Prognostic impact of atherogenic index of plasma (AIP) in type 2 diabetes mellitus patients with acute coronary syndrome undergoing percutaneous coronary intervention

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Abstract

Background and purposes

The association of atherogenic index of plasma (AIP), an emerging lipid index which can predict risk for cardiovascular (CV) disease, with adverse outcomes in type 2 diabetes mellitus (T2DM) patients with acute coronary syndrome (ACS) undergoing percutaneous coronary intervention (PCI) has been undetermined. Therefore, the aim of this study was to investigate whether AIP could independently predict adverse CV events in T2DM patients with ACS undergoing PCI.

Methods

This study was a retrospective analysis of a single centre prospective registry involving 826 consecutive T2DM patients who underwent coronary angiography for ACS and were treated with primary or elective PCI at our CV center from June 2016 to November 2017. This study eventually included 798 patients (age, 61 ± 10 years, male, 72.7%). AIP was calculated as the base 10 logarithm of the ratio of plasma concentration of triglycerides to high density lipoprotein-cholesterol (HDL-C). All patients were divided into 4 groups based on the AIP quartiles. The primary endpoint was a composite of all-cause death, non-fatal ischemic stroke, non-fatal myocardial infarction (MI), or unplanned repeat revascularization. The key secondary endpoint was a composite of cardiovascular death, non-fatal ischemic stroke, or non-fatal MI.

Results

During a median follow-up period of 927 days, 198 patients developed at least one event. Unadjusted Kaplan–Meier analysis showed the incidence of the primary endpoint increased gradually with rising AIP quartiles (log-rank test, $P = 0.001$). Adjusted multivariate Cox proportional hazards analyses revealed that compared with the lowest AIP quartile, the top AIP quartile was associated with significantly increased risk for the primary and key secondary endpoints (hazard ratio [HR]: 2.153; 95% confidence interval [CI]: 1.355 to 3.421; $P = 0.001$, and HR: 2.613; 95% CI: 1.024 to 6.666; $P = 0.044$, respectively). Inclusion of AIP quartiles in a baseline prediction model for the primary endpoint increased the Harrell's C statistic from 0.697 to 0.707. More importantly, addition of AIP quartiles to the above model significantly improved the continuous net reclassification improvement (continuous NRI = 19.1%, $P < 0.001$).

Conclusion

A higher AIP value on admission was independently and strongly associated with adverse CV events in T2DM patients with ACS undergoing PCI.

Background

Type 2 diabetes mellitus (T2DM) has been established as an important risk factor for adverse outcomes in patients with acute coronary syndrome (ACS) [1–3]; this may be due to a rapid development of atherosclerosis related to T2DM [4]. T2DM patients with ACS remain at a very high residual risk of

adverse cardiovascular (CV) events and mortality, despite receiving percutaneous coronary intervention (PCI) and guideline-recommended first-line medication therapies [5–8]. Therefore, further risk assessment of such patients may help better determine prognosis and guide better medical management.

Dyslipidemia is a common comorbidity in T2DM and ACS patients. The dyslipidemic pattern in diabetic patients [mainly characterized by high levels of fasting and postprandial triglyceride-rich lipoproteins, reduced high density lipoprotein-cholesterol (HDL-C), normal or slightly elevated low density lipoprotein-cholesterol (LDL-C), and the appearance of small dense LDL-C particles] is somewhat different from that in non-diabetic patients [9]. Atherogenic index of plasma (AIP), readily calculated from the lipid profile as $\log_{10}$ (triglycerides/HDL-C), is considered an alternative and simple marker of plasma atherogenicity based on an observed significant, positive relationship between AIP and cholesterol esterification rates in apoB-lipoprotein-depleted plasma (FER(HDL)), very low density lipoprotein particle size, remnant lipoprotein particle cholesterol, and LDL density, and inverse correlation of AIP with particle sizes of HDL and LDL [10–16]. As a consequence, we presume that AIP can better reflect the lipid characteristics of diabetic patients. Recently, AIP has been demonstrated to be associated with CV morbidity and mortality in general population and different patients groups [17–28]. However, the prognostic impact of AIP on admission among T2DM patients with ACS undergoing PCI has not been exclusively studied. We hypothesized that AIP on admission is an independent predictor of adverse CV events in T2DM and ACS patients who underwent PCI.

Methods

Study population

This study was a retrospective analysis of a single centre prospective registry involving 826 consecutive T2DM patients who underwent coronary angiography for ACS and were treated with primary or elective PCI at our CV center from June 2016 to November 2017 [29]. For purposes of this study, we excluded patients with prior coronary artery bypass graft surgery, cardiogenic shock, left ventricular ejection fraction (LVEF) <30%, and severe renal impairment requiring hemodialysis. Three patients were also excluded because of missing follow-up data despite at least 4 separate attempts to contact them. Finally, 798 patients were included in the present analysis. None of these patients were treated with drugs specifically designed to lower triglycerides or raise HDL-C, such as fibrates, niacin, and omega-3 fatty acids, before admission and at discharge.

Measurement

Data on demographics, personal medical history, and medication history were collected using a standard questionnaire. The levels of plasma triglycerides, total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and glucose in the first fasting blood samples during the stay in the hospital, which were obtained after 12 h of fasting, were determined at the central laboratory of Beijing Anzhen Hospital. The low-density lipoprotein cholesterol (LDL-C) level was calculated using the

Friedewald equation. AIP was calculated as the base 10 logarithm of the ratio of plasma concentration of triglycerides to high density lipoprotein-cholesterol (HDL-C) [10].

Follow-up and endpoints

All patients were followed up at 1 month and then every 6 months after hospital discharge. Trained personnel who were blinded to the baseline data of patients obtained information on adverse events via telephone contact with patients or their family members using a standardized questionnaire; the adverse events were then ascertained from a careful review of corresponding medical records. The primary endpoint was a composite of all-cause death, non-fatal ischemic stroke, non-fatal myocardial infarction (MI), or unplanned repeat revascularization. The key secondary endpoint was a composite of cardiovascular death, non-fatal ischemic stroke, or non-fatal MI. Adverse events were defined in accordance with our previous publications [29, 30]. The most severe endpoint event was selected for the primary endpoint analysis if >1 event occurred during follow-up (death > stroke > MI > revascularization). If more than one stroke or MI or revascularization occurred, the first stroke or MI or revascularization was selected. The follow-up period of the present study lasted until November 2019.

Statistical analysis

All patients were stratified into 4 groups (Q1 [AIP ≤0.0147], Q2 [0.0147< AIP ≤0.1850], Q3 [0.1850< AIP ≤0.3517] and Q4 [AIP >0.3517]) according to the AIP quartiles. Continuous variables with parametric distributions are shown as the means ± standard deviations and those with nonparametric distributions are shown as medians and interquartile ranges. Categorical variables are shown as frequencies and percentages. Unpaired t-test or Mann-Whitney U test and Analysis of Variance or Kruskal-Wallis H test were used to assess the statistical significance of differences for continuous variables between groups. The statistical significance of differences for categorical variables between groups was analyzed using chi-squared test or Fisher's exact test. Survival analyses of the primary and key second endpoints were performed using Kaplan-Meier curves and Cox proportional hazards model. Differences among Kaplan-Meier estimates were evaluated with the log-rank test. Results of Cox proportional hazards analyses were presented as hazard ratios (HRs) with 95% confidence intervals (CIs). Variables with statistical significance and those with clinical importance were entered into the multivariate regression model. Post-hoc subgroup analyses stratified by age (<60 versus ≥60 years), sex (female versus male), body mass index (BMI) (<28 versus ≥28 kg/m^2), LDL-C (≤1.8 versus >1.8 mmol/L), hypertension (yes versus no), and clinical presentation (non-ST versus ST segment elevation ACS) were employed to examine the consistence of the prognostic significance of AIP for the primary endpoint. Harrell's C statistic for the primary endpoint was calculated after the addition of AIP quartiles to other independent predictors identified in the multivariate Cox proportional hazards analyses; it is generally considered Harrell's C statistic above 0.7 acceptable discriminatory power, that above 0.8 excellent discriminatory power, and that above 0.9 outstanding discriminatory power. The incremental effect of adding AIP quartiles to other independent predictors in predicting the primary endpoint was evaluated using the continuous net reclassification improvement (NRI). Analyses were performed using SPSS version 24.0 (IBM Corp.,

Armonk, New York, US) and R software version 3.5.3 (R Foundation for Statistical Computing, Beijing, China). A 2-sided *P*-value <0.05 was considered significant.

Results

A total of 798 T2DM and ACS patients who underwent PCI were included in the present study. The mean age of these patients was 61 ± 10 years, and 72.7% of patients were men. The baseline clinical and laboratory characteristics of the study patients according to the AIP quartiles are listed in Table 1. Patients with higher AIP values tended to be younger, were predominantly male, had higher rates of current smoking and dyslipidaemia, and had lower rates of never smoking and diagnosis with unstable angina pectoris. Patients with higher AIP values were more likely to have higher levels of BMI, serum creatinine (SCr), uric acid, TC, LDL-C, triglycerides, and fasting plasma glucose (FPG), while have lower levels of pulse pressure (PP) and HDL-C. Use of medications, agiographic findings, and procedural results of the study patients according to the AIP quartiles are summarized in Table 2. Medications before admission, intraoperative anticoagulants, and periprocedural medications, except for β-blockers, did not differ among the different AIP groups. Medications at discharge, except for P2Y12 inhibitors, angiotensin converting enzyme inhibitors/angiotensin II receptor blockers (ACEIs/ARBs), and oral antidiabetic agents, were similar across the different AIP groups. More patients who had higher AIP values were treated with ACEIs/ARBs at discharge. The proportions of left main/three-vessel disease and two-vessel disease were different among the different AIP groups. Patients with higher AIP values tended to have a higher rate of chronic total occlusions, and a lower rate of heavy calcification lesions. The proportions of left circumflex artery and right coronary artery interventions were different among the different AIP groups. Patients with higher AIP values tended to have a lower rate of complete revascularization.

Table 1
Baseline clinical and laboratory characteristics of the study patients according to the AIP quartiles

Variable	Q1 n = 199	Q2 n = 200	Q3 n = 200	Q4 n = 199	*P* value
Demographics					
Age (years)	63 ± 8	63 ± 10	61 ± 9	58 ± 12	< 0.001
Male sex, n (%)	125 (62.8)	146 (73.0)	153 (76.5)	156 (78.4)	0.002
Clinical values (on admission)					
BMI (kg/m^2)	25.3 ± 3.1	25.4 ± 2.8	26.1 ± 3.1	27.0 ± 3.5	< 0.001
SBP (mm Hg)	133 ± 18	133 ± 17	130 ± 16	131 ± 16	0.116
DBP (mm Hg)	75 ± 11	76 ± 10	75 ± 10	77 ± 11	0.203
PP (mm Hg)	58 ± 16	58 ± 15	55 ± 15	54 ± 14	0.015
Risk factors					
Smoking status					
Current smoking, n (%)	60 (30.2)	77 (38.5)	76 (38.0)	111 (55.8)	< 0.001
Former smoking, n (%)	33 (16.6)	33 (16.5)	38 (19.0)	26 (13.1)	0.455
Never smoking, n (%)	106 (53.3)	90 (45.0)	86 (43.0)	62 (31.2)	< 0.001
Chronically daily drinking, n (%)	14 (7.0)	18 (9.0)	26 (13.0)	21 (10.6)	0.234
Family history of CHD, n (%)	54 (27.1)	60 (30.0)	69 (34.5)	56 (28.1)	0.386
Hypertension, n (%)	138 (69.3)	137 (68.5)	141 (70.5)	130 (65.3)	0.715
Dyslipidaemia, n (%)	107 (53.8)	174 (87.0)	192 (96.0)	195 (98.0)	< 0.001
Previous MI, n (%)	36 (18.1)	43 (21.5)	40 (20.0)	51 (25.6)	0.301

AIP indicates atherogenic index of plasma; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure; CHD, coronary heart disease; MI, myocardial infarction; PCI, percutaneous coronary intervention; TIA, transient ischemic attack; PAD, peripheral artery disease; LVEF, left ventricular ejection fraction; UAP, unstable angina pectoris; NSTEMI, non ST-segment elevation myocardial infarction; STEMI, ST-segment elevation myocardial infarction; BUN, blood urea nitrogen; SCr, serum creatinine; UA, uric acid; TC, total cholesterol; LDL-C, low-density lipoprotein-cholesterol; HDL-C, high-density lipoprotein-cholesterol; FPG, fasting plasma glucose.

Variable	Q1 n = 199	Q2 n = 200	Q3 n = 200	Q4 n = 199	*P* value
Past PCI, n (%)	47 (23.6)	50 (25.0)	50 (25.0)	44 (22.1)	0.891
Previous ischemic stroke or TIA, n (%)	13 (6.5)	13 (6.5)	17 (8.5)	8 (4.0)	0.338
PAD, n (%)	27 (13.6)	29 (14.5)	31 (15.5)	35 (17.6)	0.713
Cardiac failure, n (%)	12 (6.0)	13 (6.5)	23 (11.5)	19 (9.5)	0.156
LVEF (%)	64 (60–67)	64 (60–68)	65 (60–68)	65 (59–68)	0.963
Clinical presentation					
UAP, n (%)	171 (85.9)	153 (76.5)	150 (75.0)	153 (76.9)	0.033
NSTEMI, n (%)	19 (9.5)	28 (14.0)	28 (14.5)	25 (12.6)	0.493
STEMI, n (%)	9 (4.5)	19 (9.5)	22 (11.0)	21 (10.6)	0.088
Laboratory measurements (fasting state)					
BUN (mmol/L)	5.2 (4.3–6.3)	5.4 (4.5–6.5)	5.4 (4.6–6.2)	5.5 (4.6–6.7)	0.173
SCr (μmol/L)	66.5 (59.3–73.6)	69.2 (61.9–80.3)	70.3 (62.2–81.3)	71.5 (63.2–82.2)	< 0.001
UA (μmol/L)	303.2 (271.7-347.2)	321.3 (279.6–373.0)	323.8 (282.5–386.0)	368.5 (307.0-410.3)	< 0.001
TC (mmol/L)	3.90 ± 0.96	4.06 ± 1.01	4.10 ± 0.99	4.47 ± 1.03	< 0.001
LDL-C (mmol/L)	2.23 ± 0.85	2.48 ± 0.84	2.48 ± 0.77	2.53 ± 0.76	0.001
HDL-C (mmol/L)	1.23 ± 0.22	1.04 ± 0.17	0.95 ± 0.17	0.87 ± 0.14	< 0.001
Triglycerides (mg/dl)	0.88 (0.72-1.00)	1.31 (1.18–1.48)	1.71 (1.51–1.99)	2.66 (2.25–3.38)	< 0.001
FPG (mg/dl)	6.80 (6.12–8.23)	7.17 (6.32–8.25)	6.80 (5.91–7.88)	7.65 (6.61–8.49)	< 0.001

AIP indicates atherogenic index of plasma; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure; CHD, coronary heart disease; MI, myocardial infarction; PCI, percutaneous coronary intervention; TIA, transient ischemic attack; PAD, peripheral artery disease; LVEF, left ventricular ejection fraction; UAP, unstable angina pectoris; NSTEMI, non ST-segment elevation myocardial infarction; STEMI, ST-segment elevation myocardial infarction; BUN, blood urea nitrogen; SCr, serum creatinine; UA, uric acid; TC, total cholesterol; LDL-C, low-density lipoprotein-cholesterol; HDL-C, high-density lipoprotein-cholesterol; FPG, fasting plasma glucose.

Variable	Q1 n = 199	Q2 n = 200	Q3 n = 200	Q4 n = 199	*P* value
Glycated haemoglobin (%)	7.0 (6.6–8.1)	7.3 (6.7–8.2)	7.2 (6.6–8.1)	7.3 (6.7-8.0)	0.409
AIP	-0.1581 ± 0.1373	0.1029 ± 0.0482	0.2631 ± 0.0504	0.5272 ± 0.1773	< 0.001

AIP indicates atherogenic index of plasma; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure; CHD, coronary heart disease; MI, myocardial infarction; PCI, percutaneous coronary intervention; TIA, transient ischemic attack; PAD, peripheral artery disease; LVEF, left ventricular ejection fraction; UAP, unstable angina pectoris; NSTEMI, non ST-segment elevation myocardial infarction; STEMI, ST-segment elevation myocardial infarction; BUN, blood urea nitrogen; SCr, serum creatinine; UA, uric acid; TC, total cholesterol; LDL-C, low-density lipoprotein-cholesterol; HDL-C, high-density lipoprotein-cholesterol; FPG, fasting plasma glucose.

Table 2
Use of medications, agiographic findings, and procedural results of the study patients according to the AIP quartiles

Variable	Q1 n = 199	Q2 n = 200	Q3 n = 200	Q4 n = 199	*P* value
Medications before admission					
Aspirin, n (%)	145 (72.9)	149 (74.5)	154 (77.0)	146 (73.4)	0.784
P2Y12 inhibitors, n (%)	81 (40.7)	81 (40.5)	74 (37.0)	80 (40.2)	0.858
Statins, n (%)	150 (75.4)	143 (71.5)	155 (77.5)	142 (71.4)	0.418
ACEIs/ARBs, n (%)	55 (27.6)	65 (32.5)	72 (36.0)	69 (34.7)	0.300
β-blockers, n (%)	70 (35.2)	79 (39.5)	93 (46.5)	63 (31.7)	0.016
Insulin, n (%)	75 (37.7)	73 (36.5)	79 (39.5)	63 (31.7)	0.406
Oral antidiabetic agents, n (%)	89 (44.7)	98 (49.0)	110 (55.0)	90 (45.2)	0.145
Intraoperative anticoagulants					
Unfractionated heparin, n (%)	168 (84.4)	170 (85.0)	154 (77.0)	156 (78.4)	0.086
LMWH, n (%)	6 (3.0)	7 (3.5)	16 (8.0)	10 (5.0)	0.089
Bivalirudin, n (%)	25 (12.6)	23 (11.5)	30 (15.0)	33 (16.6)	0.448
Perioperative medications					
Aspirin, n (%)	196 (98.5)	198 (99.0)	200 (100.0)	196 (98.5)	0.308
P2Y12 inhibitors, n (%)	199 (100.0)	200 (100.0)	200 (100.0)	199 (100.0)	-
GP Ⅱb/Ⅲa receptor antagonist, n (%)	29 (14.6)	38 (19.0)	45 (22.5)	37 (18.6)	0.246
Medications at discharge					
Aspirin, n (%)	196 (98.5)	198 (99.0)	200 (100.0)	196 (98.5)	0.308
Cilostazol, n (%)	3 (1.5)	2 (1.0)	1 (0.5)	4 (2.0)	0.473
Clopidogrel, n (%)	174 (87.4)	183 (91.5)	178 (89.0)	190 (95.5)	0.031
Ticagrelor, n (%)	25 (12.6)	17 (8.5)	22 (11.0)	9 (4.5)	0.031

AIP indicates atherogenic index of plasma; ACEIs, angiotensin converting enzyme inhibitors; ARBs, angiotensin II receptor blockers; LM, left-main artery; LAD, left anterior descending artery; LCX, left circumflex artery; RCA; right coronary artery; DES, drug-eluting stent; BRS, bioresorbable scaffold; DCB, drug-coated balloon.

Variable	Q1 n = 199	Q2 n = 200	Q3 n = 200	Q4 n = 199	*P* value
Statins, n (%)	199 (100.0)	200 (100.0)	200 (100.0)	199 (100.0)	-
ACEIs/ARBs, n (%)	81 (40.7)	93 (46.5)	105 (52.5)	121 (60.8)	0.001
β-blockers, n (%)	138 (69.3)	147 (73.5)	155 (77.5)	136 (68.3)	0.155
Insulin, n (%)	65 (32.7)	76 (38.0)	72 (36.0)	57 (28.6)	0.213
Oral antidiabetic agents, n (%)	87 (43.7)	120 (60.0)	119 (59.5)	105 (52.8)	0.003
Angiographic findings					
One-vessel disease, n (%)	22 (11.1)	15 (7.5)	18 (9.0)	25 (12.6)	0.347
Two-vessel disease, n (%)	68 (34.2)	41 (20.5)	42 (21.0)	46 (23.1)	0.004
LM/three-vessel disease, n (%)	109 (54.8)	144 (72.0)	140 (70.0)	128 (64.3)	0.001
Proximal LAD stenosis, n (%)	94(47.2)	110 (55.0)	97 (48.5)	100 (50.3)	0.428
Restenotic lesions, n (%)	26 (13.1)	26 (13.0)	30 (15.0)	29 (14.6)	0.913
Trifurcation or bifurcation lesions, n (%)	155 (77.9)	162 (81.0)	151 (75.5)	148 (74.4)	0.403
Chronic total occlusions, n (%)	36 (18.1)	46 (23.0)	44 (22.0)	57 (28.6)	0.093
Thrombus lesions, n (%)	7 (3.5)	14 (7.0)	12 (6.0)	12 (6.0)	0.478
Heavy calcification lesions, n (%)	75 (37.7)	69 (34.5)	73 (36.5)	48 (24.1)	0.016
Lesions > 20 mm long, n (%)	108 (54.3)	112 (56.0)	122 (61.0)	117 (58.8)	0.537
Procedural results					
Target vessel territory					
LM, n (%)	13 (6.5)	16 (8.0)	9 (4.5)	18 (9.0)	0.313
LAD, n (%)	104 (52.3)	97 (48.5)	100 (50.0)	99 (49.7)	0.899
LCX, n (%)	64 (32.2)	69 (34.5)	42 (21.0)	48 (24.1)	0.007
RCA, n (%)	69 (34.7)	82 (41.0)	100 (50.0)	74 (37.2)	0.011
DES use, n (%)	174 (87.4)	172 (86.0)	161 (80.5)	159 (79.9)	0.097

AIP indicates atherogenic index of plasma; ACEIs, angiotensin converting enzyme inhibitors; ARBs, angiotensin II receptor blockers; LM, left-main artery; LAD, left anterior descending artery; LCX, left circumflex artery; RCA; right coronary artery; DES, drug-eluting stent; BRS, bioresorbable scaffold; DCB, drug-coated balloon.

Variable	Q1 n = 199	Q2 n = 200	Q3 n = 200	Q4 n = 199	*P* value
BRS use, n (%)	6 (3.0)	7 (3.5)	8 (4.0)	11 (5.5)	0.607
DCB use, n (%)	12 (6.0)	11 (5.5)	19 (9.5)	14 (7.0)	0.409
Complete revascularization, n (%)	136 (68.3)	115 (57.5)	110 (55.0)	107 (53.8)	0.012

AIP indicates atherogenic index of plasma; ACEIs, angiotensin converting enzyme inhibitors; ARBs, angiotensin II receptor blockers; LM, left-main artery; LAD, left anterior descending artery; LCX, left circumflex artery; RCA; right coronary artery; DES, drug-eluting stent; BRS, bioresorbable scaffold; DCB, drug-coated balloon.

The median follow-up duration was 927 days (interquartile range, 774 to 1109 days), and during the follow-up period, 198 patients suffered from at least one adverse CV event, which was recorded in 33 (16.6%) patients from the Q1 group, 45 (22.5%) from the Q2 group, 54 (27.0%) from the Q3 group, and 66 (33.2%) from the Q4 group. In the 198 patients who had at least one adverse CV event, there were 20 deaths (18 deaths from CV causes and 2 deaths from non-CV causes), 17 cases of non-fatal ischemic stroke, 24 cases of non-fatal MI, and 180 cases of unplanned revascularization. Of these, 33 patients suffered two, 2 patients suffered three, and 2 patients suffered four adverse CV events. The baseline clinical and laboratory characteristics of the study patients stratified by the primary endpoint are shown in Table 3. Compared with those without events, patients with at least one event had higher levels of AIP. Patients with at least one event had higher rates of previous MI, past PCI, peripheral arterial disease (PAD), and cardiac failure, higher levels of PP, SCr, triglycerides, and FPG, but lower levels of diastolic blood pressure, HDL-C, and LVEF. Use of medications, agiographic findings, and procedural results of the study patients stratified by the primary endpoint are presented in Table 4. Medications before admission, except for ACEIs/ARBs, were not different between patients with and without events. Intraoperative anticoagulants and perioperative medications, except for aspirin, did not differ between patients with and without events. Medications at discharge, except for aspirin, cilostazol, and insulin, were similar between patients with and without events. Compared with those without events, patients with at least one event had higher rates of left main/three-vessel disease, restenotic lesions, and lesions > 20 mm long, but lower rates of one-vessel and two-vessel diseases. In terms of procedural results, more patients who suffered from at least one event used drug-coated balloon, and fewer patients who suffered from at least one event achieved complete revascularization.

Table 3
Baseline clinical and laboratory characteristics of the study patients stratified by the primary endpoint

Variable	No such events n = 600	Primary endpoint n = 198	*P* value
Demographics			
Age (years)	61 ± 10	62 ± 10	0.435
Male sex, n (%)	436 (72.7)	144 (72.7)	0.987
Clinical values (on admission)			
BMI (kg/m^2)	26.1 ± 3.2	25.6 ± 3.1	0.087
SBP (mm Hg)	131 ± 17	133 ± 16	0.399
DBP (mm Hg)	77 ± 10	72 ± 10	< 0.001
PP (mm Hg)	55 ± 15	60 ± 15	< 0.001
Risk factors			
Smoking status			
Current smoking, n (%)	244 (40.7)	80 (40.4)	0.948
Former smoking, n (%)	93 (15.5)	37 (18.7)	0.292
Never smoking, n (%)	263 (43.8)	81 (40.9)	0.471
Chronically daily drinking, n (%)	61 (10.2)	18 (9.1)	0.660
Family history of CHD, n (%)	173 (28.8)	66 (33.3)	0.231
Hypertension, n (%)	408 (68.0)	138 (69.7)	0.656
Dyslipidaemia, n (%)	496 (82.7)	172 (86.9)	0.165
Previous MI, n (%)	114 (19.0)	56 (28.3)	0.006
Past PCI, n (%)	123 (20.5)	68 (34.3)	< 0.001
Previous ischemic stroke or TIA, n (%)	39 (6.5)	12 (6.1)	0.827
PAD, n (%)	66 (11.0)	56 (28.3)	< 0.001
Cardiac failure, n (%)	39 (6.5)	28 (14.1)	0.001
LVEF (%)	65 (60–68)	63 (57–67)	0.002

Abbreviations as in Tables 1 and 2.

Variable	No such events n = 600	Primary endpoint n = 198	*P* value
Clinical presentation UAP, n (%)	467 (77.8)	160 (80.8)	0.376
NSTEMI, n (%)	82 (13.7)	18 (9.1)	0.092
STEMI, n (%)	51 (8.5)	20 (10.1)	0.493
Laboratory measurements (fasting state)			
BUN (mmol/L)	5.4 (4.5–6.3)	5.6 (4.5–6.7)	0.179
SCr (μmol/L)	68.5 (60.9–78.5)	70.7 (63.1–83.5)	0.010
UA (μmol/L)	333.2 ± 77.2	344.4 ± 78.9	0.079
TC (mmol/L)	4.10 ± 1.03	4.24 ± 0.98	0.093
LDL-C (mmol/L)	2.41 ± 0.83	2.47 ± 0.74	0.382
HDL-C (mmol/L)	1.04 ± 0.22	0.96 ± 0.20	< 0.001
Triglycerides (mmol/L)	1.46 (1.04-2.00)	1.67 (1.12–2.31)	0.003
FPG (mmol/L)	6.88 (6.12–8.01)	7.89 (6.70–9.23)	< 0.001
Glycated haemoglobin (%)	7.2 (6.6–8.1)	7.4 (6.8–8.3)	0.079
AIP	0.1608 ± 0.2653	0.2535 ± 0.2919	< 0.001
AIP			0.001
Q1, n (%)	166 (27.7)	33 (16.7)	-
Q2, n (%)	155 (25.8)	45 (22.7)	-
Q3, n (%)	146 (24.3)	54 (27.3)	-
Q4, n (%)	133 (22.2)	66 (33.3)	-
Abbreviations as in Tables 1 and 2.			

Table 4
Use of medications, agiographic findings, and procedural results of the study patients stratified by the primary endpoint

Variable	No such events n = 600	Primary endpoint n = 198	*P* value
Medications before admission			
Aspirin, n (%)	442 (73.7)	152 (76.8)	0.386
P2Y12 inhibitors, n (%)	234 (39.0)	82 (41.4)	0.547
Statins, n (%)	438 (73.0)	152 (76.8)	0.295
ACEIs/ARBs, n (%)	183 (30.5)	78 (39.4)	0.021
β-blockers, n (%)	233 (38.8)	72 (36.4)	0.535
Insulin, n (%)	212 (35.3)	78 (39.4)	0.303
Oral antidiabetic agents, n (%)	289 (48.2)	98 (49.5)	0.746
Intraoperative anticoagulants			
Unfractionated heparin, n (%)	486 (81.0)	162 (81.8)	0.798
LMWH, n (%)	29 (4.8)	10 (5.1)	0.902
Bivalirudin, n (%)	85 (14.2)	26 (13.1)	0.715
Perioperative medications			
Aspirin, n (%)	600 (100.0)	190 (96.0)	< 0.001
P2Y12 inhibitors, n (%)	600 (100.0)	198 (100.0)	-
GP □b/□a receptor antagonist, n (%)	105 (17.5)	44 (22.2)	0.139
Medications at discharge			
Aspirin, n (%)	600 (100.0)	190 (96.0)	< 0.001
Cilostazol, n (%)	2 (0.3)	8 (4.0)	< 0.001
Clopidogrel, n (%)	545 (90.8)	180 (90.9)	0.974
Ticagrelor, n (%)	55 (9.2)	18 (9.1)	0.974
Statins, n (%)	600 (100.0)	198 (100.0)	-
ACEIs/ARBs, n (%)	294 (49.0)	106 (53.5)	0.268
β-blockers, n (%)	442 (73.7)	134 (67.7)	0.103

Abbreviations as in Tables 1 and 2.

Variable	No such events n = 600	Primary endpoint n = 198	*P* value
Insulin, n (%)	190 (31.7)	80 (40.4)	0.024
Oral antidiabetic agents, n (%)	324 (54.0)	106 (53.5)	0.909
Angiographic findings			
One-vessel disease, n (%)	72 (12.0)	8 (4.0)	0.001
Two-vessel disease, n (%)	165 (27.5)	32 (16.2)	0.001
LM/three-vessel disease, n (%)	363 (60.5)	158 (79.8)	< 0.001
Proximal LAD stenosis, n (%)	295 (49.2)	106 (53.5)	0.286
Restenotic lesions, n (%)	62 (10.3)	49 (24.7)	< 0.001
Trifurcation or bifurcation lesions, n (%)	460 (76.7)	156 (78.8)	0.537
Chronic total occlusions, n (%)	141 (23.5)	42 (21.2)	0.507
Thrombus lesions, n (%)	38 (6.3)	7 (3.5)	0.139
Heavy calcification lesions, n (%)	197 (32.8)	68 (34.3)	0.696
Lesions > 20 mm long, n (%)	319 (53.2)	140 (70.7)	< 0.001
Procedural results			
Target vessel territory			
LM, n (%)	40 (6.7)	16 (8.1)	0.499
LAD, n (%)	302 (50.3)	98 (49.5)	0.838
LCX, n (%)	168 (28.6)	52 (27.7)	0.808
RCA, n (%)	243 (40.5)	82 (41.4)	0.820
DES use, n (%)	502 (83.7)	164 (82.8)	0.783
BRS use, n (%)	27 (4.5)	5 (2.5)	0.219
DCB use, n (%)	34 (5.7)	22 (11.1)	0.009
Complete revascularization, n (%)	384 (64.0)	84 (42.4)	< 0.001
Abbreviations as in Tables 1 and 2.			

Kaplan-Meier analyses revealed a significantly higher incidence of the primary endpoint (log-rank test, $P = 0.001$; Fig. 1a) and a marginally (but non-significantly) higher incidence of the key secondary endpoint (log-rank test, $P = 0.114$; Fig. 1b) in patients with higher AIP values. The difference of the incidence of the

primary endpoint was mainly driven by the increase in unplanned repeat revascularization (log-rank test, $P = 0.005$; Fig. 1f) across the AIP quartiles. However, the incidence of all-cause death (log-rank test, $P = 0.168$; Fig. 1c), CV death (log-rank test, $P = 0.459$), non-fatal ischemic stroke (log-rank test, $P = 0.167$; Fig. 1d), and non-fatal MI (log-rank test, $P = 0.636$; Fig. 1e) at follow-up were similar among the AIP quartiles.

Table 5 shows univariate and multivariate Cox proportional hazards regression analyses for the primary endpoint at follow up, which includes AIP quartiles, age, BMI, PP, LVEF, SCr, LDL-C, FPG, glycosylated haemoglobin, sex, current smoking, hypertension, previous MI, past PCI, PAD, cardiac failure, clinical presentation, coronary artery disease (CAD) severity, restenotic lesions, lesions > 20 mm long, use of drug-coated balloon, complete revascularization, and use of insulin at discharge. Taking Q1 as the reference, multivariate analysis showed that the AIP for Q2, Q3, and Q4 increased the HRs for the incidence of the primary endpoint (Q2: HR 1.164, 95% CI 0.728–1.860; Q3: HR 1.640, 95% CI 1.032–2.606; Q4: HR 2.153, 95% CI 1.355–3.421). Moreover, AIP used as a continuous variable was independently predictive of the primary endpoint (HR, 2.581; 95% CI, 1.499–4.444; $P = 0.001$). Table 6 shows univariate and multivariate Cox proportional hazards regression analyses for the key secondary endpoint at follow up, which includes AIP quartiles, age, BMI, PP, LVEF, blood urea nitrogen, SCr, LDL-C, FPG, glycosylated haemoglobin, current smoking, hypertension, past PCI, PAD, cardiac failure, clinical presentation, CAD severity, lesions > 20 mm long, complete revascularization, and use of ACEIs/ARBs at discharge. Taking Q1 as the reference, multivariate analysis revealed that the AIP for Q2, Q3, and Q4 increased the HRs for the incidence of the key secondary endpoint (Q2: HR 1.063, 95% CI 0.397–2.849; Q3: HR 1.762, 95% CI 0.690–4.497; Q4: HR 2.613, 95% CI 1.024–6.666). Moreover, AIP used as a continuous variable was independently predictive of the key secondary endpoint (HR, 3.412; 95% CI, 1.086–10.723; $P = 0.036$).

Table 5
Relationship between the incidence of the primary endpoint and the AIP expressed as a categorical variable

Variables	Univariate analysis HR (95% CI)	*P*-value	Multivariate analysis HR (95% CI)	*P*-value
AIP quartiles				
Q1	Reference		Reference	
Q2	1.376 (0.878–2.156)	0.164	1.164 (0.728–1.860)	0.525
Q3	1.710 (1.109–2.636)	0.015	1.640 (1.032–2.606)	0.036
Q4	2.265 (1.491–3.440)	< 0.001	2.153 (1.355–3.421)	0.001
Age	1.005 (0.991–1.019)	0.472	0.989 (0.972–1.007)	0.219
BMI	0.959 (0.916–1.005)	0.078	0.931 (0.884–0.982)	0.008
PP	1.021 (1.012–1.029)	< 0.001	1.019 (1.008–1.029)	< 0.001
LVEF	0.974 (0.959–0.990)	0.002	0.987 (0.965–1.009)	0.242
SCr	1.013 (1.006–1.021)	0.001	1.011 (1.003–1.020)	0.010
LDL-C	1.078 (0.916–1.269)	0.366	1.021 (0.842–1.239)	0.832
FPG	1.201 (1.132–1.274)	< 0.001	1.192 (1.108–1.281)	< 0.001
Glycosylated haemoglobin	1.067 (0.955–1.193)	0.252	0.861 (0.739–1.003)	0.055
Male sex	0.966 (0.706–1.320)	0.827	0.834 (0.549–1.266)	0.394
Current smoking	1.003 (0.755–1.332)	0.983	1.256 (0.874–1.805)	0.219
Hypertension	1.068 (0.789–1.447)	0.669	1.040 (0.732–1.478)	0.825
Previous MI	1.492 (1.095–2.033)	0.011	0.812 (0.549–1.202)	0.299
Past PCI	1.723 (1.285–2.310)	< 0.001	1.157 (0.687–1.949)	0.583
PAD	2.511 (1.836–3.435)	< 0.001	1.601 (1.096–2.338)	0.015
Cardiac failure	1.951 (1.308–2.909)	0.001	1.167 (0.661–2.062)	0.594
Clinical presentation				
UAP	Reference		Reference	
NSTEMI	0.677 (0.416–1.102)	0.117	0.531 (0.310–0.909)	0.021
STEMI	1.098 (0.690–1.747)	0.695	1.114 (0.649–1.913)	0.695

Abbreviations as in Tables 1 and 2.

Variables	Univariate analysis HR (95% CI)	*P*-value	Multivariate analysis HR (95% CI)	*P*-value
CAD severity				
One-vessel disease	Reference		Reference	
Two-vessel disease	1.756 (0.809–3.810)	0.154	1.324 (0.589–2.975)	0.497
LM/three-vessel disease	3.541 (1.740–7.205)	< 0.001	1.876 (0.882–3.990)	0.103
Restenotic lesions	2.290 (1.658–3.163)	< 0.001	1.724 (0.947–3.138)	0.075
Lesions > 20 mm long	1.984 (1.461–2.695)	< 0.001	1.574 (1.132–2.189)	0.007
DCB use	1.913 (1.228–2.980)	0.004	1.025 (0.589–1.784)	0.931
Complete revascularization	0.467 (0.352–0.619)	< 0.001	0.736 (0.538–1.008)	0.056
Insulin at discharge	1.396 (1.051–1.854)	0.021	1.135 (0.818–1.574)	0.448
Abbreviations as in Tables 1 and 2.				

Table 6
Relationship between the incidence of the key secondary endpoint and the AIP expressed as a categorical variable

Variables	Univariate analysis HR (95% CI)	*P*-value	Multivariate analysis HR (95% CI)	*P*-value
AIP quartiles				
Q1	Reference		Reference	
Q2	1.380 (0.555–3.432)	0.488	1.063 (0.397–2.849)	0.903
Q3	2.020 (0.865–4.720)	0.104	1.762 (0.690–4.497)	0.236
Q4	2.477 (1.085–5.659)	0.031	2.613 (1.024–6.666)	0.044
Age	1.042 (1.013–1.072)	0.004	1.017 (0.982–1.053)	0.343
BMI	0.915 (0.834–1.004)	0.062	0.844 (0.751–0.948)	0.004
PP	1.030 (1.014–1.046)	< 0.001	1.012 (0.991–1.034)	0.265
LVEF	0.924 (0.902–0.946)	< 0.001	0.945 (0.906–0.984)	0.007
BUN	1.166 (1.018–1.335)	0.026	0.868 (0.724–1.041)	0.127
SCr	1.025 (1.014–1.036)	< 0.001	1.016 (1.001–1.030)	0.031
LDL-C	1.064 (0.774–1.463)	0.702	1.081 (0.714–1.636)	0.713
FPG	1.097 (0.967–1.243)	0.150	1.017 (0.880–1.176)	0.818
Glycated haemoglobin	1.090 (0.882–1.347)	0.425	1.220 (0.932–1.597)	0.148
Current smoking	1.014 (0.589–1.746)	0.959	1.534 (0.824–2.855)	0.177
Hypertension	1.333 (0.725–2.450)	0.354	1.266 (0.608–2.636)	0.528
Past PCI	1.904 (1.096–3.309)	0.022	2.247 (1.170–4.313)	0.015
PAD	5.804 (3.402–9.902)	< 0.001	2.888 (1.545–5.399)	0.001
Cardiac failure	6.939 (3.993–12.061)	< 0.001	1.888 (0.767–4.648)	0.167
Clinical presentation				
UAP	Reference		Reference	
NSTEMI	1.333 (0.622–2.857)	0.460	0.501 (0.199–1.258)	0.141
STEMI	1.920 (0.896–4.115)	0.094	1.056 (0.427–2.610)	0.906
CAD severity				

Abbreviations as in Tables 1 and 2.

Variables	Univariate analysis HR (95% CI)	*P*-value	Multivariate analysis HR (95% CI)	*P*-value
One-vessel disease	Reference		Reference	
Two-vessel disease	0.201 (0.037–1.096)	0.064	0.059 (0.009–0.402)	0.004
LM/three-vessel disease	1.910 (0.689–5.296)	0.214	0.418 (0.121–1.444)	0.168
Lesions > 20 mm long	2.681 (1.411–5.029)	0.003	1.828 (0.882–3.789)	0.105
Complete revascularization	0.403 (0.232-0.700)	0.001	0.684 (0.348–1.343)	0.270
ACEIs/ARBs at discharge	2.933 (1.596–5.391)	0.001	1.782 (0.883–3.599)	0.107
Abbreviations as in Tables 1 and 2.				

Further evaluation of predictive value of AIP as a continuous variable for the primary endpoint was performed in different subgroups of the study population. Increased AIP value (per 1-unit) was consistently associated with the primary endpoint in different subgroups, including age < 60 versus ≥ 60 years, BMI < 28 versus ≥ 28 kg/m^2, LDL-C ≤ 1.8 versus > 1.8 mmol/L, female versus male, with versus without hypertension, and non-ST versus ST segment elevation ACS (Fig. 2).

From the results of the multivariate Cox proportional hazards regression analyses, we calculated the Harrell's C statistic for the predictive value of the primary endpoint. The Harrell's C statistic of the variables, including BMI, PP, SCr, FPG, PAD, clinical presentation, and lesions > 20 mm long, was 0.697 versus 0.707 after the addition of AIP quartiles; the continuous NRI was 19.1% (7.9–35.6%; $P < 0.001$).

Discussion

The main findings of the present study were as follows: (1) patients with higher AIP values had a significantly higher probability of adverse CV events by the log-rank test; (2) multivariate Cox proportional hazards analyses showed that AIP was independently and strongly associated with the primary and key secondary endpoints in T2DM and ACS patients who underwent PCI, suggesting that AIP might have a potential role in early risk stratification of such patients; (3) a significant continuous NRI showed that predictive model was improved after adding AIP to the model of other independent predictors. To the best of our knowledge, this is the first report to describe the prognostic impact of AIP in T2DM patients with ACS undergoing PCI.

Dyslipidemia plays a crucial role in the pathogenesis and progression of coronary atherosclerosis. Diabetic patients are more likely to develop coronary atherosclerosis than non-diabetic patients, which may be significantly associated with so-called diabetic dyslipidemia, which consists of elevated plasma concentrations of triglyceride-rich lipoproteins, small dense LDL-C particles and low levels of HDL-C. The different components of diabetic dyslipidemia are not isolated abnormalities but closely linked to each other metabolically [9]. Triglycerides and HDL-C are two lipid parameters measured routinely in clinical

practice; however, neither is a consistently good proxy for plasma atherogenicity. AIP, a novel lipid index defined as $\log_{10}$ (triglycerides/HDL-C), has been demonstrated to be closely correlated with FER(HDL) and lipoprotein particle size both of which are directly involved in the pathogenesis and development of atherosclerosis, and thus AIP is regarded as an excellent indicator of atherosclerosis and can offer a benefit to identify the risk of CV disease [31].

Multiple cross-sectional studies reported that AIP was a strong predictor of CAD independent of diabetes [23, 24, 26]. Notably, the Indian Atherosclerosis Research Study revealed that addition of AIP and family history to traditional risk factors improved risk discrimination (C-index: from 0.864 to 0.873) in Asian Indians with CAD [19]. Intriguingly, Frohlich J, et al. found that AIP was an independent predictor of angiographically defined CAD only when FER(HDL) was omitted from multivariate analysis, which may be due to a clear internal correlation between AIP and FER(HDL) [17]. Moreover, Nam JS, et al. found that there is a significant correlation between AIP and the progression of coronary artery calcification measured by using a multi-detector computed tomography in subjects without cardiovascular disease [28]. Furthermore, in a prospective cohort study including 2676 middle-aged adults followed for 7.8 years, researchers demonstrated that the top quartiles of AIP predicted significantly age-adjusted incident CAD in both sexes, more strongly in women, after adjustment for C-reactive protein and traditional risk factors [18].

AIP has been demonstrated to be associated with mortality in elder patients and dialysis patients. Edwards MK, et al. analyzed data from the 1999–2006 National Health and Nutrition Examination Survey with follow-up through 2011 to find that AIP was positively and independently associated with mortality risk and predicted mortality risk better than individual cholesterol risk factors, among an older adult population [20]. Bendzala M, et al. also found that AIP was positively associated with the risk of all-cause death in elderly women with hypertension [21]. However, a Korean nationwide prospective cohort study including 1174 incident dialysis patients showed that AIP had a non-linear relationship with survival; both the highest and the lowest AIP quintiles were independently associated with all-cause mortality, showing a U-shaped association [22].

The predictive value of AIP has also been explored in ACS patients. Cai G, et al. retrospectively enrolled 1478 very young participants (≤ 35 years of age) undergoing coronary angiography and divided them into two groups: ACS group (n = 1058) and non-CAD group (n = 419). They found that AIP was independently associated with the presence and severity of ACS in a gender-dependent manner and the prevalence of ACS, acute MI, unstable angina pectoris and the value of Gensini Score (a scoring system for evaluating CAD severity) were elevated as AIP quartiles increased [25]. Qin Z, et al. retrospectively enrolled 2356 T2DM patients who underwent PCI and followed them for 4 years. They found that AIP was an independent predictor of major cardiovascular and cerebrovascular adverse events including cardiac death, MI, repeated revascularization, and stroke, regardless of clinical presentation [27].

AIP was reported to be positively correlated with serum malondialdehyde in menopausal women with CV disease [32]. And we know malondialdehyde can reflect the status of oxidative stress which is

significantly associated with coronary atherosclerosis [33]. AIP was found to be associated with epicardial adipose tissue measured by using a transthoracic echocardiography or an electrocardiogram-gated multidetector computed tomography [34, 35]. Evidence indicates that epicardial adipose tissue directly affects coronary atherosclerosis [36]. AIP was shown to be directly and independently associated with arterial stiffness in normotensive and never-treated hypertensive subjects [37]. Increased aortic stiffness often results in early wave reflection of the aortic pulse wave which increases systolic blood pressure but decreases diastolic blood pressure, and these hemodynamic changes impair coronary perfusion, which can promote adverse CV events [30]. AIP was demonstrated to be a marker for reduced coronary flow reserve [38], and the latter was positively associated with adverse CV events. Of note, AIP includes triglycerides and HDL-C in its formula. High triglycerides and low HDL-C levels were shown to be associated with adverse CV events after ACS, independent of diabetic status [39, 40].

Glucose-lowering regiments including pioglitazone have been shown to be effective in reducing AIP values, thereby reducing CV risk [41, 42]. Moreover, moderate-to-vigorous physical activity, increasing aerobic exercise time, decreased sedentary behavior, and consequent high levels of cardiorespiratory fitness were reported to be inversely correlated with AIP, which implies that a healthy lifestyle helps attenuate the risk for CV disease via improvements in AIP [43–47]. As a result, use of pioglitazone and early initiation of physical activity and aerobic exercise may be important to reduce future CV risk in T2DM patients with ACS undergoing PCI who have received first-line medication therapy but still have significantly increased values of AIP.

Our study also had several important limitations. First, this was a retrospective analysis of a single centre prospective registry, which could not definitively establish causality. Second, the baseline concentrations of triglycerides and HDL-C might be affected by the use of statins before admission and glycemic control status. However, there were no significant differences among the four groups on the basis of the AIP quartiles with respect to the use of statins before admission and glycated haemoglobin which can consistently reflect glycemic control status in diabetic patients. Third, follow-up data were obtained merely via telephone; however, we confirm the authenticity of adverse events by reviewing corresponding medical records. Finally, whether the findings from the present study including only Chinese patients can be extrapolated to other ethnic groups will require further studies.

Conclusions

A higher AIP value on admission was independently and strongly associated with adverse CV events in T2DM patients with ACS undergoing PCI, suggesting that AIP might have a potential role in early risk stratification of such patients. Medical management optimization according to AIP could result in a reduced risk of subsequent CV events.

Abbreviations

ACEIs/ARBs: angiotensin converting enzyme inhibitors/angiotensin II receptor blockers; ACS:acute coronary syndrome; AIP:atherogenic index of plasma; BMI:body mass index; CABG:coronary artery bypass grafting; CAD:coronary artery disease; CI:confidence interval; CV:cardiovascular; FER(HDL):cholesterol esterification rates in apoB-lipoprotein-depleted plasma; FPG:fasting plasma glucose; HDL-C:high-density lipoprotein cholesterol; HR:hazard ratio; LDL-C:low-density lipoprotein cholesterol; LVEF:left ventricular ejection fraction; MI:myocardial infarction; NRI:net reclassification improvement; PAD:peripheral artery disease; PCI:percutaneous coronary intervention; PP:pulse pressure; SCr:serum creatinine; T2DM:type 2 diabetes mellitus; TC:total cholesterol.

Declarations

Conflict of interest

The authors declare that they have no conflict of interest.

Availability of data and materials

The data, analytic methods, and study materials will not be made available to other researchers for purposes of reproducing the results or replicating the procedure.

Ethics approval and consent to participate

This study was approved by the institutional review board of Beijing Anzhen Hospital, Capital Medical University. Given the retrospective nature of this study, the requirement for informed consent was waived.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Authors’ contributions

Xiaoteng Ma, Yan Sun, and Yujing Cheng contributed equally to this paper. All authors were involved in the conception and design of the study and in the collection, analysis, and interpretation of the data. All authors reviewed the final manuscript. All authors read and approved the final manuscript.

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Figures

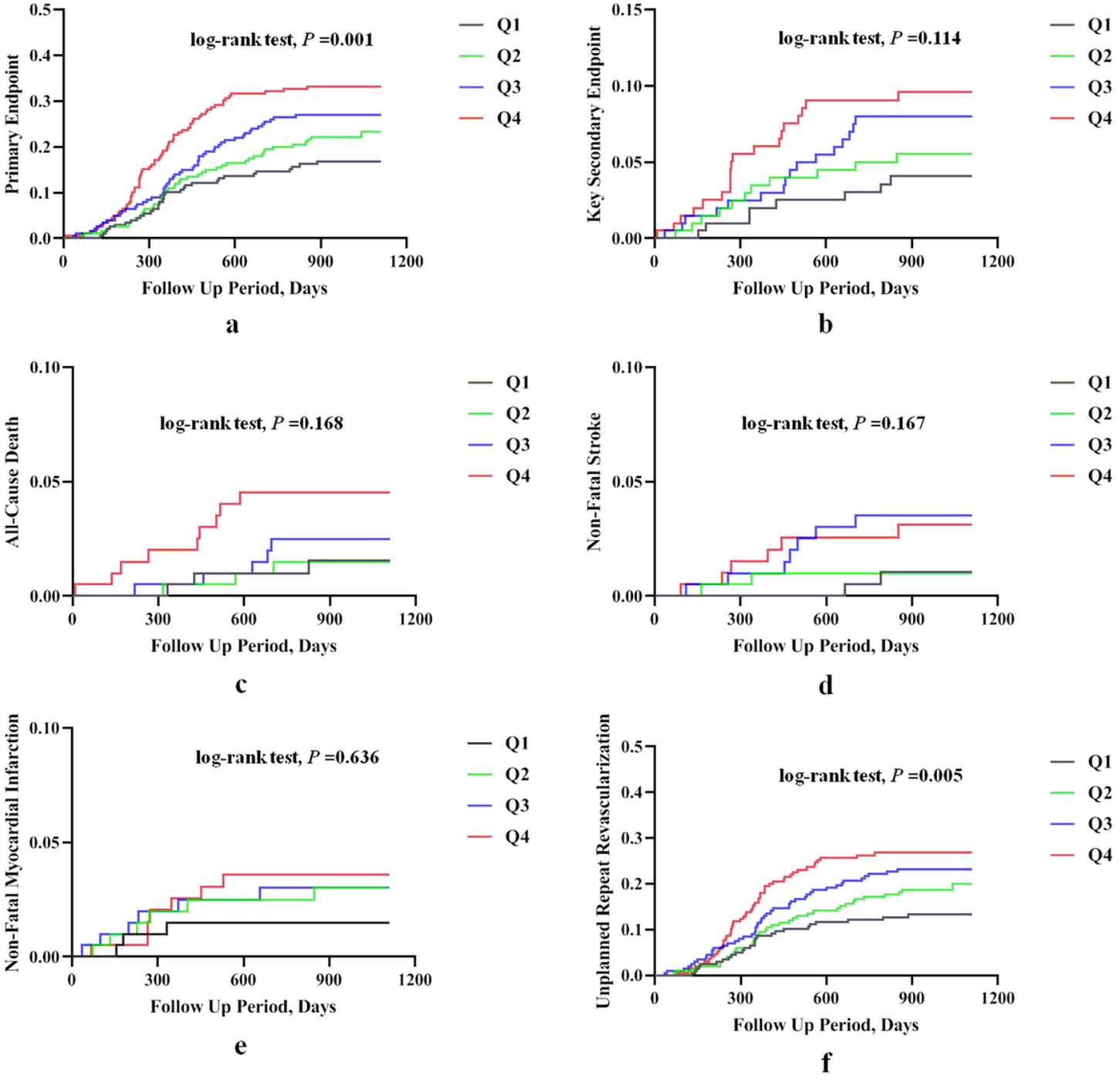

Figure 1

Kaplan-Meier curves of the incidences of the primary and key secondary endpoints and each component event of the primary endpoint for the AIP quartiles. The primary endpoint was defined as a composite of all-cause death, non-fatal ischemic stroke, non-fatal myocardial infarction, and unplanned repeat revascularization. The key secondary endpoint was a composite of CV death, non-fatal ischemic stroke, or non-fatal myocardial infarction.

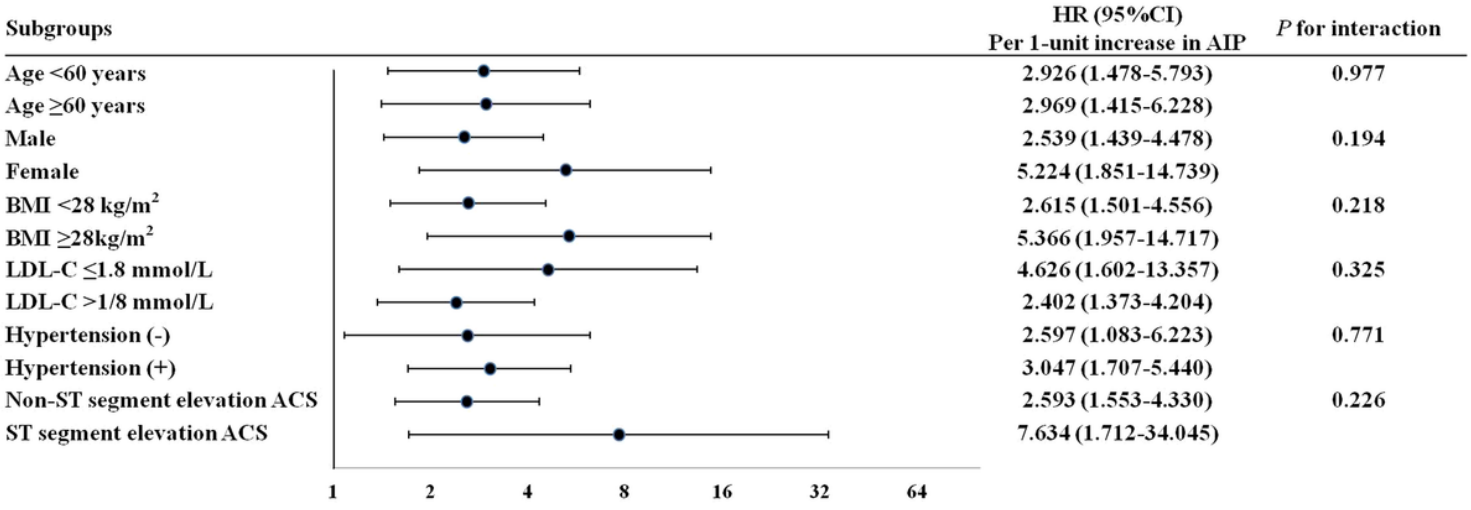

Figure 2

Cox proportional hazards analyses for the primary endpoint at follow up in different subgroups. HR was evaluated by per 1-unit increase in AIP. BMI indicates body mass index; LDL-C, low-density lipoprotein cholesterol; ACS acute coronary syndrome; HR, hazard ratio; 95% CI, 95% confidence interval.