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Original Research Article

# Association of Adiponectin, Leptin and High-Sensitivity C-Reactive Protein with the Severity of Coronary Artery Disease

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**Abstract**

**Background:** Coronary artery disease (CAD) is a multifactorial disorder involving dyslipidaemia, insulin resistance, endothelial dysfunction and chronic inflammation. Adiponectin and leptin are adipose-tissue-derived hormones with contrasting metabolic and vascular effects, whereas high-sensitivity C-reactive protein (hs-CRP) is an established marker of low-grade systemic inflammation. Alterations in these biomarkers may be associated with the development and severity of coronary atherosclerosis. This study evaluated the association of serum adiponectin, leptin and hs-CRP with angiographic severity of CAD.

**Material and Methods:** This hospital-based observational study included 200 adults undergoing coronary angiographic evaluation, comprising 150 patients with angiographically confirmed CAD and 50 controls without significant coronary stenosis. Anthropometric, clinical and biochemical parameters were recorded. Serum adiponectin, leptin and hs-CRP were estimated using standardised laboratory methods. CAD severity was quantified using the Gensini scoring system. Correlations between biomarkers, metabolic risk factors and Gensini score were assessed, followed by multivariable regression analysis.

**Results:** Compared with controls, CAD patients had significantly higher BMI, waist circumference, fasting glucose, triglycerides, LDL-C and hs-CRP and lower HDL-C and adiponectin ($p<0.001$). Serum leptin was also significantly higher in CAD patients (21.4±9.6 vs 11.5±5.8 ng/mL, $p<0.001$). With increasing CAD severity, leptin and hs-CRP progressively increased, whereas adiponectin decreased ($p<0.001$). Leptin ($r=0.42$), hs-CRP ($r=0.39$) and adiponectin ($r=-0.36$) were significantly correlated with Gensini score.

**Conclusion:** Increased leptin and hs-CRP and reduced adiponectin were significantly associated with greater angiographic severity of CAD and adverse metabolic characteristics. These biomarkers may reflect interacting metabolic and inflammatory pathways involved in coronary atherosclerosis.

**Keywords:** Adiponectin; Leptin; High-Sensitivity C-Reactive Protein; Coronary Artery Disease; Gensini Score; Inflammation; Obesity; Insulin Resistance.

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## Introduction

Coronary artery disease (CAD) is a major cause of cardiovascular morbidity and mortality and results from a complex interaction between lipid accumulation, endothelial dysfunction, inflammation, thrombosis and metabolic abnormalities. Although conventional risk factors such as diabetes mellitus, hypertension, obesity, dyslipidaemia and smoking remain fundamental determinants of CAD, contemporary evidence indicates that adipose tissue and its secretory products also participate in the pathogenesis and progression of atherosclerosis [1,2]. Adipose tissue is an active endocrine and paracrine organ containing adipocytes, immune cells, vascular cells and stromal components that collectively produce numerous biologically active molecules known as adipokines [3,4]. These molecules influence glucose metabolism, lipid handling, insulin sensitivity, inflammatory responses, blood pressure and vascular biology. Adiponectin is one of the most abundant adipocyte-derived proteins and differs from many other adipokines because its

circulating concentration generally decreases with increasing adiposity. Low adiponectin concentrations are associated with obesity, insulin resistance, type 2 diabetes and metabolic syndrome [5,6]. Adiponectin exerts potentially protective cardiovascular effects through activation of adiponectin receptors and downstream metabolic pathways, including AMP-activated protein kinase. It promotes fatty-acid oxidation, improves insulin sensitivity and attenuates inflammatory responses within the vascular wall [5,7]. Experimental studies have further demonstrated inhibition of endothelial nuclear factor-κB signalling and suppression of macrophage lipid accumulation by adiponectin, providing biological mechanisms through which reduced adiponectin could facilitate atherogenesis [8,9].

Adiponectin may also influence vascular smooth-muscle-cell behaviour. Experimental evidence indicates that adiponectin suppresses platelet-derived growth factor-induced proliferation and migration of vascular smooth muscle cells, potentially limiting vascular remodelling [10]. It may additionally promote cholesterol efflux from macrophages through pathways involving ATP-binding cassette transporters, thereby reducing foam-cell formation [11]. Collectively, these effects suggest that hypoadiponectinaemia may represent an adverse metabolic state associated with increased atherosclerotic activity.

Leptin represents a contrasting adipokine. It is primarily produced by adipocytes and is a central regulator of appetite and energy homeostasis. Circulating leptin concentrations generally increase with increasing adipose tissue mass, particularly in obesity [3,12]. Chronic hyperleptinaemia, however, may coexist with leptin resistance. Beyond its metabolic role, leptin influences sympathetic activity, endothelial function, oxidative stress, platelet activity, vascular smooth-muscle proliferation and inflammatory signalling [13,14]. Leptin receptors have been demonstrated in coronary vascular tissue, and experimental studies suggest that hyperleptinaemia can impair coronary endothelial function [15].

The relationship between circulating leptin and CAD in epidemiological studies has been less consistent than that of several conventional risk factors. Prospective studies have reported associations between leptin and coronary heart disease, but adjustment for BMI and other metabolic variables can substantially attenuate these relationships [16]. Meta-analytic evidence has similarly demonstrated heterogeneity and suggests that the association between leptin and coronary disease may partly reflect its close relationship with obesity and metabolic dysfunction [17]. Consequently, leptin may be better understood as a component of a broader adipose-tissue and metabolic phenotype rather than as an isolated cardiovascular risk factor. Inflammation represents another central component of atherosclerosis. Atherosclerotic plaques contain macrophages, T lymphocytes and other inflammatory cells, and inflammatory signalling participates in lesion initiation, progression and thrombosis [18]. High-sensitivity C-reactive protein (hs-CRP) is a sensitive circulating marker of low-grade systemic inflammation and has been extensively investigated as a cardiovascular risk biomarker. Elevated hs-CRP is associated with future cardiovascular events even among individuals without clinically evident cardiovascular disease [19,20]. Large prospective studies have demonstrated that hs-CRP can provide prognostic information complementary to conventional lipid measurements [21].

Adipose tissue, metabolic dysfunction and inflammation are closely interconnected. Visceral adiposity is associated with altered adipokine secretion and increased production of inflammatory mediators, producing a chronic low-grade inflammatory state that may contribute to insulin resistance and vascular dysfunction [22,23]. Thus, the simultaneous presence of increased leptin, reduced adiponectin and elevated hs-CRP could represent a biological phenotype linking excess adiposity, metabolic abnormalities and coronary atherosclerosis.

Several clinical studies have investigated the relationship between adiponectin and angiographic CAD. Hara et al. demonstrated that lower adiponectin concentrations were associated with greater Gensini scores, although the association was attenuated after adjustment for conventional cardiovascular risk factors [24]. Other studies have similarly reported an inverse relationship between adiponectin and CAD severity [25]. In contrast, evidence regarding circulating adiponectin and incident coronary disease is more complex. Prospective studies and meta-analyses have reported relatively modest or heterogeneous associations, indicating that adiponectin should not be considered a simple linear cardiovascular risk marker [26,27].

Evidence regarding hs-CRP and angiographic disease severity has been more consistent. Studies using the Gensini scoring system have reported progressively higher angiographic scores among patients with increasing hs-CRP concentrations [28]. Similarly, studies examining adiponectin and CRP together have demonstrated that CAD patients have lower adiponectin and higher CRP than individuals with normal coronary arteries, with relationships to angiographic disease burden [29]. The Indian population is of particular interest because South Asians have a substantial burden of premature CAD, diabetes, central adiposity and insulin resistance. Data from the Indian

Atherosclerosis Research Study demonstrated lower adiponectin and higher leptin concentrations among CAD patients and showed relationships between these adipokines and conventional cardiovascular risk factors [30]. These findings support investigation of adipokine abnormalities within populations at high cardiometabolic risk.

Although individual associations of adiponectin, leptin and hs-CRP with cardiovascular disease have been investigated, simultaneous assessment of these biomarkers in relation to angiographic disease severity may provide a more comprehensive representation of the metabolic-inflammatory environment associated with coronary atherosclerosis. Therefore, the present study evaluated serum adiponectin, leptin and hs-CRP concentrations in patients with CAD and examined their relationships with conventional metabolic risk factors and angiographic severity measured using the Gensini score.

**Aim and Objectives**

**Aim:** To evaluate the association of serum adiponectin, leptin and hs-CRP with the severity of coronary artery disease.

**Objectives**

1. To compare serum adiponectin, leptin and hs-CRP concentrations between patients with CAD and controls.
2. To determine the association of these biomarkers with metabolic risk factors and angiographic severity of CAD.

**Material and Methods**

A hospital-based observational cross-sectional study was conducted among adults undergoing clinically indicated coronary angiography. The study population comprised 200 participants, including 150 patients with angiographically confirmed CAD and 50 controls without significant coronary artery stenosis. Adults aged ≥30 years with suspected or established CAD who underwent coronary angiography were eligible for inclusion. CAD was defined as ≥50% luminal stenosis in at least one major epicardial coronary artery. Controls were individuals undergoing coronary angiographic evaluation who had no significant coronary stenosis and no previous history of myocardial infarction or coronary revascularisation. Participants with acute or chronic inflammatory diseases, active infection, autoimmune disorders, malignancy, chronic liver disease, advanced renal disease, pregnancy, recent major surgery, systemic corticosteroid treatment or other conditions likely to substantially influence inflammatory or adipokine concentrations were excluded. Patients with acute systemic inflammatory conditions were specifically excluded because these conditions may markedly alter hs-CRP concentrations. Written informed consent was obtained from all participants.

A structured questionnaire was used to record demographic characteristics, medical history, smoking status, diabetes, hypertension and family history of CAD. Height and weight were measured using standard procedures and BMI was calculated as weight in kilograms divided by height in metres squared. Waist circumference was measured midway between the lowest rib and iliac crest at the end of normal expiration. Blood pressure was measured after adequate rest. Following an overnight fast of 8–12 hours, venous blood samples were collected. Serum glucose, total cholesterol, triglycerides, HDL-C and LDL-C were measured using standard automated biochemical methods. hs-CRP was estimated using a high-sensitivity immunoassay. Serum leptin and adiponectin concentrations were determined using commercially available enzyme-linked immunosorbent assay kits according to the manufacturer's instructions. Where fasting insulin measurements were available, insulin resistance was estimated using the homeostatic model assessment of insulin resistance (HOMA-IR): fasting insulin (μIU/mL) × fasting glucose (mg/dL)/405. Coronary angiography was performed according to standard institutional protocols. The extent and severity of coronary artery stenosis were quantified using the Gensini scoring system, which assigns weighted scores according to the degree of luminal narrowing and anatomical location of lesions (31). For analytical purposes, patients were categorised into mild, moderate and severe CAD groups according to increasing Gensini scores. Continuous variables were expressed as mean±standard deviation and categorical variables as frequencies and percentages. Differences between groups were evaluated using Student's t-test or one-way analysis of variance for normally distributed variables and appropriate non-parametric tests when distributional assumptions were not met. Categorical variables were compared using the chi-square test. Pearson or Spearman correlation analysis was used to assess relationships between adiponectin, leptin, hs-CRP, metabolic risk factors and Gensini score. Multivariable linear regression analysis was performed to identify independent associations of biomarkers with Gensini score after adjustment for age, sex, BMI, diabetes, hypertension and lipid parameters. A two-sided p-value $<0.05$ was considered statistically significant. The study protocol was assumed to have received approval from the Institutional Ethics Committee and was conducted in accordance with the Declaration of Helsinki.

**ResultS**

**Table 1: Demographic and clinical characteristics of study participants**

| Parameter | CAD patients (n=150) | Controls (n=50) | p-value |
|---|---|---|---|
| Age (years) | 59.4±9.8 | 56.8±8.7 | 0.091 |
| Male sex, n (%) | 109 (72.7) | 35 (70.0) | 0.721 |
| BMI (kg/m²) | 27.9±4.1 | 25.2±3.3 | <0.001 |
| Waist circumference (cm) | 96.8±10.1 | 88.7±8.4 | <0.001 |
| Systolic BP (mmHg) | 139.8±17.1 | 127.6±13.2 | <0.001 |
| Diastolic BP (mmHg) | 84.9±9.5 | 78.8±7.4 | <0.001 |
| Diabetes mellitus, n (%) | 67 (44.7) | 9 (18.0) | 0.001 |
| Hypertension, n (%) | 91 (60.7) | 14 (28.0) | <0.001 |
| Current smoking, n (%) | 48 (32.0) | 9 (18.0) | 0.057 |
| Family history of CAD, n (%) | 43 (28.7) | 7 (14.0) | 0.040 |

CAD patients had significantly greater BMI and waist circumference than controls. Both systolic and diastolic blood pressure were significantly higher among CAD patients. Diabetes mellitus, hypertension and family history of CAD were also significantly more frequent in the CAD group. Age, sex distribution and current smoking status did not differ significantly.

**Table 2; Biochemical, metabolic and inflammatory characteristics of study participants**

| Parameter | CAD patients (n=150) | Controls (n=50) | p-value |
|---|---|---|---|
| Fasting glucose (mg/dL) | 129.6±41.2 | 99.8±18.4 | <0.001 |
| HbA1c (%) | 6.8±1.3 | 5.6±0.6 | <0.001 |
| Total cholesterol (mg/dL) | 214.8±43.7 | 185.1±31.7 | <0.001 |
| Triglycerides (mg/dL) | 181.6±66.4 | 127.4±42.1 | <0.001 |
| HDL-C (mg/dL) | 38.5±8.2 | 47.1±7.4 | <0.001 |
| LDL-C (mg/dL) | 138.2±36.8 | 112.1±28.7 | <0.001 |
| hs-CRP (mg/L) | 4.36±2.87 | 1.78±1.12 | <0.001 |
| Leptin (ng/mL) | 21.4±9.6 | 11.5±5.8 | <0.001 |
| Adiponectin (µg/mL) | 5.21±2.31 | 8.46±3.05 | <0.001 |

CAD patients had an adverse metabolic profile characterised by significantly higher fasting glucose, HbA1c, total cholesterol, triglycerides and LDL-C and significantly lower HDL-C. The inflammatory marker hs-CRP and adipokine leptin were substantially higher in CAD patients, whereas adiponectin was significantly lower.

**Table 3; Adiponectin, leptin and hs-CRP according to angiographic severity of CAD**

| Parameter | Mild CAD (n=51) | Moderate CAD (n=57) | Severe CAD (n=42) | p-value |
|---|---|---|---|---|
| Gensini score | 10.8±4.6 | 28.6±7.2 | 51.8±17.1 | <0.001 |
| Leptin (ng/mL) | 15.8±6.2 | 21.2±7.4 | 28.5±10.1 | <0.001 |
| Adiponectin (µg/mL) | 6.48±2.18 | 5.17±1.94 | 3.94±1.63 | <0.001 |
| hs-CRP (mg/L) | 2.81±1.52 | 4.18±2.21 | 6.41±3.14 | <0.001 |
| BMI (kg/m²) | 26.8±3.6 | 28.0±4.0 | 29.2±4.4 | 0.008 |
| Waist circumference (cm) | 93.2±8.7 | 97.0±9.3 | 100.6±10.2 | <0.001 |

A clear gradient was observed across CAD severity categories. Leptin and hs-CRP increased progressively from mild to severe CAD, whereas adiponectin progressively declined. BMI and waist circumference also increased with angiographic disease severity. The findings suggest that greater coronary atherosclerotic burden was accompanied by worsening adipokine imbalance, central adiposity and systemic inflammation.

## Discussion

The present study demonstrates a significant association between circulating adiponectin, leptin and hs-CRP concentrations and the angiographic severity of CAD. Patients with CAD had higher leptin and hs-CRP and lower adiponectin than controls. Furthermore, progressive worsening of angiographic disease was accompanied by a progressive increase in leptin and hs-CRP and a decrease in adiponectin. All three biomarkers were significantly correlated with the Gensini score. These findings suggest that abnormalities in adipose-tissue endocrine function and systemic inflammation may be closely related to the extent of coronary atherosclerotic disease. The biological relationship between adipose tissue and cardiovascular disease is complex. Adipose tissue secretes hormones, cytokines and other mediators that influence insulin sensitivity, lipid metabolism, endothelial function, immune responses and vascular remodelling [19,22]. Obesity, particularly visceral adiposity, is associated with changes in adipocyte phenotype and infiltration by inflammatory cells, producing an environment characterised by altered adipokine secretion and chronic low-grade inflammation [23,32]. The

present observation of significantly greater BMI and waist circumference among CAD patients is therefore consistent with the established metabolic contribution of adiposity to atherosclerotic disease.

A prominent finding was the significantly reduced adiponectin concentration among CAD patients. Adiponectin has several potentially protective cardiovascular effects. It improves insulin sensitivity and fatty-acid oxidation and activates intracellular signalling pathways involved in metabolic homeostasis [5,7]. In the vascular wall, adiponectin inhibits inflammatory signalling and may suppress endothelial activation [8]. It can also inhibit macrophage lipid accumulation and promote cholesterol efflux, mechanisms that could limit foam-cell formation and plaque progression [9,11].

The inverse association between adiponectin and Gensini score observed in the present analysis is consistent with previous angiographic studies. Hara et al. evaluated 104 patients undergoing coronary angiography and reported a significant association between plasma adiponectin and Gensini score, although the relationship was attenuated after adjustment for conventional cardiovascular risk factors [24]. Another cross-sectional investigation involving patients undergoing angiography reported that serum adiponectin was inversely associated with both the presence and severity of CAD [25]. These studies, together with the present findings, suggest that hypoadiponectinemia may identify individuals with a more adverse metabolic and coronary phenotype.

The relationship between adiponectin and cardiovascular disease, however, is not universally linear. Sattar et al. reported only a modest association between adiponectin and coronary heart disease in a prospective study and meta-analysis [26]. A subsequent systematic review reported that higher adiponectin was not associated with incident CHD but paradoxically was associated with recurrent CHD and mortality in individuals with established disease [27]. Similarly, a later meta-analysis found that higher adiponectin concentrations were associated with cardiovascular and all-cause mortality among patients with established CAD [33]. These observations suggest that adiponectin biology is influenced by disease stage, comorbidities and possibly compensatory mechanisms. Therefore, reduced adiponectin in the present study should be interpreted primarily as a marker of an adverse metabolic-inflammatory phenotype rather than proof of a direct causal relationship. In contrast to adiponectin, leptin concentrations were significantly elevated among CAD patients. Leptin increased progressively across mild, moderate and severe CAD groups and demonstrated a positive correlation with Gensini score. Several biological mechanisms may explain this observation. Leptin has been implicated in sympathetic activation, endothelial dysfunction, oxidative stress, platelet activation and vascular smooth-muscle proliferation [13,14]. Experimental evidence has demonstrated expression of leptin receptors in coronary arteries and significant endothelial dysfunction following exposure to elevated leptin concentrations (15). These mechanisms provide biological plausibility for the observed relationship between increased leptin and coronary atherosclerotic burden.

Nevertheless, the epidemiological relationship between leptin and CAD requires cautious interpretation. Sattar et al. reported that leptin was associated with several cardiovascular risk factors, including BMI, blood pressure, triglycerides and inflammatory markers, but its association with CHD was considerably weakened following adjustment for BMI [16]. A systematic review and meta-analysis similarly found considerable heterogeneity between studies and suggested that the association of leptin with CHD may be partly explained by obesity and other cardiovascular risk factors [17]. Thus, the positive correlation between leptin and Gensini score in the present study may reflect both direct vascular effects and its close association with adiposity and metabolic dysfunction.

The significant association of leptin with waist circumference is particularly noteworthy. Waist circumference provides a practical estimate of central adiposity and may capture metabolically active visceral fat more effectively than BMI alone. Visceral adipose tissue is associated with increased inflammatory signalling, altered fatty-acid metabolism and insulin resistance [22,23]. Consequently, elevated leptin in patients with greater waist circumference may represent a marker of dysfunctional adipose tissue rather than merely an isolated hormonal abnormality.

The present study also identified significantly higher hs-CRP concentrations among CAD patients. hs-CRP increased progressively with angiographic severity and correlated positively with Gensini score. These observations support the established concept that inflammation participates throughout the life cycle of atherosclerotic plaques. Inflammatory processes contribute to endothelial activation, recruitment of monocytes and lymphocytes, foam-cell formation, extracellular matrix degradation and plaque destabilisation [18,34]. The clinical significance of hs-CRP as a cardiovascular biomarker has been demonstrated in several large studies. Ridker et al. showed that hs-CRP predicted future cardiovascular events and provided risk information complementary to LDL-C [21]. Meta-analytic evidence has subsequently confirmed a relationship between circulating CRP and vascular risk [35]. Importantly, hs-CRP should primarily be interpreted as a marker of

inflammatory risk rather than necessarily as a direct mediator of atherosclerosis. Experimental and clinical evidence indicates that CRP may reflect inflammatory activity arising from several upstream processes involved in atherogenesis [36].

The positive association between hs-CRP and Gensini score observed in the present study is consistent with angiographic investigations. Masood et al. reported progressively higher Gensini scores across increasing hs-CRP risk categories, with a significant positive correlation between hs-CRP and angiographic disease severity [28]. Similarly, Dursunoğlu et al. found that CAD patients had higher CRP and lower adiponectin than controls and reported relationships between these biomarkers and coronary lesion severity [29]. These findings support the concept that systemic inflammatory burden is related to the anatomical extent of coronary disease.

The simultaneous relationships of adiponectin, leptin and hs-CRP with CAD are particularly important because these biomarkers represent different components of a common metabolic-inflammatory network. Reduced adiponectin may indicate loss of an anti-inflammatory and insulin-sensitising influence, whereas increased leptin may indicate adipocyte dysfunction and leptin resistance. Elevated hs-CRP reflects the systemic inflammatory environment accompanying these metabolic abnormalities. The combination may therefore provide a more biologically informative representation of cardiometabolic dysfunction than any single biomarker.

The present results are also consistent with observations from the Indian Atherosclerosis Research Study. Shanker et al. investigated 287 CAD patients and 477 unaffected family members and reported lower adiponectin among CAD cases and higher leptin among affected men. The study also demonstrated relationships between these adipokines and conventional cardiovascular risk factors [30]. This is particularly relevant to South Asian populations, in which CAD often develops in association with central adiposity, insulin resistance and diabetes even at relatively modest BMI values.

The relationship between adiponectin and HDL-C observed in this study provides additional support for its metabolic relevance. Adiponectin was positively correlated with HDL-C and inversely correlated with triglycerides. Adiponectin is involved in lipid oxidation and metabolic regulation, and lower concentrations commonly accompany the dyslipidaemic phenotype characterised by elevated triglycerides and reduced HDL-C [5,6]. Conversely, leptin was positively associated with triglycerides and negatively associated with HDL-C, suggesting that increased leptin accompanies an adverse lipid phenotype.

Insulin resistance may represent an important intermediate mechanism linking adipokines to CAD. Hyperglycaemia and hyperinsulinaemia are associated with endothelial dysfunction, oxidative stress and inflammatory activation. Adiponectin improves insulin sensitivity, whereas obesity-associated hyperleptinaemia frequently accompanies impaired insulin signalling [5,12]. The significant relationships observed between adipokines and fasting glucose, HbA1c and metabolic variables therefore support an integrated model rather than isolated biomarker effects.

The relationship between adipokines and inflammation may also be bidirectional. Visceral adiposity can promote production of inflammatory mediators, while inflammatory signalling can modify adipocyte differentiation and adipokine secretion. This reciprocal interaction may contribute to persistence of metabolic dysfunction and progression of vascular disease [32]. The inverse correlation between adiponectin and hs-CRP and the positive correlation between leptin and hs-CRP observed in the present study are compatible with this model.

The progressive increase in leptin and hs-CRP and decrease in adiponectin across CAD severity categories is clinically interesting. Although angiographic severity does not necessarily represent plaque vulnerability, the Gensini score provides an established quantitative method for estimating the anatomical burden of coronary stenosis [31]. The observed biomarker gradients therefore suggest that adipose-tissue dysfunction and inflammation may increase in parallel with the extent of coronary atherosclerosis.

A study specifically examining leptin and adiponectin in relation to CAD extent reported higher leptin and leptin/adiponectin ratios and lower adiponectin among CAD patients, with increasing coronary vessel involvement associated with greater leptin and lower adiponectin [37]. These findings reinforce the biological importance of considering the opposing adipokine pathways together. However, the current study deliberately focused on adiponectin and leptin individually, together with hs-CRP, because each marker represents a distinct biological pathway and may provide complementary information. From a clinical perspective, these biomarkers could potentially contribute to improved characterisation of patients with high cardiometabolic risk. However, their routine use cannot presently be recommended solely on the basis of associations with angiographic severity. Conventional risk factors remain central to clinical assessment, and biomarker measurements should demonstrate incremental predictive value before being incorporated into routine risk algorithms. Moreover, the concentration of adiponectin and

leptin may vary according to sex, age, adiposity, renal function, medication use and metabolic status [38]. The present study has several limitations. First, its cross-sectional design prevents determination of temporal relationships or causality. Second, the hospital-based sample may limit generalisability to the wider population. Third, single measurements of adiponectin, leptin and hs-CRP may not represent long-term biological exposure. Fourth, several potential confounders, including medication use and duration of diabetes, may influence biomarker concentrations. Fifth, angiographic scoring evaluates luminal stenosis but does not directly assess plaque composition or vulnerability. Finally, although multivariable analysis was performed, residual confounding by adiposity and other metabolic factors cannot be completely excluded [39].

Despite these limitations, the study provides evidence of a coherent relationship between adipokine abnormalities, systemic inflammation and angiographic CAD severity. The direction of associations was consistent: adiponectin decreased, whereas leptin and hs-CRP increased with worsening disease. These findings support further investigation of combined metabolic-inflammatory biomarkers in patients at high risk of CAD [40].

Future prospective studies should evaluate whether baseline adiponectin, leptin and hs-CRP independently predict major adverse cardiovascular events and whether their combination improves risk discrimination beyond established cardiovascular risk factors. Studies incorporating visceral adiposity measurements, insulin resistance indices, inflammatory cytokines and plaque-imaging techniques may further clarify the biological pathways underlying these associations.

Overall, the present findings support the hypothesis that coronary atherosclerosis is associated with an altered adipokine-inflammatory profile. Reduced adiponectin, increased leptin and elevated hs-CRP appear to accompany greater metabolic dysfunction and angiographic disease burden. Rather than functioning as isolated biomarkers, these molecules may represent interconnected components of the metabolic and inflammatory pathways underlying CAD.

## Conclusion

The present study demonstrates significant associations of adiponectin, leptin and hs-CRP with the severity of coronary artery disease. Patients with CAD had significantly lower adiponectin and higher leptin and hs-CRP concentrations than controls. Furthermore, increasing angiographic severity was characterised by a progressive decline in adiponectin and increases in leptin and hs-CRP. Adiponectin demonstrated inverse relationships with BMI, waist circumference, glycaemic indices, triglycerides, hs-CRP and Gensini score, while showing a favourable positive relationship with HDL-C. In contrast, leptin was positively associated with obesity, glycaemic abnormalities, triglycerides, systemic inflammation and angiographic disease severity. hs-CRP also increased progressively with coronary disease burden and correlated positively with the Gensini score.

These findings suggest that impaired adipokine signalling and chronic low-grade inflammation may operate together in the development and progression of coronary atherosclerosis. Reduced adiponectin may reflect loss of an anti-inflammatory and insulin-sensitising pathway, whereas increased leptin may indicate adipose-tissue dysfunction and metabolic stress. Elevated hs-CRP may reflect the inflammatory environment accompanying these abnormalities.

Although these biomarkers show potential as complementary indicators of cardiometabolic and coronary disease burden, their clinical application requires prospective validation. Larger multicentre studies should determine whether adiponectin, leptin and hs-CRP provide incremental prognostic information beyond conventional risk factors and whether their combined assessment can improve prediction of cardiovascular events.

## References

1. Libby P, Buring JE, Badimon L, Hansson GK, Deanfield J, Bittencourt MS, et al. Atherosclerosis. Nat Rev Dis Primers. 2019; 5(1):56. doi:10.1038/s41572-019-0106-z.
2. Libby P, Ridker PM, Maseri A. Inflammation and atherosclerosis. Circulation. 2002;105(9): 1135-1143. doi:10.1161/hc0902.104353.
3. Kershaw EE, Flier JS. Adipose tissue as an endocrine organ. J Clin Endocrinol Metab. 2004;89(6):2548-2556. doi:10.1210/jc.2004-0395.
4. Ronti T, Lupattelli G, Mannarino E. The endocrine function of adipose tissue: an update. Clin Endocrinol (Oxf). 2006;64(4):35 5-365. doi:10.1111/j.1365-2265.2006.02474.x.
5. Kadowaki T, Yamauchi T, Kubota N, Hara K, Ueki K, Tobe K. Adiponectin and adiponectin receptors in insulin resistance, diabetes, and the metabolic syndrome. J Clin Invest. 2006; 116(7):1784-1792. doi:10.1172/JCI2912 6.
6. Gil-Campos M, Cañete R, Gil A. Adiponectin, the missing link in insulin resistance and obesity. Clin Nutr. 2004;23(5):963-974. doi:10.1016/j.clnu.2004.04.010.
7. Han SH, Quon MJ, Kim JA, Koh KK. Adiponectin and cardiovascular disease: response to therapeutic interventions. J Am

Coll Cardiol. 2007;49(5):531-538. doi:10.10 16/j.jacc.2006.08.061.
8. Ouchi N, Kihara S, Arita Y, Okamoto Y, Maeda K, Kuriyama H, et al. Adiponectin, an adipocyte-derived plasma protein, inhibits endothelial NF-kappaB signaling through a cAMP-dependent pathway. Circulation. 2000;102(11):1296-1301. doi:10.1161/01.CIR. 102.11.1296.
9. Ouchi N, Kihara S, Arita Y, Nishida M, Matsuyama A, Okamoto Y, et al. Adipocyte-derived plasma protein adiponectin suppresses lipid accumulation and class A scavenger receptor expression in human monocyte-derived macrophages. Circulation. 2001;103 (8):1057-1063. doi:10.1161/01.CIR.103.8.10 57.
10. Ouchi N, Kihara S, Arita Y, Maeda K, Kuriyama H, Okamoto Y, et al. Adiponectin, an adipocyte-derived plasma protein, inhibits endothelial NF-kappaB signaling through a cAMP-dependent pathway. Circulation. 2000;102(11):1296-1301. doi:10.1161/01.CIR. 102.11.1296.
11. Tsubakio-Yamamoto K, Matsuura F, Koseki M, Oku H, Sandoval JC, Inagaki M, et al. Adiponectin prevents atherosclerosis by increasing cholesterol efflux from macrophages. Biochem Biophys Res Commun. 2008;375(3):390-394. doi:10.1016/j.bbrc.2008. 08.009.
12. Ahima RS. Adipose tissue as an endocrine organ. Obesity (Silver Spring). 2006;14 Suppl 5:242S-249S. doi:10.1038/oby.2006.317.
13. Knudson JD, Payne GA, Borbouse L, Tune JD. Leptin and mechanisms of endothelial dysfunction and cardiovascular disease. Curr Hypertens Rep. 2008;10(6):434-439. doi:10.10 07/s11906-008-0082-2.
14. Beltowski J. Leptin and atherosclerosis. Atherosclerosis. 2006;189(1):47-60. doi:10.10 16/j.atherosclerosis.2006.03.003.
15. Knudson JD, Dincer UD, Zhang C, Swafford AN Jr, Koshida R, Picchi A, et al. Leptin receptors are expressed in coronary arteries, and hyperleptinemia causes significant coronary endothelial dysfunction. Am J Physiol Heart Circ Physiol. 2005;289(1). doi:10.1152/ajpheart.01159.2004.
16. Sattar N, Wannamethee G, Sarwar N, Chernova J, Lawlor DA, Kelly A, et al. Leptin and coronary heart disease: prospective study and systematic review. J Am Coll Cardiol. 2009;53(2):167-175. doi:10.1016/j.jacc.2008. 09.035.
17. Chai SB, Sun F, Nie XL, Wang J. Leptin and coronary heart disease: a systematic review and meta-analysis. Atherosclerosis. 2014;233 (1):3-10. doi:10.1016/j.atherosclerosis.2013.11.069.
18. Libby P. Inflammation in atherosclerosis. Nature. 2002;420(6917):868-874. doi:10.1038 /nature01323.
19. Ridker PM, Morrow DA. C-reactive protein, inflammation, and coronary risk. Cardiol Clin. 2003;21(3):315-325. doi:10.1016/S0733-8651(03)00079-1.
20. Ridker PM. High-sensitivity C-reactive protein, inflammation, and cardiovascular risk: from concept to clinical practice to clinical benefit. Am Heart J. 2004;148(1 Suppl). doi:10.1016/j.ahj.2004.04.028.
21. Ridker PM, Rifai N, Rose L, Buring JE, Cook NR. Comparison of C-reactive protein and low-density lipoprotein cholesterol levels in the prediction of first cardiovascular events. N Engl J Med. 2002;347(20):1557-1565. doi:10.1056/NEJMoa021993.
22. Molica F, Morel S, Kwak BR, Rohner-Jeanrenaud F, Steffens S. Adipokines at the crossroad between obesity and cardiovascular disease. Thromb Haemost. 2015;113(3):553-566. doi:10.1160/TH14-06-0513.
23. Galic S, Oakhill JS, Steinberg GR. Adipose tissue as an endocrine organ. Mol Cell Endocrinol. 2010;316(2):129-139. doi:10.101 6/j.mce.2009.08.018.
24. Hara K, Yamauchi T, Imai Y, Manabe I, Nagai R, Kadowaki T. Reduced adiponectin level is associated with severity of coronary artery disease. Int Heart J. 2007;48(2):149-153. doi:10.1536/ihj.48.149.
25. Li S, et al. The relationship between serum adiponectin levels with the presence and severity of coronary artery disease. J Cardiovasc Dis Res. 2012;3(4):?
26. Sattar N, Wannamethee G, Sarwar N, Tchernova J, Cherry L, Wallace AM, et al. Adiponectin and coronary heart disease: a prospective study and meta-analysis. Circulation. 2006;114(7):623-629. doi:10.116 1/CIRCULATIONAHA.106.618918.
27. Kanhai DA, Kranendonk ME, Uiterwaal CSPM, van der Graaf Y, Kappelle LJ, Visseren FLJ. Adiponectin and incident coronary heart disease and stroke. A systematic review and meta-analysis of prospective studies. Obes Rev. 2013;14(7): 555-567. doi:10.1111/obr.12027.
28. Masood A, Jafar SS, Akram Z. Serum high sensitivity C-reactive protein levels and the severity of coronary atherosclerosis assessed by angiographic Gensini score. J Pak Med Assoc. 2011;61(4):325-327.
29. Dursunoğlu D, Göksoy H, Oztürk M, Rota S. A relationship between CRP, adiponectin and Gensini score in the patients with coronary artery disease. Anadolu Kardiyol Derg. 2011;11(2):?

30. Shanker J, Kakkar V, Jauhari S, et al. Relationship of adiponectin and leptin to coronary artery disease, classical cardiovascular risk factors and atherothrombotic biomarkers in the IARS cohort. Thromb Haemost. 2012;108(4):769-779. doi:10.1160/TH12-04-0263.
31. Gensini GG. A more meaningful scoring system for determining the severity of coronary heart disease. Am J Cardiol. 1983;51 (3):606. doi:10.1016/S0002-9149(83)80105-2.
32. Wozniak SE, Gee LL, Wachtel MS, Frezza EE. Adipose tissue: the new endocrine organ? A review article. Dig Dis Sci. 2009;54(9): 1847-1856. doi:10.1007/s10620-008-0585-3.
33. Yang L, Li B, Zhao Y, Zhang Z. Prognostic value of adiponectin level in patients with coronary artery disease: a systematic review and meta-analysis. Lipids Health Dis. 2019;18:174. doi:10.1186/s12944-019-1168-3.
34. Libby P, Ridker PM, Hansson GK. Inflammation in atherosclerosis: from pathophysiology to practice. J Am Coll Cardiol. 2009;54(23):2129-2138. doi:10.101 6/j.jacc.2009.09.009.
35. Danesh J, Wheeler JG, Hirschfield GM, Eda S, Eiriksdottir G, Rumley A, et al. C-reactive protein and other circulating markers of inflammation in the prediction of coronary heart disease. N Engl J Med. 2004;350 (14):1387-1397. doi:10.1056/NEJMoa032804.
36. Ridker PM. From C-reactive protein to interleukin-6 to interleukin-1: moving upstream to identify novel targets for atheroprotection. Circ Res. 2016;118(1):145-156. doi:10.1161/CIRCRESAHA.115.306656.
37. Mohammadi M, et al. Association between plasma leptin/adiponectin ratios with the extent and severity of coronary artery disease. BMC Cardiovasc Disord. 2020;20:197. doi:10.11 86/s12872-020-01723-7.
38. Kajikawa Y, Ikeda M, Takemoto S, Tomoda J, Ohmaru N, Kusachi S. Association of circulating levels of leptin and adiponectin with metabolic syndrome and coronary heart disease in patients with various coronary risk factors. Int Heart J. 2011;52(1):17-22. doi:10. 1536/ihj.52.17.
39. Pischon T, Girman CJ, Hotamisligil GS, Rifai N, Hu FB, Rimm EB. Plasma adiponectin levels and risk of myocardial infarction in men. JAMA. 2004;291(14):1730-1737. doi:10.100 1/jama.291.14.1730.
40. Choi KM, Lee J, Lee KW, Seo JA, Oh JH, Kim SG, et al. Serum adiponectin concentrations predict the developments of type 2 diabetes and the metabolic syndrome in elderly Korean subjects. Clin Endocrinol (Oxf). 2004;61(1):75-80. doi:10.1111/j.1365-2265.2004.02056.x.