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Atherogenic index of plasma combined with carotid crouse score predicts coronary artery disease in young and middle-aged adults

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This retrospective study included 642 patients aged 18–59 years who underwent carotid ultrasound and coronary angiography. Patients were grouped by coronary artery disease (CAD) status and median Gensini score. Clinical characteristics, the atherogenic index of plasma (AIP), and carotid Crouse scores were compared. Multivariate logistic regression analysis was performed to identify independent predictors of CAD and severe coronary stenosis. Receiver operating characteristic (ROC) curve analyses assessed the diagnostic performance of AIP, Crouse score, and their combination. Both AIP and Crouse score were significantly higher in CAD patients compared to non-CAD controls ($P < 0.001$) and in high versus low Gensini score groups ($P < 0.001$). Multivariate analyses identified AIP (odds ratio [OR] = 1.219 for CAD; OR = 1.575 for severe stenosis) and Crouse score (OR = 1.543 for CAD; OR = 1.253 for severe stenosis) as independent predictors. ROC curve analysis revealed that the combined model had higher area under the curve (AUC) values for predicting CAD (AUC = 0.700) and severe coronary stenosis (AUC = 0.754) compared to either AIP or Crouse score alone. Both the AIP and carotid Crouse score are independent predictors of CAD presence and severity. Their combined use significantly improves diagnostic performance, offering a practical, non-invasive strategy for early CAD screening and risk stratification in this population.

Keywords Coronary artery disease, Atherogenic index of plasma, Crouse score, Carotid ultrasound, Young and middle-aged populations, Risk prediction, Atherosclerosis

Despite substantial declines in coronary artery disease (CAD) mortality owing to advancements in medical technology and heightened public health awareness, CAD persists as a major global cause of death[1]. Alarmingly, its prevalence is shifting towards younger demographics, a trend attributed to accelerated lifestyles, elevated occupational stress, disrupted daily routines, and suboptimal dietary habits[2]. Although young CAD patients exhibit lower early mortality, their long-term outcomes remain unfavorable[1]. Additionally, asymptomatic CAD is frequently observed in this age group, often culminating in sudden cardiac death upon acute manifestation. Therefore, early identification and intervention for even subclinical CAD are imperative to avert adverse clinical events[3].

While coronary angiography (CAG) remains the definitive diagnostic standard for CAD, its invasive nature, high cost, and limited acceptability among young and middle-aged individuals necessitate alternative screening strategies. As CAD is fundamentally driven by lipid metabolic abnormalities and chronic inflammatory processes[4]its underlying pathology of atherosclerosis has gained attention. Recent findings indicate that the incidence of CAD among young and middle-aged populations has surged by 1.5-fold compared to prior decades[1].

Carotid ultrasound offers a non-invasive and reliable approach to assess both the presence and extent of atherosclerosis[5]. Due to the carotid arteries' accessibility to ultrasound examination, atherosclerotic lesions causing vascular narrowing or occlusion can be effectively evaluated[6]. Notably, carotid atherosclerosis generally precedes coronary artery involvement, and plaque morphology is comparable across these vascular territories[6]. The Crouse score, calculated by summing the maximal plaque thicknesses within the common carotid artery, bifurcation, and internal carotid artery, has been extensively adopted in clinical carotid plaque assessment[7]. Evidence suggests that detection of carotid atherosclerosis (CAS) signifies a heightened CAD risk and in type 2 diabetes mellitus (T2DM) populations, carotid plaques serve as superior predictors of cardiovascular events compared to carotid intima-media thickness (CIMT) alone[8]. Owing to its non-invasiveness, rapid performance,

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and convenience, carotid ultrasound has become the preferred modality for CAS evaluation[9]. Moreover, elevated Crouse scores are positively correlated with CAD severity[10].

Beyond structural imaging indices such as the Crouse score, biochemical markers indicative of lipid metabolism are equally significant. Dyslipidemia is a critical factor in CAD pathogenesis[11]and while low-density lipoprotein cholesterol (LDL-C) remains important, its small dense fraction (small dense LDL-C, sdLDL-C) exhibits stronger atherogenic potential[12]. Nevertheless, sdLDL-C measurement in clinical practice is often challenging. The atherogenic index of plasma (AIP), computed as log10(triglycerides [TG]/high-density lipoprotein cholesterol [HDL-C]), functions as an indirect marker for sdLDL-C levels and has been recognized as an independent predictor of CAD risk[13]. Compared to individual lipid parameters, AIP provides a more integrated representation of the balance between atherogenic and protective lipoproteins[14]. Prior research has demonstrated that AIP predicts CAD severity, major adverse cardiac events (MACE), and stroke severity, underscoring its promising clinical utility[15].

This study seeks to elucidate the associations between AIP, carotid Crouse score, and the presence and severity of CAD among young and middle-aged adults. Furthermore, it aims to assess whether integrating AIP with the Crouse score enhances CAD predictive accuracy. By combining a practical blood-based biomarker with imaging evaluation, this research aspires to provide valuable clinical references for timely detection and early intervention of CAD within this target population.

Materials and methods

Study participants

This retrospective, single-center observational study was conducted in the Department of Cardiology at Xiangtan Central Hospital. From June 2019 to December 2022, a total of 642 patients aged 18 to 59 years who presented with intermittent chest pain or tightness and underwent both carotid artery ultrasound and CAG for suspected CAD were evaluated for eligibility. The inclusion criteria encompassed: (1) an age range between 18 and 59 years, categorizing them as young and middle-aged adults; and (2) completion of both carotid ultrasound and CAG during hospitalization. Patients were excluded if they met any of the following conditions: (1) presence of malignancies, active infections, or severe hepatic or renal impairment; (2) severe congenital heart disease, valvular heart disease, pericardial disease, or heart failure classified as New York Heart Association (NYHA) class III or IV; (3) a history of coronary artery bypass grafting (CABG), percutaneous coronary intervention (PCI), or contraindications to coronary angiography; (4) thyroid dysfunction, autoimmune diseases such as systemic lupus erythematosus, or hematologic disorders like multiple myeloma that could influence lipid metabolism or carotid plaque formation; (5) current or recent use (within the preceding three months) of lipid-lowering therapies; and (6) a known diagnosis of hyperlipidemia (Fig. 1). The study protocol received approval from the Ethics Committee of Xiangtan Central Hospital (Approval No. X2020642) and adhered to the principles outlined in the Declaration of Helsinki (2013 revision). Written informed consent was obtained from all participants, and where written consent was impractical, verbal consent was documented according to institutional policy.

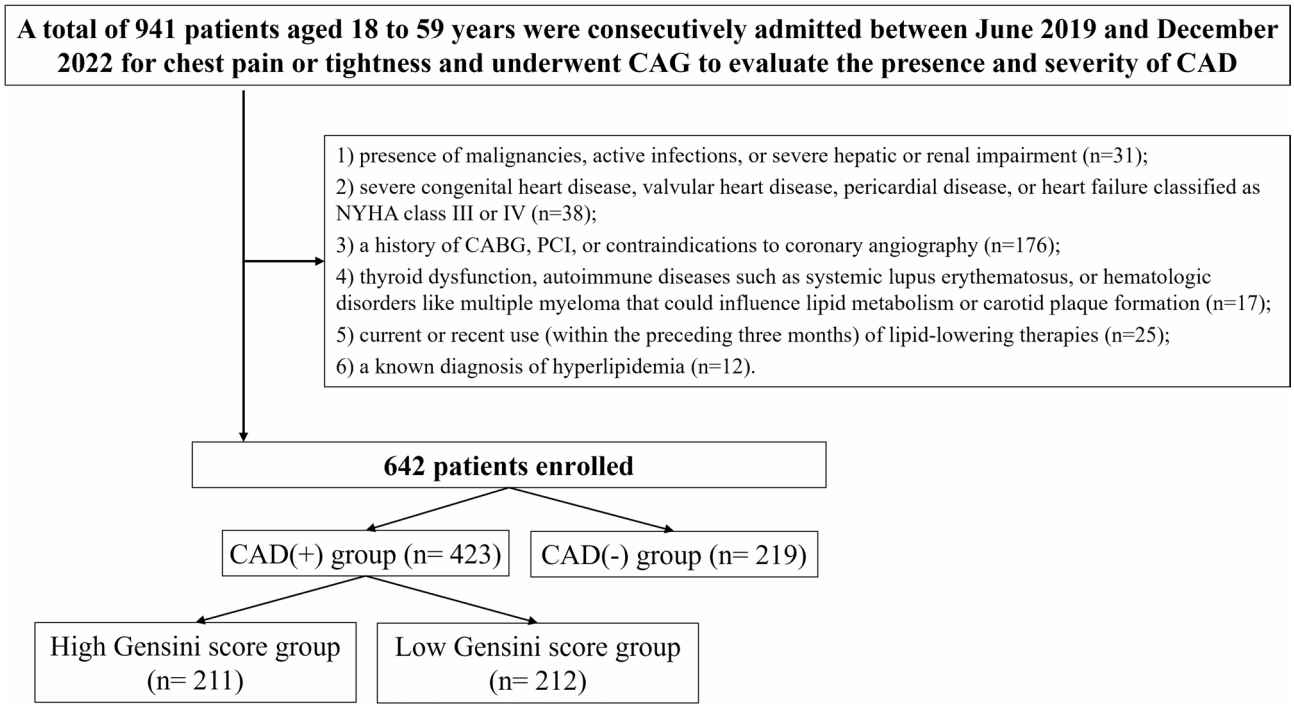

Fig. 1. Study flowchart. CAD, Coronary artery disease; PCI, Percutaneous coronary intervention; CABG, Coronary artery bypass grafting; NYHA, New york heart association; CAG, Coronary angiography.

Data collection and laboratory measurements

Demographic and clinical information for all eligible patients was retrospectively obtained from the hospital's electronic medical record system. Collected variables included age, sex, body mass index (BMI), history of hypertension, history of diabetes mellitus, and smoking status. Each variable was documented along with its corresponding units and exact values.

For laboratory data, standard pre-test instructions—documented in patient records—indicated that patients were routinely advised to avoid high-fat foods for 12–24 h and to fast overnight prior to blood collection. Venous blood samples (approximately 5 mL) were collected in the early morning and analyzed by the Department of Laboratory Medicine at Xiangtan Central Hospital using the Roche C8000 automated biochemical analyzer. The evaluated parameters included white blood cell count (WBC), neutrophil count (NEU), lymphocyte count (LYM), platelet count (PLT), fasting blood glucose (FBG), HDL-C, LDL-C, TG, total cholesterol (TC), and serum creatinine (Scr). All biochemical data were retrospectively extracted and recorded in accordance with standard laboratory protocols and units.

The AIP was calculated as log10(TG/HDL-C), with TG and HDL-C concentrations expressed in mmol/L.

Carotid ultrasound examination and Crouse score assessment

Prior to undergoing CAG, all participants received carotid ultrasound examinations performed by experienced sonographers in the Department of Ultrasound at Xiangtan Central Hospital. The assessments were carried out using a GE LOGIQ E9 color Doppler ultrasound system (GE Healthcare, Chicago, IL, USA) equipped with an 11-MHz linear array transducer. During the procedure, patients were positioned supine without a pillow, allowed to rest for 5–10 min, and instructed to turn their heads contralaterally to optimize exposure of the carotid arteries.

Both left and right carotid arteries, encompassing the common carotid artery (CCA), carotid bulb, and internal carotid artery (ICA), were comprehensively examined in short-axis and long-axis views. CIMT measurements were obtained at the carotid bifurcation, specifically 1.0–1.5 cm proximal and distal to the bifurcation point. Multiple readings were taken, and the mean CIMT value was calculated for analysis. Plaque classification was based on CIMT measurements[16]: CIMT ≤ 0.9 mm was regarded as normal; values between 1.0 and 1.4 mm indicated intimal thickening; and CIMT ≥ 1.5 mm was defined as plaque formation. The Crouse score was determined by summing the maximal thicknesses of all distinct atherosclerotic plaques identified in the bilateral carotid arteries, resulting in a total plaque score that reflected the overall plaque burden.

Coronary angiography and Gensini score assessment

All participants underwent coronary angiography during hospitalization, performed by experienced interventional cardiologists at Xiangtan Central Hospital. The procedure was carried out using the Judkins technique via either radial or femoral artery access. Imaging was acquired with a GE INNOVA 2100IQ digital subtraction angiography system (GE Healthcare, Chicago, IL, USA), obtaining multiple projections of the left and right coronary arteries and their branches from various angles and positions. The extent of coronary artery stenosis was evaluated using the diameter method by at least two independent cardiologists. A diagnosis of CAD was established when there was ≥ 50% stenosis in any major coronary artery or its branches.

Lesion severity was further assessed using the Gensini scoring system[17]. Each coronary lesion was assigned a severity score based on the degree of luminal narrowing (1 for 1–25% stenosis, 2 for 26–50%, 4 for 51–75%, 8 for 76–90%, 16 for 91–99%, and 32 for total occlusion), which was subsequently multiplied by a weighting factor reflecting the significance of the lesion's anatomical location within the coronary circulation. The sum of these weighted scores represented the overall severity of coronary artery stenosis.

Grouping description

Patients were divided into CAD(+) ($n = 423$) and CAD(−) ($n = 219$) groups based on coronary angiography findings. In the CAD(+) group, patients were further categorized into a high Gensini score group ($n = 211$, Gensini score > 54.91) and a low Gensini score group ($n = 212$, Gensini score ≤ 54.91) according to the median Gensini score level. The median Gensini score in the CAD(+) group was 54.91.

Statistical analysis

All statistical analyses were performed using SPSS software version 26.0 (IBM Corp., Armonk, NY, USA). Categorical variables were presented as frequencies with percentages, whereas continuous variables were expressed as mean ± standard deviation if normally distributed or as median with interquartile range when data did not follow a normal distribution. The Kolmogorov–Smirnov test was utilized to assess the normality of continuous variables. For comparisons between two groups, Student's t-test was applied for normally distributed continuous data, while the Mann–Whitney U test was used for non-normally distributed data. Comparisons of categorical variables were conducted using the Chi-square (χ^2) test. Spearman correlation analysis was employed to evaluate associations between variables. Multivariate logistic regression analyses were conducted to identify independent predictors of CAD and severe coronary artery stenosis among young and middle-aged patients. Variables with a P-value < 0.05 in univariate analyses were entered into the respective multivariate logistic regression models for CAD and severe coronary stenosis. All statistical tests were two-tailed, with a significance threshold set at $P < 0.05$. Receiver operating characteristic (ROC) curve analyses were performed to determine the optimal cutoff values, sensitivity, specificity, and area under the curve (AUC) for AIP, Crouse score, and their combined use in predicting CAD and severe coronary artery stenosis in this population. The DeLong test was utilized to compare the AUCs of AIP, Crouse score, and their combination.

Results

Table 1 summarizes the baseline clinical characteristics and laboratory biomarkers of the study cohort. Compared with the CAD(−) group, patients in the CAD(+) group exhibited significantly higher prevalences of hypertension (60.5% vs. 49.8%, $P=0.011$) and diabetes mellitus (18.4% vs. 11.0%, $P=0.019$). No significant differences were observed between the groups in terms of age, sex distribution, smoking status, BMI, blood pressure, or heart rate. In laboratory analyses, the CAD(+) group demonstrated significantly elevated triglyceride levels, fasting plasma glucose, white blood cell counts, AIP, and Crouse scores, while HDL-C levels were significantly reduced compared to the CAD(−) group (all $P<0.001$). No significant differences were noted for TC, LDL-C, Scr, hemoglobin A1c, apolipoproteins, or other hematological parameters. Importantly, the median Crouse score and mean AIP were markedly higher in CAD(+) patients, indicating a greater carotid atherosclerotic burden and a more atherogenic lipid profile.

Table 2 compares baseline characteristics and laboratory biomarkers between high and low Gensini score subgroups within the CAD(+) population. Age, sex, BMI, blood pressure, heart rate, and the prevalences of hypertension, diabetes, and smoking history did not differ significantly between the subgroups. However, patients in the high Gensini score group had significantly elevated triglyceride levels, AIP, and Crouse scores, alongside significantly lower HDL-C levels (all $P<0.001$). No significant differences were found in LDL-C, TC,

	ALL ($n=642$)	CAD(+) group ($n=423$)	CAD(−) group ($n=219$)	*P* value
Age, years	52.55 ± 3.83	52.71 ± 3.75	52.25 ± 3.96	0.153
Male, n%	371 (57.8%)	245 (57.9%)	126 (57.5%)	0.992
Smoking history, n%	186 (29.0%)	122 (28.8%)	64 (29.2%)	0.992
Hypertension, n%	365 (56.9%)	256 (60.5%)	109 (49.8%)	0.011
Diabetes mellitus, n%	102 (15.9%)	78 (18.4%)	24 (11.0%)	0.019
Family history of premature CAD, n%	100 (15.6%)	62 (14.7%)	38 (17.4%)	0.436
SBP, mmHg	135.46 ± 18.89	135.94 ± 18.65	134.53 ± 19.30	0.370
DBP, mmHg	81.80 ± 11.82	82.06 ± 11.36	81.29 ± 12.64	0.435
Heart rate, bpm	76.21 ± 14.44	76.47 ± 14.43	75.72 ± 14.46	0.535
Body mass index, kg/m^2	24.95 ± 2.57	25.07 ± 2.40	24.72 ± 2.84	0.104
LVEF, %	52.77 ± 6.32	52.98 ± 6.05	52.38 ± 6.80	0.255
LVEDD, mm	49.98 ± 5.57	49.85 ± 5.28	50.22 ± 6.10	0.420
Laboratory biomarkers				
TC, mmol/L	4.57 (4.16–5.05)	4.62 (4.20–5.06)	4.50 (4.03–4.97)	0.056
TG, mmol/L	1.38 (1.12–1.68)	1.51 (1.29–1.78)	1.12 (0.97–1.35)	< 0.001
HDL-C, mmol/L	1.15 (0.96–1.37)	1.09 (0.91–1.27)	1.29 (1.10–1.53)	< 0.001
LDL-C, mmol/L	2.76 ± 1.01	2.76 ± 1.05	2.77 ± 0.92	0.917
Scr, umo/L	89.22 (86.13–92.05)	89.09 (85.95–92.05)	89.42 (86.79–92.04)	0.416
WBC, 10^9/L	8.32 (6.65–10.19)	9.52 (7.97–10.98)	6.24 (5.17–7.41)	< 0.001
RBC, 10^{12}/L	4.99 (4.82–5.14)	4.98 (4.82–5.14)	4.99 (4.81–5.15)	0.696
PLT, 10^9/L	247.52 (229.33-269.02)	247.53 (228.62-268.31)	247.51 (230.66-270.76)	0.722
FPG, mmol/L	5.50 ± 0.48	5.61 ± 0.47	5.28 ± 0.41	< 0.001
NEU, 10^9/L	4.29 (3.68–5.07)	4.35 (3.71–5.07)	4.21 (3.51–4.96)	0.143
LYM, 10^9/L	2.09 (1.74–2.43)	2.11 (1.77–2.44)	2.04 (1.69–2.42)	0.170
HbA1C, %	5.91 ± 0.60	5.91 ± 0.57	5.92 ± 0.66	0.865
Lp(a), mg/L	197.56 (168.85-235.89)	199.24 (168.84-235.69)	195.71 (168.98-235.96)	0.633
ApoA1, g/L	1.19 ± 0.35	1.19 ± 0.37	1.18 ± 0.31	0.908
ApoB, g/L	0.92 ± 0.23	0.92 ± 0.23	0.92 ± 0.24	0.875
TBIL, umol/L	16.45 (15.30-17.49)	16.47 (15.34–17.44)	16.43 (15.24–17.59)	0.985
Uric acid, umol/L	479.68 (435.47-527.56)	480.49 (436.67-527.09)	478.74 (428.79-527.89)	0.749
AIP	2.10 ± 0.27	2.16 ± 0.27	1.98 ± 0.21	< 0.001
Crouse score	3.24 (0.95–7.27)	4.99 (2.63–9.05)	0.55 (0.00-2.01)	< 0.001
Gensini score	40.07 ± 15.11	54.30 ± 18.69	12.59 ± 5.21	< 0.001

Table 1. Baseline clinical characteristics and laboratory biomarkers between CAD(+) and CAD(−) group. Continuous variables were expressed as mean ± SD, or median (interquartile range). Categorical variables were expressed as number (percentage). CAD, Coronary artery disease; SBP, Systolic blood pressure; DBP, Diastolic blood pressure; LVEF, Left ventricular ejection fraction; LVEDD, Left ventricular end-diastolic diameter; TC, Total cholesterol; TG, Triglycerides; HDL, High-density lipoprotein; LDL, Low-density lipoprotein; Scr, Serum creatinine; WBC, White blood cell; RBC, Red blood cell; PLT, Platelet count; NEU, Neutrophil count; LYM, Lymphocyte count; HbA1C, Hemoglobin A1c; ApoA1, Apolipoprotein A1; ApoB, Apolipoprotein B; TBIL, Total bilirubin; AIP, Atherogenic index of plasma; Lp(a), Lipoprotein(a); FPG, Fasting blood glucose.

	ALL ($n=423$)	High Gensini score group ($n=211$)	Low Gensini score group ($n=212$)	*P* value
Age, years	52.71 ± 3.75	52.57 ± 3.75	52.84 ± 3.75	0.457
Male, n%	245 (57.9%)	137 (64.9%)	108 (50.9%)	0.060
Smoking history, n%	122 (28.8%)	58 (27.5%)	64 (30.2%)	0.613
Hypertension, n%	256 (60.5%)	124 (58.8%)	132 (62.3%)	0.524
Diabetes mellitus, n%	78 (18.4%)	33 (15.6%)	45 (21.2%)	0.175
Family history of premature CAD, n%	62 (14.7%)	32 (15.2%)	30 (14.2%)	0.874
SBP, mmHg	135.94 ± 18.65	134.50 ± 19.11	137.37 ± 18.16	0.114
DBP, mmHg	82.06 ± 11.36	81.62 ± 11.12	82.50 ± 11.64	0.425
Heart rate, bpm	76.47 ± 14.43	76.44 ± 14.60	76.50 ± 14.32	0.967
Body mass index, kg/m^2	25.07 ± 2.40	24.98 ± 2.40	25.16 ± 2.41	0.457
LVEF, %	52.98 ± 6.05	52.76 ± 6.06	53.20 ± 6.07	0.457
LVEDD, mm	49.85 ± 5.28	49.40 ± 5.26	50.30 ± 5.28	0.079
Laboratory biomarkers				
TC, mmol/L	4.66 ± 0.68	4.61 ± 0.67	4.73 ± 0.69	0.081
TG, mmol/L	1.52 ± 0.25	1.57 ± 0.29	1.20 ± 0.19	< 0.001
HDL-C, mmol/L	1.13 ± 0.20	1.00 ± 0.19	1.29 ± 0.20	< 0.001
LDL-C, mmol/L	2.76 ± 1.05	2.71 ± 1.06	2.81 ± 1.05	0.336
Scr, umo/L	89.10 ± 4.45	89.00 ± 4.36	89.13 ± 4.58	0.764
WBC, $10^9/L$	9.73 ± 2.44	9.65 ± 2.49	9.81 ± 2.39	0.496
RBC, $10^{12}/L$	4.99 ± 0.24	4.97 ± 0.24	5.01 ± 0.24	0.078
PLT, $10^9/L$	249.82 ± 30.04	249.63 ± 29.97	250.01 ± 30.19	0.895
FPG, mmol/L	5.61 ± 0.47	5.60 ± 0.47	5.62 ± 0.47	0.661
NEU, $10^9/L$	4.48 ± 1.11	4.39 ± 1.11	4.57 ± 1.10	0.087
LYM, $10^9/L$	2.16 ± 0.54	2.14 ± 0.55	2.17 ± 0.53	0.496
HbA1C, %	5.91 ± 0.57	5.86 ± 0.57	5.96 ± 0.57	0.079
Lp(a), mg/L	206.41 ± 52.30	206.06 ± 52.03	206.76 ± 52.69	0.890
ApoA1, g/L	1.19 ± 0.37	1.18 ± 0.37	1.20 ± 0.38	0.661
ApoB, g/L	0.92 ± 0.23	0.93 ± 0.22	0.90 ± 0.24	0.172
TBIL, umol/L	16.49 ± 1.60	16.44 ± 1.61	16.55 ± 1.60	0.464
Uric acid, umol/L	485.75 ± 71.54	479.67 ± 71.31	491.81 ± 71.43	0.081
AIP	2.16 ± 0.27	2.38 ± 0.28	1.98 ± 0.27	< 0.001
Crouse score	4.56 ± 1.69	5.09 ± 1.73	3.47 ± 0.81	< 0.001
Gensini score	54.30 ± 18.69	69.15 ± 12.00	39.52 ± 10.76	< 0.001

Table 2. Baseline clinical characteristics and laboratory biomarkers between high Gensini score and low Gensini score in CAD group. Continuous variables were expressed as mean ± SD. Categorical variables were expressed as number (percentage). CAD, Coronary artery disease; SBP, Systolic blood pressure; DBP, Diastolic blood pressure; LVEF, Left ventricular ejection fraction; LVEDD, Left ventricular end-diastolic diameter; TC, Total cholesterol; TG, Triglycerides; HDL, High-density lipoprotein; LDL, Low-density lipoprotein; Scr, Serum creatinine; WBC, White blood cell; RBC, Red blood cell; PLT, Platelet count; NEU, Neutrophil count; LYM, Lymphocyte count; HbA1C, Hemoglobin A1c; ApoA1, Apolipoprotein A1; ApoB, Apolipoprotein B; TBIL, Total bilirubin; AIP, Atherogenic index of plasma; Lp(a), Lipoprotein(a); FPG, Fasting blood glucose.

fasting plasma glucose, hemoglobin A1c, Scr, uric acid, apolipoproteins, or hematological parameters. Notably, both AIP and Crouse scores were substantially higher in the high Gensini score subgroup, suggesting strong associations between atherogenic lipid profiles, carotid plaque burden, and coronary lesion severity.

Table 3 and Fig. 2 present the correlations between study parameters and Gensini scores among CAD patients. Of all indicators evaluated, AIP showed the strongest positive correlation with Gensini score ($r=0.558$, $P<0.001$), followed by Crouse score ($r=0.513$, $P<0.001$) and TG levels ($r=0.407$, $P<0.001$). In contrast, HDL-C was negatively correlated with Gensini score (r=-0.433, $P<0.001$). Other variables, including TC, LDL-C, BMI, diabetes status, Scr, and apolipoproteins, did not exhibit significant correlations with coronary lesion severity.

Table 4 summarizes the univariate and multivariate logistic regression analyses for predictors of CAD in young and middle-aged patients. In univariate analyses, both AIP (OR = 1.156, 95% CI: 1.053–1.270, $P<0.001$) and Crouse score (OR = 1.522, 95% CI: 1.297–1.787, $P<0.001$) were significantly associated with CAD. After multivariate adjustment, AIP (OR = 1.219, 95% CI: 1.102–1.348, $P<0.001$) and Crouse score (OR = 1.543, 95% CI: 1.309–1.820, $P<0.001$) remained as independent predictors, while other variables, including hypertension, diabetes mellitus, TG, HDL-C, WBC, FPG, and Gensini score, were not significant. The additional variables, including age, sex, and smoking history, were not statistically significant.

Parameters	*r*	*P* value
Diabetes mellitus	0.054	0.383
Body mass index	0.079	0.181
TC	0.094	0.073
TG	0.407	< 0.001
HDL-C	-0.433	< 0.001
LDL-C	0.154	0.353
Scr	0.086	0.328
WBC	0.103	0.123
Lp(a)	0.089	0.296
ApoA1	0.094	0.263
ApoB	0.106	0.082
AIP	0.558	< 0.001
Crouse score	0.513	< 0.001

Table 3. Correlation coefficient between research indicators and Gensini score in CAG group. CAD, Coronary artery disease; TC, Total cholesterol; TG, Triglycerides; HDL, High-density lipoprotein; LDL, Low-density lipoprotein; Scr, Serum creatinine; WBC, White blood cell; ApoA1, Apolipoprotein A1; ApoB, Apolipoprotein B; TBIL, Total bilirubin; AIP, Atherogenic index of plasma; Lp(a), Lipoprotein(a).

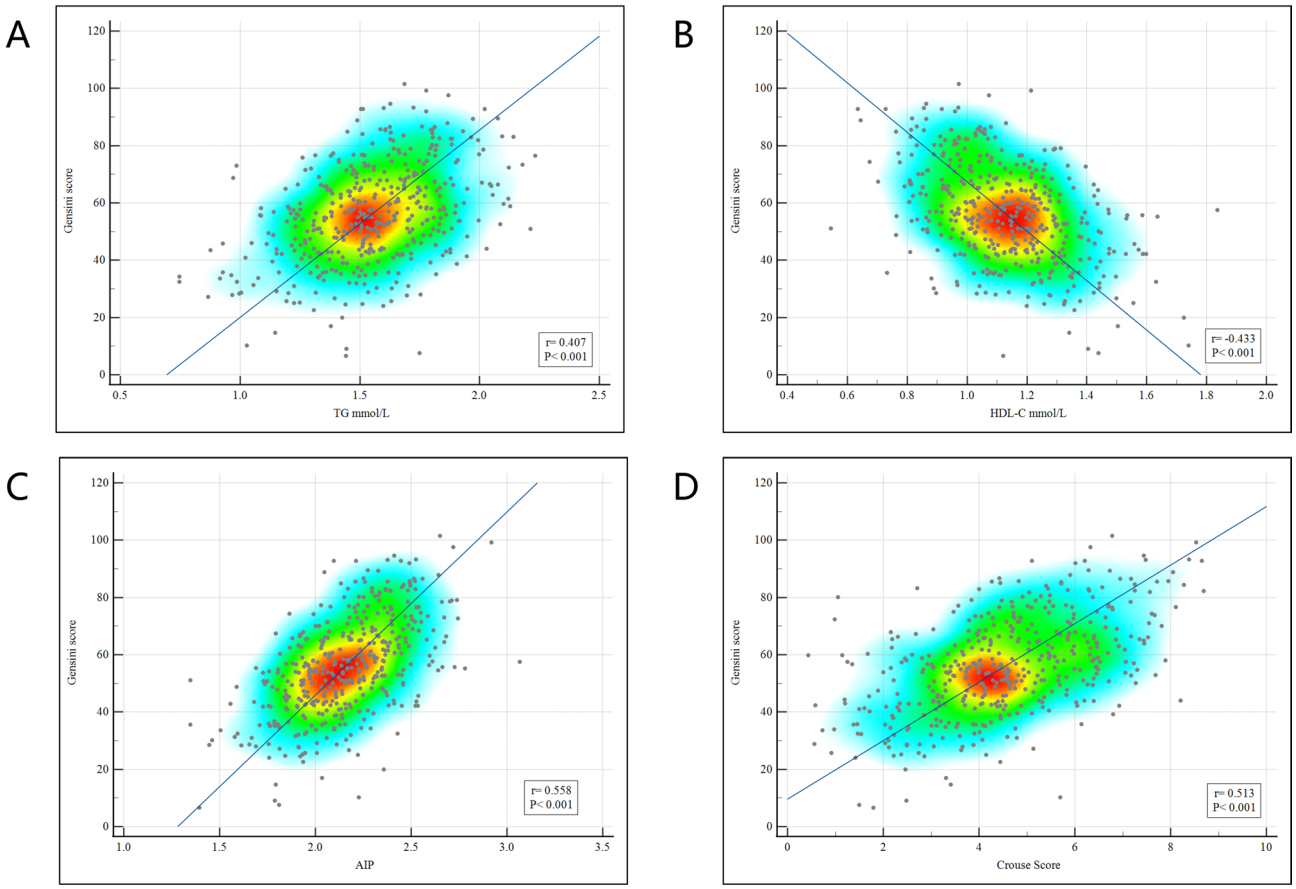

Fig. 2. Correlations between lipid parameters, AIP, carotid Crouse score, and Gensini score in CAD patients. (**A**) Positive correlation between TG levels and Gensini score ($r = 0.407$, $P < 0.001$). (**B**) Negative correlation between HDL-C levels and Gensini score (r=-0.433, $P < 0.001$). (**C**) Positive correlation between AIP and Gensini score ($r = 0.558$, $P < 0.001$). (**D**) Positive correlation between Crouse score and Gensini score ($r = 0.513$, $P < 0.001$). Scatter plots are overlaid with density heatmaps, with linear regression lines shown. The color gradient from blue to red indicates increasing point density. AIP, Atherogenic index of plasma; CAD, Coronary artery disease; TG, Triglyceride; HDL-C, High-density lipoprotein cholesterol.

Variables	Univariate analysis			Multivariate analysis		
	OR	95% CI	*P* value	OR	95% CI	*P* value
Hypertension	1.002	0.997–1.007	0.518			
Diabetes mellitus	0.892	0.513–1.551	0.685			
TG, mmol/L	1.333	0.733–2.427	0.347			
HDL-C, mmol/L	0.822	0.465–1.455	0.502			
WBC, 10^9/L	0.993	0.935–1.056	0.829			
FPG, mmol/L	0.988	0.793–1.230	0.912			
AIP	1.156	1.053–1.270	< 0.001	1.219	1.102–1.348	< 0.001
Crouse score	1.522	1.297–1.787	< 0.001	1.543	1.309–1.820	< 0.001
Gensini score	1.295	0.416–4.025	0.531			
Age, years	0.269	0.096–1.751	0.235			
Male	0.877	0.325–2.363	0.795			
Smoking history	0.815	0.225–2.957	0.756			

Table 4. Univariate and multivariate Cox regression analyses of the presence of CAD in young and middle-aged patients. OR, Odds ratios; CI, Confidence interval; CAD, Coronary artery disease; AIP, Atherogenic index of plasma; WBC, White blood cell; TG, Triglycerides; HDL, High-density lipoprotein; FPG, Fasting blood glucose

Variables	Univariate analysis			Multivariate analysis		
	OR	95% CI	*P* value	OR	95% CI	*P* value
TG, mmol/L	1.013	0.994–1.021	0.827			
HDL-C, mmol/L	0.892	0.732–1.087	0.237			
AIP	1.519	1.358–1.699	< 0.001	1.575	1.379–1.791	< 0.001
Crouse score	1.376	1.190–1.591	0.003	1.253	1.082–1.452	0.002
Gensini score	0.408	0.161–1.011	0.065			
Age, years	0.995	0.967–1.024	0.732			
Male	1.026	0.907–1.167	0.686			
Smoking history	1.009	0.985–1.034	0.456			

Table 5. Multivariate logistic regression analysis of severe coronary artery stenosis in young and middle-aged patients. OR, Odds ratios; CI, Confidence interval; CAD, Coronary artery disease; AIP, Atherogenic index of plasma; TG, Triglycerides; HDL, High-density lipoprotein

Table 5 displays the multivariate logistic regression analysis for predictors of severe coronary artery stenosis. Univariate analysis showed that both AIP (OR = 1.519, 95% CI: 1.358–1.699, $P < 0.001$) and Crouse score (OR = 1.376, 95% CI: 1.190–1.591, $P = 0.003$) were significantly associated with severe stenosis. After adjusting for traditional risk factors (age, gender, and smoking), as well as other covariates, AIP (OR = 1.575, 95% CI: 1.379–1.791, $P < 0.001$) and Crouse score (OR = 1.253, 95% CI: 1.082–1.452, $P = 0.002$) remained significant predictors, while none of the other variables were statistically significant.

Table 6 and Fig. 3 illustrate the diagnostic performance of AIP, Crouse score, and their combination for predicting CAD and severe coronary artery stenosis. In predicting CAD (Fig. 3A), the AUCs were 0.658 (95% CI: 0.617–0.704) for AIP and 0.639 (95% CI: 0.599–0.684) for Crouse score, with sensitivities of 55.6% and 57.7%, and specificities of 68.9% and 66.2%, respectively. The combined model yielded a higher AUC of 0.700 (95% CI: 0.658–0.745), with improved sensitivity (63.6%) and specificity (68.0%). DeLong's test showed the combined model had a significantly superior AUC compared to either marker alone ($P < 0.05$). For predicting severe coronary artery stenosis (Fig. 3B), AIP alone demonstrated an AUC of 0.687 (95% CI: 0.637–0.734), while Crouse score alone had an AUC of 0.678 (95% CI: 0.622–0.727). Their combination achieved the highest AUC of 0.754 (95% CI: 0.706–0.796), significantly outperforming individual markers ($P < 0.05$), with sensitivity and specificity of 58.8% and 83.0%, respectively.

Discussion

This study investigated the associations of AIP and carotid Crouse score with both the presence and severity of CAD among young and middle-aged individuals, as well as the predictive utility of their combined application. Findings revealed that both AIP and Crouse score independently predicted the occurrence of CAD and severe coronary stenosis within this population. Furthermore, the combined model incorporating both markers demonstrated superior diagnostic accuracy compared to either parameter alone, suggesting that their integration could serve as an effective non-invasive approach for early CAD screening and risk stratification. Specifically, the combination of AIP and Crouse score may facilitate the early identification of high-risk individuals, enabling

	AUC	95% CI	Youden index	Cut-off point	Sensitivity, %	Specificity, %	*P* value		
							AIP	Crouse score	AIP + Crouse score
Predicting CAD									
AIP	0.658	0.617–0.704	0.245	2.041	55.6	68.9	–	0.519	0.012
Crouse score	0.639	0.599–0.684	0.239	3.451	57.7	66.2	0.519	–	< 0.001
AIP + Crouse score	0.700	0.658–0.745	0.316	0.659	63.6	68.0	0.012	< 0.001	–
Predicting severe coronary artery stenosis									
AIP	0.687	0.637–0.734	0.290	2.240	53.6	75.5	–	0.812	0.002
Crouse score	0.678	0.622–0.727	0.394	4.686	51.2	88.2	0.812	–	< 0.001
AIP + Crouse score	0.754	0.706–0.796	0.418	0.544	58.8	83.0	0.002	< 0.001	–

Table 6. Comparative analysis of area under the receiver operating characteristic curves. Sensitivity and specificity were determined using the optimal cutoff defined by the Youden index. *P* values were calculated using DeLong's test to compare the differences in AUC between scoring models. A two-sided *P* value < 0.05 was considered statistically significant. AIP, Atherogenic index of plasma; AUC, Area under the receiver operating characteristic curve; CI, Confidence interval.

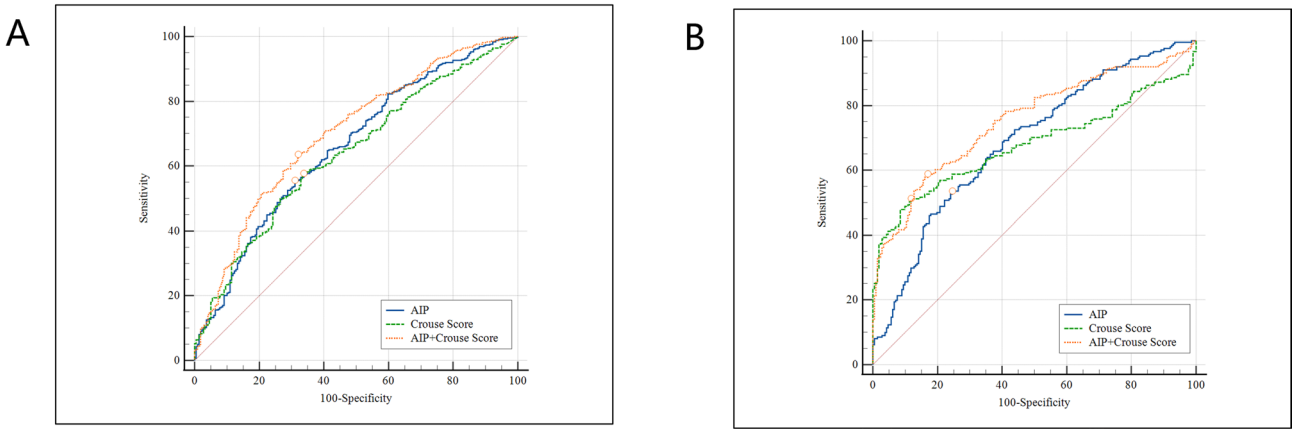

Fig. 3. ROC curves for predicting CAD and severe coronary artery stenosis. (**A**) ROC curves comparing AIP (blue solid line), Crouse score (green dashed line), and their combination (orange dotted line) for predicting CAD. The combination model showed the highest AUC (0.700). (**B**) ROC curves for predicting severe coronary artery stenosis, demonstrating superior diagnostic performance of the combined AIP and Crouse score model (AUC = 0.754) compared to either indicator alone. Sensitivity and specificity were calculated based on optimal cut-off points determined by the Youden index. Statistical comparisons were performed using DeLong's test. AIP, Atherogenic index of plasma; CAD, Coronary artery disease; ROC, Receiver operating characteristic; AUC, Area under the curve

an initial evaluation of coronary stenosis severity prior to CAG and informing decisions regarding the necessity of subsequent CAG for definitive diagnosis. This strategy holds important clinical implications for the timely detection and intervention of CAD in young and middle-aged patients, supporting individualized lifestyle modifications, pharmacological management, and pre-procedural assessments.

Increasing CAD burden in young and Middle-Aged populations

In recent years, the incidence of CAD among young and middle-aged individuals has exhibited a clear upward trend, driven by factors such as accelerated lifestyles, heightened occupational stress, and suboptimal dietary patterns[18]. Compared with older patients, young individuals with CAD often lack prodromal symptoms due to the shorter duration of disease and underdeveloped collateral circulation, leading to delays in diagnosis and treatment[19]. Given their pivotal roles within both families and society, the onset of CAD in this population imposes considerable health and economic burdens[19]. Nonetheless, awareness and management of cardiovascular risk factors in young CAD patients remain insufficient, despite evidence indicating that effective control of smoking, hypertension, diabetes, and dyslipidemia can markedly lower disease incidence and improve prognosis[20]. Therefore, proactive identification and intervention targeting high-risk young individuals are crucial for preventing premature CAD and its associated complications, underscoring the clinical significance of the findings in this study.

Predictive value of AIP for CAD

LDL-C plays a pivotal role in the initiation and progression of CAD[21]. Further research has demonstrated that LDL-C comprises various subfractions with differing atherogenicity, among which sdLDL-C is particularly implicated in CAD development[22]. These small, dense LDL particles possess enhanced atherogenic properties due to their greater ability to penetrate the endothelium and their increased susceptibility to oxidative modification. However, the direct measurement of sdLDL-C is technically demanding and expensive, limiting its widespread clinical application. The AIP, calculated as log(TG/HDL-C), was proposed by Dobiasova as a novel integrated lipid index and has been shown to inversely correlate with LDL particle size, thereby serving as an indirect marker for sdLDL-C levels[23]. In patients undergoing coronary angiography, AIP has been identified as an independent risk factor for premature CAD and has demonstrated effective predictive capacity[24].

AIP reflects the combined influence of TG, a recognized cardiovascular risk factor, and HDL-C, a protective factor against atherosclerosis[24]. Therefore, it not only indicates the plasma lipoprotein distribution pattern but also indirectly reflects LDL particle size, serving as a reliable predictor of cardiovascular risk[24]. Consistent with previous reports[25–27]our findings revealed significantly higher AIP levels in CAD patients, which were associated with both disease presence and severity as indicated by elevated Gensini scores. Spearman correlation analysis showed a positive association between AIP and Gensini scores, indicating that increased AIP levels correspond to more severe coronary lesions. Importantly, AIP emerged as an independent predictor for both CAD and severe coronary stenosis in our study, with ROC analysis demonstrating good discriminatory performance.

Beyond its role in CAD prediction, elevated AIP levels have also been observed in patients with in-stent restenosis[28]and AIP has been recognized as a predictor of chronic total occlusion percutaneous coronary intervention (CTO-PCI) complexity, thereby aiding procedural planning[29]. Furthermore, studies have identified AIP as an independent predictor of acute myocardial infarction (AMI)[25]and elevated AIP levels have been reported in patients undergoing CABG, where it is associated with disease progression[26]. These findings underscore AIP's potential as a comprehensive marker for CAD onset, severity, and progression, warranting further investigation.

Since its introduction in 2001 by Dobiasova and Frohlich[23]AIP has been recognized as a sensitive indicator of plasma lipoprotein distribution, correlating with insulin sensitivity, LDL particle size, and HDL-C esterification rate. Large-scale studies have demonstrated its associations with waist circumference, BMI, and levels of physical activity[30]while its strong correlations with biomarkers such as ADMA and FABP4 further support its utility as an early diagnostic marker for cardiovascular events[31].

Notably, a decade-long study involving 1,059 young ACS patients demonstrated a positive correlation between AIP and ACS prevalence, indicating its superiority over conventional lipid parameters in predicting premature ACS[32]. Similarly, a cohort study of 6,465 young individuals showed a significant association between AIP and obesity, highlighting its stronger predictive value compared to traditional lipid indices[33]. Given its simplicity, cost-effectiveness, and robust predictive capability for CAD incidence, severity, and progression, AIP offers practical utility for risk assessment and early prevention strategies in young and middle-aged populations. Importantly, our study is among the first to evaluate the combined predictive value of AIP with carotid Crouse score in this population, underscoring its potential to enhance early CAD screening and intervention strategies.

Furthermore, the systemic relevance of AIP in atherosclerotic disease has been highlighted in recent vascular research. For instance, a study by Evsen et al. demonstrated that both AIP and the LDL/HDL ratio were associated with the complexity of peripheral arterial disease (PAD), reinforcing their value as markers of dyslipidemia-driven atherosclerosis beyond coronary beds[34]. Another study by Altunova et al. further confirmed the prognostic potential of AIP by showing that elevated AIP levels independently predicted long-term major adverse limb events (MALE) in patients undergoing endovascular therapy for superficial femoral artery lesions[35]. These findings together emphasize that AIP reflects a global atherogenic burden, further supporting its utility as a cost-effective and comprehensive cardiovascular risk indicator.

Predictive value of carotid Crouse score for CAD

Carotid atherosclerosis is widely recognized as a window into CAD[6]. Due to shared systemic atherosclerotic mechanisms, including endothelial dysfunction, lipid deposition, and inflammatory pathways, carotid plaques are closely linked to the progression of coronary atherosclerosis and serve as visual surrogate markers for coronary pathology[36]. Moreover, the burden of carotid plaques has been shown to predict both the severity of coronary atherosclerosis and the risk of future cardiovascular events[37]. The Crouse score, calculated as the sum of the maximal thicknesses of all discrete plaques in bilateral carotid arteries, quantifies carotid plaque burden. Recent studies have demonstrated its predictive value for ischemic stroke in patients with diabetes mellitus[38]highlighting its prognostic significance. However, its utility in predicting CAD presence and severity specifically among young and middle-aged populations has not been previously investigated.

In our study, Crouse scores were significantly higher in CAD patients compared to non-CAD controls and were also elevated in patients with high Gensini scores relative to those with low scores. Multivariate logistic regression analysis identified Crouse score as an independent predictor for both CAD and severe coronary stenosis. Furthermore, Spearman correlation analysis demonstrated a significant positive correlation between Crouse score and Gensini score, suggesting that a greater carotid plaque burden is associated with increased coronary lesion severity. ROC analysis confirmed the predictive value of Crouse score alone for CAD presence and severe coronary stenosis, supporting its role as a non-invasive screening tool in young and middle-aged individuals.

The superficial anatomical position of the carotid arteries facilitates their evaluation by ultrasound, which is a simple, non-invasive, cost-effective imaging modality that permits repeated assessments. Importantly, Crouse score increases proportionally with the number and thickness of plaques and is minimally influenced by operator subjectivity, thereby providing a reliable measure of carotid atherosclerosis severity and systemic

plaque burden. The TOOTH study[39]a prospective cohort study involving 347 Japanese participants aged ≥ 85 years without baseline CAD, utilized Crouse scoring to assess plaque burden and demonstrated that higher scores were significantly associated with cardiovascular disease-related mortality (HR = 3.90; 95% CI: 1.47–10.39). Similarly, Tada et al.[40] reported that after adjusting for traditional ASCVD risk factors, Crouse score remained significantly associated with major adverse cardiovascular events (MACE), whereas CIMT did not. Compared to CIMT, Crouse score more accurately reflects carotid plaque burden, suggesting its superiority as a marker for predicting elevated MACE risk in secondary prevention settings.

Combined use of AIP and Crouse score for CAD risk prediction

CAG remains the gold standard for diagnosing CAD; however, its invasive nature, associated procedural risks, and high costs limit its routine application. Combining AIP with carotid Crouse score offers a practical and relatively accurate method to predict CAD presence and coronary stenosis severity in young and middle-aged individuals using readily obtainable laboratory and imaging parameters. Our findings demonstrated that the combined predictive value of AIP and Crouse score for both CAD and severe coronary stenosis was significantly superior to that of either parameter alone, with statistically significant differences observed in both CAD and high Gensini score groups.

AIP serves as an indicator of dyslipidemia, reflecting the balance between triglycerides and HDL-C as a biochemical snapshot of lipid metabolism at a specific time point, whereas carotid plaque formation, assessed by the Crouse score, represents the cumulative structural burden of atherosclerosis over time. Thus, integrating these two dimensions – the horizontal biochemical profile and the longitudinal structural manifestation – provides a more comprehensive evaluation of vascular health and CAD risk.

In our study, both AIP and Crouse scores differed significantly between CAD and non-CAD groups, as well as between high and low Gensini score groups. Multivariate logistic regression analyses confirmed that each was an independent predictor for CAD and severe coronary stenosis, while Spearman correlation analyses revealed significant positive associations with Gensini scores. ROC curve analyses further indicated that the combined model of AIP and Crouse score achieved higher AUCs compared to either marker alone for predicting CAD and severe coronary stenosis, with statistically significant improvements.

Collectively, integrating AIP with Crouse score, which combines biochemical and imaging assessments, enables clinicians to more conveniently and accurately estimate CAD risk and stenosis severity prior to performing invasive CAG. This integrated approach holds particular clinical value for young and middle-aged populations, facilitating early identification and timely intervention, ultimately improving outcomes and reducing the overall burden of CAD.

Limitations

This study has several limitations. First, it was a retrospective, single-center observational study, which may introduce selection bias and limit the generalizability of the findings to broader populations. Second, only patients who underwent both carotid ultrasound and coronary angiography were included, potentially introducing referral bias. Third, this study lacked long-term follow-up data to evaluate the prognostic value of AIP and Crouse score for cardiovascular events or mortality outcomes. Although such outcomes (e.g., myocardial infarction, cardiovascular death, or recurrent ischemic events) are of significant clinical interest, the retrospective design of our study limited the availability and completeness of follow-up records. In particular, the number of patients with clearly documented adverse events was insufficient to support a valid prognostic analysis. Therefore, these endpoints were not included in the current analysis. We acknowledge this limitation and emphasize that future prospective studies with systematic follow-up and adequate event capture will be necessary to determine the true prognostic utility of AIP and the Crouse score. Fourth, residual confounding factors, such as inflammatory biomarkers, insulin resistance parameters, or genetic predisposition, were not assessed and may have influenced the observed associations. Fifth, due to the retrospective nature of this study, we were unable to collect key clinical variables—such as chest pain characteristics—required to calculate the risk factor weighted clinical likelihood (RF-CL) score as recommended in the 2024 ESC CCS guidelines. Therefore, a direct comparison between our model and the RF-CL model could not be performed. Finally, sdLDL-C was not directly measured due to technical and cost limitations, preventing direct validation of the proposed mechanistic link between AIP and sdLDL-C in this population. Therefore, future prospective, multicenter studies with larger sample sizes and long-term follow-up are needed to validate these findings and explore their impact on clinical outcomes.

Conclusion

In conclusion, this study demonstrated that both AIP and carotid Crouse score are independent predictors of CAD presence and severity in young and middle-aged individuals. Importantly, their combined use significantly improves the diagnostic performance for identifying CAD and assessing coronary stenosis severity compared to either marker alone. Given their simplicity, non-invasiveness, and cost-effectiveness, integrating AIP and Crouse score assessments may serve as an effective screening strategy for early CAD detection and risk stratification in this population, enabling timely lifestyle interventions, pharmacological management, and pre-procedural planning to reduce the burden of CAD.

Data availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Author contributions
X.W. and L.W. had the idea for the paper, reviewed and edited it critically for important intellectual content. H.B.H. and H.H. performed the literature search and analysis. X.W., M.X.W., L.W., Z.L. and H.H. substantially contributed to the conception of the paper, drafted and critically revised the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

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Declarations

Competing interests
The authors declare no competing interests.

Ethics approval and consent to participate
The present research was carried out in accordance with the tenets mentioned in the Helsinki Declaration and was approved by the Ethical Board of Xiangtan Central Hospital (approval number: X2020642). Prior to the commencement of the research, our team obtained written informed consent from each patient.

Additional information

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