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Multi-Biomarker Stratification of Coronary Artery Disease in Diabetic and Non-Diabetic Patients: Adiponectin, Inflammation, and Insulin Resistance

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ABSTRACT

Background: Coronary artery disease [CAD] remains a leading cause of global mortality, with higher prevalence among individuals with type 2 diabetes mellitus [T2DM]. Limited data exist on biomarker interactions in CAD patients with and without T2DM.

Objective: This study aimed to investigate correlations among adiponectin, inflammatory markers, and metabolic factors in CAD patients and evaluate their association with T2DM status.

Methods: A cross-sectional study enrolled 225 participants: 75 healthy controls, 75 CAD patients with T2DM, and 75 CAD patients without T2DM. Serum levels of adiponectin, hs-CRP, IL-6, E-selectin, insulin, and C-peptide were measured using ELISA. Lipid profiles were analyzed via automated analyzer. Statistical analysis included ANOVA, correlation analysis, multicollinearity assessment, regression, and ROC analysis.

Results: All biomarkers showed significant differences across groups [$p<0.05$]. Adiponectin levels were lowest in CAD with T2DM [4.2 ± 1.0 mg/L vs 7.4 ± 1.6 mg/L in controls, $p<0.001$]. Inflammatory markers were elevated in both CAD groups, with highest levels in diabetic patients. ROC analysis revealed moderate discriminative ability: adiponectin [AUC=0.79], hs-CRP [AUC=0.83], E-selectin [AUC=0.75], and insulin [AUC=0.72]. In the multivariable regression model, insulin emerged as the superior insulin-secretion marker over C-peptide, after accounting for multicollinearity and excluding participants with renal impairment.

Conclusion: This study demonstrates significant associations between reduced adiponectin, elevated inflammatory markers, and metabolic dysfunction in CAD patients, particularly those with T2DM. An adiponectin threshold of ≤5.0 mg/L may serve as a practical clinical alert for high cardiovascular risk in diabetic patients. These findings warrant further prospective investigation to determine their potential clinical utility. These findings warrant further prospective investigation to determine their potential clinical utility.

Keywords: adiponectin, biomarkers, coronary artery disease, hs-CRP, insulin resistance, type 2 diabetes mellitus.

Introduction

One of the leading causes of morbidity and death in the world today is coronary artery disease [CAD], which is defined by the accumulation of atherosclerotic plaques in the coronary arteries [1]. Other metabolic anomalies that, when combined with hereditary predisposition, cause the condition include dyslipidaemia, hypertension, obesity, and type 2 diabetic mellitus [T2DM] [2]. Lipoprotein deposition, endothelial activation, vascular smooth muscle cell proliferation, and persistent arterial wall inflammation are all intricately linked to atherosclerosis [3].

The identification of molecular biomarkers has helped to develop the knowledge on CAD and highlight the central roles of adipokines, pro-inflammatory cytokines, and endothelial markers in its pathophysiology. Adiponectin, a 30kDa compound released by adipocytes has proven to be the main controller of metabolic and cardiovascular homeostasis [4]. In contrast to other adipokines, adiponectin improves the work of endothelium, suppresses the growth of smooth-muscle-cells, reduces the vascular inflammation, and increases the insulin sensitivity [5]. Reduced levels of adiponectin in the circulation have been linked with increased risk of CAD especially in diabetic patients with T2DM and metabolic syndrome [6].

Inflammation is the primary cause of atherosclerosis and CAD. An independent predictor of unfavourable cardiovascular events is high sensitivity C-reactive protein [hs-CRP], which is generated by hepatic cells in response to pro-inflammatory cytokines such interleukin-6 [IL-6] [7]. Strong hs-CRP is linked to plaque instability, endothelial dysfunction, and artery stiffness [8]. In order to attract leukocytes to the sites of vascular damage, IL-6 stimulates acute-phase protein production and increases endothelial adhesion factors like E-selectin [9,10].

The phenomenon of insulin resistance, which is characteristic of T2DM, increases atherosclerosis due to hyperinsulinemia that contributes to vascular inflammation, dysfunction of endothelium, and proliferation of smooth-muscle-cells [11]. In addition, C-peptide, a product of insulin production can be also involved in pro-inflammatory signaling pathways that are activated during CAD development especially in insulin-resistant groups [12]. Although C-peptide is traditionally regarded as a more stable marker of endogenous insulin secretion owing to its longer half-life and absence of first-pass hepatic metabolism, its circulating levels are also influenced by renal clearance, which may introduce variability in populations with subclinical renal dysfunction. Dyslipidemia is a heart attack risk factor as it is an established risk factor of CAD [13].

The interaction between these metabolic and inflammatory biomarkers can provide information on how these biomarkers can be used in the early detection and risk stratification of CAD, particularly in diabetic groups. Adiponectin exhibits well-documented gender specificity, with higher concentrations in females, a pattern that may be further modulated by sex steroid levels and menopausal status, particularly in the 30–50-year age group. The current study aims at enhancing the understanding of the pathophysiology of CAD under the presence of insulin resistance and diabetes.

Aim: This study aims to evaluate the relationships between circulating levels of adiponectin and a number of inflammatory biomarkers, including high-sensitivity C-reactive protein, interleukin-6, and E-selectin, as well as metabolic factors, such as insulin and C-peptide concentrations in the blood of individuals with coronary artery disease. Additionally, the study will be stratified based on whether type 2 diabetes mellitus is present, and lipid profiles will be compared based on these subgroups.

Methods

Study Design and Setting

The study was a cross-sectional research based on observation of the general medicine and cardiology outpatient units of a tertiary care hospital in Coimbatore, India. The intrinsic ethics committee gave its ethical approval (Approval No: IHEC/305/Biochemistry/08/2023). Informed consent was gathered in the form of written consent. The research was not prospectively registered, because no interventional procedures were involved in the research.

Sample Size Calculation

Sample size calculation was performed using G*Power 3.1.9.7 software based on a one-way ANOVA design with three groups. Using an effect size of 0.8 [derived from previous adiponectin studies], $\alpha = 0.05$, and power = 0.80, the minimum required sample was 64 participants per group. We enrolled 75 participants per group [n = 225 total] to ensure robust statistical power and account for potential data variability.

Participants

A total of 225 subjects was divided into three groups, namely Group 1 (Control) consisted of 75 healthy adults who had never had a history of cardiovascular disease or diabetes mellitus; Group 2 (CAD with T2DM) consisted of 75 patients with both coronary artery disease and type 2 diabetes mellitus; and Group 3 (CAD without diabetes) comprised 75 patients with coronary artery disease but without diabetes.

The inclusion criteria included individuals with a clinical diagnosis of CAD through coronary angiography and electrocardiography between the ages of 30 and 50 years. Diabetes was assessed based on the criteria of American Diabetes Association.

The exclusion criteria included active or chronic infections, autoimmune disease, malignancy, pregnancy, or recent coronary bypass grafting, or administration of drugs that may affect cardiovascular or metabolic values. Participants with known chronic kidney disease or an estimated glomerular filtration rate [eGFR] below 60 mL/min/1.73 m² were also excluded to minimise the potential confounding effect of impaired renal clearance on C-peptide concentrations. Additionally, participants receiving insulin sensitizers such as metformin or thiazolidinediones were documented separately; those on active injectable insulin therapy were excluded, as exogenous insulin administration directly confounds the measurement of circulating insulin and related indices.

Sample Collection and Processing

Aseptic methodology was used to collect venous blood samples following 12 hours of an overnight fast. The plasma was separated out of tubes filled with EDTA anticoagulant and serum was obtained out of tubes lacking anticoagulant. Samples were treated instantly; plasma, serum, was centrifuged at 3000 rpm and 10 min at 4°C and stored at -80°C until analysis.

Biochemical Analyses

Standardised enzyme-immunoassay techniques were used to evaluate serum levels of adiponectin, high sensitivity C-reactive protein (hs-CRP), interleukin-6 (IL-6), E-selectin, insulin, and C-peptide. Every test was performed twice in compliance with the manufacturer's instructions. Each biomarker had coefficients of variation of less than 10% both within and across assays. A Roche automated analyser was used to measure

lipid parameters, including total cholesterol, triglycerides, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol, while rigorous quality control procedures were followed. Fasting plasma glucose was measured on the same venous sample, and the homeostasis model assessment of insulin resistance [HOMA-IR] was calculated using the standard formula: HOMA-IR = [fasting insulin (μU/mL) × fasting glucose (mmol/L)] / 22.5, to provide a standardised index of insulin resistance in addition to absolute fasting insulin values.

Statistical Analysis

Data processing was done using version 25 of the SPSS Statistical Package for the Social Sciences. Categorical variables were reported as frequencies, whereas continuous variables were presented as mean±standard deviations. To compare group differences, a one-way analysis of variance was performed with post hoc comparisons using Tukey's test. The linear associations between biomarkers were assessed using Pearson's correlation coefficients. Multiple linear regression models were used to investigate clinical outcome predictors. Prior to finalising the regression models, multicollinearity among predictors was assessed using variance inflation factors [VIF] and tolerance statistics. Given the high inter-correlation between insulin and C-peptide [$r = 0.76$, $p < 0.001$], both variables were initially entered into the model simultaneously. C-peptide yielded a non-significant regression coefficient [$\beta = 0.14$, $p = 0.08$] with a VIF indicating shared variance with insulin, and was therefore excluded from the final model to avoid redundancy and statistical noise. Insulin was retained as the superior predictor of insulin secretory activity in this population after this sequential selection. To evaluate the discriminative power of biomarkers, receiver operating characteristic curves were developed, and areas under the curve and ideal cutoff points were computed. The threshold for statistical significance was set at $p<0.05$.

Results

Demographic Characteristics

The study included 225 participants with no statistically significant difference in gender distribution across groups [$p = 0.85$]. Mean age showed a non-significant trend toward higher values among CAD patients [$p = 0.08$], while BMI was significantly elevated in the CAD with T2DM group compared to controls [$p < 0.001$] (Table 1).

iochemical Marker Levels

According to biochemical tests, patients with coronary artery disease (CAD) had significantly lower blood adiponectin levels than control participants (p 0.001). Patients with CAD who also had type 2 diabetic mellitus (T2DM) had the lowest levels. High-sensitivity C-reactive protein (hs-CRP), interleukin-6 (IL-6), and E-selectin are pro-inflammatory biomarkers that were considerably greater than controls in both CAD subgroups ($p < 0.001$), with the diabetic CAD subset showing the largest rises. In the CAD population, insulin resistance markers significantly increased, particularly for individuals with T2DM ($p < 0.001$). High levels of total cholesterol, low density lipoprotein cholesterol, and triglycerides, together with a reduction in high density lipoprotein cholesterol ($p < 0.001$; see Table 2), were indicative of dyslipidemic profiles. HOMA-IR was significantly elevated in CAD patients with T2DM compared to CAD patients without T2DM and controls, confirming a gradient of insulin resistance across groups ($p < 0.001$), consistent with the pattern observed for absolute fasting insulin values.

Table 1 Demographic Characteristics of Study Participants

Characteristic	Control [n=75]	CAD with T2DM [n=75]	CAD without T2DM [n=75]	p-value
Age [years]	45.2 ± 6.1	53.5 ± 7.2	52.6 ± 6.4	0.08
Gender [Male/ Female]	38/37	45/30	44/31	0.85
BMI [kg/m^2]	23.5 ± 2.8	27.4 ± 3.1	26.9 ± 2.7	< 0.001

Table 2 Biochemical Marker Levels in Study Groups

Marker	Control [n=75]	CAD with T2DM [n=75]	CAD without T2DM [n=75]	p-value
Adiponectin [mg/L]	7.4 ± 1.6	4.2 ± 1.0	5.1 ± 1.3	< 0.001
hs-CRP [mg/L]	1.2 ± 0.3	5.8 ± 1.4	4.5 ± 1.0	< 0.001
IL-6 [pg/mL]	3.8 ± 1.2	9.2 ± 3.4	6.6 ± 2.2	< 0.001
E-selectin [ng/mL]	45.2 ± 12.1	92.7 ± 23.2	67.5 ± 18.3	< 0.001
Insulin [μU/mL]	12.3 ± 4.1	28.9 ± 6.5	20.7 ± 5.0	< 0.001
C-peptide [ng/mL]	2.9 ± 0.9	6.5 ± 2.1	4.2 ± 1.5	< 0.001
HOMA-IR	1.9 ± 0.6	6.1 ± 1.8	3.8 ± 1.2	< 0.001
Total Cholesterol [mg/dL]	187.4 ± 20.2	216.5 ± 30.4	204.1 ± 23.8	< 0.05
Triglycerides [mg/ dL]	125.3 ± 45.2	186.3 ± 58.5	159.2 ± 49.8	< 0.001
LDL Cholesterol [mg/dL]	112.4 ± 18.5	145.3 ± 25.3	139.4 ± 21.0	< 0.01
HDL Cholesterol [mg/dL]	52.1 ± 10.3	41.2 ± 9.4	46.1 ± 8.6	< 0.01

Correlation Analysis

Correlation analysis demonstrated statistically significant inverse associations between adiponectin and inflammatory markers: hs-CRP [$r = -0.45$, $p < 0.001$], IL-6 [$r = -0.38$, $p = 0.001$], and E-selectin [$r = -0.32$, $p = 0.004$]. Adiponectin exhibited negative correlations with serum insulin [$r = -0.28$, $p = 0.006$] and C-peptide [$r = -0.21$, $p = 0.03$]. Positive correlations were observed among inflammatory markers and between these markers and insulin resistance indices (Table 3). Notably, insulin and C-peptide showed a strong positive inter-correlation [r =

Table 3 Correlation of Adiponectin and Other Biochemical Markers

Marker	Adipo-nectin	hs-CRP	IL-6	E-selec-tin	Insulin	C-pep-tide
Adipone-ctin	1	-0.45**	-0.38**	-0.32**	-0.28*	-0.22*
hs-CRP	-0.45**	1	0.59**	0.56**	0.41**	0.37**
IL-6	-0.38**	0.59**	1	0.64**	0.38**	0.32*
E-selectin	-0.32**	0.56**	0.64**	1	0.34**	0.29*
Insulin	-0.28*	0.41**	0.38**	0.34**	1	0.76**
C-peptide	-0.22*	0.37**	0.32*	0.29*	0.76**	1

**Correlation is significant at the 0.05 level; **Correlation is significant at the 0.01 level*

Table 4 Multiple Linear Regression Analysis for Factors Associated with CAD

Predictor Variable	β [Standardized Coefficient]	p-value
Adiponectin [μg/mL]	-0.35	< 0.001
hs-CRP [mg/L]	0.42	< 0.001
Insulin [μU/mL]	0.27	< 0.01
E-selectin [ng/mL]	0.23	0.02
C-peptide [ng/mL]	0.14	0.08

**Correlation is significant at the 0.05 level; **Correlation is significant at the 0.01 level*

Table 5 Post Hoc Analysis [Tukey's Test] Between Study Groups

Marker	Control vs CAD with T2DM	Control vs CAD without T2DM	CAD with T2DM vs CAD without T2DM
Adiponectin	< 0.001	< 0.001	0.03
hs-CRP	< 0.001	< 0.001	0.05
IL-6	< 0.001	< 0.001	0.02
E-selectin	< 0.001	< 0.001	0.001
Insulin	< 0.001	< 0.001	0.03
C-peptide	< 0.001	< 0.001	0.04

0.76, p < 0.001], indicating substantial shared variance, which informed the multicollinearity assessment conducted during regression modelling.

Multiple Linear Regression Analysis

Multiple linear regression analysis identified adiponectin [β = -0.35, p = 0.002], hs-CRP [β = 0.42, p < 0.001], insulin [β = 0.27, p = 0.01], and E-selectin [β = 0.23, p = 0.02] as independent factors associated with CAD after adjusting for age, BMI, and lipid parameters. C-peptide showed a marginal association [p = 0.08] but did not reach statistical significance (Table 4).

The exclusion of C-peptide from the final model was informed by multicollinearity diagnostics: the VIF for C-peptide when entered simultaneously with insulin exceeded the acceptable threshold, indicating that its bivariate correlation with adiponectin [r = -0.21, p = 0.03] does not translate into an independent regression effect once the shared variance with insulin is accounted for. This does not imply that C-peptide lacks physiological relevance; rather, it reflects the statistical redundancy between these two markers of endogenous insulin secretion in this cross-sectional sample. Future studies incorporating C-peptide in populations stratified by renal function may better delineate its independent contribution.

Post Hoc Analysis

When comparing patients with coronary artery disease (CAD) to healthy controls, post-hoc analysis using Tukey's Honestly Significant Difference test revealed statistically significant intergroup differences (p < 0.001). Table 5 summarises the significant changes between the groups in adiponectin, interleukin-6 (IL-6), E-selectin, insulin, and high-sensitivity C-reactive protein (hs-CRP).

ROC Analysis

ROC curve analysis was employed to evaluate discriminative performance of biomarkers. hs-CRP exhibited the highest area under the curve [AUC = 0.83], followed by adiponectin [AUC = 0.79], E-selectin [AUC = 0.75], and insulin [AUC = 0.72], indicating moderate discriminative ability for differentiating CAD with T2DM from healthy controls (Table 6).

At its optimal Youden index-derived cutoff, adiponectin demonstrated a sensitivity of 74% and specificity of 78% at a threshold of ≤5.0 mg/L for identifying CAD patients with T2DM, providing a clinically interpretable reference point for risk stratification.

Table 6 ROC Analysis for Biomarkers

Marker	AUC	95% Confidence Interval	p-value
Adiponectin	0.79	0.72 - 0.86	< 0.001
hs-CRP	0.83	0.77 - 0.89	< 0.001
E-selectin	0.75	0.68 - 0.82	< 0.001
Insulin	0.72	0.64 - 0.80	< 0.001

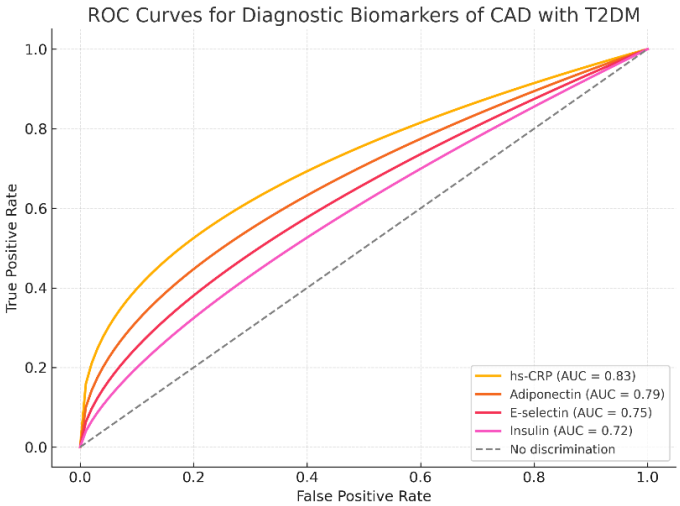

Figure 1 – Regression Coefficients of Biochemical Predictors Associated with the Outcome Variable

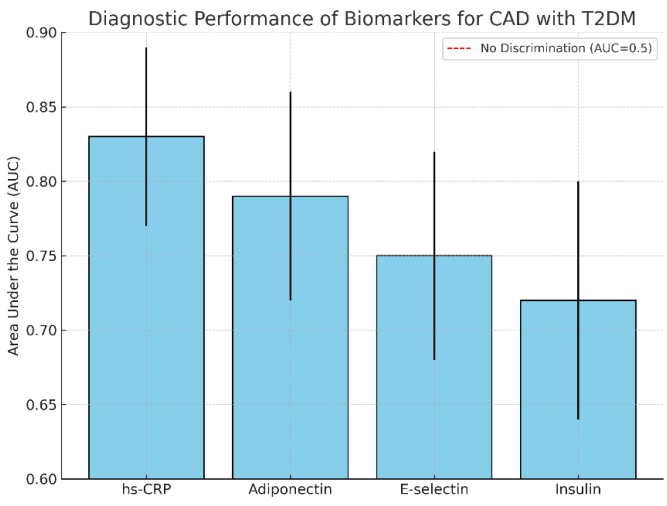

Figure 2 – Regression Coefficients of Biochemical Predictors Associated with the Outcome Variable

Discussion

The current study investigated the relationships between adiponectin, inflammatory and metabolic indices in a patient group diagnosed with coronary artery disease (CAD), including patients with and without type 2 diabetes mellitus (T2DM). The results provide improvements in our understanding of pathophysiological mechanisms that underlie cardiovascular disease in the diabetic state and the clinical significance of adiponectin as a biomarker that indicates cardiovascular health.

When compared to CAD patients without diabetes and healthy volunteers, observations indicate that plasma concentrations of adiponectin were significantly lower in patients with coronary artery disease (CAD) concurrently with type 2 diabetes mellitus (T2DM). These results are in line with existing research that associates hypoadiponectinemia with a higher risk of cardiovascular disease, particularly in those who experience metabolic disturbances [14,15].

Adiponectin reduces vascular inflammation, enhances endothelial function, and increases nitric oxide generation, among other mechanisms that contribute to its cardioprotective benefits [16, 17]. Adiponectin concentrations and insulin resistance have been found to be consistently inversely correlated. By triggering the AMP-activated protein kinase (AMPK) signalling cascade, adiponectin is thought to improve insulin sensitivity [18,19].

In the present study, HOMA-IR confirmed a gradient of insulin resistance across groups and showed a pattern consistent with absolute fasting insulin values, supporting the validity of fasting insulin as a surrogate marker of insulin resistance in this cohort. While standardised indices such as HOMA-IR and HOMA2 are preferable for precise insulin resistance quantification in future studies, the strong inter-group differences observed herein for both fasting insulin and HOMA-IR indicate that the core findings are not artefactual.

Systemic inflammation is a major factor in pathogenesis of both CAD and T2DM. The present study reported a significantly higher level of high sensitivity C-reactive protein (hs-CRP) and interleukin-6 (IL-6) in CAD patients with T2DM, in line with the chronic low grade inflammation milieu described in this group of patients. hs-CRP is an independent predictor of cardiovascular risk, particularly in diabetic populations, and its elevation closely correlates with endothelial dysfunction and atherogenic progression [20,21]. Similarly, IL-6 encourages cardiovascular pathology by promoting vascular inflammation and endothelial dysfunction on top of promoting insulin resistance and lipid dysregulation [22,23].

E-selectin is involved in leukocyte adhesion to the vascular endothelium and activates the inflammatory cascade on which atherogenesis is based. Elevated plasma E-selectin levels were detected in CAD patients with T2DM in this study and suggest increased endothelial activation and dysfunction. These observations are in concert with previous reports characterizing a relationship between elevated E-selectin and incident cardiovascular events [24,25].

Patients with coronary artery disease (CAD) who also had type 2 diabetic mellitus (T2DM) had significantly different serum lipid profiles from those who did not have the metabolic condition. High levels of total cholesterol, low-density LDL cholesterol and triglycerides, and low levels of high-density HDL cholesterol were seen in subjects with both T2DM and CAD [26, 27]. This constellation is characteristic of diabetic dyslipidaemia and is linked to the acceleration of atherogenesis.

Adiponectin, high sensitivity C-reactive protein (hsCRP), and insulin are independent predictors of CAD, according to multivariate regression analysis, with adiponectin exhibiting the highest inverse connection with insulin levels and inflammatory markers. The decision to prioritise insulin over C-peptide in the final regression model was based on multicollinearity assessment revealing high inter-correlation between these two markers [$r = 0.76$], causing C-peptide to lose significance [$p = 0.08$] when included simultaneously. Although C-peptide is a more stable marker with superior pharmacokinetic properties owing to its absence of first-pass hepatic metabolism, its circulating levels are subject to renal filtration; all participants with eGFR < 60 mL/min/1.73 m² were excluded to mitigate this confound. The loss of C-peptide significance in the adjusted model should therefore be interpreted as a statistical consequence of redundancy rather than absence of biological relevance. All three biomarkers had modest discriminative performance according to receiver operating characteristic (ROC) curves; adiponectin's area under the curve (AUC) was 0.79, which was in line with findings from other research [28, 29].

Adiponectin demonstrated a well-characterised gender specificity, with female individuals generally exhibiting higher concentrations than males. In the 30–50 age group studied here, circulating adiponectin in women may be additionally modulated by endogenous sex steroid levels and menopausal transition. Although the overall gender distribution was balanced across groups [$p = 0.85$], formal gender-stratified sub-analyses were not performed, which represents a limitation of the current study and may have attenuated the precision of adiponectin-based risk estimates, particularly in female participants. Future investigations should incorporate gender-stratified analyses and account for menopausal status when evaluating adiponectin as a cardiovascular biomarker.

Regarding the potential impact of ongoing hypoglycaemic therapy, participants receiving injectable insulin were excluded from the study; however, oral hypoglycaemic agents, particularly insulin sensitizers such as metformin and thiazolidinediones, were documented among enrolled patients. These agents are known to modulate adiponectin levels and insulin sensitivity independently of glycaemic control. The absence of a formal pharmacological adjustment for these agents in the multivariable model represents an additional limitation. Future research should stratify participants by medication class or introduce pharmaceutical exposure as a covariate to obtain unconfounded biomarker estimates.

From a translational perspective, the ROC-derived optimal cutoff for adiponectin [≤5.0 mg/L] offers a clinically actionable threshold that cardiologists could incorporate into routine metabolic screening of patients presenting with suspected CAD, particularly those with concurrent T2DM. We propose the following simple decision algorithm: (1) measure fasting adiponectin alongside standard lipid and glycaemic panels; (2) classify patients with adiponectin ≤5.0 mg/L and hs-CRP ≥3.0 mg/L as high-risk for CAD with metabolic comorbidity; (3) prioritise these patients for early coronary angiographic evaluation, intensified glycaemic optimisation, and adiponectin-targeted therapeutic strategies. Validation of this threshold in prospective cohorts and in populations with broader age ranges and diverse ethnicities is essential before clinical implementation.

The present study did not include a systematic comparison of biomarker levels with angiographic severity scores such as the Syntax score, which would have provided objective anatomical grounding for the biomarker hierarchy reported. While all CAD patients were diagnosed through coronary angiography as part of the inclusion criteria, the degree of vascular involvement

was not quantitatively correlated with circulating biomarker concentrations. This represents a notable gap, and future work should examine whether the adiponectin–hs-CRP–insulin profile correlates with Syntax score-derived lesion complexity, which would considerably strengthen the risk stratification framework proposed here.

Study Limitations

There are a number of limitations to consider. The cross-sectional nature of the study makes causal inferences impossible and prospective studies are needed to confirm temporal links between biomarker changes and the onset of CAD. Furthermore, the sample was obtained from a limited demography to extrapolate upon heterogeneous ethnic cohorts and other studies should determine the external validity of the findings within different populations. The study population was restricted to the 30–50-year age range, which limits generalisability to older patient cohorts in whom adiponectin dynamics and insulin resistance patterns may differ substantially. Gender-stratified sub-analyses for adiponectin were not performed; given the known gender specificity of adiponectin and the influence of sex steroids and menopausal status in this age range, this limits the precision of adiponectin-based risk estimates in female participants. The study did not formally adjust for the effects of ongoing oral hypoglycaemic therapy on adiponectin and insulin levels; insulin sensitizers such as metformin and thiazolidinediones may independently modulate these markers and represent a potential source of residual confounding. Insulin resistance was quantified using both absolute fasting insulin and HOMA-IR; however, standardised indices such as HOMA2 or the hyperinsulinaemic-euglycaemic clamp, which offer more precise quantification, were not employed. The study did not correlate biomarker levels with the anatomical severity of coronary artery disease as assessed by the Syntax score; such correlation would have provided stronger mechanistic and clinical validation of the proposed risk stratification markers. Prospective research should also question the therapeutic implications of modulating adiponectin in patients with CAD, especially in patients with T2DM.

Conclusion

The present study establishes significant associations between reduced levels of adiponectin, increased inflammatory markers and metabolic aberrations in patients with CAD, specifically in patients with T2DM. These biomarkers are related to the systemic inflammatory processes that are intrinsic to CAD, and they should further evaluated in a prospective evaluation to determine their clinical applicability. The ROC-derived optimal cutoff for adiponectin [≤5.0 mg/L], combined with elevated hs-CRP, identifies a high-risk metabolic profile that may guide early clinical decision-making in cardiology practice. Multicollinearity diagnostics confirmed the statistical primacy of insulin over C-peptide in the regression model, though the biological contribution of C-peptide in renally-intact populations warrants dedicated investigation. The findings support the proposition of adiponectin as a therapeutic target in order to attenuate cardiovascular risk in the diabetic population.

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