Research Square

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Admission Atherogenic Index of Plasma Predicts 3-Year Major Adverse Cardiovascular Events After Percutaneous Coronary Intervention for Acute Myocardial Infarction: A Retrospective Cohort Study

Xiaolong Kang
Ningxia Medical University
Xiaolan Liang
Ningxia Medical University
Wenhao Cui
Ningxia Medical University
Yichen Song
Ningxia Medical University
Xin Wang
Ningxia Medical University
Xinrui Hai
Ningxia Medical University
Peng Wu
Ningxia Medical University
Yu Hao
Ningxia Medical University General Hospital
Xueping Ma
Ningxia Medical University General Hospital
Ning Yan
yanning169@yahoo.com
Ningxia Medical University General Hospital

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Abstract

Background: The atherogenic index of plasma (AIP), calculated as $\log_{10}$(triglycerides/high-density lipoprotein cholesterol), reflects atherogenic dyslipidemia and insulin resistance. This study evaluated the association between admission AIP and 3-year major adverse cardiovascular events (MACE), as well as its incremental prognostic value beyond established clinical predictors and the GRACE score, in patients with acute myocardial infarction (AMI) undergoing percutaneous coronary intervention (PCI).

Methods: In this single-center retrospective cohort study, consecutive patients with AMI undergoing successful PCI between January 1, 2014 and December 31, 2019 were classified by admission AIP tertiles. The primary outcome was 3-year MACE, defined as a composite of cardiovascular death, non-fatal reinfarction, ischemia-driven revascularization, and heart failure hospitalization. Cox proportional hazards models, restricted cubic splines, mediation analysis, ROC/time-dependent ROC, net reclassification improvement (NRI), integrated discrimination improvement (IDI), and decision curve analysis were used.

Results: Among 3,781 patients, 556 (14.71%) developed MACE during a median follow-up of 36 months. MACE incidence increased across AIP tertiles (log-rank P < 0.001). In the fully adjusted model, the highest AIP tertile was associated with a higher MACE risk than the lowest tertile (adjusted HR 1.53, 95% CI 1.13–2.09), and each 1-unit increase in AIP was associated with higher MACE risk (adjusted HR 1.86, 95% CI 1.29–2.69). Adding AIP to traditional risk factors and the GRACE score significantly improved reclassification (continuous NRI 0.1799, P < 0.001) and discrimination (IDI 0.0039, P = 0.001). HbA1c and neutrophil count mediated 8.16% and 5.18% of the association, respectively.

Conclusions: Admission AIP was independently associated with 3-year MACE in patients with AMI undergoing PCI and provided modest but significant incremental prognostic information beyond traditional risk factors and the GRACE score.

Introduction

Acute myocardial infarction (AMI), including ST-segment elevation myocardial infarction (STEMI) and non-ST-segment elevation myocardial infarction (NSTEMI), remains a major cause of morbidity and mortality worldwide [1–4]. Although early revascularization and contemporary evidence-based therapies have substantially improved short-term survival, a considerable burden of recurrent ischemic events, heart failure hospitalization, and cardiovascular death persists after PCI [1–7]. This residual risk underscores the need for practical biomarkers that can complement traditional clinical assessment and help identify patients with an adverse cardiometabolic profile who may otherwise be insufficiently recognized by routine parameters alone. Among the mechanisms implicated in post-AMI residual risk, atherogenic dyslipidemia has attracted increasing attention because it reflects not only quantitative lipid abnormalities but also qualitative lipoprotein disturbances associated with plaque progression, thrombogenicity, and impaired vascular healing. In clinical practice, LDL-C remains central to lipid-lowering strategies. However, even when strict guideline-recommended LDL-C targets are achieved (e.g., <1.4 mmol/L for very-high-risk patients), a substantial residual cardiovascular risk persists. LDL-C alone does not fully capture triglyceride-rich lipoproteins, remnant burden, or the prevalence of small dense LDL particles, all of which may contribute to this persistent risk despite standard therapy [5–8].

Atherogenic dyslipidemia is typically characterized by elevated triglycerides, low HDL-C, and an increased burden of small dense LDL particles—a combination closely linked to insulin resistance, endothelial dysfunction, and accelerated atherosclerosis [5, 6, 8]. Small dense LDL is particularly relevant because it more readily penetrates the arterial wall, is

more susceptible to oxidation and glycation, and may better reflect a pro-atherogenic milieu than conventional LDL-C concentration alone [8]. However, direct measurement of lipoprotein subfractions or particle size is not routinely available in many centers. Therefore, there is sustained interest in pragmatic composite markers derived from standard lipid testing that can be obtained rapidly at admission and incorporated into real-world risk assessment without additional cost.

The atherogenic index of plasma (AIP), defined as $\log_{10}$(TG/HDL-C), has emerged as one such marker [9–11]. Experimental and epidemiological studies suggest that AIP correlates with lipoprotein particle size, reflects atherogenic dyslipidemia, and is closely related to insulin resistance, chronic low-grade inflammation, and broader cardiometabolic dysfunction [12–16]. Because triglycerides and HDL-C are routinely measured in AMI care, AIP is appealing as an immediately available biomarker with potential utility for bedside risk stratification. Recent studies have linked higher AIP to the presence and severity of coronary artery disease, incident major adverse cardiovascular events, and worse outcomes in selected ACS and PCI populations [13–26]. Importantly, newer ACS-specific studies have shown that elevated AIP is associated with more advanced coronary disease at first presentation, stent thrombosis, BMI-dependent risk heterogeneity, higher post-PCI event rates, and poorer prognosis even in patients without standard modifiable risk factors [18–25]. Meta-analytic evidence has further strengthened the association of AIP with both coronary artery disease burden and ACS outcomes [17, 21].

Nevertheless, several clinically important gaps remain. Data specifically focusing on patients with AMI undergoing contemporary PCI are still limited; the incremental value of AIP beyond established risk tools such as the GRACE score has not been sufficiently examined in large hospital-based cohorts; and the metabolic-inflammatory pathways linking AIP to long-term outcomes remain incompletely understood [13, 17–22, 24–27]. Therefore, the present study aimed to (1) evaluate the association between admission AIP and 3-year MACE in patients with AMI undergoing PCI, (2) assess whether AIP provides incremental prognostic information beyond traditional cardiovascular risk factors and the GRACE score, and (3) explore whether metabolic and inflammatory markers mediate this association.

Methods

Study Design and Population

This retrospective observational cohort study was conducted at the General Hospital of Ningxia Medical University. Consecutive patients with STEMI or NSTEMI who underwent successful PCI between January 1, 2014 and December 31, 2019 were screened for inclusion. AMI was diagnosed according to the Fourth Universal Definition of Myocardial Infarction [4].

Eligible patients were required to be aged >18 years, have a confirmed diagnosis of AMI, and have undergone successful primary or early routine PCI. Successful PCI was defined as residual stenosis <20% with restoration of Thrombolysis in Myocardial Infarction (TIMI) grade 3 flow.

Patients were excluded if they were managed conservatively without PCI or had failed PCI, died during hospitalization, had severe non-cardiovascular comorbidities (including advanced liver failure, end-stage renal failure, or active malignancy), had systemic infectious or autoimmune diseases, or lacked essential baseline lipid data, particularly fasting TG and HDL-C. After application of these criteria, 3,781 patients were included in the final analysis.

Data Collection and AIP Calculation

Demographic characteristics, clinical variables, laboratory findings, procedural data, and discharge medications were extracted from the hospital electronic medical record system. Recorded variables included age, sex, body mass index

(BMI), blood pressure, heart rate, Killip class at presentation, medical history, and cardiovascular medication use. Definitions and coding of variables used in the supplementary analyses are provided in Supplementary Table S1.

Fasting venous blood samples obtained within 24 hours of admission were analyzed using standard laboratory methods. Lipid parameters included total cholesterol, LDL-C, HDL-C, and TG. Additional biomarkers included HbA1c, high-sensitivity C-reactive protein (hs-CRP), N-terminal pro-B-type natriuretic peptide (NT-proBNP), serum creatinine, and neutrophil count. AIP was calculated as $\log_{10}$(TG/HDL-C), with both TG and HDL-C expressed in mmol/L. Patients were categorized into tertiles according to baseline AIP values: tertile 1 (T1, lowest AIP), tertile 2 (T2, intermediate AIP), and tertile 3 (T3, highest AIP). The observed tertile cutoffs in the study dataset are presented in Supplementary Table S5.

Study Endpoint and Follow-up

The primary endpoint was 3-year MACE, defined as a composite of cardiovascular death, non-fatal reinfarction, ischemia-driven target lesion or target vessel revascularization, and unplanned hospitalization for heart failure. Follow-up was performed by trained research coordinators who were blinded to baseline AIP status. Outcome information was obtained from scheduled outpatient visits, electronic readmission records, and standardized telephone interviews with patients or their relatives. Follow-up assessments were conducted at 1, 6, 12, 24, and 36 months after discharge.

Statistical Analysis

Baseline characteristics were summarized according to AIP tertiles. Continuous variables were expressed as mean ± standard deviation and categorical variables as number (percentage). Kaplan-Meier curves were used to compare event-free survival across AIP tertiles. The association between AIP and 3-year MACE was assessed using Cox proportional hazards regression. Three incrementally adjusted multivariable models were constructed: Model I adjusted for age, sex, BMI, Killip class, heart rate, shock index, intra-aortic balloon pump use, and diabetes mellitus; Model II additionally adjusted for left ventricular ejection fraction, use of direct oral anticoagulants, use of ACEI/ARB, and D-dimer; and Model III further adjusted for previous cardiovascular disease, hypertension, previous coronary artery disease, previous myocardial infarction, atrial fibrillation, chronic heart failure, chronic kidney disease, active smoking, C-reactive protein, NT-proBNP, lactate dehydrogenase, serum creatinine, and beta-blocker use. Restricted cubic spline analysis was used to examine the dose-response relationship between AIP and MACE. Prespecified subgroup analyses were also performed. To evaluate incremental predictive value, four hierarchical models were constructed: Model 1, traditional risk factors (age, sex, hypertension, diabetes mellitus, current smoking, and LDL-C); Model 2, GRACE score alone; Model 3, Model 1 plus GRACE score; and Model 4, Model 3 plus AIP. The GRACE score was selected because of its established prognostic role across the ACS spectrum [27]. Although originally developed to predict in-hospital and 6-month outcomes, subsequent iterations and extensive external validations have confirmed the sustained prognostic validity of the GRACE risk model over extended follow-up periods. Specifically, large-scale studies have demonstrated that the GRACE score maintains robust discriminative accuracy for predicting mortality and MACE at 1-year and 3-year horizons in patients undergoing PCI [28, 29]; therefore, it serves as an appropriate clinical reference model for our 3-year endpoint. The prespecified primary incremental comparison was Model 4 versus Model 3. Model discrimination was assessed by ROC analysis and time-dependent ROC analysis. Continuous NRI and IDI were calculated to quantify reclassification and discrimination improvement, and decision curve analysis (DCA) was used to assess clinical utility. Mediation analyses were performed to explore whether HbA1c and neutrophil count mediated the association between AIP and MACE. Variable completeness in the core dataset is summarized in Supplementary Table S2, and the full coefficient set for the fully adjusted Cox model is provided in Supplementary Table S4. All analyses were performed using Empower Stats version 4.2 (www.empowerstats.com, X&Y Solutions, Inc., Boston, MA) and R version 3.6.1. A two-sided $P < 0.05$ was considered statistically significant.

Results

Baseline Characteristics

The final study cohort consisted of 3,781 patients with AMI undergoing PCI, including 1,260 patients in tertile 1, 1,260 in tertile 2, and 1,261 in tertile 3 (Table 1). Patients in the highest AIP tertile were younger and more frequently male than those in the lowest tertile. They also had higher BMI, higher systolic and diastolic blood pressure, and a more adverse cardiometabolic profile, including a higher prevalence of diabetes mellitus, hypertension, hyperlipidemia, current smoking, and current alcohol use. Detailed baseline characteristics stratified by 3-year MACE status are presented in Supplementary Table S3. As expected, substantial gradients were observed in lipid parameters: triglyceride levels increased progressively from 0.77 ± 0.25 mmol/L in T1 to 2.99 ± 1.61 mmol/L in T3, whereas HDL-C levels decreased from 1.06 ± 0.23 mmol/L to 0.79 ± 0.17 mmol/L. HbA1c values also increased across tertiles, ranging from 6.22 ± 1.41% in T1 to 6.75 ± 1.67% in T3. Serum creatinine was slightly but significantly higher in the highest tertile.

Clinical Outcomes and Association Between AIP and MACE

During a median follow-up of 36 months, 556 patients experienced MACE, corresponding to an overall incidence of 14.71%. Kaplan-Meier analysis demonstrated a graded increase in cumulative event rates across AIP tertiles (log-rank $P < 0.001$). In Cox regression analysis, AIP as a continuous variable was not significantly associated with MACE in the unadjusted model but became significantly associated after multivariable adjustment. In the fully adjusted model (Model III), each 1-unit increase in AIP was independently associated with a higher risk of 3-year MACE (adjusted HR 1.86; 95% CI 1.29–2.69; $P = 0.001$) (Table 2). The full coefficient set for Model III is presented in Supplementary Table S4. When AIP was analyzed categorically, patients in tertile 2 had an intermediate risk (adjusted HR 1.37; 95% CI 1.05–1.77; $P = 0.019$), whereas those in tertile 3 had a significantly higher risk than those in tertile 1 (adjusted HR 1.53; 95% CI 1.13–2.09; $P = 0.003$). A significant linear trend was observed across tertiles in the fully adjusted model (P for trend = 0.002). Observed tertile cutoffs and crude 3-year MACE incidence across tertiles are shown in Supplementary Table S5.

Dose-Response Relationship

Restricted cubic spline analysis demonstrated a positive association between baseline AIP and the log hazard of 3-year MACE. The overall association was statistically significant, and no significant evidence of nonlinearity was observed, supporting an approximately linear dose-response relationship.

Subgroup Analyses

The association between higher AIP and increased MACE risk was generally consistent across most clinically relevant subgroups. A significant interaction was observed for age (P for interaction = 0.047). Among patients aged ≤60 years, elevated AIP was associated with a markedly higher risk of MACE (HR 2.06; 95% CI 1.38–3.09; $P < 0.001$), whereas the association was not statistically significant among patients aged >60 years (HR 1.20; 95% CI 0.85–1.70; $P = 0.307$).

Mediation Analysis

Mediation analysis indicated that the association between AIP and 3-year MACE was partially mediated by both metabolic and inflammatory pathways. HbA1c mediated 8.16% of the total effect ($P < 0.001$), while neutrophil count mediated 5.18% ($P = 0.027$). These findings support a potential mechanistic contribution of chronic hyperglycemic stress and systemic inflammation to the adverse cardiovascular risk associated with elevated AIP.

Incremental Predictive Value and Clinical Utility

Four hierarchical models were constructed to assess the incremental prognostic value of AIP (Table 3). Model 1, which included traditional risk factors, yielded an AUC of 0.647 (95% CI 0.621–0.671). Model 2, consisting of the GRACE score alone, yielded an AUC of 0.634 (95% CI 0.609–0.662). Model 3, combining traditional risk factors with the GRACE score, improved discrimination to an AUC of 0.665 (95% CI 0.641–0.691). Model 4, which additionally incorporated AIP, demonstrated the highest discrimination, with an AUC of 0.672 (95% CI 0.648–0.698). Time-dependent ROC analysis further showed that Model 4 maintained consistently higher predictive accuracy than the other three models over the 3-year follow-up period. In the prespecified primary comparison, Model 4 significantly improved performance compared with Model 3—which already included both traditional risk factors and the GRACE score—with a continuous NRI of 0.1799 (95% CI 0.0913–0.2684; P < 0.001) and an IDI of 0.0039 (95% CI 0.0017–0.0063; P = 0.001). Compared with Model 1, Model 4 also improved reclassification (continuous NRI 0.2435; 95% CI 0.1539–0.3341; P < 0.001) and discrimination (IDI 0.0292; 95% CI 0.0219–0.0382; P < 0.001). Compared with Model 2, Model 4 yielded further improvement (continuous NRI 0.2625; 95% CI 0.1745–0.3486; P < 0.001; IDI 0.0114; 95% CI 0.0071–0.0155; P < 0.001). Decision curve analysis showed that Model 4 provided a consistently higher net benefit than Models 1, 2, and 3 across a broad range of clinically relevant threshold probabilities, indicating superior clinical utility.

Discussion

In this retrospective cohort study of 3,781 patients with AMI undergoing PCI, elevated admission AIP was independently associated with a higher risk of 3-year MACE. This association remained significant after extensive multivariable adjustment and followed an approximately linear dose-response pattern. In addition, AIP provided incremental prognostic information beyond traditional cardiovascular risk factors and the GRACE score. The prognostic effect of AIP was particularly evident in younger patients, and mediation analysis suggested that the association was partly explained by metabolic and inflammatory pathways. Overall, these findings indicate that AIP is not merely a lipid-derived index but a clinically relevant marker of residual cardiometabolic risk in patients with AMI after PCI.

Our results extend a growing body of literature suggesting that AIP captures clinically important information beyond conventional lipid measures alone. Previous studies have demonstrated associations between elevated AIP and the presence and severity of coronary artery disease, incident major cardiovascular events in general populations, and adverse outcomes in selected coronary cohorts [13–17, 21, 24, 26]. In patients with first-diagnosed ACS, higher AIP has been associated with greater angiographic complexity and worse 12-month outcomes [24]. Among ACS patients, elevated AIP has also been linked to stent thrombosis [23], differential prognostic value across BMI categories [22], enhanced prediction when combined with glycated albumin in postmenopausal women undergoing PCI [19], and poorer outcomes after STEMI-PCI or in SMuRF-less ACS cohorts [18, 25]. Together with the recent ACS and CAD meta-analyses [17, 21], these findings support the view that AIP captures clinically relevant residual risk across diverse presentations of coronary artery disease.

A notable strength of the present study is the hierarchical evaluation of incremental predictive value. Although the increase in AUC from Model 3 to Model 4 was modest, the addition of AIP significantly improved both continuous NRI and IDI, indicating better patient-level risk reclassification beyond established clinical predictors and the GRACE score. This distinction is clinically important because a biomarker may meaningfully improve individual risk assignment even when the change in the global C-statistic appears numerically small. Thus, AIP should not be interpreted as a replacement for established clinical risk scores, but rather as a pragmatic adjunct that may refine long-term prognostic assessment when added to accepted tools such as the GRACE score [27]. The DCA findings further

support the potential clinical utility of incorporating AIP into post-AMI risk evaluation. The subgroup analysis is also clinically informative: we observed a stronger association between AIP and MACE in patients aged ≤60 years, suggesting that AIP may be particularly informative in comparatively younger patients whose absolute risk may otherwise appear lower because of age weighting within standard models. This pattern differs from some community-based analyses and from at least one ACS meta-analysis in which stronger associations were reported in older populations [14, 21], but is not incompatible with previous reports of effect modification by metabolic phenotype, such as BMI strata [22]. Collectively, these observations suggest that the prognostic expression of AIP may be influenced by age structure, body composition, and background metabolic status rather than reflecting a single universal effect size.

The mediation analysis provides biologically plausible support for the observed association. HbA1c mediated 8.16% of the relationship between AIP and MACE, reinforcing the close connection between triglyceride-rich dyslipidemia, insulin resistance, and chronic dysglycemia [13, 26, 28, 29]. Neutrophil count mediated 5.18%, suggesting a contribution from systemic inflammatory activation. Prior cohort data demonstrating joint effects of AIP and hs-CRP [13], together with randomized evidence that targeting inflammation reduces recurrent cardiovascular events [30], make it plausible that elevated AIP reflects a broader metabolic-inflammatory milieu rather than an isolated lipid abnormality. In this context, AIP may be viewed as a clinically accessible surrogate for several converging pathways that promote recurrent events after AMI.

From a clinical perspective, AIP is an attractive biomarker because it is inexpensive, easily calculated, and derived from routine lipid testing. Its integration into post-AMI risk evaluation may help identify patients with a metabolically unfavorable profile who warrant closer follow-up and more intensive risk factor management. This interpretation is further supported by reports linking higher AIP to additional clinically relevant vulnerabilities, including contrast-associated kidney injury after NSTEMI-PCI [31] and future diabetes risk [32, 33]. However, our results should not be interpreted as evidence that AIP is a standalone predictor sufficient to replace established risk scores. Rather, AIP appears to function as a complementary biomarker that modestly but significantly improves long-term risk stratification when combined with conventional predictors and the GRACE score.

At the same time, the present findings should not be overinterpreted as evidence that modifying AIP itself will necessarily improve outcomes. More reasonably, AIP may serve as a convenient clinical marker of a residual-risk phenotype that could be addressed through comprehensive secondary prevention, including aggressive lipid lowering, weight management, optimization of glycemic control, and treatment of associated cardiometabolic disease when indicated. Emerging cardiovascular outcome data for modern metabolic therapies further emphasize the importance of addressing residual risk beyond LDL-C alone [34–37]. Future multicenter prospective studies are warranted to determine whether incorporating AIP into structured post-AMI risk algorithms can improve treatment allocation and patient outcomes.

Limitations

Several limitations should be acknowledged. First, this was a retrospective observational study, and causal inference cannot be established. Despite multivariable adjustment and mediation analyses, residual confounding from unmeasured factors—such as socioeconomic status, dietary patterns, frailty, residual ischemic burden, apolipoprotein measurements, and longitudinal treatment adherence—cannot be excluded. Furthermore, while the mediation analysis provides biologically plausible insights into the potential pathways linking AIP to MACE, it is constrained by inherent methodological limitations. Standard mediation analysis assumes a strict temporal sequence in which the exposure precedes the mediator and the mediator precedes the outcome. In the present study, the exposure (AIP) and the proposed mediators (HbA1c and neutrophil count) were all measured simultaneously from fasting venous blood samples obtained within 24 hours of admission. Because of the cross-sectional nature of these baseline

assessments, the true causal directionality cannot be definitively established; consequently, these mediation effects should be interpreted cautiously as exploratory and associative rather than strictly causal. Second, the study was conducted at a single center, which may limit the generalizability of the findings to other ethnic, geographic, or therapeutic settings. Third, AIP was assessed only at baseline, and dynamic changes in lipid profile, inflammatory activity, and glycemic control during follow-up were not evaluated, although emerging evidence suggests that cumulative or changing AIP exposure may carry additional prognostic information [14, 29]. Fourth, detailed data on long-term adherence to lipid-lowering therapy, glucose-lowering therapy, and lifestyle interventions after discharge were unavailable. Fifth, because routine advanced lipid phenotyping was not available, we could not directly compare AIP with apolipoprotein B, remnant cholesterol, or measured small dense LDL. Finally, the predictive findings were not externally validated in an independent cohort. Therefore, the current results should be interpreted as robust associative evidence that requires confirmation in prospective multicenter studies.

Conclusions

In this large single-center cohort, elevated admission AIP was independently associated with an increased risk of 3-year MACE in patients with AMI undergoing PCI. Beyond traditional cardiovascular risk factors and the GRACE score, AIP provided incremental prognostic value and may improve long-term risk stratification, particularly in younger patients. The observed association appears to be partially mediated by chronic hyperglycemic stress and systemic inflammation, supporting the view that AIP reflects a broader cardiometabolic risk phenotype rather than an isolated lipid abnormality.

Abbreviations

ACEI/ARB, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; AF, atrial fibrillation; AIP, atherogenic index of plasma; AMI, acute myocardial infarction; AUC, area under the curve; BMI, body mass index; CAD, coronary artery disease; CHF, chronic heart failure; CI, confidence interval; CKD, chronic kidney disease; CRP, C-reactive protein; DAPT, dual antiplatelet therapy; DM, diabetes mellitus; DOAC, direct oral anticoagulant; GRACE, Global Registry of Acute Coronary Events; HbA1c, glycated hemoglobin; HDL-C, high-density lipoprotein cholesterol; HR, hazard ratio; hs-CRP, high-sensitivity C-reactive protein; IABP, intra-aortic balloon pump; IDI, integrated discrimination improvement; LDL-C, low-density lipoprotein cholesterol; LDH, lactate dehydrogenase; LVEF, left ventricular ejection fraction; MACE, major adverse cardiovascular events; MI, myocardial infarction; NRI, net reclassification improvement; NSTEMI, non-ST-segment elevation myocardial infarction; NT-proBNP, N-terminal pro-B-type natriuretic peptide; PCI, percutaneous coronary intervention; ROC, receiver operating characteristic; SCr, serum creatinine; SD, standard deviation; STEMI, ST-segment elevation myocardial infarction; TC, total cholesterol; TG, triglycerides.

Declarations

Ethics approval and consent to participate

This study involving human participants was approved by the Ethics Committee of the General Hospital of Ningxia Medical University. The study was conducted in accordance with local legislation, institutional requirements, and the

Declaration of Helsinki. The requirement for written informed consent was waived by the Ethics Committee because this was a retrospective study using de-identified clinical data.

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated and/or analysed during the current study are not publicly available due to patient privacy and institutional restrictions but are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Xiaolong Kang: conceptualization, data curation, formal analysis, investigation, methodology, software, validation, visualization, and writing - original draft. Xiaolan Liang and Xin Wang: investigation and writing - original draft. Wenhao Cui and Yichen Song: writing - review and editing, and supervision. Xinrui Hai and Peng Wu: investigation, supervision, validation, and writing - review and editing. Yu Hao, Ning Yan, and Xueping Ma: supervision, project administration, and writing - review and editing. All authors read and approved the final manuscript.

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Use of AI and AI-assisted technologies

During manuscript revision, AI-assisted tools were used to improve language readability, formatting consistency, and reference-style checking. The authors reviewed and edited the output and take full responsibility for the content of the publication.

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Tables

Table 1. Baseline characteristics by AIP tertiles

Variables	Tertile 1 (n=1260)	Tertile 2 (n=1260)	Tertile 3 (n=1261)	P-value
General conditions				
Age (years)	62.68 ± 11.30	60.73 ± 11.24	56.72 ± 11.36	<0.001
Male, n (%)	983 (78.02%)	940 (74.60%)	1034 (82.00%)	<0.001
BMI (kg/m2)	23.40 ± 4.71	24.52 ± 4.36	25.72 ± 3.63	<0.001
SBP (mmHg)	119.28 ± 21.28	121.69 ± 21.46	124.01 ± 21.71	<0.001
DBP (mmHg)	74.79 ± 13.67	75.47 ± 13.62	77.77 ± 13.90	<0.001
GRACE Score (points)	156.59 ± 30.29	152.11 ± 29.92	143.34 ± 29.66	<0.001
Laboratory test				
hs-CRP (mg/L)	24.09 ± 39.41	25.82 ± 39.09	21.27 ± 36.82	0.060
cTNI (ng/L)	21.83 ± 21.80	17.31 ± 19.96	15.53 ± 18.49	<0.001
LDH (mmol/L)	1208.66 ± 1141.26	1003.78 ± 923.85	860.75 ± 792.55	<0.001
SCr (umol/L)	71.46 ± 38.11	74.12 ± 26.20	76.60 ± 41.41	0.002
TG (mmol/L)	0.77 ± 0.25	1.43 ± 0.35	2.99 ± 1.61	<0.001
HDL-C (mmol/L)	1.06 ± 0.23	0.92 ± 0.18	0.79 ± 0.17	<0.001
LDL-C (mmol/L)	2.13 ± 0.70	2.30 ± 0.76	2.26 ± 0.77	<0.001
TC (mmol/L)	3.99 ± 0.92	4.16 ± 1.00	4.49 ± 1.07	<0.001
D-dimer (mg/mL)	0.71 ± 2.26	0.74 ± 2.33	0.52 ± 1.05	0.014
HbA1c (%)	6.22 ± 1.41	6.46 ± 1.51	6.75 ± 1.67	<0.001
Neutrophils (10^9/L)	8.20 ± 2.50	7.55 ± 2.63	7.34 ± 2.71	<0.001
Risk factor				
DM	200 (15.87%)	286 (22.70%)	362 (28.71%)	<0.001
Hypertension	576 (45.71%)	652 (51.75%)	670 (53.13%)	<0.001
Prior CVD	159 (12.62%)	139 (11.03%)	98 (7.77%)	<0.001
Prior PVD	42 (3.33%)	48 (3.81%)	44 (3.49%)	0.805
Hyperlipidemia	312 (24.76%)	496 (39.37%)	875 (69.39%)	<0.001
Prior CAD	149 (11.83%)	153 (12.14%)	187 (14.83%)	0.047
Current smoking	768 (60.95%)	761 (60.40%)	821 (65.11%)	0.029
Current alcohol use	214 (16.98%)	246 (19.52%)	307 (24.35%)	<0.001
M**edications**				
Beta-blockers	897 (71.19%)	966 (76.67%)	974 (77.24%)	<0.001
ACEI/ARB	489 (38.81%)	572 (45.40%)	611 (48.45%)	<0.001
DAPT	1034 (82.06%)	1077 (85.54%)	1052 (83.36%)	0.058

Variables	Tertile 1 (n=1260)	Tertile 2 (n=1260)	Tertile 3 (n=1261)	P-value
Statins	1258 (99.84%)	1256 (99.76%)	1257 (99.60%)	0.497
Infarction related artery				
RCA	952 (75.56%)	963 (76.49%)	1006 (79.71%)	0.033
LM	122 (11.61%)	144 (14.65%)	119 (12.77%)	0.122
LAD	1168 (92.70%)	1170 (92.93%)	1156 (91.60%)	0.404
LCX	820 (65.08%)	839 (66.64%)	904 (71.63%)	0.001
Total stent length (mm)	40.96 ± 25.30	43.92 ± 26.76	47.97 ± 30.24	<0.001

Values are presented as mean ± SD or number (%). AIP, atherogenic index of plasma; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; hs-CRP, high-sensitivity C-reactive protein; cTnI, cardiac troponin I; LDH, lactate dehydrogenase; SCr, serum creatinine; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; HbA1c, glycated hemoglobin; DM, diabetes mellitus; CVD, cardiovascular disease; PVD, peripheral vascular disease; CAD, coronary artery disease; ACEI/ARB, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; DAPT, dual Antiplatelet therapy; RCA, right coronary artery; LM, left main coronary artery; LAD, left anterior descending artery; LCX, left circumflex artery.

Table 2. AIP and 3-year MACE risk

Variable	Non-adjusted		Model I		Model II		Model III	
	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
AIP	1.20(0.93,1.55)	0.1576	1.70 (1.28, 2.26)	0.0002	1.86 (1.37,2.52)	<0.0001	1.86 (1.29,2.69)	0.0010
AIP index tertile								
Low	1.00 (Reference)	-	1.00 (Reference)	-	1.00 (Reference)	-	1.00 (Reference)	-
Middle	1.15 (0.94,1.42)	0.1762	1.26 (1.02, 1.55)	0.0331	1.29 (1.03,1.61)	0.0248	1.37 (1.05,1.77)	0.0192
High	1.16 (0.94,1.43)	0.1510	1.46 (1.18,1.82)	0.0006	1.49 (1.18,1.88)	0.0007	1.53 (1.13,2.09)	0.0027
P-trend	1.08 (0.97,1.19)	0.1545	1.21 (1.08,1.35)	0.0006	1.22 (1.09,1.37)	0.0007	1.24 (1.08,1.42)	0.0022

HR, hazard ratio; CI, confidence interval; AIP, atherogenic index of plasma; BMI, body mass index; IABP, intra-aortic balloon pump; LVEF, left ventricular ejection fraction; DOAC, direct oral anticoagulant; ACEI/ARB, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker. Model I was adjusted for age, sex, BMI, Killip class, heart rate, shock index, IABP use, and diabetes mellitus. Model II was additionally adjusted for LVEF, DOAC use, ACEI/ARB use, and D-dimer. Model III was further adjusted for previous cardiovascular disease, hypertension, previous coronary artery disease, previous myocardial infarction, atrial fibrillation, chronic heart failure, chronic kidney disease, active smoking, C-reactive protein, NT-proBNP, lactate dehydrogenase, serum creatinine, and beta-blocker use.

Table 3. Incremental predictive value of AIP

Comparison and metric	Estimate	95% confidence interval	P-value
Model 4 vs. Model 1 (Traditional Risk Model)			
Continuous NRI	0.2435	15.39% – 33.41%	<0.001
IDI	0.0292	0.0219 – 0.0382	<0.001
Model 4 vs. Model 2 (GRACE Score Only)			
Continuous NRI	0.2625	17.45% – 34.86%	<0.001
IDI	0.0114	0.0071 – 0.0155	<0.001
Model 4 vs. Model 3 (Traditional Risk + GRACE)			
Continuous NRI	0.1799	9.13% – 26.84%	<0.001
IDI	0.0039	0.0017 – 0.0063	0.001

Model 1 included traditional cardiovascular risk factors (age, sex, hypertension, diabetes mellitus, current smoking, and LDL-C). Model 2 included the GRACE score alone. Model 3 included traditional cardiovascular risk factors plus the GRACE score. Model 4 included Model 3 plus AIP. AUC, area under the curve; CI, confidence interval; NRI, net reclassification improvement; IDI, integrated discrimination improvement; AIP, atherogenic index of plasma; GRACE, Global Registry of Acute Coronary Events.

Figures

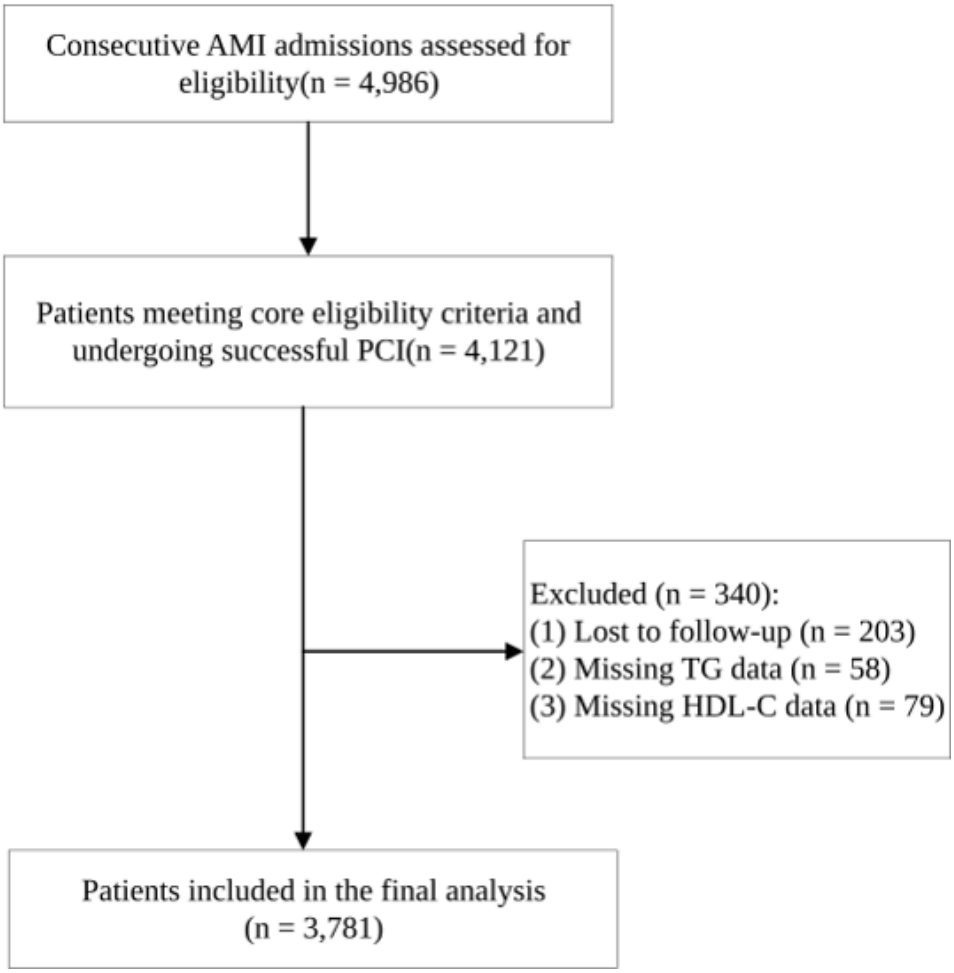


Figure 1

Patient selection flow diagram. Flowchart showing the screening and selection of patients with acute myocardial infarction (AMI) who underwent percutaneous coronary intervention (PCI) at the General Hospital of Ningxia Medical University between January 1, 2014 and December 31, 2019.

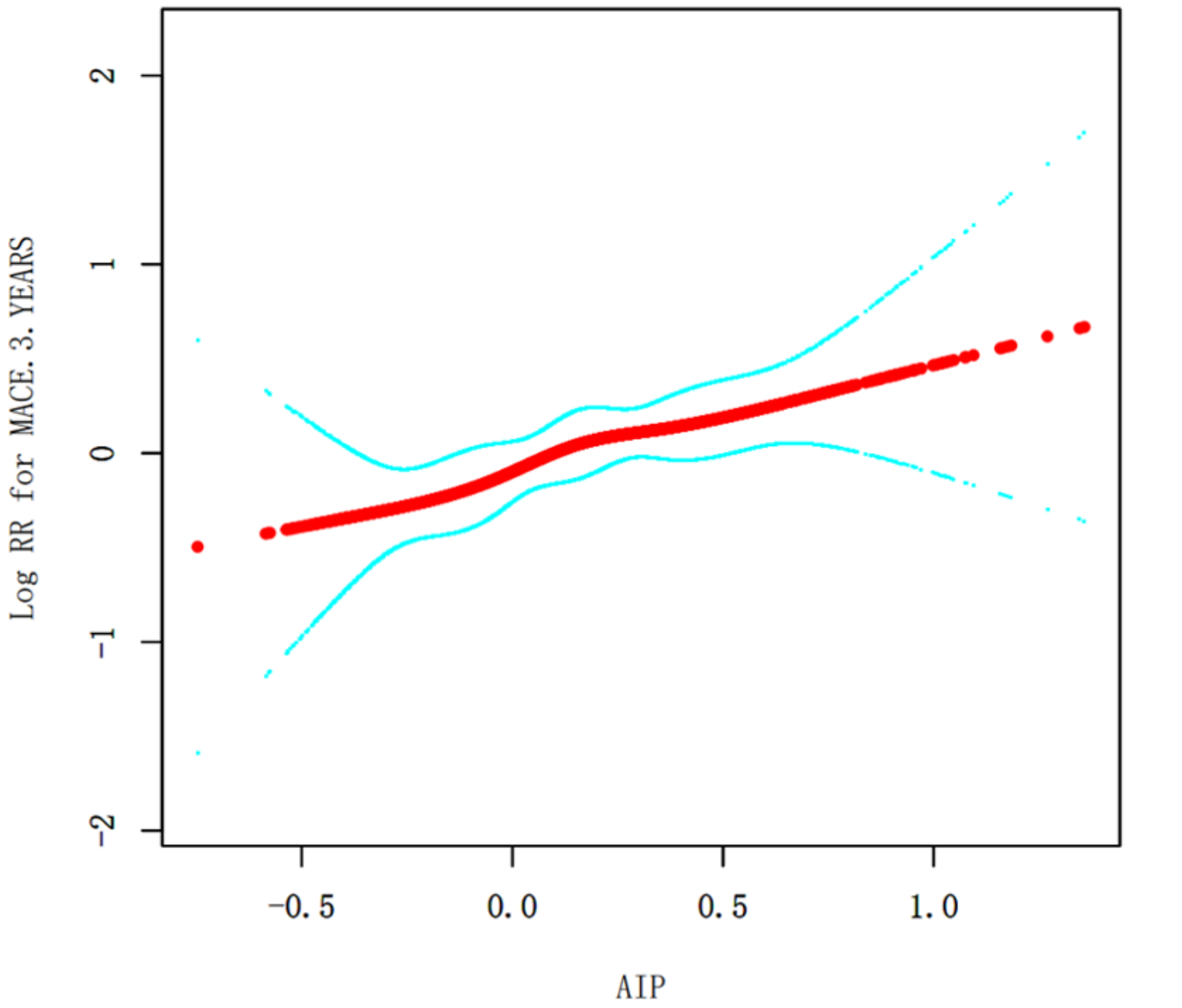


Figure 2

Restricted cubic spline for AIP and MACE. The solid line represents the adjusted log hazard ratio for 3-year major adverse cardiovascular events (MACE) across the continuous spectrum of baseline atherogenic index of plasma (AIP), and the dashed lines indicate the 95% confidence intervals. The model was adjusted for age, sex, body mass index, Killip class, heart rate, shock index, intra-aortic balloon pump use, diabetes mellitus, previous cardiovascular disease, hypertension, previous coronary artery disease, previous myocardial infarction, atrial fibrillation, chronic heart failure, chronic kidney disease, active smoking, C-reactive protein, N-terminal pro-B-type natriuretic peptide, lactate

dehydrogenase, serum creatinine, D-dimer, left ventricular ejection fraction, beta-blocker use, ACEI/ARB use, and direct oral anticoagulant use.

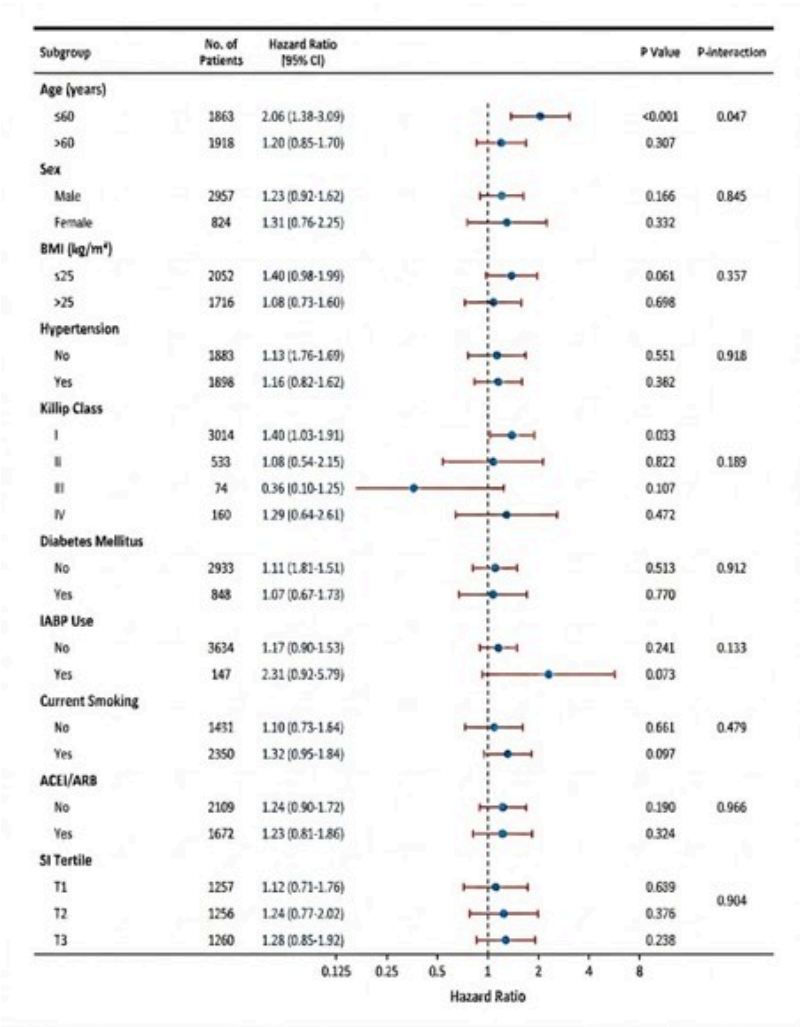


Figure 3

Subgroup analysis of AIP and MACE. Forest plot showing hazard ratios and 95% confidence intervals for the association between baseline AIP and 3-year MACE across prespecified clinical subgroups. A significant interaction was observed for age.

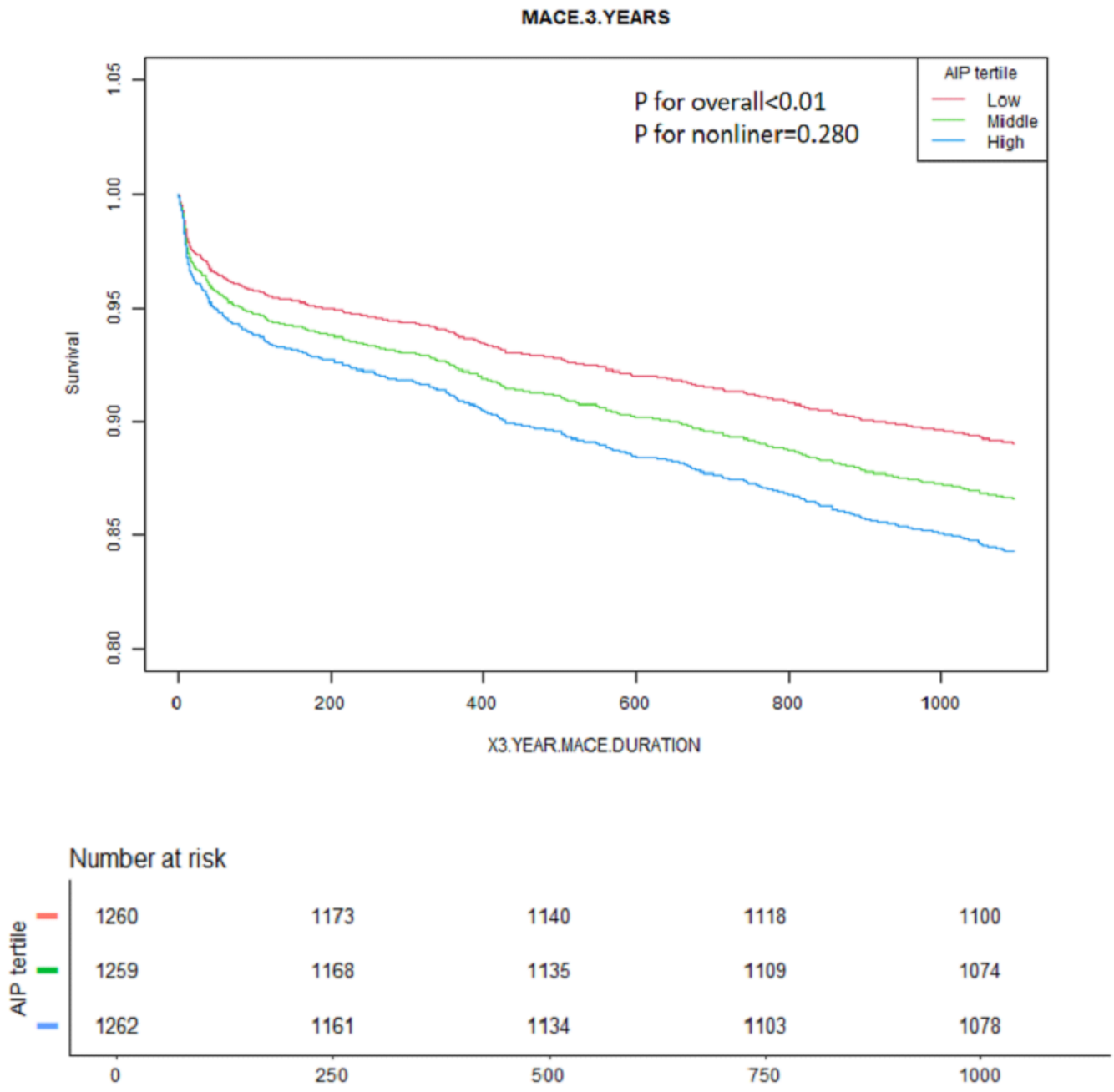


Figure 4

Kaplan-Meier curves by AIP tertiles. Kaplan-Meier estimates of event-free survival for 3-year MACE stratified by baseline AIP tertiles. Patients in the highest AIP tertile had the lowest MACE-free survival. The difference among groups was significant by log-rank test.

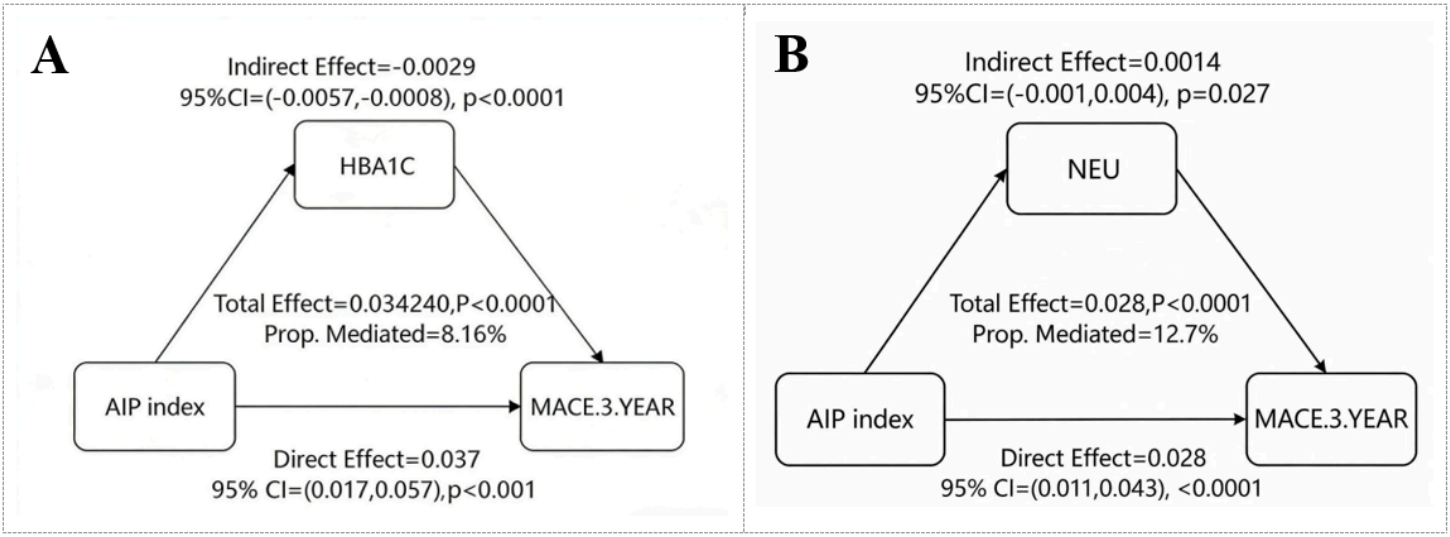


Figure 5

Mediation analysis. (A) Mediation effect of glycated hemoglobin (HbA1c) on the association between baseline AIP and 3-year MACE. (B) Mediation effect of neutrophil count on the association between baseline AIP and 3-year MACE. HbA1c and neutrophil count mediated 8.16% and 5.18% of the total association, respectively. CI, confidence interval.

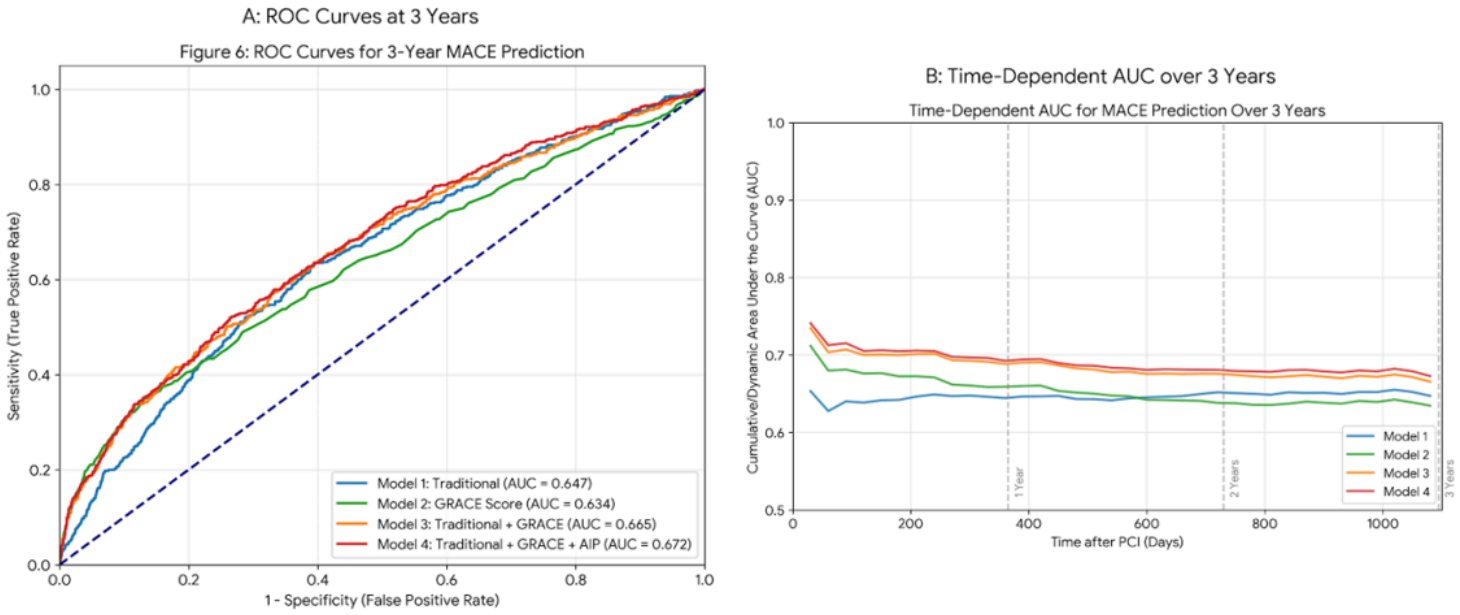


Figure 6

ROC analysis for 3-year MACE prediction. (A) Conventional ROC curves comparing the discrimination performance of the hierarchical prediction models for 3-year MACE. (B) Time-dependent ROC curves comparing the predictive performance of the four models during follow-up. Model 1 included traditional risk factors; Model 2 included the GRACE score; Model 3 combined traditional risk factors and the GRACE score; Model 4 further incorporated AIP.

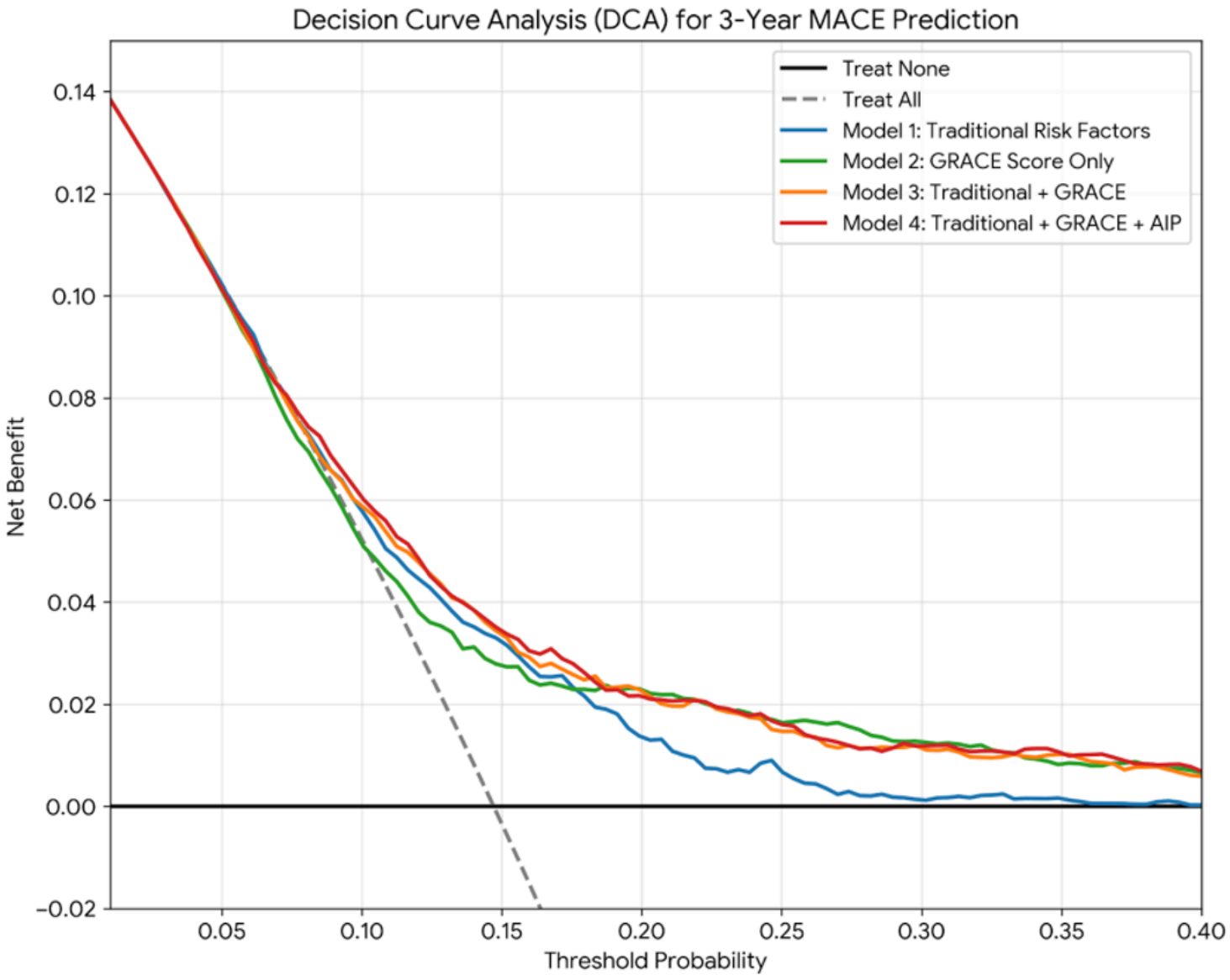


Figure 7

Decision curve analysis. Decision curve analysis comparing the clinical net benefit of the four predictive models across a range of threshold probabilities. Model 4 provided the highest net benefit across most clinically relevant thresholds.

Supplementary Files

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