Original article

Association between atherogenic index of plasma and major adverse cardiovascular events in hypertensive patients at Khok Samrong Hospital: A retrospective cohort study

Kittipan Wongtuntakorn[1], Tanawat Kerdsawat[1], and Wisit Kaewput[2]

[1] Sixth-year Medical Student, Phramongkutklao College of Medicine, Bangkok 10400, Thailand

[2] Department of Community Medicine, Phramongkutklao College of Medicine, Bangkok 10400, Thailand

Abstract

Introduction: Cardiovascular disease (CVD) remains a leading cause of morbidity and mortality worldwide, particularly among hypertensive individuals. Hypertension is a significant risk factor for major adverse cardiovascular events (MACEs), including myocardial infarction, stroke, and cardiovascular-related mortality. In Thailand, cardiovascular risk assessment tools such as the Thai ASCVD Risk Score are commonly used, incorporating factors such as age, sex, blood pressure, total cholesterol, smoking status, and diabetes history. However, the use of total cholesterol alone may not fully capture the complexity of lipid abnormalities associated with cardiovascular risk. The Atherogenic Index of Plasma (AIP), calculated as log (TG/HDL-C), has gained interest as a potential marker for cardiovascular risk assessment due to its ability to reflect dyslipidemia and arterial stiffness more effectively. Despite its potential utility, data on AIP in Thai hypertensive populations remain limited, and its predictive accuracy may vary across different demographic contexts. **Objective:** This study aims to evaluate the association between AIP and MACEs in hypertensive patients and to determine the predictive value of AIP for assessing cardiovascular risk. **Materials and Method:** A retrospective cohort study was conducted using medical records from hypertensive patients treated at Khok Samrong Hospital between January 1, 2014, and January 1, 2025. The study included patients aged 40 years or older with at least one lipid panel test available for AIP calculation and followed for a minimum of one year or until the occurrence of a cardiovascular event. The primary outcome was the incidence of MACEs, including nonfatal myocardial infarction, nonfatal stroke, and cardiovascular-

related death. Statistical analysis was performed using Cox proportional hazards regression to assess hazard ratios (HRs). **Results:** AIP was independently associated with MACEs (HR = 1.97, 95% CI: 1.117-3.490, p = 0.019). Harrell's C-index improved from 0.58 (AIP alone) to 0.67 when combined with other covariates, indicating enhanced risk stratification. **Conclusion**: The findings of this study suggest that AIP is a significant independent predictor of MACEs in hypertensive patients. Its integration into cardiovascular risk assessment models could enhance predictive accuracy and help identify high-risk individuals who may benefit from targeted interventions. Given its accessibility and ease of calculation from routine lipid panels, AIP could be a valuable adjunct to existing risk assessment tools. Future prospective studies are warranted to validate these findings and explore the potential of AIP-guided clinical decision-making in hypertensive populations.

Keywords ● *Atherogenic Index of Plasma* ● *Major Adverse Cardiovascular Events* ● *Hypertension*

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Correspondence should be addressed to Author: Wisit Kaewput, Department of community medicine, Phramongkutklao college of medicine E-mail: wisit_nephro@hotmail.com

นิพนธ์ต้นฉบับ

ความสัมพันธ์ระหว่างดัชนีไขมันในพลาสมาและเหตุการณ์ไม่พึงประสงค์ทางหัวใจและหลอดเลือดในผู้ป่วยความดันโลหิตสูงที่โรงพยาบาลโคกสำโรง: การศึกษาแบบย้อนหลัง

กิตติพันธ์ วงศ์ทันตกร[1] ธนวัฒน์ เกิดสวัสดิ์[1] และ วิศิษฐ์ แก้วพุด[2]

[1] นักศึกษาแพทย์ชั้นปีที่ 6 วิทยาลัยแพทยศาสตร์พระมงกุฎเกล้า

[2] ภาควิชาเวชศาสตร์ทหารและชุมชน วิทยาลัยแพทยศาสตร์พระมงกุฎเกล้า

บทคัดย่อ

บทนำ: โรคหัวใจและหลอดเลือดยังคงเป็นสาเหตุสำคัญของการเจ็บป่วยและการเสียชีวิตทั่วโลก โดยเฉพาะในผู้ป่วยที่มีภาวะความดันโลหิตสูง ซึ่งเป็นปัจจัยเสี่ยงสำคัญของเหตุการณ์ไม่พึงประสงค์ทางหัวใจและหลอดเลือด (Major Adverse Cardiovascular Events; MACEs) เช่น กล้ามเนื้อหัวใจตายเฉียบพลัน (Myocardial infarction), โรคหลอดเลือดสมอง (Stroke), ภาวะหัวใจล้มเหลว (Heart Failure) และการเสียชีวิตจากโรคหัวใจและหลอดเลือด ในประเทศไทยมีการใช้เครื่องมือประเมินความเสี่ยงของโรคหัวใจและหลอดเลือดที่เรียกว่า Thai ASCVD Risk Score ซึ่งพิจารณาจากปัจจัยเสี่ยงหลายประการ ได้แก่ อายุ เพศ ค่าความดันโลหิต ค่าคอเลสเตอรอลรวม (Total Cholesterol) ประวัติการสูบบุหรี่ และประวัติโรคเบาหวาน อย่างไรก็ตาม การใช้ค่าคอเลสเตอรอลรวมเพียงอย่างเดียวอาจไม่สามารถสะท้อนลักษณะของไขมันในเลือดที่สัมพันธ์กับความเสี่ยงของโรคหัวใจและหลอดเลือดได้อย่างครบถ้วน ค่าดัชนีไขมันในพลาสมา (Atherogenic Index of Plasma; AIP) ซึ่งคำนวณจากอัตราส่วนของไตรกลีเซอไรด์ต่อคอเลสเตอรอลชนิดดี (TG/HDL-C) ได้รับความสนใจมากขึ้น เนื่องจากสามารถสะท้อนถึงภาวะไขมันในเลือดผิดปกติและภาวะหลอดเลือดแข็งตัวได้อย่างแม่นยำมากขึ้น อย่างไรก็ตาม ข้อมูลเกี่ยวกับ AIP ในกลุ่มผู้ป่วยความดันโลหิตสูงในประเทศไทยยังมีจำกัด และความแม่นยำของการทำนายความเสี่ยงอาจแตกต่างกันไปตามบริบทประชากรที่ศึกษา **วัตถุประสงค์:** ศึกษาความสัมพันธ์ระหว่างค่าดัชนีไขมันในพลาสมา (AIP) กับการเกิดเหตุการณ์ไม่พึงประสงค์ทางหัวใจและหลอดเลือด (MACEs) ในผู้ป่วยที่มีภาวะความดันโลหิตสูง และประเมินความสามารถของ AIP ในการทำนายความเสี่ยงของโรคหัวใจและหลอดเลือด **วัสดุและวิธีการ:** การศึกษาย้อนหลังแบบกลุ่มประชากร (Retrospective cohort study) โดยใช้เวชระเบียนของผู้ป่วยความดันโลหิตสูงที่เข้ารับการรักษาที่โรงพยาบาลโคกสำโรงระหว่างวันที่ 1 มกราคม 2557 ถึง 1 มกราคม 2568 โดยคัดเลือกผู้ป่วยที่มีอายุตั้งแต่ 40ปีขึ้นไป และมีข้อมูลตรวจระดับไขมันในเลือดที่สามารถใช้คำนวณ AIP ได้ และติดตามอาการอย่างน้อย 1 ปี หรือจนกระทั่งเกิดเหตุการณ์ทางหัวใจและหลอดเลือดที่ร้ายแรง (MACEs) ซึ่ง

รวมถึงภาวะกล้ามเนื้อหัวใจตายเฉียบพลัน (Nonfatal myocardial infarction), โรคหลอดเลือดสมองตีบ (Nonfatal stroke) และการเสียชีวิตจากโรคหัวใจและหลอดเลือด การวิเคราะห์ทางสถิติใช้ Cox proportional hazards regression เพื่อประเมินค่าสัมพันธ์ความเสี่ยง (Hazard ratios, HRs) **ผลการวิจัย:** AIP มีความสัมพันธ์กับการเกิด MACEs อย่างมีนัยสำคัญทางสถิติ (HR = 1.97, 95% CI: 1.117-3.490, p = 0.019) นอกจากนี้ Harrell's C-index เพิ่มขึ้นจาก 0.58 (เมื่อใช้ AIP เพียงอย่างเดียว) เป็น 0.67 เมื่อนำ AIP รวมกับตัวแปรอื่น ๆ แสดงให้เห็นถึงความสามารถในการทำนายความเสี่ยงที่ดีขึ้น **สรุปผล:** ผลการศึกษานี้ชี้ให้เห็นว่า AIP เป็นตัวทำนายอิสระที่สำคัญของ MACEs ในผู้ป่วยที่มีภาวะความดันโลหิตสูง การนำ AIP มาประยุกต์ใช้ร่วมกับแบบจำลองการประเมินความเสี่ยงโรคหัวใจและหลอดเลือดอาจช่วยเพิ่มความแม่นยำในการพยากรณ์โรค และช่วยระบุผู้ป่วยกลุ่มเสี่ยงสูงที่อาจได้รับประโยชน์จากมาตรการป้องกันโรคที่เหมาะสม ด้วยความสะดวกในการคำนวณจากข้อมูลระดับไขมันในเลือดที่ตรวจตามปกติ AIP อาจเป็นเครื่องมือเสริมที่มีประโยชน์ในการประเมินความเสี่ยงของโรคหัวใจและหลอดเลือด อย่างไรก็ตาม ควรมีการศึกษาเชิงทดลองเพิ่มเติมเพื่อยืนยันผลลัพธ์นี้ และสำรวจบทบาทของ AIP ในการตัดสินใจทางคลินิกในประชากรที่มีภาวะความดันโลหิตสูง

คำสำคัญ *● ดัชนีไขมันในพลาสมา ● เหตุการณ์ทางหัวใจและหลอดเลือดที่ร้ายแรง ● ความดันโลหิตสูง*

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ได้รับต้นฉบับ 27 กันยายน 2568 แก้ไขบทความ 3 ธันวาคม 2568 รับลงตีพิมพ์ 5 ธันวาคม 2568

ต้องการสำเนาต้นฉบับติดต่อ วิศิษฐ์ แก้วพุด ภาควิชาศาสตร์ทหารและชุมชน วิทยาลัยแพทยศาสตร์พระมงกุฎเกล้า

E-mail wisit_nephro@hotmail.com

Introduction

Cardiovascular disease (CVD) is a leading cause of morbidity and mortality worldwide, particularly among individuals with hypertension, which significantly increases the risk of major adverse cardiovascular events (MACEs), including myocardial infarction, stroke, heart failure, and cardiovascular-related mortality. Given the high prevalence of hypertension and its contribution to CVD, effective risk assessment tools are essential for early identification and management of high-risk individuals.

In Thailand, the Thai ASCVD Risk Score is widely used to assess cardiovascular risk based on factors such as age, sex, blood pressure, total cholesterol, smoking status, and diabetes history. While this model is specifically tailored for the Thai population, its reliance on total cholesterol alone as a lipid marker may not sufficiently capture the complexity of dyslipidemia associated with cardiovascular risk. Emerging evidence suggests that other lipid indices may provide additional prognostic value for assessing cardiovascular risk, particularly in populations with high metabolic risk.

The Atherogenic Index of Plasma (AIP) has gained attention as a potential marker for cardiovascular risk assessment. AIP, calculated as the logarithm of the triglyceride-to-HDL cholesterol ratio (log [TG/HDL-C]), is associated with increased arterial stiffness, endothelial dysfunction, and heightened cardiovascular risk. Unlike total cholesterol, AIP reflects the balance between pro-atherogenic and protective lipoproteins, making it a more dynamic marker of lipid metabolism. Studies have shown that elevated AIP is linked to insulin resistance, metabolic syndrome, and an increased likelihood of cardiovascular events.

Despite growing evidence supporting AIP's predictive utility, data on its role in cardiovascular risk assessment among Thai hypertensive patients remains limited. The accuracy of AIP in predicting MACEs may vary across different populations, necessitating further investigation into its applicability in the Thai context. Understanding whether AIP provides additional predictive value beyond conventional risk factors could help refine cardiovascular risk assessment strategies and improve early intervention efforts.

Therefore, this study aims to investigate the association between AIP and MACEs in hypertensive patients and to assess whether incorporating AIP into existing risk models enhances predictive accuracy. By addressing these gaps, the findings may support the integration of AIP as

a complementary tool for cardiovascular risk assessment, particularly in resource-limited settings such as community hospitals.

Methods

Study Design and Protocol

This is a retrospective cohort study conducted on hypertensive patients who received follow-up and treatment at Khok Samrong Hospital. The data used for this study were retrieved from the hospital's Information and Technology Center, which stores medical records of patients. Permission was obtained from the hospital director to access the medical records of hypertensive patients, identified by the International Classification of Diseases (ICD-10) codes related to hypertension. The data were collected over an 11-year period, from January 2014 to January 2025.

Inclusion criteria were patients aged 40 years or older at the time of their first follow-up during the study period, diagnosed with hypertension, and having at least one available lipid profile for AIP calculation. Exclusion criteria were patients with pre-existing cardiovascular disease at baseline, and those with incomplete key laboratory data, such as triglyceride levels, HDL-C, or LDL-C.

Patient confidentiality was strictly maintained throughout the data collection process. All personal identifiers were removed, and each patient was assigned a unique code corresponding to their first recorded visit within the study period to ensure anonymity.

Measurement and Study Outcomes

The primary outcome of the study was the association between the Atherogenic Index of Plasma (AIP) and the occurrence of major adverse cardiovascular events (MACEs) in hypertensive patients. The secondary outcome was the comparison of MACEs risk prediction between AIP alone and AIP combined with traditional cardiovascular risk factors such as age, gender, smoking, alcohol consumption, systolic blood pressure (SBP), diabetes mellitus (DM), and serum LDL-C levels.

Other key variables analyzed included age, gender, body mass index (BMI), dyslipidemia, and comorbidities. Patient clinical characteristics such as smoking history, alcohol consumption history, and BMI classification were also examined.

Data Collection

In this study, data were collected from existing medical records. These records contained treatment details, follow-up information, and laboratory results, which were extracted from the Information and Technology Center at Khok Samrong Hospital.

The data collection process was divided into three main steps:

1. **Approval Process:** Permission was obtained from the hospital director to access patient data while ensuring compliance with ethical standards and patient confidentiality regulations.
2. **Data Extraction:** Necessary clinical and laboratory information was retrieved from the hospital's Information and Technology Center, including demographics, comorbidities, and lipid profile data.
3. **Data Analysis:** The collected data were analyzed to examine the relationship between AIP and MACEs, as well as to compare the predictive performance of AIP alone versus AIP combined with traditional cardiovascular risk factors.

Statistical analysis and sample size

Continuous variables were summarized as mean ± standard deviation (SD), while categorical variables were presented as frequency and percentage. The Shapiro-Wilk test was used to assess the normality of continuous variables. For descriptive statistics, the Chi-square test was applied to evaluate the relationship between categorical variables, whereas the Mann-Whitney U test was used for non-normally distributed continuous variables.

For analytical statistics, a competing risk regression model was used to determine factors associated with major adverse cardiovascular events (MACEs) among hypertensive patients. The Cox proportional hazards model was applied to estimate hazard ratios (HR) and 95% confidence intervals (CI) for both univariable and multivariable analyses. A two-tailed p-value ≤ 0.05 was considered statistically significant.

The sample size was determined using Freedman's formula, incorporating an expected event rate and power of 80% ($Z_{\beta} = 0.84$) at a 95% confidence level ($Z_{\alpha/2} = 1.96$). The calculation accounted for four groups, resulting in a required sample size of 132 participants per group, leading to a total sample size of 528 hypertensive patients.

Patient Selection and Flowchart Description

A total of 3,234 hypertensive patients were assessed for eligibility at Khok Samrong Hospital in 2014. Of these, 1,354 patients were excluded due to incomplete laboratory data (n=1,270) or age below 40 years (n=84). The remaining 1,880 patients met the initial criteria for inclusion in the study.

Further exclusion was applied to 255 patients who had a history of myocardial infarction (MI) or stroke prior to enrollment, leaving a final cohort of 1,625 patients eligible for analysis. Among this cohort, 1,094 patients (67.4%) did not experience MACEs during the follow-up period, 194 patients (11.9%) experienced MACEs, and 335 patients (20.6%) died from other causes.

The patient selection process and distribution of study participants are summarized in the STROBE diagram.

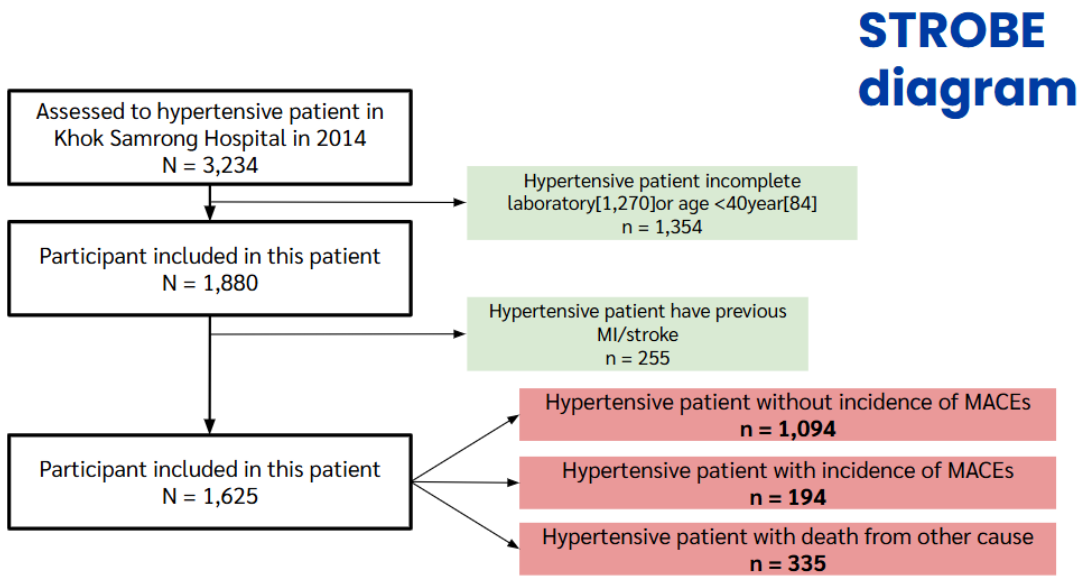

Figure 1 STROBE diagram

Table 1: Demographic data of general characteristic

	n (%)
Age (year-old) (n=1,625)	
Mean ± SD	62.88 ± 10.84
Median (Min-Max)	60 (40-93)
Age group (n=1,625)	
<60-year-old	656 (40.37)
≥60-year-old	969 (59.63)
Gender (n=1,625)	
Male	449 (27.63)
Female	1,176 (72.37)
Status (n=1,625)	
Single	188 (11.57)
Married	1,429 (87.94)
Widow	3 (0.18)
Divorced	1 (0.06)
Smoking (n=1,617)	
No	1.577 (97.53)
Yes	40 (2.47)
Alcoholic drinking (n=1,618)	
No	1,597 (98.70)
Yes	21 (1.30)
Diabetes mellitus (n=1,625)	
No	830 (51.08)
Yes	795 (48.92)
Systolic blood pressure (SBP) (mmHg) (n=1,616)	
Mean ± SD	136.65 ± 18.76
Median (Min-Max)	135 (79-221)
SBP group (n=1,616)	
<140 mmHg	980 (60.64)
≥140 mmHg	636 (39.36)
LDL-C (mg/dl) (n=1,625)	
Mean ± SD	110.10 ± 27.73
Median (Min-Max)	108 (36-292)

	n (%)
LDL group (n=1,625)	
<100 mg/dl	602 (37.05)
≥100 mg/dl	1,023 (62.95)
Atherogenic index of plasma (AIP) (n=1,625)	
Mean ± SD	0.53 ± 0.26
Median (Min-Max)	0.52 (-0.19-1.52)
Outcome (n=1,625)	
No MACEs	1,096 (67.45)
MACES	194 (11.94)
Death from other cause	335 (20.62)
Major adverse cardiovascular events (MACEs) (n=194)	
Myocardial infarction	98 (50.52)
Stroke	74 (38.14)
Death from cardiovascular cause	22 (11.34)

Results

Demographic data

From **table 1**, the study included a total of 1,625 hypertensive patients, with a mean age of 62.88 ± 10.84 years and a median age of 60 years (range: 40–93 years). Most of the participants (59.63%) were aged 60 years or older, reflecting an older hypertensive population. In terms of sex distribution, female patients constituted 72.37% of the cohort, while male patients accounted for 27.63%.

Regarding lifestyle factors, the prevalence of smoking was relatively low, with only 2.47% of participants reporting current smoking. Similarly, alcohol consumption was uncommon, with 1.30% of patients indicating current alcohol use. Diabetes mellitus was present in 48.92% of the study population, highlighting a high prevalence of metabolic comorbidities that could contribute to increased cardiovascular risk.

For clinical parameters, systolic blood pressure (SBP) levels varied across participants, with a mean of 136.65 ± 18.76 mmHg and a median of 135 mmHg (range: 79–221 mmHg). A total of 39.36% of patients had SBP ≥140 mmHg, whereas 60.64% had SBP below this threshold. Low-density lipoprotein cholesterol (LDL-C) levels were also assessed, with a mean value of

110.10 ± 27.73 mg/dL and a median of 108 mg/dL (range: 36–292 mg/dL). Notably, 62.95% of patients had LDL-C levels ≥100 mg/dL, indicating a substantial prevalence of dyslipidemia in this cohort.

The atherogenic index of plasma (AIP) was analyzed as a key lipid marker, with a mean value of 0.53 ± 0.26 and a median of 0.52 (range: -0.19 to 1.52). These findings suggest that a significant proportion of patients exhibited elevated AIP levels, supporting its potential role as a marker for cardiovascular risk in hypertensive populations.

With respect to clinical outcomes, 11.94% (n=194) of patients experienced a major adverse cardiovascular event (MACE) during the follow-up period, while 67.45% remained free of cardiovascular events. Additionally, 20.62% (n=335) of patients died from non-cardiovascular causes, emphasizing the presence of competing risks in this population. Among patients who developed MACEs, 50.52% experienced myocardial infarction, 38.14% suffered a stroke, and 11.34% died due to cardiovascular causes.

Table 2 Factors Associated with Major Adverse Cardiovascular Events (MACEs) in Hypertensive Patients - An Analysis Using Multiple Competing Risk Regression

	Events	Person-years	Incidence (1,000Person-years)	Univariable analysis			Multivariable analysis		
				Hazard ratio (HR)	95%CI	p-value	Hazard ratio (HR)	95%CI	p-value
Major adverse cardiovascular events (MACEs)	194	14,377	13.49	-	-	-	-	-	-
Age, years									
<60	50	6,308	7.93	1 (reference)			1 (reference)		
≥60	141	8,069	17.47	2.22	1.608-3.066	<0.001*	2.22	1.601-3.067	<0.001*
Gender									
female	128	10,637	12.03	1 (reference)			1 (reference)		
Male	63	3,740	16.84	1.40	1.040-1.903	0.027*	1.40	1.025-1.916	0.034*
Smoking									
No	182	13,980	13.02	1 (reference)			1 (reference)		
Yes	8	334	23.95	1.84	0.908-3.743	0.091	1.66	0.768-3.597	0.197
Alcoholic drinking									
No	188	14,130	13.30	1 (reference)			1 (reference)		
Yes	3	190	15.79	1.18	0.378-3.700	0.773	1.06	0.313-3.597	0.924
SBP group									
<140	102	8,810	11.58	1 (reference)			1 (reference)		
≥140	88	5,498	16.01	1.38	1.041-1.838	0.025*	1.18	0.886-1.586	0.253
Diabetes mellitus									
No	67	7,741	8.66	1 (reference)			1 (reference)		
Yes	124	6,637	18.68	2.17	1.612-2.922	<0.001*	2.14	1.576-2.914	<0.001*
LDL-C, mg/dl	-	-	-	1.01	1.001-1.011	0.021*	1.01	1.002-1.011	0.008*
Atherogenic index of plasma (AIP)	-	-	-	2.81	1.647-4.782	<0.001*	1.97	1.117-3.490	0.019*

Comparisons of factors between risk factors and MACEs incidence

From **table 2**, The univariable and multivariable competing risk regression analyses identified several factors significantly associated with major adverse cardiovascular events (MACEs). Age was a strong predictor, with patients aged ≥60 years demonstrating a significantly higher risk of MACEs (HR = 2.220, $p < 0.001$). This finding reinforces the well-established association between aging and increased cardiovascular risk.

Male sex was also identified as an independent risk factor, with a hazard ratio of 1.4 ($p = 0.034$), indicating a higher susceptibility to MACEs among male patients compared to females. Although smoking showed an increased hazard ratio in the univariable analysis (HR = 1.84, $p = 0.091$), it did not remain statistically significant in the multivariable model (HR = 1.66, $p = 0.197$), suggesting that other confounding factors may have influenced this association. Similarly, alcohol consumption did not reach statistical significance in either model.

Among metabolic factors, diabetes mellitus emerged as a strong independent risk factor, with diabetic patients exhibiting a significantly higher risk of MACEs (HR = 2.14, $p < 0.001$). This underscores the critical role of diabetes management in reducing cardiovascular risk in hypertensive populations. Serum LDL-C was also significantly associated with MACEs, though with a modest effect size (HR = 1.01, $p = 0.008$), suggesting that even small elevations in LDL-C contribute to an increased cardiovascular risk.

Importantly, Atherogenic Index of Plasma (AIP) demonstrated a significant independent association with MACEs, with a hazard ratio of 1.97 ($p = 0.019$) in the multivariable model. This finding suggests that higher AIP values are indicative of an elevated cardiovascular risk, supporting its potential utility as a predictive biomarker in clinical practice. The significant association between AIP and MACEs highlights the need for further exploration of AIP as an adjunctive tool in cardiovascular risk assessment among hypertensive patients.

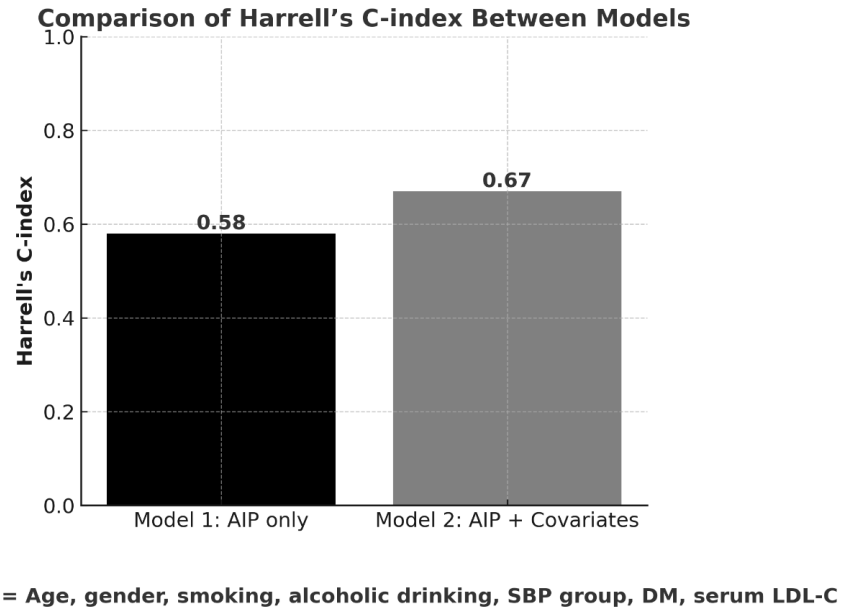

Figure 2 Comparison of Harrell's C-index between Models

Predictive value of AIP and MACEs incidence

The predictive performance of Atherogenic Index of Plasma (AIP) was evaluated both independently and in combination with traditional cardiovascular risk factors. When assessed alone, AIP demonstrated a Harrell's C-index of 0.58, indicating a moderate predictive capability for major adverse cardiovascular events (MACEs). However, when integrated with additional covariates, including age, gender, smoking, alcohol consumption, systolic blood pressure (SBP), diabetes mellitus, and serum LDL-C levels, the C-index improved to 0.67.

This enhancement in predictive accuracy suggests that while AIP is a valuable marker for cardiovascular risk, its predictive strength is significantly improved when incorporated into a comprehensive risk model. These findings support the potential utility of AIP as an adjunctive biomarker in cardiovascular risk stratification, reinforcing the importance of a multifactorial approach in assessing MACEs risk among hypertensive patients.

Discussion

Comparison of our study with other Studies

The findings of this study align with previous research conducted in United States (2023), which demonstrated a significant association between Atherogenic Index of Plasma (AIP) and

cardiovascular mortality in hypertensive patients.[1] Similarly, a study from Iran (2015) identified AIP as a reliable biomarker for cardiovascular disease risk.[2]

Further evidence supporting our results, research from the China (2024) explored the relationship between AIP and metabolic disorders, reinforcing the importance of lipid imbalance in cardiovascular risk assessment.[3] Additionally, a study conducted in Iraq (2013) found that AIP was superior to conventional lipid markers (e.g., total cholesterol and LDL-C) in predicting cardiovascular events, a finding consistent with our study's results.[4]

Our study contributes to this body of research by evaluating AIP's predictive performance both independently and in combination with traditional cardiovascular risk factors. The improvement in Harrell's C-index from 0.58 (AIP alone) to 0.67 (AIP + covariates) supports the notion that AIP enhances cardiovascular risk prediction when used alongside conventional metrics.[5]

Key Findings to Emphasize

Several important findings from our study emphasize AIP's role as a significant predictor of MACEs:

- Age: Patients aged ≥60 years exhibited a significantly higher risk of MACEs (HR = 2.220, $p < 0.001$). This finding is consistent with studies showing that aging contributes to vascular dysfunction, endothelial damage, and increased cardiovascular risk.[6]
- Male Sex: Male patients were at a higher risk of MACEs than females (HR = 1.4, p = 0.034), supporting findings from previous research suggesting that men have a higher prevalence of cardiovascular risk factors such as dyslipidemia, hypertension, and oxidative stress.[7]
- Diabetes Mellitus (DM): Diabetes was found to be an independent risk factor for MACEs (HR = 2.14, $p < 0.001$), reinforcing its well-documented role in atherosclerosis, endothelial dysfunction, and chronic inflammation, which contribute to cardiovascular disease.[8]
- LDL-C: Although LDL-C was significantly associated with MACEs (HR = 1.01, $p = 0.008$), its effect size was modest. This finding is in line with studies suggesting that LDL-C alone may not fully capture lipid-related cardiovascular risk and should be complemented with additional biomarkers such as AIP.[4]

- AIP: Our study confirms that higher AIP values are independently associated with an increased risk of MACEs (HR = 1.97, p = 0.019). This supports research from Southeast Asia (2023), which identified AIP as a crucial lipid marker in high-risk cardiovascular populations.[9]

Possible Explanations for Findings

The observed association between AIP and MACEs can be explained by its role in lipid metabolism and cardiovascular pathophysiology:

1. AIP reflects the ratio of triglycerides to HDL-C, a key indicator of lipid metabolism dysfunction, insulin resistance, and endothelial damage.[10]
2. Elevated AIP levels are associated with increased small, dense LDL particles and decreased HDL-C, leading to atherogenic lipid profiles and higher cardiovascular risk.[11]
3. The strong link between AIP and metabolic syndrome suggests that AIP is a better predictor of cardiovascular risk than LDL-C alone, particularly in populations with diabetes and hypertension.[12]

The improvement in predictive accuracy when AIP is combined with traditional cardiovascular risk factors (C-index = 0.67) suggests that AIP should not be used in isolation but rather integrated into multifactorial risk assessment models.[13]

Clinical Implications

The findings of this study underscore the potential of AIP as an adjunctive biomarker in cardiovascular risk stratification, particularly in hypertensive patients. While traditional models, such as the cardiovascular risk assessment tools used in Thailand and other countries, rely primarily on LDL-C, they do not account for the impact of triglyceride-HDL imbalance, which AIP effectively captures.[14]

Given its ease of calculation (log [Triglycerides/HDL-C]) and strong predictive value, AIP could be integrated into routine lipid panels to enhance cardiovascular risk prediction in hypertensive populations. Clinicians may consider monitoring AIP levels to identify high-risk individuals who may benefit from early intervention, lifestyle modification, and aggressive lipid management.[15]

Furthermore, AIP is modifiable through interventions such as dietary changes, lipid-lowering medications (e.g., fibrates, statins), and glucose control, making it a valuable marker for both risk prediction and therapeutic monitoring.[15]

Limitations and Future Research

- Single-center retrospective design: The findings may not be generalizable to diverse populations or multi-center settings. Future studies should validate these results in larger, multi-center cohorts across different populations.
- Potential confounding factors: While adjustments were made for major risk factors, unmeasured variables such as inflammatory biomarkers, genetic predisposition, and lifestyle factors were not included in this study.
- Longitudinal impact: This study establishes an association but not causation. Future prospective and interventional studies should investigate whether AIP modification can reduce cardiovascular risk and improve long-term outcomes.

Conclusion

This study demonstrated that the Atherogenic Index of Plasma (AIP) is significantly associated with major adverse cardiovascular events (MACEs) in hypertensive patients. Our findings suggest that AIP serves as an independent predictor of cardiovascular risk, even when adjusted for traditional risk factors such as age, gender, smoking, systolic blood pressure (SBP), diabetes mellitus, and LDL-C levels.

The predictive performance analysis showed that AIP alone has moderate predictive capability (Harrell's C-index = 0.58), but its accuracy improves significantly (C-index = 0.67) when combined with traditional cardiovascular risk factors. This highlights the potential of AIP as an adjunctive marker for cardiovascular risk stratification, offering additional insights beyond conventional lipid parameters.

Given its simple calculation from routine lipid profiles (log [Triglycerides/HDL-C]) and its strong predictive value, AIP could be a practical tool for identifying high-risk hypertensive patients who may benefit from earlier intervention and more aggressive cardiovascular risk management strategies.

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