night-time)/mean daytime] multiplied by 100. The morning surge was calculated as the difference between the average BP during the 2 h after awakening (four BP readings) and the lowest nighttime BP.

#### 2.4 Coronary Angiography and Assessment of the Severity of Coronary Artery Disease

All participants in the study underwent coronary angiography, and then the degree of coronary narrowing was analyzed by two cardiologists. The diagnosis of coronary artery disease (CAD) required at least 50% stenosis in one of the four main coronary arteries: left main, anterior descending, left circumflex, and right coronary [13]. The Gensini score was calculated by summing the values for the location and luminal narrowing of each lesion. The severity of coronary artery stenosis was categorized into three forms based on the number of affected coronary arteries: single-vessel ( $n=155$ ), double-vessel ( $n=174$ ), and triple-vessel ( $n=222$ ). The Gensini score (GS) was employed to assess the intensity of CAD. The GS assigns points on a scale that corresponds to the degree of coronary artery narrowing: 1 point for <25% narrowing, 2 points for 26–50% narrowing, 4 points for 51–75% narrowing, 8 points for 76–90% narrowing, 16 points for 91–99% narrowing, and 32 points for total occlusion [14]. Patients with angiographically confirmed CAD were then divided into three groups based on the tertiles of the GS: low GS, <24 points ( $n=178$ ); medium GS, 24–47 points ( $n=193$ ); and high GS, >48 points ( $n=180$ ).

#### 2.5 Statistical Analysis

All data were analyzed using IBM SPSS Statistics version 26.0 (Chicago, IL, USA), GraphPad Prism 9.4 (San Diego, California, USA). The Shapiro–Wilk test was used to assess the normality of the continuous variable distribution. Normally distributed data were presented as mean and standard deviation, while non-normally distributed data were presented as median with interquartile range. Categorical variables were described as frequency and percentage (%).

To compare continuous variables with a normal distribution, independent samples *t* test or analysis of variance (ANOVA) was employed. The Mann–Whitney *U* test or Kruskal–Wallis test was used for continuous variables with non-normal distribution. Categorical variables were analyzed using the chi-squared test or Fisher's exact test. The association between Gensini score (GS) and

Ambulatory Arterial Stiffness Index (AASI) was assessed using Spearman's correlation analysis.

Univariate logistic regression analysis was performed to analyze the variables, and variables with a *P* value <0.05 in the univariate analysis were included in the multivariate logistic regression analysis. The variance inflation factor (VIF) was calculated to address the potential issue of multicollinearity. Variables with a VIF >10 were excluded from the analysis to mitigate the impact of multicollinearity.

ROC curves were generated for the combined model, adjusted models, and AASI. The optimal cutoff value was determined based on the maximum Youden index. The area under the curve (AUC) was used to compare the diagnostic utility of CAD presence and a high GS. A *P* value of less than 0.05 was considered statistically significant.

### 3 Results

#### 3.1 Baseline Patient Characteristics

A total of 619 patients were included in this study, with 551 patients belonging to the CAD group (patients with angiographically confirmed CAD) and 68 patients in the control group (patients with normal coronary angiography). The baseline clinical and demographic characteristics of the participants are summarized in Table 1. The specific composition of the patient groups is illustrated in Fig. 1A.

The two groups of participants did not differ significantly in terms of gender, smoking, drinking, TG, dsLDL-C, Hb, prealbumin, Average DBP, Average HR, Average MAP, Awake HR, Awake MAP, Nocturnal DBP, Average PP and morning surge.

Meanwhile, the CAD group exhibited a higher prevalence of ST-segment depression. Additionally, the CAD group had higher average age, elevated levels of LDL-C, FBG, HbA1c, Average SBP, Average MAP, Awake SBP, Nocturnal SBP, Nocturnal HR, Nocturnal MAP, Average PP and BMI, as well as lower LVEF, TC, HDL-C, albumin, A/G, and Night-Time Dipping levels (all  $P < 0.05$ ). Moreover, the CAD group exhibited a significantly higher AASI in comparison to the control group [0.47 (0.4, 0.58) vs. 0.32 (0.24, 0.41),  $P < 0.001$ , respectively].

The baseline characteristics of the patients, categorized according to the tertiles of the Gensini score (GS), are presented in Table 2. The table indicates significant differences in various factors including gender, BMI, LVEF, TG, LDL-C, HDL-C, Hb, prealbumin, albumin, A/G, FBG, Nocturnal SBP, Morning surge, Average PP and AASI.

Comparison of AASI between the CAD and control participants.

**Table 1** Baseline characteristics of the study population

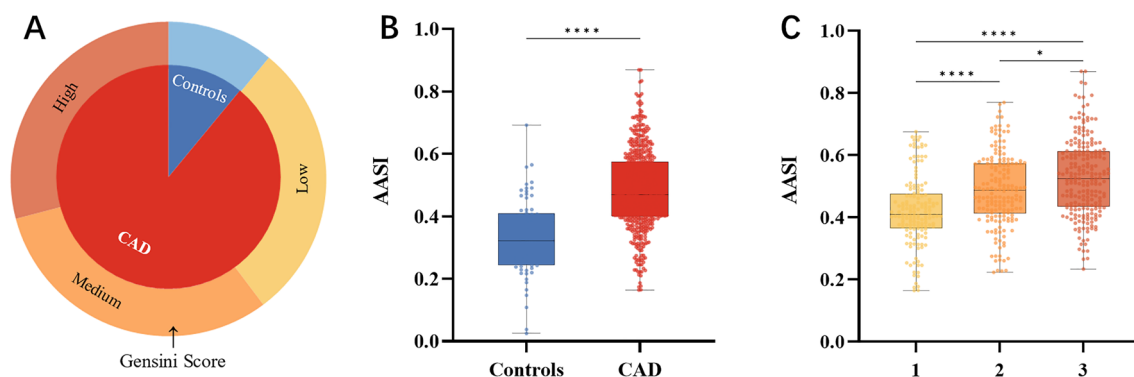
Variables	Total (N=619)	Control group (n=68)	CAD group (n=551)	P value
General conditions				
Male, n (%)	395 (63.81%)	40 (58.82%)	355 (64.43%)	0.364
Age (years)	62 (54, 70)	57 (54.75, 64.25)	63 (54, 70)	0.004
BMI (kg/m <sup>2</sup> )	25.1 (24.02, 26.61)	24.52 (22.84, 25.75)	25.24 (24.09, 26.82)	0.001
STD, n (%)	429 (69.31%)	35 (51.47%)	394 (71.51%)	0.001
LVEF (%)	59 (57, 61)	60 (59, 62)	59 (57, 61)	<0.001
Risk factors, n (%)				
HTN, n (%)	517 (83.52%)	48 (70.59%)	469 (85.12%)	0.002
DM, n (%)	189 (30.53%)	10 (14.71%)	179 (32.49%)	0.003
Smoking, n (%)	203 (32.79%)	17 (25%)	186 (33.76%)	0.147
Drinking, n (%)	112 (18.09%)	10 (14.71%)	102 (18.51%)	0.442
Laboratory test				
TC (mmol/dl)	3.85 (3.14, 4.56)	4.13 (3.55, 4.87)	3.82 (3.08, 4.53)	0.016
TG (mmol/dl)	1.35 (0.97, 1.86)	1.22 (0.88, 1.69)	1.36 (0.98, 1.93)	0.052
LDL-C (mmol/dl)	2.54 (2.02, 2.96)	2.36 (1.94, 2.58)	2.57 (2.03, 2.99)	0.001
sdLDL-C (mmol/dl)	0.55 (0.4, 0.79)	0.55 (0.4, 0.74)	0.54 (0.4, 0.79)	0.728
HDL-C (mmol/dl)	1.12 (0.94, 1.29)	1.25 (1.04, 1.53)	1.11 (0.93, 1.27)	<0.001
Hb (g/dl)	135 (124, 145)	135.5 (128, 145)	135 (124, 145)	0.29
Prealbumin (mg/dl)	275 (231, 316)	289.5 (240.25, 315.75)	273 (230, 316)	0.253
Albumin (g/dl)	42.6 (40, 45.8)	44.3 (41.45, 47.53)	42.45 (39.62, 45.48)	<0.001
A/G	1.7 (1.5, 1.9)	1.8 (1.58, 2)	1.7 (1.49, 1.9)	0.005
FBG (mmol/dl)	5.55 (5, 6.69)	5.14 (4.75, 5.85)	5.66 (5.07, 6.82)	<0.001
HbA1c (%)	5.9 (5.6, 6.8)	5.7 (5.42, 6.06)	6 (5.6, 6.9)	<0.001
ABPM				
Average SBP (mmHg)	126 (117, 135)	118.5 (113, 128)	127 (118, 136)	<0.001
Average DBP (mmHg)	72 (67, 79)	72 (66, 78)	72 (67, 79)	0.601
Average HR (bpm)	70 (65, 76)	68.5 (65, 76)	71 (65, 76.5)	0.089
Average MAP (mmHg)	90 (84, 97)	88 (82, 95)	90 (85, 97)	0.02
Awake SBP (mmHg)	127 (117, 135)	120.5 (115, 128)	128 (118, 136)	<0.001
Awake DBP (mmHg)	73 (68, 80)	74 (67.75, 79)	73 (68, 81)	1
Awake HR (bpm)	72 (67, 79)	70.5 (67, 77.5)	72 (67, 79)	0.199
Awake MAP (mmHg)	90 (85, 97.5)	89.5 (82, 94.25)	91 (85, 98)	0.06
Nocturnal SBP (mmHg)	125 (112, 134)	116 (106.75, 124.5)	126 (114, 135)	<0.001
Nocturnal DBP (mmHg)	70 (63, 78)	69.5 (60, 76)	70 (63, 78)	0.108
Nocturnal HR (bpm)	65 (59, 71)	61 (55, 68.25)	65 (59.5, 71)	0.003
Nocturnal MAP (mmHg)	88 (80.5, 95)	84.5 (76, 91.25)	88 (81, 96)	0.001
Night-time dipping (%)	3.33 (-2.15, 9.38)	5.96 (0, 10.61)	2.9 (-2.17, 9.09)	0.03
Morning surge (mmHg)	24.4 ± 12.93	23.03 ± 11.73	24.57 ± 13.08	0.355
Average PP (mmHg)	53 (45, 60)	46 (42, 53)	53 (45, 60)	<0.001
AASI	0.46 (0.39, 0.57)	0.32 (0.24, 0.41)	0.47 (0.4, 0.58)	<0.001

Data were given as mean ± SD, median with interquartile range or n (%)

BMI body mass index, LVEF left ventricular ejection fraction, STD ST-segment depression, HTN hypertension, DM diabetes mellitus, TC total cholesterol I, TG triglyceride, LDL-C low-density lipoprotein-cholesterol, HDL-C high-density lipoprotein-cholesterol, sdLDL-C small dense low-density lipoprotein cholesterol, Hb hemoglobin, A/G albumin/globulin ratio, FBG fasting blood glucose, HbA1c hemoglobin A1c, SBP systolic blood pressure, DBP diastolic blood pressure, HR heart rate, MAP mean blood pressure, PP pulse pressure, AASI ambulatory arterial stiffness index

The CAD group presented a significantly higher AASI compared to the control group [0.47 (0.4, 0.58) vs.0.32 (0.24, 0.41),  $P < 0.0001$ , respectively] (Fig. 1B). Subgroup analysis was then conducted in CAD patients based on

the number of diseased vessels using the Kruskal–Wallis test, revealing a significant difference among the one-, two-, and three-vessel diseased groups ( $P < 0.001$ ) (Fig. 1C). Further multiple group comparison was



**Fig. 1** **A** Subjects: 68 patients without CAD and 551 patients with CAD. The group with CAD was further divided into three subgroups according to Gensini score. Low-score group ( $n=178$ ), medium-score group ( $n=193$ ), high-score group ( $n=180$ ). **B** AASI levels in CAD group and control group. **C** Relationship between AASI and the number of coronary artery lesions; \* $P<0.05$ ; \*\*\*\* $P<0.0001$

calculated by the Dunn-Bonferroni test. As depicted in Fig. 1C, significantly higher AASI levels were observed in the three-vessel diseased group [median (quartile): 0.524 (0.434–0.612)] and the two-vessel diseased group [0.485 (0.412–0.573)] compared to the one-vessel diseased group [0.409 (0.364–0.475)] ( $P<0.0001$ ). And the AASI was higher in the three-vessel diseased group than in the two-vessel diseased group ( $P=0.011$ ). The levels of AASI exhibited a progressive increase with a higher number of diseased coronary arteries.

### 3.2 Association between AASI and Gensini scores

The Gensini score is an angiographic tool utilized to assess the extent and severity of coronary artery disease (CAD). In comparison to the control group, patients in the low, medium, and high Gensini score groups exhibited significantly higher levels of Ambulatory Arterial Stiffness Index (AASI) in an increasing trend (Kruskal–Wallis test,  $P<0.001$ ). However, no statistically significant difference was observed among the medium-, and high-GS group followed by Dunn's multiple comparisons test, possibly due to the limitations of the sample volume (Fig. 2A).

To further elucidate the relationship between AASI levels and the extent of coronary artery lesions, Spearman's correlation analysis was used to examine the correlations of the AASI with GS in patients with CAD. As shown in Fig. 2B, a significantly positive correlation was established between the two factors (AASI vs. Gensini score,  $R=0.375$ ,  $P<0.001$ ). Interestingly, the correlation between AASI and Gensini score in low, medium, and high groups did not increase gradually ( $R=0.283$ ,  $P=0.001$ ;  $R=0.024$ ,  $P=0.738$ ;  $R=0.039$ ,  $P=0.605$ ) (Table 3).

### 3.3 Univariate and Multivariate Analyses of Factors Associated with CAD and Severe CAD

Univariate analysis revealed that several factors were associated with the presence of CAD, including AASI, HDL-C, LDL-C, TG, Albumin, A/G, FBG, HbA1c, Average SBP; Average PP, Night-Time Dipping, LVEF, ST-segment depression, diabetes mellitus and hypertension. (Table 4).

Multivariate logistic regression analysis demonstrated that AASI, HDL-C and LDL-C remained significant after adjusting for confounders. These associations remained significant (all  $P<0.001$ ) even after controlling for gender and age (Model I), or after considering additional characteristics such as gender, age, BMI, smoking status, diabetes, and hypertension (Model II). For each standard deviation increase in AASI, the adjusted odds ratio (95% CI) was 4.04 (2.79, 5.84).

Logistic regression analysis of the severe CAD risk for the high-GS group using low and medium GS groups as the control group showed that, the following factors were associated with the presence of the high-GS group: AASI, HDL-C, LDL-C, Prealbumin, A/G, HbA1c, morning surge, BMI; Average SBP; ST-segment depression; LVEF; gender and hypertension. (Table 5).

Multivariate logistic regression analysis demonstrated that AASI, HDL-C, LDL-C, morning surge, and BMI remained significant after adjusting for confounders. These associations remained significant (all  $P<0.001$ ) even after controlling for gender and age (Model I). Furthermore, after adjusting for traditional CAD risk factors including age, sex, hypertension, diabetes mellitus, and smoking, significant differences were still observed (Model II). For each standard deviation increase in AASI, the adjusted odds ratio (95% CI) was 1.73 (1.30, 2.28).

**Table 2** Baseline characteristics of the study population according to the tertile of the Gensini score

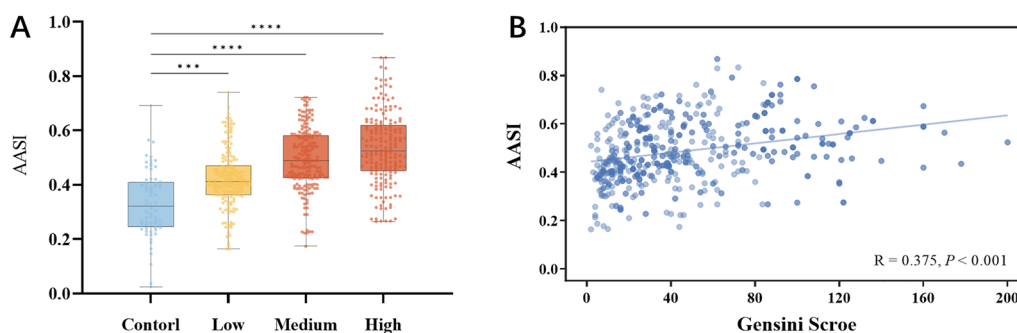
Variables	Low GS (GS < 24, n = 178)	Medium GS (GS:24–47, n = 193)	High GS (GS ≥ 48, n = 180)	P value
General conditions				
Male, n (%)	96 (53.93%)	127 (65.8%)	132 (73.33%)	0.001
Age (years)	63 (56, 71)	63 (53, 71)	64 (54, 70)	0.732
BMI (kg/m <sup>2</sup> )	24.51 (23.5, 25.78)	25 (24.06, 26.61)	25.71 (24.77, 27.3)	<0.001
STD, n (%)	110 (61.8%)	133 (68.91%)	151 (83.89%)*#	
LVEF (%)	59 (58, 62)	59 (57, 61)	58 (56, 60)	0.011
Risk factors, n (%)				
HTN, n (%)	145 (81.46%)	162 (83.94%)	162 (90%)*#	0.065
DM, n (%)	49 (27.53%)	63 (32.64%)	67 (37.22%)*#	0.147
Smoking, n (%)	49 (27.53%)	70 (36.27%)	67 (37.22%)*#	0.1
Drinking, n (%)	28 (15.73%)	37 (19.17%)	37 (20.56%)	0.48
Laboratory test				
TC (mmol/dl)	3.94 (3.09, 4.66)	3.82 (3.2, 4.44)	3.64 (2.91, 4.47)	0.262
TG (mmol/dl)	1.22 (0.91, 1.83)	1.56 (1.09, 2.01)	1.26 (0.97, 1.72)	0.001
LDL-C (mmol/dl)	2.5 (1.91, 2.95)	2.56 (2.02, 2.87)	2.7 (2.17, 3.16)	0.026
sdLDL-C (mmol/dl)	0.55 (0.41, 0.78)	0.61 (0.43, 0.84)	0.51 (0.38, 0.72)*#	0.029
HDL-C (mmol/dl)	1.15 (0.95, 1.34)	1.12 (0.94, 1.25)	1.08 (0.9, 1.2)*#	0.002
Hb (g/dl)	137 (128, 147)	133 (123.5, 145)	134 (121, 144)	0.019
Prealbumin (mg/dl)	290.5 (246, 317)	273 (227, 319)	262.5 (219, 297)	0.003
Albumin (g/dl)	43 (40.4, 45.8)	42.7 (40.4, 45.3)	41.2 (38.7, 45.3)	0.004
A/G	1.7 (1.5, 2)	1.74 (1.5, 1.9)	1.6 (1.4, 1.8)*#	0.014
FBG (mmol/dl)	5.5 (4.93, 6.33)	5.53 (5, 6.85)	6.05 (5.21, 6.98)	0.044
HbA1c (%)	5.93 (5.6, 6.4)	6 (5.6, 6.8)	6.1 (5.6, 7.29)	0.175
ABPM				
Average SBP (mmHg)	126.19 ± 13.07	126.64 ± 13.76	128.27 ± 14.18	0.315
Average DBP (mmHg)	73 (69, 79)	71 (67, 79)	72 (67, 79.25)	0.144
Average HR (bpm)	71 (66, 78)	71 (65, 77)	70 (64, 74)	0.176
Average MAP (mmHg)	89 (85, 97)	90 (84, 96)	90 (85, 99)	0.749
Awake SBP (mmHg)	126 (117, 135)	128 (119, 135)	129 (120.75, 138.25)	0.266
Awake DBP (mmHg)	74 (68.25, 81)	72 (68, 81)	74 (67, 80)	0.389
Awake HR (bpm)	72 (68, 79)	73 (67, 79)	71.5 (66, 77)	0.203
Awake MAP (mmHg)	90 (85, 98.75)	91 (85, 97)	92 (85, 99)	0.888
Nocturnal SBP (mmHg)	124 (112, 133)	126 (116, 135)	128 (116.75, 137)	0.041
Nocturnal DBP (mmHg)	71 (64.25, 79)	70 (63, 77)	69 (63, 77)	0.103
Nocturnal HR (bpm)	64.5 (59, 71)	66 (61, 72)	65 (58, 70.25)	0.053
Nocturnal MAP (mmHg)	90 (80, 96)	88 (81, 95)	88.5 (81, 96)	0.703
Night-time dipping (%)	3.74 (– 1.2, 9.8)	2.9 (– 2.2, 8.22)	2.33 (– 2.8, 8.37)	0.688
Morning surge (mmHg)	25.56 ± 11.57	21.65 ± 12.82	26.71 ± 14.21	<0.001
Average PP (mmHg)	49 (43, 55)	53 (45, 60)	55 (46.75, 61)*	<0.001
AASI	0.41 (0.36, 0.47)	0.49 (0.43, 0.58)	0.53 (0.45, 0.62)*#	<0.001

Data were given as mean ± SD, median with interquartile range or n (%)

BMI body mass index, LVEF left ventricular ejection fraction, STD ST-segment depression, HTN hypertension, DM diabetes mellitus, TC total cholesterol I, TG triglyceride, LDL-C low-density lipoprotein-cholesterol, HDL-C high-density lipoprotein-cholesterol, sdLDL-C small dense low-density lipoprotein cholesterol, Hb hemoglobin, A/G albumin/globulin ratio, FBG fasting blood glucose, HbA1c hemoglobin A1c, SBP systolic blood pressure, DBP diastolic blood pressure, HR heart rate, MAP mean blood pressure, PP pulse pressure, AASI ambulatory arterial stiffness index

\*p < 0.05 vs. Low GS; #p < 0.05 vs. Medium GS





**Fig. 2** **A** AASI levels from low to high tertile groups according to Gensini score. **B** Correlation between AASI and Gensini score; \*\*\* $P < 0.001$ ; \*\*\*\* $P < 0.0001$

**Table 3** Correlation of AASI with Gensini score

Group	Correlation coefficient	P value
CAD	0.375	<0.001
Low GS	0.283	<0.001
Medium GS	0.023	0.023
High GS	0.061	0.412

### 3.4 The Predictive Performance of AASI for CAD and Severe CAD

Figure 3 illustrates the ROC curves of Ambulatory Arterial Stiffness Index (AASI) for predicting the presence of coronary artery disease (CAD) and severe CAD. Comparing AASI with other models based on ROC curves, it was observed that the AUC for Model II was greater. The ROC analysis revealed that the optimal cutoff value for AASI in predicting CAD was 0.423, corresponding to a sensitivity of 68.1% and a specificity of 80.9% (Fig. 3A and Table 6). Moreover, an AASI value of 0.451 was identified as the optimal cutoff point for detecting high Gensini score (GS), with a sensitivity of 54.2% and a specificity of 75.6% (Fig. 3B and Table 7).

## 4 Discussion

In 2006, Li [15] first proposed the concept of “Ambulatory Arterial Stiffness Index (AASI)”. AASI is an index that was projected as a surrogate measure of arterial stiffness through statistical regression analysis based on 24-h dynamic blood pressure parameters. There was a significant positive correlation with PWV, which is currently recognized as an evaluation of arteriosclerosis ( $r=0.51, P<0.01$ ). The values of AASI range from 0 to 1, with values closer to 0 indicating better arterial elasticity and values closer to 1 indicating poorer arterial function. The principle of AASI is mainly related to the compliance of blood vessels, which can be determined

by the elasticity of the vessel wall. When risk factors such as hypertension, hyperlipidemia, and smoking act on the blood vessels, arterial elasticity decreases and vascular compliance decreases. This decrease in compliance leads to a faster wave reflection, causing the reflected wave to appear earlier at the end of the systolic phase of the arterial pressure wave, increasing systolic blood pressure, while at the same time, during the diastolic phase, due to the loss of synergy of the reflected wave that should have appeared during the diastolic phase, the pressure decay increases, which leads to a decrease in diastolic blood pressure. Thus, the functional relationship between systolic and diastolic blood pressure can reflect the degree of arterial sclerosis, and AASI is based on this principle [16]. AASI has been found to have application value in the fields of hypertension, cerebrovascular disease, and coronary artery disease. In studies examining the correlation between AASI and hypertension, researchers have found associations with blood pressure variability, target organ damage in hypertension, and assessment of anti-hypertensive medication efficacy [17–19]. In the field of cerebrovascular disease, significant results have also been obtained, such as a positive correlation between AASI and the incidence of acute ischemic stroke [20], as well as a significant correlation with the cerebral vascular function score (a novel indicator for assessing cerebral embolism) [21]. However, there is no statistically significant correlation between AASI and the incidence of acute intracerebral hemorrhage. Nevertheless, there is limited and controversial research regarding the predictive value of AASI for coronary artery disease and its assessment of coronary artery lesions [6, 7, 9]. The main focus of this study is to explore the correlation between AASI and Gensini score in patients with suspected coronary artery disease and their predictive value for coronary artery disease and severe coronary artery disease.

In this study, the AASI of coronary artery disease (CAD) patients was significantly higher than that of the

**Table 4** Univariate and multivariate logistic regression analyses for the presence of CAD

Variables	Univariate		Multivariate		Non-adjusted		Model I		Model II	
	OR [95% CI]	P	OR [95% CI]	P	OR [95% CI]	P	OR [95% CI]	P	OR [95% CI]	P
Average PP (per SD)	2.19 [1.07, 1.83]	<0.001	0.69 [0.26, 2.87]	0.062						
Average SBP (per SD)	1.78 [1.36, 2.33]	<0.001	1.67 [0.98, 7.52]	0.118						
Night-time dipping (%)	0.96 [0.93, 1.00]	0.026	0.95 [0.90, 1.00]	0.095						
STD	2.37 [1.42, 3.94]	0.001	0.98 [0.44, 2.20]	0.954						
LVEF (%)	0.92 [0.88, 0.97]	0.002	0.94 [0.87, 1.02]	0.184						
HTN	2.38 [1.35, 4.22]	0.003	0.65 [0.23, 1.84]	0.248						
DM	2.79 [1.39, 5.59]	0.004	0.48 [0.14, 1.64]	0.414						
TG (mmol/dl)	1.48 [1.03, 2.14]	0.034	1.25 [0.73, 2.14]	0.327						
FBG (mmol/dl)	1.38 [1.11, 1.72]	0.004	0.82 [0.55, 1.22]	0.057						
HbA1c (%)	1.7 [1.14, 2.52]	0.009	2.11 [1.00, 4.43]	<0.001						
AASI (per SD)	4.09 [2.89, 5.80]	<0.001	3.85 [2.19, 6.77]	0.002	4.04 [2.79, 5.84]	<0.001	4.26 [2.82, 6.42]	<0.001	4.15 [2.74, 6.28]	<0.001
LDL-C (mmol/dl)	1.78 [1.22, 2.59]	0.003	2.83 [1.47, 5.45]	0.009	2.19 [1.39, 3.45]	0.001	2.26 [1.43, 3.57]	<0.001	2.17 [1.37, 3.44]	0.001
HDL-C (mmol/dl)	0.14 [0.06, 0.32]	<0.001	0.16 [0.04, 0.62]	0.045	0.15 [0.06, 0.38]	<0.001	0.12 [0.05, 0.34]	<0.001	0.14 [0.05, 0.40]	<0.001

Model I was adjusted for age and gender. Model II was adjusted for age, gender, hypertension, diabetes mellitus and smoking history

OR odds ratio, CI confidence interval, PP pulse pressure, SBP systolic blood pressure, STD ST-segment depression, LVEF left ventricular ejection fraction, HTN hypertension, DM diabetes mellitus, TG triglyceride, FBG fasting blood glucose, HbA1c hemoglobin A1c, AASI ambulatory arterial stiffness index, LDL-C low-density lipoprotein-cholesterol, HDL-C high-density lipoprotein-cholesterol

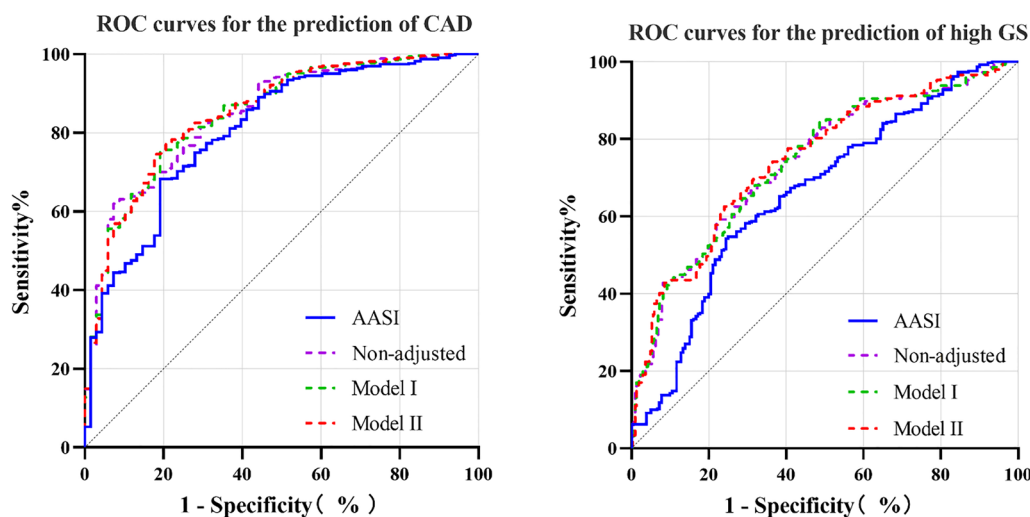


**Table 5** Univariate and multivariate logistic regression analyses for the presence of high GS

Variables	Univariate		Multivariate		Non-adjusted		Model I		Model II	
	OR	P	OR [95% CI]	P	OR [95% CI]	P	OR [95% CI]	P	OR [95% CI]	P
Average PP (per SD)	1.41 [1.18, 1.68]	<0.001	1.01 [0.74, 1.36]	0.974						
Average SBP (per SD)	0.98 [0.96, 1.00]	0.016	1.02 [0.79, 1.32]	0.864						
male	1.83 [1.24, 2.70]	0.003	0.81 [0.45, 1.46]	0.479						
STD	2.74 [1.75, 4.31]	<0.001	0.54 [0.29, 1.00]	0.052						
LVEF (%)	0.95 [0.92, 0.98]	0.001	0.97 [0.93, 1.00]	0.111						
A/G	0.42 [0.23, 0.79]	0.007	0.64 [0.28, 1.48]	0.297						
HbA1c (%)	1.21 [1.02, 1.42]	0.025	1.19 [0.97, 1.45]	0.092						
AASI (per SD)	2.16 [1.77, 2.65]	<0.001	1.73 [1.30, 2.28]	<0.001	2.14 [1.73, 2.66]	<0.001	2.2 [1.74, 2.79]	<0.001	2.15 [1.69, 2.73]	<0.001
LDL-C (mmol/dl)	1.39 [1.11, 1.73]	0.004	1.63 [1.19, 2.24]	0.003	1.54 [1.19, 1.99]	0.001	1.53 [1.19, 1.98]	0.001	1.51 [1.16, 1.95]	0.002
HDL-C (mmol/dl)	0.34 [0.16, 0.70]	0.004	0.20 [0.07, 0.61]	0.005	0.19 [0.09, 0.44]	<0.001	0.21 [0.09, 0.49]	<0.001	0.22 [0.09, 0.52]	0.001
Morning surge (mmHg)	1.02 [1.01, 1.03]	0.008	1.03 [1.01, 1.05]	0.004	1.02 [1.01, 1.04]	0.002	1.02 [1.01, 1.04]	0.002	1.02 [1.01, 1.04]	0.002
BMI (kg/m <sup>2</sup> )	1.17 [1.09, 1.25]	<0.001	1.12 [1.02, 1.24]	0.018	1.14 [1.06, 1.23]	0.001	1.14 [1.05, 1.23]	0.001	1.14 [1, 1.23]	0.001

Model I was adjusted for age and gender. Model II was adjusted for age, gender, hypertension, diabetes mellitus and smoking history

OR odds ratio, CI confidence interval, SBP systolic blood pressure, PP pulse pressure, STD ST-segment depression, LVEF left ventricular ejection fraction, A/G albumin/globulin ratio, HbA1c hemoglobin A1c, AASI ambulatory arterial stiffness index, LDL-C low-density lipoprotein-cholesterol, HDL-C high-density lipoprotein-cholesterol, BMI body mass index



**Fig. 3** **A** The ROC analysis for AASI and different models in coronary artery disease (CAD) prediction. **B** The ROC analysis for AASI and different models in severe coronary artery disease (CAD) prediction

control group without coronary artery lesions. Moreover, there was a statistically significant increasing trend in AASI across the low, moderate, and high Gensini score groups. A positive correlation was observed between AASI and Gensini score, which was evident in the CAD group. However, this correlation was not observed within different Gensini score subgroups, possibly due to a small sample size and further subdivision of the groups. Additionally, the calculation of the GS considered only two factors: the severity score and the regional multiplying factor for each lesion. However, it did not take into account the additional third parameter, which is the effect of the severity score adjustment factor on collateral modification [22]. As a result, the complexity of measuring CAD with GS is overestimated in patients with total collateral coronary artery occlusion. Therefore, in CAD patients, AASI may reflect the extent of coronary artery lesions, and monitoring AASI could provide a non-invasive and convenient method for predicting coronary artery disease. Additionally, in this study, coronary artery disease patients had higher age, BMI, LDL-C, FBG, and HbA1c levels compared to non-coronary artery disease patients. The proportion of hypertensive and diabetic patients was also higher in the coronary artery disease group, which is consistent with previous research findings [23, 24]. The demographic characteristics of our study population are similar to those in previous studies, which enhances the generalizability of our research results.

In the multivariate analysis, multiple influencing or confounding factors were comprehensively considered. Further analysis revealed that AASI was an independent predictor for the presence of coronary artery disease

(CAD) and high Gensini score. Additionally, apart from the well-established CAD predictors such as HDL-C, LDL-C, and BMI, we identified independent predictors for high Gensini score (morning surge). The morning surge were found to be associated with the severity of coronary artery lesions [25, 26]. However, despite the strong correlation between AASI and Average PP, the univariate analysis did not reveal a significant association between Average PP and the presence of CAD and in the high-GS group. These results may be potentially influenced by the limitations imposed by the sample size. Subsequent ROC curve analysis showed that the area under the ROC curve for AASI in predicting coronary artery disease was 0.806 (95% CI 0.751–0.861,  $P < 0.001$ ), and for predicting high Gensini score was 0.663 (95% CI 0.615–0.712,  $P < 0.001$ ) (Table 7). This suggests that AASI has a certain predictive value for coronary artery disease and severe coronary artery disease, and when combined with other independent risk factors and traditional coronary artery disease risk factors in our study, the predictive ability of the model was further enhanced. Therefore, AASI can be considered as a novel predictive reference index for CAD, providing evidence for the prediction, screening, and assessment of the severity of coronary artery lesions.

Coronary angiography has long been used as the gold standard for diagnosing coronary artery disease, but its application has been limited by the high price of the measurement equipment and the high professionalism required of the operators. AASI is derived from 24 h-ABPM, and ambulatory blood pressure monitoring is a straightforward and easily executed procedure, and studies have confirmed that there is a positive correlation

**Table 6** Comparison of the predictive value of different models for predicting the presence of CAD

Variables	Sensitivity (%)	Specificity (%)	Cutoff value	AUC (95% CI)	P value
AASI	68.1	80.9	> 0.423	0.806 (0.751–0.861)	< 0.001
Non-adjusted	92.65	61.99	–	0.847 (0.800–0.894)	< 0.001
Model I	75.09	80.88	–	0.849 (0.802–0.897)	< 0.001
Model II	74.53	82.35	–	0.852 (0.804–0.890)	< 0.001

Model I was adjusted for age and gender. Model II was adjusted for age, gender, hypertension, diabetes mellitus and smoking history  
AUC area under the curve, AASI ambulatory arterial stiffness index

**Table 7** Comparison of the predictive value of different models for predicting the presence of high GS

Variables	Sensitivity (%)	Specificity (%)	Cutoff value	AUC (95% CI)	P value
AASI	54.2	75.6	< 0.451	0.663 (0.615–0.712)	< 0.001
Non-adjusted	59.2	77.6	–	0.740 (0.691–0.789)	< 0.001
Model I	68.0	68.1	–	0.741 (0.692–0.791)	< 0.001
Model II	62.6	76.0	–	0.746 (0.697–0.795)	< 0.001

Model I was adjusted for age and gender. Model II was adjusted for age, gender, hypertension, diabetes mellitus and smoking history  
AUC area under the curve, AASI ambulatory arterial stiffness index

between AASI and Pulse Wave Velocity (PWV), and that AASI can be used to assess arteriosclerosis. AASI as a test indicator is non-invasive, and has the advantage of being convenient, economical and reliable, and can be accepted by a broader spectrum of patients, and its advantages provide a new choice for the diagnosis of coronary artery disease. Ambulatory blood pressure monitoring, a non-invasive blood pressure measurement method, bears no absolute contraindications and is predominantly employed for hypertension monitoring and diagnosis. And the findings of this study suggest that AASI holds predictive value in diagnosing patients presenting with suspected symptoms of angina, especially those with high GS confirmed after coronary angiography.

Therefore, in clinical practice, 24-h ambulatory blood pressure monitoring can be used to screen patients with asymptomatic and suspected coronary heart disease, especially those patients who refuse coronary angiography due to economic time and other reasons, but this does not mean that these patients do not need to undergo coronary angiography. It is difficult to obtain AASI through continuous and accurate blood pressure monitoring in clinical practice, which makes this index prone to fluctuations, and may be poor in stability and repeatability. In addition, there is not enough evidence to show that coronary arteries change before AASI is slightly elevated, and more in-depth basic research is needed in order to obtain accurate evidence in this regard.

This study has several limitations that should be acknowledged. Firstly, it is a small-sample cross-sectional study conducted at a single center, which may introduce bias and limit the generalizability of the findings. The

small sample size reduces the statistical power and may affect the reliability of the results. Secondly, the exclusion of patients with severe coronary artery disease, such as those with heart failure or previous revascularization therapy, may underestimate the predictive efficacy of AASI for coronary artery disease. Including these patients in future studies would provide a more comprehensive understanding of AASI's predictive value. Therefore, further research with larger sample sizes, multicenter collaborations, and comprehensive analysis of influencing factors is needed to provide a solid theoretical basis for the prediction of coronary artery disease and severe coronary artery disease using AASI.

## 5 Conclusions

In conclusion, the findings of this study indicate that AASI is increased in patients with coronary artery disease and shows a positive correlation with the severity of coronary artery lesions. AASI is identified as a valuable predictor for the presence and severity of CAD. Therefore, our study suggests that incorporating AASI into the assessment of patients with suspected coronary artery disease can help identify individuals who are more likely to have severe and significant CAD, thereby potentially reducing the need for invasive coronary angiography. Thus, these findings suggested that the AASI exerted a predictive potential for both CAD and severe CAD. It serves as a simple, inexpensive, and timely predictor for both conditions.

## Abbreviations

AASI Ambulatory arterial stiffness index

CAD	Coronary artery disease
GS	Gensini score
ABPM	Ambulatory blood pressure monitoring
ROC	Receiver operating characteristic
CAG	Coronary angiography
SBP	Systolic blood pressure
DBP	Diastolic blood pressure
BMI	Body mass index
LVEF	Left ventricular ejection fraction
STD	ST-segment depression
HTN	Hypertension
DM	Diabetes mellitus
TC	Total cholesterol I
TG	Triglyceride
LDL-C	Low-density lipoprotein-cholesterol
HDL-C	High-density lipoprotein-cholesterol
sdLDL-C	Small dense low-density lipoprotein cholesterol
Hct	Hematocrit
Hb	Hemoglobin
A/G	Albumin/globulin ratio
Dbil	Direct bilirubin
Ibil	Indirect bilirubin
FBG	Fasting blood glucose
HbA1c	Hemoglobin A1c
Fib	Fibrinogen
IMA	Ischemia-modified albumin
HR	Heart rate
MAP	Mean blood pressure
PP	Pulse pressure

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#### Author Contributions

JLG conceived and supervised the study; QXT and YQG: designed experiments; QXT, YQG, ZYD, JP, JXT and YZ: contributed to data collection and manuscript editing; QXT and YQG: analyzed data; QXT: wrote the manuscript; QXT and YQG: made manuscript revisions. All authors read and approved the final manuscript.

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#### Availability of Data and Materials

The data that support the findings of this study are available from the corresponding author upon reasonable request.

#### Declarations

#### Conflict of Interest

The authors declare that they have no competing interests.

#### Ethics Approval and Consent to Participate

The study protocol was approved by the ethics committee of the second affiliated hospital of Zhengzhou University and conformed to the principles of the Declaration of Helsinki. Informed consent was obtained from all participants. Consent for publication.

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