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RESEARCH PAPER

Association of Calculated Lipid Indices with Coronary Artery Disease severity (assessed by SYNTAX score) and Their Role as Biomarker for Detection of Severe Coronary Artery Disease

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Abstract

Background: Coronary Artery Disease (CAD) is a leading cause of morbidity and mortality globally, with its rising prevalence, especially in South Asia. Dyslipidemia is a well-established risk factor for CAD. Recent research has focused on novel lipid indices like atherogenic Index (AI), atherogenic index of plasma (AIP), lipoprotein combine index (LCI), castelli risk index- I (CRI-I) & castelli risk index-II (CRI-II). These are calculated simply from fasting lipid profile components and they can act as potential predictors of CAD severity. Therefore, these lipid indices offer more comprehensive assessment of atherogenic risk and CAD severity compared to individual lipid components.

Objective: To evaluate the association of calculated lipid indices with severity of CAD and to assess their role as diagnostic biomarker for detection of coronary artery disease severity (assessed by SYNTAX score).

Methods: This cross-sectional study was conducted at Sir Salimullah Medical College (SSMC) from March 2024 to February 2025. Total 218 patients (age 18- 70 years) with CAD were purposively selected as study subjects from the Cardiology department of Sir Salimullah Medical College Mitford Hospital (SSMCMH) and National Institute of Cardiovascular Diseases (NICVD), Dhaka. The demographic, clinical, and biochemical data were collected. Fasting lipid profile was measured in every patient and lipid indices were calculated using the values of lipid profile components. For all patients coronary angiogram were done, SYNTAX score were calculated to assess CAD severity. All (218) subjects were divided into three groups according to their SYNTAX score; mild CAD (low risk, SYNTAX Score 0 - 22), moderate CAD (intermediate risk; SYNTAX Score 23 - 32) and severe CAD (high risk; SYNTAX Score of > 32). The associations of lipid indices with CAD severity was analyzed by unpaired t-test, spearman rank correlation coefficient test and logistic regression test. To evaluate the diagnostic performance of lipid indices for detection of CAD severity, their cutoff points were determined by Youden Index. Using those cutoff points diagnostic performance of lipid indices were evaluated by ROC (receiver operator characteristic) curve analysis, AUC (area under curve) and performance tests (sensitivity, specificity, positive predictive value, negative predictive value, accuracy). Statistical significance was set at $p \leq 0.05$.

Results: Unpaired t-test, Spearman rank correlation coefficient test, logistic regression analysis revealed positive correlation and association of calculated lipid indices with the CAD severity. The CRI-II had the highest (0.647) area under the curve (AUC), and AIP had lowest (0.606) AUC. As predictors of CAD severity AI, and CRI-I showed 68.8% sensitivity, 54.8% specificity, 86.43% PPV, 29.48% NPV, 66.05% accuracy with cutoff point 3.0 and 4.0 respectively. AIP and LCI showed 71.6% sensitivity, 52.4% specificity, 86.3% PPV, 30.55% NPV, 67.89% accuracy with cutoff point 0.13 for both. CRI-II showed 62.5% sensitivity, 59.5% specificity, 86.61% PPV, 27.47% NPV, 61.93% accuracy with cutoff point 4.0

Conclusion: The calculated lipid indices were found to be positively associated with CAD severity and positively correlated with SYNTAX score. The diagnostic performance of calculated lipid indices for detection of CAD severity was not satisfactory because their AUC, sensitivity and specificity were not promising.

Keywords: Coronary Artery Disease (CAD), Atherogenic Index (AI), Atherogenic Index of Plasma (AIP), Lipoprotein Combine Index (LCI), Castelli Risk Index I (CRI-I), Castelli Risk Index II (CRI-II), SYNTAX Score (SS)

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Introduction

Coronary artery disease (CAD) is the most common cardiovascular condition that poses a serious risk to the people in both developed and developing countries.[1, 2] Increasing socioeconomic status in the

developing countries has led to an epidemic rise in the risk factors for coronary artery disease in younger adults.[3] Disproportionately, it is more common in South Asians.[4] In Bangladesh, the prevalence ranges from 0.33% to 19.6% as reported in many studies. Despite marked disparity in values, there seems to be a rising prevalence & mortality from CAD.[5]

The main cause of coronary artery disease (CAD) is atherosclerosis, which is influenced by a number of factors such as oxidative stress, inflammation and endothelial dysfunction.[6] The development of atherosclerosis is largely dependent on plasma lipid's capacity to migrate into the sub intimal layer.[7] Dyslipidemia has been widely studied and found to have significant association with the development and progression of CAD.[6] Dyslipidemia is characterized by raised levels of serum total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and reduced level of serum high-density lipoprotein cholesterol (HDL-C).[8]

The primary goal of lipid lowering therapy in clinical practice targets to reduce LDL-C, but residual cardiovascular risk remains even after reduction of LDL-C to the reference range.[9] Thus rather than depending just one lipid measure, using a variety of lipid indices may provide a more thorough assessment of lipid state.[6] Recently calculated lipid indices, such as the Atherogenic index of plasma (AIP), Atherogenic index (AI), Lipoprotein combine index (LCI) , Castelli risk index-I (CRI-I), and Castelli risk index-II (CRI-II,) have emerged as potential predictors of CAD severity.[10.11] They are obtained from the results of fasting lipid profile by calculation according to individual equation. May be a person's TG, TC, LDL-C, HDL-C within normal range but the ratios calculated from these parameters show a significant difference ($p<0.05$).[12]

The atherogenic index of plasma (AIP),is the logarithm of the molar ratio of triglyceride (TG) to high-density lipoprotein cholesterol (HDL-C) levels, is inversely proportional to the diameter of LDL-C particles and hence indirectly indicates sdLDL levels.[13] Compared to buoyant low-density lipoprotein small dense low-density lipoprotein (sdLDL) is more atherogenic.[14] The 2002 National Cholesterol Education Program documented sdLDL as a new hazard for CAD.[15] However, the application of this measurement in clinical practice has been limited because of the high cost and complexity of the test.[13]

Atherogenic Index (AI) or Atherogenic Coefficient is the ratio of Non-HDL Cholesterol and HDL Cholesterol. Non-high-density lipoprotein cholesterol (non-HDL-C) has become a new target in the fight against cardiovascular events.[16] All potentially atherogenic particles, including remnant lipoproteins, very low-density lipoproteins, intermediate density lipoproteins, and LDL-C, carry cholesterol that is classified as non-HDL-C. In both baseline and treatment settings, non-HDL-C showed a stronger correlation with cardiovascular risk than LDL-C, according to multiple meta-analyses.[17,18]

Lipoprotein combine index (LCI), is calculated as (TC×TG×LDL-C)/HDL-C. The predictive efficacy of classic single lipid indicators has been surpassed by this LCI, which may act as a potential predictor of CAD severity.[19] William Castelli reported Castelli's risk indexes, also called the cardiac risk indexes which are two lipid ratios. CRI-I is the ratio of TC to HDL-C and CRI-II is the ratio of LDL-C to HDL-C. These two ratios (CRI-I, CRI-II) are positively associated with CAD risk. [20,21]

SYNTAX score is a coronary angiography-based anatomical scoring system.[22] It is used to assess the extent and severity of coronary artery disease (CAD). SYNTAX score > 32 has been defined as high risk, 23 – 32 as intermediate-risk and 0–22 as low risk.[23] The greater the score, the worse the prognosis.[13]

To improve cardiovascular disease diagnostic and treatment approaches, new biomarkers are required. In clinical practice, biomarkers are valuables tools. SYNTAX score could be a reliable indicator of CAD expansion to link with coronary atherosclerosis biomarkers.[24] Study reveals that CAD subjects has a significantly higher values of Atherogenic Index, Atherogenic Index of Plasma, Lipoprotein Combine Index, and Castelli Risk Index-I, Castelli Risk Index-II.[6] Considering all these, this study was designed to evaluate the association of lipid indices with the SYNTAX score in patients with established CAD.

Materials and Methods

This cross-sectional study was carried out in the department of biochemistry, Sir Salimullah Medical

College, Dhaka, Bangladesh, from March 2024 to February 2025. Purposive sampling was used to select 218 patients who were scheduled for coronary angiography and clinically diagnosed of having coronary artery disease (CAD). Participants were recruited from the department of Cardiology, Sir Salimullah Medical College Mitford Hospital (SSMCMH), and the National Institute of Cardiovascular Diseases (NICVD), Dhaka. Individuals with a history of coronary artery bypass grafting (CABG) or coronary stenting, hepatic or renal dysfunction, thyroid disorders, malignancy, diabetes mellitus, or decompensated heart failure were excluded from the study. Both dependent and independent variables were analyzed in this study. The independent variables included the calculated lipid indices—Atherogenic Index (AI), Atherogenic Index of Plasma (AIP), Lipoprotein Combine Index (LCI), Castelli Risk Index I (CRI-I), and Castelli Risk Index II (CRI-II). The dependent variable was the SYNTAX score, which represents the angiographic severity of CAD.

Venous blood samples (3 mL) were collected from all participants after 10–12 hours of over night fasting using standard aseptic precautions. The samples were centrifuged, and serum was separated for biochemical analysis. Lipid profile parameters were analyzed in the Biochemistry laboratory of Sir Salimullah Medical College using standard enzymatic methods: total cholesterol (TC) was measured by the cholesterol oxidase (CHOD-PAP) method, triglycerides (TG) by the GPO-PAP method, and high-density lipoprotein cholesterol (HDL-C) by the CHOD-PAP method. Low-density lipoprotein cholesterol (LDL-C) was calculated using the Friedewald formula. All the lipid indices were then calculated: Atherogenic Index (AI) = non-HDL-C / HDL-C; Atherogenic Index of Plasma (AIP) = log (TG / HDL-C); Lipoprotein Combine Index (LCI) = (TC × TG × LDL-C) / HDL-C; Castelli Risk Index I (CRI-I) = TC / HDL-C; and Castelli Risk Index II (CRI-II) = LDL-C / HDL-C.

All patients underwent coronary angiography according to standard institutional protocols. The SYNTAX score, which quantifies the extent and complexity of coronary artery disease, was calculated using a web-based tool. The angiograms were evaluated independently by experienced cardiologists who were blinded to the study protocol, the participant's baseline clinical and biochemical data. SYNTAX score is a coronary angiography-based anatomical scoring system.[22] It is used to assess the extent and severity of coronary artery disease (CAD). SYNTAX score > 32 has been defined as high risk, 23 – 32 as intermediate-risk and 0–22 as low risk.[23] The greater the score, the worse the prognosis.[13]

Ethical approval for this study was obtained from the Institutional Ethics Committee of Sir Salimullah Medical College, Dhaka, Bangladesh. All participants were fully informed about the purpose, procedures, and potential risks of the study, and written informed consent was obtained before enrollment. Socio-demographic and clinical data were collected using a pretested structured questionnaire.

Statistical analyses were performed using SPSS Version 26. Continuous variables were expressed as mean ± SD, and categorical variables as frequencies and percentages. Group comparisons were made using the unpaired t-test. Correlations between lipid indices and SYNTAX score were assessed by Spearman's rank correlation coefficient test. Logistic regression analysis was done to identify independent predictors of CAD severity. To evaluate the diagnostic performance of lipid indices for detection of CAD severity, their cutoff points were determined by Youden Index and using those cutoff points diagnostics performance were evaluated by ROC curve analysis and performance tests (sensitivity, specificity, positive predictive value, negative predictive value, accuracy). A p-value ≤ 0.05 was considered statistically significant.

Results

A total of 218 CAD subjects were included in this study. Out of the 218 subjects included in the study, the severity of coronary artery disease (CAD) was assessed using the SYNTAX score. Mild CAD (SYNTAX score 0–22) was observed in 42 subjects (19.3%), moderate CAD (SYNTAX score 23–32) in 94 subjects (43.1%), and severe CAD (SYNTAX score >32) in 82 subjects (37.6%)(table-I). These findings indicate that most of the study subjects had moderate to severe coronary artery involvement according to the SYNTAX scoring system.

Table I: Distribution of the study subject according to SYNTAX Score used to assess the CAD severity (N=218)

Grouping of CAD	Syntax score	Number of subjects	Percentages of subjects
Mild	0-22 (low risk)	42	19.3%
Moderate	23-32 (Intermediate risk)	94	43.1%
Severe	>32 (High risk)	82	37.6%

The severe CAD showing significantly higher values of all lipid indices AI(3.31 ± 1.68 vs 3.79 ± 0.89), AIP (0.16 ± 0.2 vs 0.2 ± 0.1), LCI (18.40 ± 8.7 vs 21.25 ± 7.53), CRI(4.31 ± 1.13 vs 4.8 ± 0.89), and CRI-II(2.69 ± 0.80 vs 3.15 ± 0.73) compared to those with mild and moderate CAD ($p < 0.05$ for all), indicating a greater atherogenic risk in the severe group (table-II).

Table II: Calculated lipid indices between mild to moderate and severe coronary artery disease (CAD)

Characteristics	Mild and Moderate (n=136)	Severe (n = 82)	*p* value
AI	3.31 ± 1.68	3.79 ± 0.89	<0.001
AIP	0.16 ± 0.2	0.2 ± 0.1	0.03
LCI	18.40 ± 8.7	21.25 ± 7.53	0.029
CRI-I	4.31 ± 1.13	4.8 ± 0.89	0.005
CRI-II	2.69 ± 0.80	3.15 ± 0.73	<0.001

Unpaired t-test done

All calculated lipid indices (AI, AIP, LCI, CRI-I, and CRI-II) have a significant positive correlation with the SYNTAX score (r = 0.353–0.376, p < 0.001), indicating that higher lipid indices are associated with increased severity of coronary artery disease(table-III).

Table III: Correlation of calculated lipid indices with SYNTAX Score (N = 218)

Calculated lipid indices	Correlation coefficient (r)	*p*-value
AI	0.376	< 0.001
AIP	0.353	< 0.001
LCI	0.368	< 0.001
CRI-I	0.376	< 0.001
CRI-II	0.361	< 0.001

Spearman rank correlation coefficient test done

The logistic regression analysis showed that among individual lipid parameters, HDL-C was significantly protective against severe CAD (adjusted OR = 0.124, 95% CI: 0.019–0.823, p = 0.031), while all lipid indices (AI, AIP, LCI, CRI-I, and CRI-II) were independently associated with increased risk of severe CAD. Specifically, AIP (adjusted OR = 3.037, 95% CI: 2.415–4.190, p = 0.007) and CRI-II (adjusted OR = 2.108, 95% CI: 1.265–3.515, p = 0.004) showed the strongest association, indicating that higher atherogenic indices significantly increase the likelihood of severe coronary artery disease. Triglycerides, total cholesterol, and LDL-C were not significant after adjustment (table-IV).

The diagnostic performance of calculated lipid indices for detecting severe CAD showed that AIP and LCI had the highest sensitivity (71.6%) and moderate specificity (52.4%), with an overall accuracy of 67.89%. AI and CRI-I had slightly lower sensitivity (68.8%) and almost similar specificity (54.8%), with an accuracy of 66.05%. CRI-II had the highest specificity (59.5%)

Table IV: Logistic regression analysis of lipid parameters with the severity of coronary artery disease (CAD)

Variables	Unadjusted		Adjusted	
	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
TG	1.565 (0.507 - 4.832)	0.436	2.151 (0.634 -7.299)	0.219
TC	1.316 (0.779 - 2.223)	0.306	1.149 (0.660 - 2.001)	0.624
LDL-C	1.94 (1.051 - 3.579)	0.034	1.797 (0.922 - 3.502)	0.085
HDL-C	0.196 (0.031 - 0.922)	0.04	0.124 (0.019 - 0.823)	0.031
AI	1.53 (1.085 - 2.157)	0.015	1.49 (1.035 - 2.144)	0.032
AIP	3.85 (1.887 - 6.279)	0.017	3.037 (2.415 - 4.190)	0.007
LCI	1.059 (1.009 - 1.112)	0.02	1.072 (1.014 - 1.133)	0.027
CRI-I	1.53 (1.085 - 2.157)	0.015	1.49 (1.035 - 2.144)	0.032
CRI-II	2.113 (1.314 - 3.399)	0.002	2.108 (1.265 – 3.515)	0.004

Table V: Comparison of the diagnostic performance of calculated lipid indices for detecting severity of CAD (N = 218)

Calculated lipid indices	Cut of point	Sensitivity	Specificity	PPV	NPV	Accuracy
AI	3.0	68.8%	54.8%	86.43%	29.48%	66.05%
AIP	0.13	71.6%	52.4%	86.3%	30.55%	67.89%
LCI	0.13	71.6%	52.4%	86.3%	30.55%	67.89%
CRI-I	4.0	68.8%	54.8%	86.43%	29.48%	66.05%
CRI-II	4.0	62.5%	59.5%	86.61%	27.47%	61.93%

but the lowest sensitivity (62.5%) and accuracy (61.93%). All indices demonstrated high positive predictive values (≈ 86%), indicating good ability to correctly identify patients with severe CAD, though negative predictive values were low (27–30%), reflecting limited ability to rule out severe disease (table-V).

The ROC curve showed the diagnostic performance of the lipid indices (AI, AIP, LCI, CRI-I, and CRI-II) in detecting the severity of CAD. All indices show curves above the reference line, indicating better-than-chance discrimination. The AI (dotted maroon) and CRI-II (purple) curves appear to have slightly better overall sensitivity and specificity across different thresholds compared to others. However, none of the indices show a markedly superior curve, suggesting comparable diagnostic abilities among these lipid indices for predicting severe CAD (figure 1).

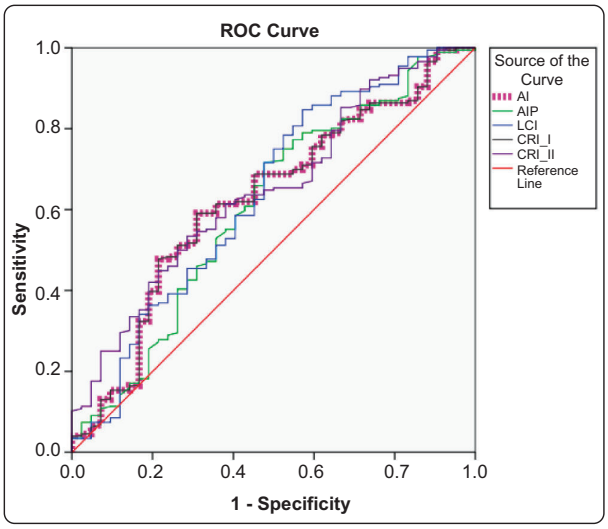

Figure 1: ROC curve analysis of Calculated Lipid Indices

AUC of AI 0.626, AIP 0.606, LCI 0.635, CRI-I 0.626, CRI-II 0.647

Discussion

The present study evaluated the role of calculated lipid indices—Atherogenic Index (AI), Atherogenic Index of Plasma (AIP), Lipoprotein Combine Index (LCI), Castelli Risk Index I (CRI-I), and Castelli Risk Index II (CRI-II)—as predictors of coronary artery disease (CAD) severity among patients attending tertiary hospitals in Bangladesh. Using the SYNTAX score as the benchmark for disease severity, we demonstrated that these indices are significantly elevated in patients with severe CAD and are positively correlated with the angiographic extent of coronary atherosclerosis.

In this study, most patients presented with moderate (43.1%) or severe CAD (37.6%), while only 19.3% had mild disease. Comparable findings have been reported in other South Asian populations, where delayed diagnosis and clustering of metabolic risk factors contribute to an increased burden of severe CAD at first presentation. This emphasizes the need for improved screening strategies and earlier identification of high-risk individuals. [6,10]

All calculated lipid indices showed significant associations with CAD severity. After adjustment for confounders, AI, AIP, LCI, CRI-I, and CRI-II remained independent predictors, with AIP and CRI-II showing the strongest associations. These findings are consistent with earlier studies reporting that lipid-derived indices, which reflect the balance between atherogenic and protective lipoproteins, offer better predictive power for CAD risk than single lipid measurements. Notably, low HDL-C was protective in our study, reaffirming the well-established inverse relationship between HDL cholesterol and atherosclerosis progression. .[6,13]

Comparison with prior literature supports the relevance of these findings. Studies from different populations

have shown that CRI-I and CRI-II, which integrate total cholesterol and HDL-C, are strongly linked to angiographic severity of CAD. Similarly, AIP has been reported to correlate with both subclinical atherosclerosis and clinical outcomes, reflecting its capacity to capture the atherogenic potential of triglyceride-rich lipoproteins relative to HDL. Our observation that AIP had the highest sensitivity is in line with its recognized role as an early marker of atherogenic dyslipidemia, particularly in South Asian patients who often present with low HDL and high triglyceride levels. [6,13]

The diagnostic accuracy of the lipid indices, however, was modest. ROC curve analysis revealed that CRI-II and LCI had the highest AUC values (0.647 and 0.635, respectively), while AIP showed the lowest (0.606). Although the discriminative power was not strong, the indices demonstrated practical utility: AIP and LCI offered higher sensitivity (71.6%), making them suitable for early screening, whereas CRI-II achieved the highest specificity (59.5%), making it more valuable for confirming disease severity.

Fourth, ROC analysis showed only moderate predictive accuracy, suggesting that lipid indices alone are insufficient for precise risk prediction. Finally, the absence of comparable ROC data from previous studies limited the scope of direct benchmarking.

In summary, this study demonstrates that calculated lipid indices are significantly associated with CAD severity and remain independent predictors even after adjustment for conventional risk factors. While their diagnostic performance is modest, they offer a low-cost, accessible tool that may complement existing strategies for early risk assessment, particularly in resource-constrained settings. These findings highlight the potential clinical utility of lipid indices in identifying high-risk individuals and underscore the importance of incorporating them into broader preventive cardiology frameworks.

Conclusion

AI, AIP, LCI, CRI-I and CRI-II were found to be positively associated with CAD severity, but as diagnostic biomarkers for detection of CAD severity their performance is not satisfactory because their AUC, sensitivity and specificity were not very high.

Conflict of Interest: There are no conflicts of interest.

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Ethical Clearance:

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