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Atherogenic Lipid Indices and the Acute Coronary Syndrome Spectrum: The Modifying Role of Type 2 Diabetes Mellitus, A Cross-Sectional Study

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ABSTRACT: Diabetic atherogenic dyslipidemia sustains residual cardiovascular burden in acute coronary syndrome (ACS) poorly reflected by LDL cholesterol. Research on non-traditional lipid indices, AIP, ACI, and LCI, has emphasized coronary disease presence or angiographic severity rather than ACS severity. Whether T2DM modifies this relationship remains unknown. This single-center study included 416 ACS patients (156 with T2DM, 260 without); lipids were sampled within 24 h of admission. AIP, ACI, and LCI were compared across UAP, NSTEMI, and STEMI by glycemic status; ROC cut-offs assessed glycemic status and coronary severity. AIP and LCI were higher in T2DM (P=0.004 and P=0.005), whereas ACI was not (P=0.091). Correlations with spectrum were weak but consistent in T2DM. ACI and LCI differed non-monotonically in the cohort and in T2DM, lowest in UAP and comparable in NSTEMI and STEMI; no index differed in non-diabetic patients. At ROC cut-offs, indices were associated with T2DM within NSTEMI (LCI OR 3.79) and STEMI, not UAP; none with vessel count. LCI was strongest and consistent. In ACS, ACI and LCI distinguish unstable angina from infarction mainly in T2DM, in a non-monotonic pattern absent in non-diabetic patients, reflecting metabolic rather than anatomical burden. T2DM modifies indices-ACS relationships, with LCI the most consistent marker. These cross-sectional findings require prospective, outcome-based validation.

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1. INTRODUCTION

Atherosclerotic cardiovascular disease continues to be the leading cause of mortality globally, with acute coronary syndrome (ACS) representing its most severe and deadly manifestation. This condition encompasses a clinical spectrum ranging from unstable angina pectoris (UAP) and non-ST-elevation myocardial infarction (NSTEMI) to ST-elevation myocardial infarction (STEMI) [1,2]. Type 2 diabetes mellitus (T2DM) increases this risk by about twofold and leads to poorer outcomes after acute coronary syndrome (ACS), a danger that is not fully accounted for by traditional risk factors [3–5].

A central driver of this excess risk is diabetic atherogenic dyslipidemia, namely hypertriglyceridemia, low and dysfunctional high-density lipoprotein (HDL), and a preponderance of small, dense, apolipoprotein B-rich low-density lipoprotein (LDL), whose atherogenicity is poorly reflected by LDL cholesterol alone [6–9]. Because LDL cholesterol is frequently at target in these patients, conventional lipid panels systematically underestimate the residual atherogenic burden that continues to drive events despite guideline-directed lipid lowering [6,7].

To address this concealed risk, non-traditional lipid indices were developed by combining various atherogenic fractions into unified measures: the atherogenic index of plasma (AIP), the atherogenic combined index (ACI), and the lipoprotein combined index (LCI) [10–15]. To date, however, these indices have been studied almost exclusively in relation to the presence of coronary disease, angiographic severity scores, or downstream outcomes [13–19], and not to the clinical severity of the ACS presentation itself.

Whether atherogenic indices differ across the ACS clinical spectrum, and whether diabetes reshapes that relationship, is essentially unknown, and we address this gap directly. To our knowledge, this is the first study to profile AIP, ACI, and LCI across the entire ACS spectrum (UAP, NSTEMI, and STEMI) with prespecified stratification by glycemic status, using lipids drawn within the first 24 hours of admission to minimize acute-phase distortion; we further test the anatomical specificity of any association against the number of diseased coronary vessels. The analysis is deliberately associative and cross-sectional, characterizing correlations and between-group differences rather than predictive or prognostic performance, so that no causal or risk inference is drawn.

2. MATERIALS AND METHODS

2.1 Study Design and Population

A cross-sectional study was conducted at Dr. Wahidin Sudirohusodo General Hospital in Makassar, Indonesia, using data collected from May to August 2026. The study included adult patients aged 18 years and above who were consecutively admitted with diagnoses of ACS, UAP, NSTEMI, or STEMI, as defined by current guidelines [2,20]. These patients underwent coronary angiography and had their lipid profiles obtained within the first 24 hours of admission. Patients with incomplete lipid data were excluded from the study. The final sample consisted of 416 patients, of whom 156 had T2DM and 260 did not.

2.2 Sample size

The sample size was estimated for a two-group comparison of means ($Z\alpha=1.96$; $Z\beta=0.84$; power 80%), using an AIP mean difference of 0.089 and a pooled standard deviation of 0.265, yielding 139 patients per group; allowing for 10% attrition, approximately 155 per group were required.

2.3 Variables and definitions

According to the criteria set by the American Diabetes Association, type 2 diabetes mellitus is characterized by a prior diagnosis of diabetes by a physician, ongoing treatment with glucose-lowering medication, an HbA1c level of 6.5% (48 mmol/mol) or higher, or a fasting plasma glucose level of at least 126 mg/dL (7.0 mmol/L) [21]. Venous blood samples were collected within 24 hours of admission to assess lipid profiles, including total cholesterol, LDL-C, HDL-C, and triglycerides. Non-HDL-C was determined by subtracting HDL-C from total cholesterol. The three indices were calculated as follows: AIP was derived from log10(triglycerides/HDL-C), ACI was obtained by dividing non-HDL-C by HDL-C, and LCI was calculated using the formula (total cholesterol × LDL-C × triglycerides)/HDL-C, with all concentrations expressed in conventional units. The ACS spectrum comprised UAP, NSTEMI and STEMI. Coronary severity was categorized angiographically by the number of vessels with significant stenosis (single-vessel [1VD] vs. multivessel [2VD+3VD]). Patients with incomplete or unavailable coronary

angiography data were excluded from the subsequent analysis of coronary severity (single-vessel vs multivessel), which was therefore restricted to 360 patients with defined obstructive coronary artery disease.

2.4 Statistical Analysis

Shapiro-Wilk test evaluated distribution; non-normal variables are presented as median with interquartile range (Q1–Q3), and categorical variables as n (%). Mann-Whitney U compared groups, and differences among the three spectra were analyzed with Kruskal-Wallis and Dunn post-hoc tests. Associations between each index and individual ACS spectrums were assessed by Spearman/point-biserial correlation using a one-versus-rest scheme. ROC analysis (Youden index) determined optimal cut-off points; relationships of values above these cut-offs with glycemic status and coronary severity were assessed by chi-square test (or Fisher's exact test for expected counts below 5) and odds ratios (OR) with 95% confidence intervals (CI). Analyses included the cohort and glycemic subgroups, using SPSS version 26 (IBM Corp.); $P<0.05$ was statistically significant. ROC-derived cut-offs were descriptive, not validated diagnostic or prognostic thresholds..

3. RESULTS AND DISCUSSION

3.1 Baseline characteristics

In a group of 416 patients, with an average age of 57.9 years (± 11.3 years) and predominantly male (79.1%), the most frequent condition was STEMI, accounting for 64.7%. This was followed by NSTEMI at 24.3% and UAP at 11.1%; the distribution did not differ by glycemic status (P=0.585). Patients with T2DM were more often female (26.9% vs. 17.3%, P=0.027) and less often smokers (53.2% vs. 66.5%, P=0.009), and more frequently had prior myocardial infarction (14.7% vs. 6.9%, P=0.015). While total cholesterol, LDL-C, and HDL-C levels remained consistent regardless of glycemic status, triglycerides (128 vs. 115 mg/dl, P=0.001) and non-HDL-C (172 vs. 160 mg/dl, P=0.035) were elevated in individuals with T2DM. Accordingly, AIP (0.25 vs. 0.18, P=0.004) and LCI (36.0 vs. 28.5, P=0.005) were significantly higher in T2DM, while ACI showed a non-significant trend (5.56 vs. 5.14, P=0.091) (Table 1).

Table 1. Baseline demographic, clinical, and lipid characteristics of patients with acute coronary syndrome

Characteristic	Total (n=416)	Non-DM (n=260)	T2DM (n=156)	P value
UAP, n (%)	46 (11.1)	27 (10.4)	19 (12.2)	0.585
NSTEMI, n (%)	101 (24.3)	60 (23.1)	41 (26.3)	0.585
STEMI, n (%)	269 (64.7)	173 (66.5)	96 (61.5)	0.585
Age (years)	57.9 ± 11.3	57.6 ± 11.9	58.5 ± 10.1	0.839
Male, n (%)	329 (79.1)	215 (82.7)	114 (73.1)	0.027*
BMI (kg/m²)	24.1 (22.0–26.0)	23.9 (22.0–25.7)	24.4 (22.2–26.6)	0.195
Creatinine (mg/dL)	1.08 (0.89–1.30)	1.05 (0.89–1.30)	1.10 (0.89–1.31)	0.106
Random glucose (mg/dL)	140 (115–201)	122.5 (107–143)	234 (161–310)	<0.001*
Total cholesterol (mg/dL)	196.5 (164–233)	193 (161–226)	201.5 (169–247)	0.052
LDL-C (mg/dL)	144 (116–179)	144 (115–177)	144.5 (116–187)	0.442
HDL-C (mg/dL)	33 (28–40)	33 (28–40)	32 (28–39)	0.633
Triglycerides (mg/dL)	120 (91–162)	115 (87–149)	128 (101–168)	0.001*
Non-HDL-C (mg/dL)	163 (131–197)	160 (130–191)	172 (134–208)	0.035*
AIP	0.20 (0.03–0.36)	0.18 (0.00–0.34)	0.25 (0.08–0.40)	0.004*
ACI	5.27 (4.09–6.64)	5.14 (4.03–6.45)	5.56 (4.17–7.12)	0.091

Characteristic	Total (n=416)	Non-DM (n=260)	T2DM (n=156)	P value
LCI	30.9 (17.9–54.9)	28.5 (16.8–51.0)	36.0 (19.9–67.2)	0.005*
Hypertension, n (%)	226 (54.3)	135 (51.9)	91 (58.3)	0.242
Smoking history, n (%)	256 (61.5)	173 (66.5)	83 (53.2)	0.009*
ASCVD history, n (%)	71 (17.1)	37 (14.2)	34 (21.8)	0.064
Prior myocardial infarction, n (%)	41 (9.9)	18 (6.9)	23 (14.7)	0.015*
Prior lipid-lowering therapy, n (%)	41 (9.9)	19 (6.9)	22 (14.1)	0.026*
Obstructive CAD	360 (86.5)	222 (85.4)	138 (88.5)	0.340
Single-vessel (1VD)	108 (26.0)	73 (28.1)	35 (22.4)	0.223
Two-vessel (2VD)	113 (27.2)	70 (26.9)	43 (27.6)	0.223
Three-vessel (3VD)	139 (33.4)	79 (30.4)	60 (38.5)	0.223
Left main involvement	33 (7.9)	22 (8.5)	11 (7.1)	0.743
In-hospital events, n (%)				
Arrhythmia	79 (19.0)	49 (18.8)	30 (19.2)	1.000
Cardiogenic shock	65 (15.6)	39 (15.0)	26 (16.7)	0.754
Heart failure	308 (74.0)	201 (77.3)	107 (68.6)	0.065
In-hospital death	29 (7.0)	17 (6.5)	12 (7.7)	0.804
Composite (death/shock/arrhythmia)	125 (30.0)	72 (27.7)	53 (34.0)	0.214

*Data are median (IQR) or n (%); age as mean ± SD. p compares non-DM versus T2DM: Mann-Whitney U test for continuous variables and chi-square test (Yates continuity correction) or Fisher's exact test for categorical variables. *p<0.05. AIP, atherogenic index of plasma; ACI, atherogenic combined index; LCI, lipoprotein combined index; BMI, body mass index; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; ASCVD, atherosclerotic cardiovascular disease; CAD, coronary artery disease; VD, vessel disease.*

3.2 Atherogenic lipid indices across the ACS spectrum

One-versus-rest correlations between the lipid indices and each ACS subtype are presented in Table 2. In the whole cohort, AIP was positively correlated with NSTEMI (r=0.104, P=0.034), whereas ACI and LCI were inversely correlated with UAP (r=−0.139, P=0.005 and r=−0.135, P=0.006, respectively). The same associations were observed in patients with T2DM; no correlation reached statistical significance in patients without diabetes.

Distributions and between-group comparisons across UAP, NSTEMI and STEMI are shown in Table 3. ACI and LCI differed across the ACS spectrum in the whole cohort (P=0.018 and P=0.025, respectively) and in patients with T2DM (P=0.011 and P=0.022, respectively). Post-hoc comparisons showed lower values in UAP than in NSTEMI or STEMI, without a significant difference between NSTEMI and STEMI. AIP did not differ significantly across the three groups, and no index differed significantly in patients without diabetes.

3.3 ROC analysis and associations with glycemic status

The ROC curves for T2DM status are shown in Figure 1. The ROC-derived cut-off values for AIP, ACI, and LCI were used to categorize participants in the analyses presented in Tables 4, 5, and 6. Their associations with T2DM in the overall ACS cohort are presented in Table 4. Values above the cut-offs for AIP (>0.24), ACI (>7.08) and LCI (>29.47) were associated with T2DM, with odds ratios of 1.82 (95% CI, 1.21–2.71), 2.09 (95% CI, 1.28–3.41) and 2.02 (95% CI, 1.34–3.04), respectively. These cut-offs were used for exploratory comparisons.

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The corresponding analyses within each ACS subtype are presented in Table 5. In NSTEMI, all three above-cut-off indices were associated with T2DM, with the largest odds ratio observed for LCI (OR, 3.79; 95% CI, 1.58–9.10; P=0.002). In STEMI, associations were significant for ACI and LCI, but not AIP. No significant association was observed in UAP.

Table 2. Correlation of atherogenic lipid indices with each acute coronary syndrome spectrum (one-versus-rest), overall and by glycemic status

Index vs subtype	Whole cohort		T2DM		Non-DM	
	r value	p value	r value	p value	r value	p value
AIP vs UAP	−0.078	0.112	−0.045	0.578	−0.109	0.079
AIP vs NSTEMI	0.104	0.034*	0.187	0.020*	0.037	0.550
AIP vs STEMI	−0.042	0.394	−0.139	0.084	0.037	0.549
ACI vs UAP	−0.139	0.005*	−0.240	0.003*	−0.073	0.238
ACI vs NSTEMI	0.032	0.518	0.077	0.337	−0.009	0.887
ACI vs STEMI	0.063	0.202	0.091	0.257	0.055	0.374
LCI vs UAP	−0.135	0.006*	−0.195	0.015*	−0.099	0.111
LCI vs NSTEMI	0.024	0.623	0.148	0.066	−0.061	0.326
LCI vs STEMI	0.067	0.175	−0.003	0.974	0.119	0.056

*Spearman/point-biserial correlation of each index with membership in each ACS spectrum (one-versus-rest). *p<0.05.*

Table 3. Distribution and between-group differences of atherogenic lipid indices across the acute coronary syndrome spectrum according to glycemic status

Variable	UAP	NSTEMI	STEMI	p value
Whole cohort (UAP n=46 / NSTEMI n=101 / STEMI n=269)				
AIP	0.135 (0.028–0.285)	0.220 (0.090–0.433)	0.200 (0.020–0.360)	0.053
ACI	4.74 (3.55–5.75)[bc]	5.54 (4.14–6.73)[a]	5.30 (4.17–6.79)[a]	0.018*
LCI	20.54 (14.95–37.86)[bc]	32.80 (16.06–61.17)[a]	31.32 (20.44–54.11)[a]	0.025*
T2DM (UAP n=19 / NSTEMI n=41 / STEMI n=96)				
AIP	0.19 (0.09–0.31)	0.29 (0.17–0.51)	0.24 (0.04–0.38)	0.067
ACI	4.69 (2.45–7.18)[bc]	5.80 (1.96–11.49)[a]	5.78 (1.98–14.57)[a]	0.011*
LCI	19.42 (7.64–147.95)[bc]	50.39 (0.82–287.12)[a]	35.59 (3.97–220.83)[a]	0.022*
Non-DM (UAP n=27 / NSTEMI n=60 / STEMI n=173)				
AIP	0.09 (0.01–0.23)	0.19 (0.00–0.38)	0.18 (0.02–0.34)	0.206
ACI	4.96 (3.68–5.87)	5.13 (3.81–6.64)	5.15 (4.11–6.46)	0.465
LCI	22.87 (14.98–42.07)	25.45 (13.99–50.31)	29.31 (20.21–52.07)	0.120

Data are median (IQR, quartiles 1–3). Kruskal-Wallis test with Dunn post-hoc analysis; variables were non-normally distributed (Shapiro-Wilk test). Superscript letters denote the spectra from which a value differs significantly on post-hoc testing: [a] differs from UAP, [b] differs from NSTEMI, [c] differs from STEMI (p<0.05). Significant post-hoc contrasts — whole cohort: ACI UAP vs NSTEMI p=0.013, UAP vs STEMI p=0.006; LCI UAP vs NSTEMI p=0.038, UAP vs STEMI p=0.005. T2DM: ACI UAP vs NSTEMI p=0.004, UAP vs STEMI p=0.006; LCI

*UAP vs NSTEMI p=0.011, UAP vs STEMI p=0.031. NSTEMI vs STEMI not significant. *p<0.05. AIP, atherogenic index of plasma; ACI, atherogenic combined index; LCI, lipoprotein combined index; UAP, unstable angina pectoris; NSTEMI, non-ST-elevation myocardial infarction; STEMI, ST-elevation myocardial infarction.*

Table 4. Association of above-cut-off atherogenic lipid indices with type 2 diabetes mellitus in the overall acute coronary syndrome cohort

Index	Cut-off	AUC (%)	OR (95% CI)	p value
AIP	>0.24	58.5	1.82 (1.21–2.71)	0.004*
ACI	>7.08	54.9	2.09 (1.28–3.41)	0.005*
LCI	>29.47	58.3	2.02 (1.34–3.04)	<0.001*

*OR = odds of T2DM for index above vs below cut-off; chi-square test. AUC for discrimination of glycemic status. *p<0.05.*

Table 5. Association of above-cut-off atherogenic lipid indices with type 2 diabetes mellitus within each acute coronary syndrome spectrum

Index	Cut-off	UAP		NSTEMI		STEMI	
		OR (95% CI)	p value	OR (95% CI)	p value	OR (95% CI)	p value
AIP	>0.24	2.04 (0.56–7.50)	0.278	2.79 (1.23–6.34)	0.013*	1.54 (0.93–2.55)	0.090
ACI	>7.08	0.44 (0.04–4.63)	0.632	2.63 (1.00–6.92)	0.046*	2.23 (1.22–4.06)	0.008*
LCI	>29.47	0.99 (0.29–3.35)	0.989	3.79 (1.58–9.10)	0.002*	1.89 (1.13–3.16)	0.015*

*Values are odds ratios (OR) with 95% confidence intervals (95% CI) for an above-cut-off index (AIP >0.24; ACI >7.08; LCI >29.47) in patients with T2DM versus without, computed for each ACS spectrum and for the overall cohort. An OR >1 indicates that an above-cut-off index was more frequent in diabetic patients. Chi-square test, or Fisher's exact test when expected counts <5. Subject numbers: UAP (T2DM 19 / non-DM 27), NSTEMI (41 / 60), STEMI (96 / 173), and the overall association is shown in Table 4. Associations were concentrated in the infarction groups (NSTEMI and STEMI) and were not significant in UAP. *p<0.05. AIP, atherogenic index of plasma; ACI, atherogenic combined index; LCI, lipoprotein combined index; UAP, unstable angina pectoris; NSTEMI, non-ST-elevation myocardial infarction; STEMI, ST-elevation myocardial infarction.*

3.4 Associations with coronary vessel disease

Associations between above-cut-off indices and single-vessel versus multivessel disease are presented in Table 6. Among the 360 patients with defined obstructive coronary artery disease, none of the three indices was significantly associated with multivessel disease in the whole cohort or in either glycemic subgroup (all P>0.05).

Table 6. Association of above-cut-off atherogenic lipid indices with coronary severity (single-vessel versus multivessel disease) according to glycemic status

Index	Cut-off	1VD, n (%)	Multivessel, n (%)	OR (95% CI)	p
Whole cohort (1VD n=108; multivessel n=252)					
AIP	>0.24	48 (44)	109 (43)	0.95 (0.61–1.50)	0.926
ACI	>7.08	22 (20)	50 (20)	0.97 (0.55–1.70)	1.000
LCI	>29.47	58 (54)	144 (57)	1.15 (0.73–1.81)	0.626
T2DM (1VD n=35; multivessel n=103)					
AIP	>0.24	21 (60)	51 (50)	0.65 (0.30–1.42)	0.380
ACI	>7.08	10 (29)	29 (28)	0.98 (0.42–2.29)	1.000

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Index	Cut-off	1VD, n (%)	Multivessel, n (%)	OR (95% CI)	p
LCI	>29.47	24 (69)	67 (65)	0.85 (0.38–1.94)	0.862
Non-DM (1VD n=73; multivessel n=149)					
AIP	>0.24	27 (37)	58 (39)	1.09 (0.61–1.94)	0.895
ACI	>7.08	12 (16)	21 (14)	0.83 (0.39–1.80)	0.794
LCI	>29.47	34 (47)	77 (52)	1.23 (0.70–2.15)	0.568

*Indices categorized by ROC cut-offs derived for glycemic status. OR = odds of multivessel disease for index above vs below cut-off; chi-square (Fisher when expected <5). Analysis restricted to defined obstructive CAD (n=360). *p<0.05.*

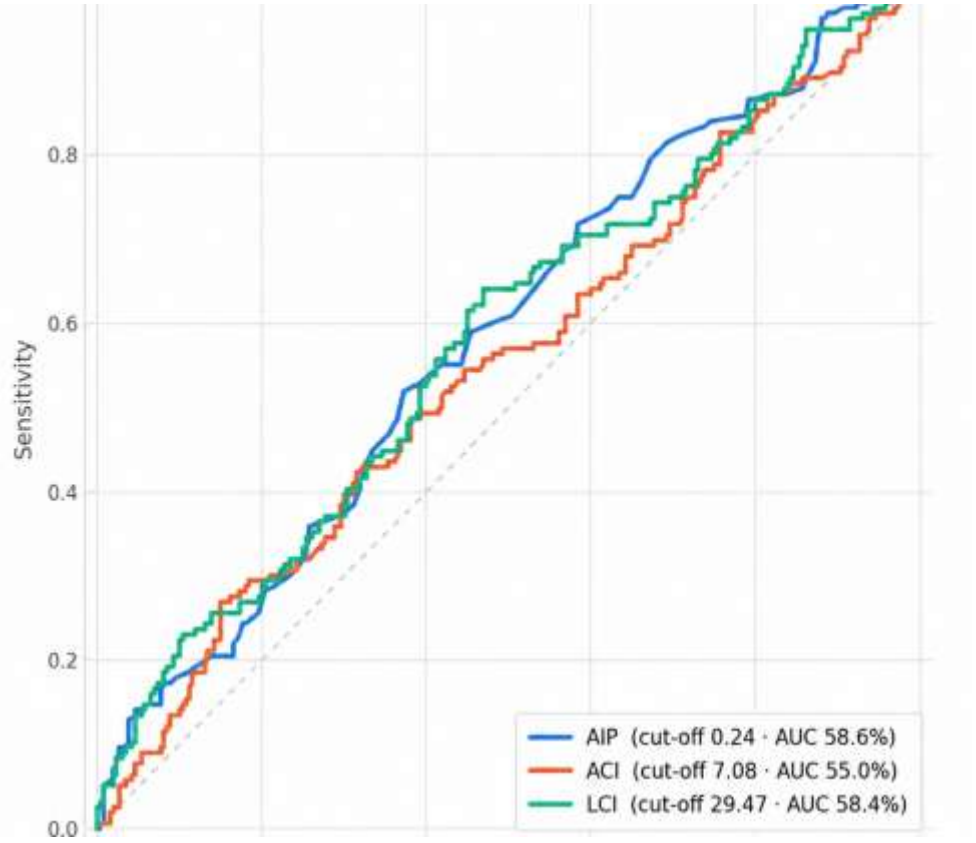


Figure 1. Receiver-operating-characteristic (ROC) curves of the non-traditional lipid indices (AIP, ACI and LCI) for type 2 diabetes mellitus status in patients with ACS. AUC: AIP 0.585; ACI 0.549; LCI 0.583.

3.5 Discussion

Composite indices and diabetic dyslipidemia

The advantage of composite indices compared to individual lipids in T2DM aligns with the biological mechanisms of diabetic dyslipidemia. Insulin resistance leads to increased production of triglyceride-rich, apolipoprotein B-containing very-low-density lipoproteins by the liver, slows their removal, and, through the action of cholesteryl ester transfer protein and hepatic lipase, results in HDL enriched with triglycerides and small, dense LDL particles. These particles are more prone to oxidation and retention within the arterial wall [6–9]. Because each LDL particle carries a single apoB molecule, this small, dense LDL phenotype markedly increases particle number and atherogenicity at any given LDL-C concentration, which explains why LDL-C alone underestimates risk in diabetes [7–9]. By combining triglycerides, non-HDL-C, and HDL-C, AIP, ACI, and LCI approximate this particle burden; AIP in particular tracks LDL particle size and the esterification rate of HDL cholesterol [10], so that the higher AIP and LCI values observed in our diabetic patients are biologically expected.

A non-monotonic relationship between the indices and the acs spectrum

A central and somewhat unexpected observation was that the indices related to the ACS spectrum in a non-monotonic fashion, with the lowest values in UAP and higher, comparable values in NSTEMI and STEMI. This pattern has a coherent pathophysiological basis. Unstable angina reflects myocardial ischemia without significant necrosis and is more often precipitated by plaque erosion or dynamic obstruction of lesions that need not carry a large lipid core, whereas myocardial infarction is more closely tied to the rupture of lipid-rich plaques with a large necrotic core and a thin fibrous cap [20–23]. Atherogenic burden, and hence the indices, therefore rises from UAP to infarction. After the infarction threshold is surpassed, the differentiation between NSTEMI and STEMI is primarily influenced by acute factors unrelated to lipids. These include the location and length of the coronary blockage, the existence of collateral circulation, and the amount of myocardium at risk, rendering the indices ineffective in distinguishing between the two. This graded-then-plateau shape reconciles the weak monotonic (one-versus-rest) correlations with the significant Kruskal-Wallis differences and indicates that a between-group difference framework, rather than correlation, best captures the relationship.

Plaque biology and effect modification by glycemic status

That the differences were confined to T2DM supports genuine effect modification by glycemic status rather than confounding. Intracoronary imaging studies show that diabetic culprit and non-culprit plaques are more lipid-rich, have thinner fibrous caps, and more frequently display features of vulnerability than those of non-diabetic patients [20,21], providing a substrate in which a higher circulating atherogenic burden translates more directly into severe coronary events. Diabetes also broadens and shifts the distribution of atherogenic particles, widening the dynamic range of the indices and improving their ability to discriminate across the spectrum, whereas in non-diabetic patients the baseline atherogenic profile is lighter and more homogeneous and spectrum severity is determined more by plaque instability and thrombosis than by chronic lipid burden. Importantly, lipids were sampled within the first 24 hours of admission, before the acute-phase response substantially lowers cholesterol fractions [24]; the differences observed in diabetic patients are therefore more likely to reflect the pre-infarction atherogenic burden than acute-phase change, which strengthens the interpretation of effect modification.

Differential behavior of the three indices

Among the three indices, ACI and LCI were consistently more discriminative than AIP, which reached only borderline significance in both the whole cohort and the T2DM subgroup. AIP rests on the triglyceride-HDL axis, whereas ACI and LCI additionally incorporate atherogenic cholesterol fractions (non-HDL-C, LDL-C, and total cholesterol) that more directly represent the plaque-forming particle burden. In a subgroup that is entirely diabetic, in which hypertriglyceridemia and low HDL are almost universal, the triglyceride-HDL axis becomes relatively saturated and loses discriminative range, so cholesterol-containing indices remain more informative [8,16]. Consistent with this, LCI, the most comprehensive composite, showed the strongest and most consistent associations across the spectrum, followed by AIP and ACI.

Comparison with previous studies

Our results not only broaden but also enhance the current body of research. Earlier studies have predominantly associated these indices with the existence or angiographic intensity of coronary disease and with negative outcomes. ACI has been confirmed as an indicator of coronary artery disease [13], AIP correlates with angiographic severity and predicts events after percutaneous coronary intervention and in diabetic ACS [14,17,18,25], and non-traditional indices have been associated with in-hospital mortality across the ACS spectrum [19]. Jin et al. also noted that the connection between AIP and the severity of coronary conditions varies depending on the glucose-metabolic state [16], echoing the effect modification we observed. Our study adds a spectrum-level perspective: rather than relating the indices to disease presence or a continuous severity score, we show that they differentiate clinical ACS categories in a non-monotonic, diabetes-dependent manner. The absence of any association with vessel count contrasts with studies that reported correlations with Gensini or SYNTAX scores; this discrepancy most likely reflects the difference between a coarse count of diseased vessels and continuous scores that capture diffuseness and lesion complexity, and it reinforces the interpretation that these indices index systemic metabolic-atherogenic burden and plaque composition rather than anatomical extent.

Clinical and research implications

Clinically, higher ACI and LCI values in diabetic ACS patients denote a heavier residual atherogenic burden that accompanies infarction rather than unstable angina, and these indices are attractive because they are derived at no additional cost from the routine lipid panel. Nonetheless, the statistical significance of between-group differences does not equate to individual discriminative accuracy; the modest AUC values indicate that the indices are best regarded as descriptive markers of metabolic-atherogenic burden rather than stand-alone diagnostic tools, and their lack of association with vessel count means they should not be used to infer anatomical severity. Whether they carry independent prognostic value will require prospective, outcome-based studies. In future research, it is advisable to use continuous angiographic scores or intracoronary imaging, include both short- and long-term clinical outcomes, and, considering the significant signal observed in diabetes, predefine glycemic stratification while ensuring sufficient power for the unstable-angina group.

Strengths and limitations

The main advantage of this study lies in the collection of lipid samples within the initial 24 hours of admission, which reduces the distortion caused by the acute phase and allows the indices to closely reflect the atherogenic burden before infarction. Additionally, the analysis was stratified based on glycemic status and utilized a large angiographic cohort. It assessed three complementary composite indices instead of relying on just one measure. Several limitations temper the findings. By design, the study characterizes associations (correlations and between-group differences) rather than predictive or prognostic performance, so no risk or outcome inference can be drawn. The study's design, being cross-sectional and conducted at a single center, restricts the ability to infer causality and might affect the extent to which the findings can be generalized. The unstable-angina subgroup was relatively small, which reduced statistical power and widened confidence intervals in some analyses. Clinical outcomes were not incorporated into the primary analysis, and residual confounding, for example from statin exposure or the degree of glycemic control, cannot be excluded.

4. CONCLUSION

In patients with ACS, the atherogenic lipid indices, particularly ACI and LCI, distinguished unstable angina from infarction in a non-monotonic pattern that was largely confined to patients with T2DM and absent in non-diabetic patients, and showed no association with the number of diseased coronary vessels, indicating that the indices capture metabolic rather than anatomical burden. Type 2 diabetes thus modified the relationship between the indices and the ACS spectrum, with LCI emerging as the strongest and most consistent marker. Because the study was cross-sectional, these findings describe associations and between-group differences rather than predictive performance, and identify ACI and LCI as inexpensive, routinely available markers of metabolic-atherogenic burden in diabetic ACS, whereas their value for risk stratification and prognosis remains to be established in prospective, outcome-based studies.

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AUTHOR CONTRIBUTIONS

M, FMSA, AMA, SB, PT, IJP, and HR contributed to the conception and design of the study. M performed data acquisition and analysis. M wrote the first draft of the manuscript. FMSA, AMA, SB, PT, IJP, and HR critically revised the manuscript. All authors approved the final version and agreed to be accountable for all aspects of the work.

CONFLICT OF INTEREST

The authors state that there is no conflict of interest concerning this study.

ETHICS STATEMENT

Approval for the study was granted by the Health Research Ethics Committee of the Faculty of Medicine at Hasanuddin University (approval no. 605/UN4.6.4.5.31/PP36/2026), and it was carried out following the guidelines of the Declaration of Helsinki.

DATA AVAILABILITY STATEMENT

Upon reasonable request, the corresponding author can provide access to the datasets examined in this study.

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