

Association of Visceral Adiposity, Core Skeletal Muscle Mass, Atherogenic Index of Plasma, and Renal Function (CKD-EPI) with Framingham Cardiovascular Risk Score in Adults: A Cross-Sectional Study

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Abstract

Background: Cardiovascular risk prediction increasingly incorporates markers of adiposity, muscle composition, and metabolic function. This study examined the associations among visceral adiposity, Core Skeletal Muscle Mass (CSMM), Atherogenic Index of Plasma (AIP), and renal function assessed using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation in relation to the Framingham Cardiovascular Risk Score (FRS) in adults, aiming to elucidate their interrelated contributions to Cardiovascular Disease (CVD) prevention.

Methods: A cross-sectional study was conducted among 520 adults aged 30–75 years. Visceral adiposity, CSMM, AIP, and CKD-EPI were measured and analyzed alongside FRS. Path analysis using SmartPLS assessed direct and indirect associations. The sample size and analytical framework followed current epidemiological standards for body composition indices and risk prediction models.

Results: Visceral adiposity demonstrated a strong positive association with AIP ($\beta = 0.339$), which in turn correlated with both CKD-EPI ($\beta = 0.030$) and the FRS ($\beta = 0.389$). CSMM was inversely related to AIP ($\beta = -0.070$), suggesting a protective effect, while CKD-EPI showed a modest negative association with the FRS ($\beta = -0.080$). The overall model indicated that visceral adiposity and AIP are key mediators in cardiovascular risk estimation among adults.

Conclusions: Visceral adiposity and AIP are significantly linked to cardiovascular risk as quantified by the FRS, with renal function and skeletal muscle mass serving as secondary modulators. These findings highlight the importance of integrating adiposity and metabolic markers into CVD risk stratification, supporting tailored preventive strategies in clinical practice.

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Introduction

Cardiovascular Disease (CVD) continues to pose a major public health challenge worldwide, reflecting complex interactions between lifestyle, metabolic, and demographic factors. Globally, CVD remains the leading cause of death, responsible for approximately 31% of all deaths worldwide, equating to over 17.9 million deaths annually.¹ Low- and middle-income countries account for nearly 80% of these fatalities.² In Asia, CVD accounts for roughly 30-40% of total mortality, with regional variation driven by population aging and lifestyle factors.³ In Indonesia, CVD is responsible for about 37% of all deaths, highlighting a significant national health burden.⁴ Prevalence data indicate that hypertension affects around 34% of adults, and metabolic syndrome prevalence ranges from 20% to 30%, underscoring the urgent need for prevention and management programs.⁵

Beyond the conventional risk factors such as hypertension, dyslipidemia, smoking, and aging, identifying modifiable determinants of cardiovascular risk has become increasingly important. Recent studies highlight that variations in body composition, lipid-related markers, and renal function may provide complementary information for more precise risk prediction.

First, the accumulation of visceral adiposity, fat deposited around internal organs, distinct from subcutaneous fat, has been increasingly implicated in cardiometabolic dysfunction. Visceral fat is metabolically active, associated with insulin resistance, inflammation, and adverse lipid profiles, and may portend a higher CVD risk even in persons with normal Body Mass Index (BMI). In parallel, skeletal muscle mass and quality have emerged as meaningful predictors: lower core or appendicular skeletal muscle mass is being linked with increased cardiovascular events and worse outcomes, highlighting the interplay between muscle health and cardiovascular risk. For example, a recent prospective cohort found that reduced skeletal muscle mass predicted cardiovascular events independent of traditional risk factors.⁶

Concurrently, skeletal muscle mass, especially core or appendicular skeletal muscle, is increasingly recognized as a relevant cardiovascular risk factor. Muscle mass has metabolic functions beyond locomotion; it contributes to glucose disposal, insulin sensitivity, and myokine secretion. A recent review suggests that higher Core Skeletal Muscle Mass (CSMM) is linked with improved cardiometabolic health. Thus, muscle-mass indices

may capture a protective dimension of body composition overlooked by measures such as BMI or Waist Circumference (WC).⁷

Second, the Atherogenic Index of Plasma (AIP), defined as the logarithm of the ratio of Triglycerides to High-Density Lipoprotein Cholesterol [$\log(\text{TG}/\text{HDL-C})$], has been proposed as a simple but robust marker of lipoprotein atherogenicity. Elevated AIP has shown independent associations with Major Adverse Cardiovascular Events (MACE) and coronary artery disease in meta-analyses.⁸⁻⁹

Third, renal function, often assessed by the estimated Glomerular Filtration Rate (eGFR) via the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation, is a recognized independent risk factor for CVD. Declining eGFR reflects both vascular and metabolic pathology, and recent work suggests that eGFR calculated by CKD-EPI is more tightly linked to incident CVD and mortality than older equations in some populations.¹⁰⁻¹¹

Widely used cardiovascular risk scores, such as the Framingham Cardiovascular Risk Score (FRS), estimate 10-year CVD risk based on demographic and traditional risk factors. However, its applicability in the Indonesian population warrants careful consideration, as it was originally developed in a Western cohort and may demonstrate variable calibration and predictive accuracy in Asian populations, including Southeast Asia. Despite these limitations, the Framingham model remains a well-established framework in epidemiological research. Importantly, it may not fully capture emerging dimensions of cardiovascular risk, such as body composition, lipoprotein quality, and renal impairment. Therefore, integrating these markers with the FRS may provide a more comprehensive approach to cardiovascular risk stratification in adults.¹²

Despite growing evidence linking individual adiposity markers, lipid-derived indices, and renal function to cardiovascular risk, there remains a notable gap in integrating these emerging markers into a unified risk assessment framework alongside established risk scores such as the FRS. Specifically, limited research has systematically evaluated the combined contribution of visceral adiposity, CSMM, AIP, and renal function (CKD-EPI eGFR) within a single adult cohort to determine whether such integration enhances cardiovascular risk stratification. Furthermore, most studies have focused on individual markers in isolation or on populations with specific diseases, leaving

uncertainty about their collective predictive value in general adult populations. This research seeks to address these gaps by simultaneously assessing these markers' independent and joint associations with cardiovascular risk, thus providing novel insights into improved risk prediction beyond traditional approaches.²⁸⁻²⁹

Against this background, our cross-sectional study aims to examine the association between visceral adiposity, CSMM, AIP, and renal function (via CKD-EPI eGFR) on one hand, and the FRS on the other, among a cohort of adults. Specifically, we hypothesize that higher visceral adiposity, lower CSMM, higher AIP values, and reduced eGFR will each be independently associated with higher predicted cardiovascular risk (via Framingham), and that combining these variables may further enhance discrimination. By exploring these relationships in a real-world adult sample, we seek to shed light on whether these emerging markers might aid in refining cardiovascular risk assessment beyond conventional approaches.

Methods

Study Design and Period

This study employed an analytical cross-sectional design to examine the associations between visceral adiposity, CSMM, AIP, and renal function (estimated by CKD-EPI) with the FRS among adults. Data collection was conducted over five months, from August to December 2025. The study was carried out in three regions of Indonesia: Jakarta, Salatiga (Central Java), and Banten (West Java), representing a diverse sample of urban and semi-rural populations. This multi-regional approach was chosen to improve external validity and capture possible variations in cardiovascular risk factors related to lifestyle, socioeconomic status, and ethnic background. All participants were provided with detailed information about the study and gave written informed consent before participation.

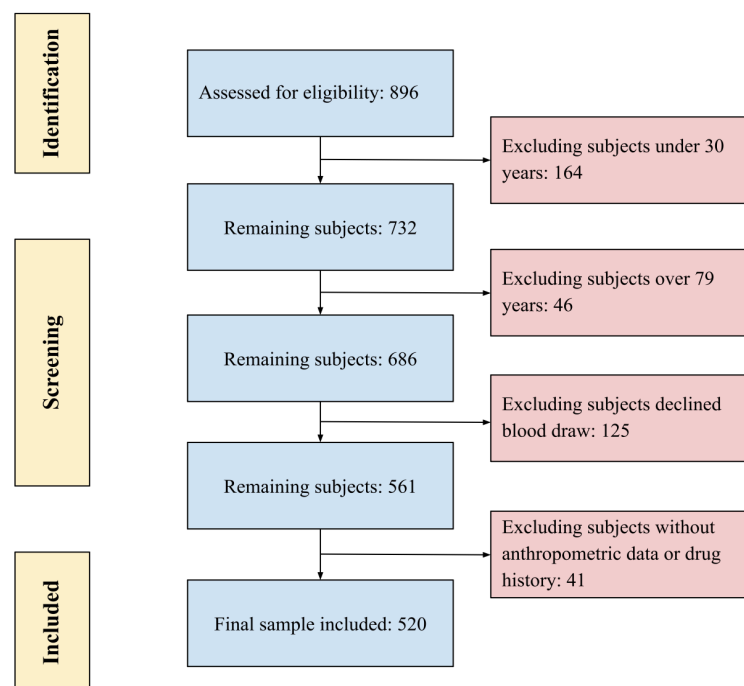


Figure 1. Flow chart of participant selection.

Study Population

A total of 896 individuals were assessed for eligibility. Of these, 376 participants were excluded due to age <30 years ($n = 164$), age >79 years ($n = 46$), refusal of blood sampling ($n = 125$), or missing anthropometric data ($n = 41$). The final analysis included 520 participants. Participants were

recruited using a purposive sampling technique, targeting adults who met the inclusion criteria and were willing to participate. Recruitment was facilitated through community health centers, local health posts, and public health campaigns conducted in collaboration with local authorities and healthcare providers (Figure 1).

Inclusion and Exclusion Criteria

The inclusion criteria were:

1. Age ≥ 30 years, <79 years
2. Residing in one of the study locations (Jakarta, Salatiga, or Banten).
3. Provided written informed consent to participate.
4. Willing to undergo anthropometric and biochemical measurements.

The exclusion criteria were:

1. Individuals with acute infection or known chronic diseases that could alter lipid or renal parameters.
2. Current use of lipid-lowering drugs, corticosteroids, or nephrotoxic agents.
3. Pregnant or lactating women.
4. Participants who refused blood collection or failed to complete essential measurements.

Data Collection

Data collection was conducted from August to December 2025 across three regions: Jakarta, Salatiga, and Banten, by a trained multidisciplinary research team consisting of physicians, nutritionists, nurses, and laboratory technicians. All team members were trained before fieldwork to ensure standardization of procedures and minimize inter-observer variation.

Data were obtained through direct measurements, fasting blood sampling, and structured interviews using a standardized questionnaire. The data collection procedures were as follows:

1. Sociodemographic and Lifestyle Data
Information on age, sex, smoking status, physical activity, alcohol consumption, medical history, and medication use was collected through face-to-face interviews using a structured and pretested questionnaire.
2. Anthropometric Measurements
Body weight and height were measured using a digital scale OMRON HBF-375 and stadiometer OneHealth HT-721, respectively, with participants wearing light clothing and no shoes. WC was measured midway between the lowest rib and the iliac crest using a non-stretchable measuring tape. BMI was calculated as weight (kg)/height (m^2).
3. Body Composition Analysis
Visceral adiposity and CSMM were assessed using a Bioelectrical Impedance Analyzer (BIA) OMRON HBF-375. The device provided estimates of Visceral Fat Area (VFA, cm^2), total body fat percentage,

and CSMM. Skeletal Muscle Index (SMI) was calculated by dividing skeletal muscle mass (kg) by height squared (m^2).

4. Blood Collection and Biochemical Analysis

After an 8–12 hour overnight fast, venous blood samples were collected by trained medical staff. Samples were analyzed for TG, HDL-C, Low-Density Lipoprotein Cholesterol (LDL-C), total cholesterol, fasting glucose, and serum creatinine using an SM 308 Semi-Auto Chemistry Analyzer.

The AIP was calculated as: $AIP = \log(TG/HDL-C)$.

Renal function was estimated using the CKD-EPI equation on the MDCalc website to obtain the eGFR (eGFR, $mL/min/1.73 m^2$).

5. Cardiovascular Risk Assessment

The FRS was computed using the MDCalc website for each participant using the standard algorithm incorporating age, sex, total cholesterol, HDL-C, systolic blood pressure, diabetes status, and smoking history. Participants were categorized into low ($<10\%$), moderate ($10\text{--}20\%$), and high ($>20\%$) 10-year CVD risk groups.

6. Data Quality Assurance

All instruments were calibrated before use, and 10% of participants were re-measured to ensure intra- and inter-observer reliability. Data entry was double-checked for accuracy, and missing or inconsistent data were verified through follow-up with the participants where possible.

Data Analysis

Sample size was determined by an a priori power analysis and cross-checked against Partial Least Squares Structural Equation Modeling (PLS-SEM) recommendations. The power analysis ($\alpha = 0.05$, power = 0.80, target effect size $f^2 = 0.15$) indicated a minimum required sample, and the PLS “10-times rule” (ten times the maximum number of structural paths into any endogenous variable) produced a comparable minimum; the recruited sample of 520 participants exceeded both criteria.

Data analysis was performed using SmartPLS version 4.0 (SmartPLS GmbH). Prior to model estimation, data were screened for missing values and outliers. The distribution of continuous variables was examined using the Shapiro–Wilk test, and since the data did not satisfy the normality assumption, a non-parametric approach was applied.

PLS-SEM was employed to assess both the measurement model and the structural model, as this method is robust against non-normal data and suitable for complex models with multiple mediating variables. Path coefficients, t-values, and p-values were calculated using the bootstrapping procedure with 5,000 resamples. Additionally, PLS-SEM is advantageous in handling multicollinearity and does not require strict distributional assumptions, making it appropriate for examining the integrated effects of body composition, metabolic markers, and renal

function on cardiovascular risk.

The relationships among visceral adiposity, CSMM, AIP, renal function (CKD-EPI), and FRS were evaluated through standardized path coefficients (β). The significance level was set at $p < 0.05$ for all analyses. Model quality was assessed based on the coefficient of determination (R^2), predictive relevance (Q^2), and the Standardized Root Mean Square Residual (SRMR) to ensure adequate model fit and predictive validity.

Table 1. Baseline sociodemographic and clinical characteristics of participants (N = 520).

Characteristic	Overall (Mean $\pm$ SD)
Age, years	49.33 $\pm$ 11.471
Sex, n(%)	
Male	133 (25.6)
Female	387 (74.4)
Smoking status, n(%)	
Yes	84 (16.2)
No	436 (83.8)
Total Cholesterol (mg/dL)	204.13 $\pm$ 37.184
HDL (mg/dL)	52.98 $\pm$ 20.931
Triglycerides (mg/dL)	175.21 $\pm$ 88.020
Systolic Blood Pressure (mmHg)	128.09 $\pm$ 18.048
Medically controlled hypertension, n(%)	
Yes	109 (21)
No	411 (79)
Creatinine (mg/dL)	1.0432 $\pm$ 1.174767
Framingham Risk Score (%)	3.949 $\pm$ 6.1298
CKD-EPI (mL/min/1.73 m ²)	83.39 $\pm$ 20.871
Visceral Fat (index/unit)	11.01 $\pm$ 6.669
Core Skeletal Muscle (kg)	19.07 $\pm$ 12.009
AIP	0.1393 $\pm$ 0.30968

Data are expressed as mean $\pm$ SD for continuous variables and as n (%) for categorical variables. Abbreviations: HDL, high-density lipoprotein; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; AIP, Atherogenic Index of Plasma.

Results

Participant Characteristics

A total of 520 participants were analyzed, with a mean age of 49.33 $\pm$ 11.47 years; 25.6% were males and 74.4% were females. Most participants were nonsmokers (83.8%), and 21.0% had medically controlled hypertension. The mean systolic blood pressure was 128.09 $\pm$ 18.05 mmHg. Mean total cholesterol, HDL, and triglyceride levels were 204.13 $\pm$ 37.18, 52.98 $\pm$ 20.93, and 175.21 $\pm$ 88.02 mg/dL, respectively. The mean eGFR (CKD-EPI) was 83.39 $\pm$ 20.87 mL/min/1.73 m², while the average FRS

was 3.95 $\pm$ 6.13%. Mean visceral fat, core skeletal muscle, and AIP were 11.01 $\pm$ 6.67, 19.07 $\pm$ 12.01, and 0.139 $\pm$ 0.310, respectively. (Table 1).

Partial Least Squares Structural Equation Modeling (PLS-SEM) Analysis

As shown in Figure 2, visceral adiposity demonstrated a strong positive association with AIP ($\beta = 0.339$), indicating that higher visceral fat levels contribute significantly to increased plasma atherogenicity. Conversely, CSMM exhibited a weak negative association with AIP ($\beta = -0.070$), suggesting that greater CSMM (lower CSMI) is related to more favorable lipid profiles.

AIP showed a positive association with renal function (CKD-EPI, $\beta = 0.030$) and a strong positive relationship with FRS ($\beta = 0.389$), implying that dyslipidemia contributes to both renal and cardiovascular risk. In contrast, CKD-EPI had a negative association with Framingham risk ($\beta = -0.080$), suggesting that better kidney function is protective against cardiovascular risk.

The R^2 values were 0.108 for AIP, 0.001 for CKD-EPI, and 0.156 for Framingham risk, indicating that the model explains 10.8% of the variance in AIP, 0.1% in CKD-EPI, and 15.6% in cardiovascular risk. Among all predictors, visceral adiposity emerged as the most influential variable, primarily through its indirect effect mediated by AIP. Overall, these findings suggest that visceral adiposity and reduced CSMM jointly contribute to increased cardiovascular risk, with AIP serving as a key mediating biomarker linking metabolic and renal dysfunction to elevated FRS. Although statistically significant, the associations involving renal function were small in magnitude and may have limited clinical relevance. Therefore, these findings should

be interpreted with caution, as statistical significance does not necessarily translate into meaningful clinical impact.

Model fit was assessed using the SRMR, R^2 , effect size (f^2), and Q^2 parameters. The SRMR value of the model was below 0.08, indicating an acceptable level of fit between the observed and predicted covariance matrices. The R^2 values for AIP (0.108), CKD-EPI (0.001), and Framingham risk (0.156) suggest that the model explained 10.8%, 0.1%, and 15.6% of the variance in each respective endogenous variable. The f^2 of the paths revealed that visceral adiposity had a moderate impact on AIP. At the same time, the effects of CSMM on AIP and CKD-EPI on Framingham risk were small, according to Cohen's classification (0.02 = small, 0.15 = medium, 0.35 = large). The Q^2 values, derived using the blindfolding procedure, were greater than zero, confirming the model's Q^2 for AIP and Framingham risk.

Overall, the model demonstrated adequate structural validity and predictive accuracy, suggesting that visceral adiposity and decreased CSMM contribute to increased cardiovascular risk through alterations in lipid metabolism and renal function.

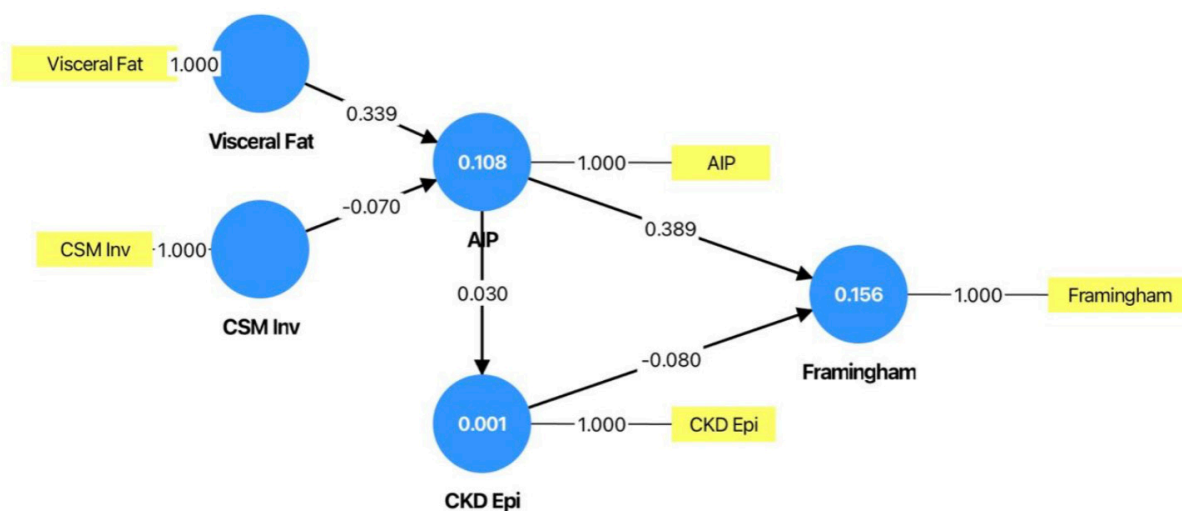


Figure 2. Structural equation model illustrating the relationships among visceral adiposity, core skeletal muscle mass inverse (CSMM Inv), AIP, renal function (CKD-EPI), and Framingham cardiovascular risk score. Values on the arrows represent standardized path coefficients (β).

Discussion

This study highlights the independent and combined roles of visceral adiposity, CSMM, AIP, and renal function (CKD-EPI) with the FRS in adults. The path analysis results demonstrate several key relationships relevant for understanding cardiovascular risk stratification.

The positive association between visceral adiposity and the FRS is consistent with evidence identifying visceral fat as a strong predictor of

cardiovascular events. Ballin et al. (2021) reported that increased visceral adipose tissue was associated with a higher risk of stroke and myocardial infarction, while Cesaro et al. (2023) demonstrated that reduction of visceral fat improved inflammatory markers. Similarly, Zhang et al. (2025) found that higher visceral fat was linked to adverse metabolic profiles, including elevated glucose, TG, and insulin resistance, as well as reduced HDL levels. Collectively,

these findings support the role of visceral adiposity in promoting metabolic dysfunction and increasing cardiovascular risk.¹³⁻¹⁵

The underlying mechanisms may involve the metabolic and inflammatory effects of visceral fat accumulation. Visceral adipose tissue secretes pro-inflammatory adipokines, such as TNF- α and IL-6, which promote insulin resistance, impair lipid metabolism, and contribute to endothelial dysfunction and atherogenic lipid profiles.¹⁶⁻¹⁷ In contrast, skeletal muscle plays a key role in glucose and lipid utilization; thus, reduced muscle mass may worsen metabolic disturbances, leading to higher AIP and cardiovascular risk. These findings underscore the importance of reducing visceral adiposity while preserving muscle mass to mitigate cardiometabolic risk.²³

Recent evidence supports these mechanisms. Kim et al. (2021) showed that individuals with visceral adiposity or sarcopenia had a significantly higher risk of metabolic syndrome, characterized by increased visceral fat and reduced muscle mass.¹⁶ Aminuddin et al. (2021) further demonstrated that reduced muscle strength was associated with increased arterial stiffness, indicating the protective role of muscle integrity.¹⁷ Similarly, Lee et al. (2023) reported that higher visceral fat was linked to adverse metabolic parameters and arterial stiffness, while skeletal muscle mass showed a protective association.²³ Collectively, these findings highlight the combined impact of excess visceral adiposity and reduced muscle mass in worsening metabolic and vascular health, thereby increasing cardiometabolic risk.

Conversely, higher CSMM (represented as inverse in the analysis, CSM Inv) is inversely associated with both AIP and the FRS, suggesting a protective role of skeletal muscle against cardiovascular risk. Low muscle mass, particularly in the context of sarcopenia or age-related muscle loss, has been implicated in poor metabolic health and increased cardiovascular events. Mechanistically, skeletal muscle serves as a primary site for insulin-mediated glucose uptake; thus, reduced muscle mass impairs metabolic flexibility, increases insulin resistance, and creates a milieu conducive to metabolic syndrome and subsequent CVD. Interventional studies also suggest that muscle preservation through resistance training and physical activity may attenuate cardiovascular risk, independent of adiposity.¹⁶⁻¹⁷

These findings are consistent with previous studies. Kim et al. (2021) reported that individuals with sarcopenia had a significantly higher risk of

metabolic syndrome, accompanied by lower skeletal muscle mass compared with those without the condition, highlighting the metabolic disadvantage of reduced muscle mass.¹⁶ Similarly, Aminuddin et al. (2021) demonstrated that muscle strength, as reflected by handgrip strength, was inversely associated with arterial stiffness, indicating a protective role of muscle integrity on vascular health.¹⁷ Collectively, these findings emphasize that maintaining skeletal muscle mass and function plays an important role in reducing insulin resistance, arterial stiffness, and overall cardiovascular risk.

The AIP, a log-transformed ratio of TG to HDL-C that functions as a mediator, reflects the balance of TG and HDL cholesterol. Elevated AIP is linked to heightened cardiovascular risk and is associated with both adiposity and muscle mass changes. In this study, AIP was shown to mediate the relationship between body composition parameters and Framingham risk, further supporting its utility as a biomarker for residual and modifiable risk.^{16,8}

Consistent with these findings, Kim et al. (2021) showed that individuals with visceral adiposity and sarcopenia exhibited adverse lipid profiles, including higher TG and lower HDL-C, contributing to an elevated AIP pattern associated with metabolic syndrome.¹⁶ Similarly, Rad et al. (2024) demonstrated that AIP is a strong independent predictor of cardiovascular risk, with a significant positive correlation with the FRS and higher values observed in high-risk individuals.⁸ Together, these findings highlight AIP as a robust integrative biomarker linking visceral adiposity, dyslipidemia, and cardiovascular risk, underscoring its role in identifying modifiable metabolic pathways beyond traditional lipid measures.

An important methodological consideration in this study is the potential for conceptual and mathematical overlap between the predictors and the outcome measure. The FRS incorporates lipid parameters such as total cholesterol and HDL-C, while AIP is derived from TG and HDL-C. This shared component may introduce a degree of circularity, potentially inflating the observed associations between AIP and cardiovascular risk. Therefore, the strength of the relationship between AIP and the FRS should be interpreted with caution, as it may partially reflect mathematical coupling rather than purely independent biological effects.

Renal function, as assessed by the CKD-EPI equation, demonstrated a complex relationship with cardiovascular outcomes. Korhonen et al. (2022) reported that both reduced and elevated eGFR

levels were associated with adverse cardiovascular events, suggesting that abnormal renal filtration reflects underlying metabolic and hemodynamic disturbances.³⁰ Specifically, individuals with renal hyperfiltration ($\text{eGFR} \geq 105 \text{ mL/min/1.73 m}^2$) had a significantly increased risk of all-cause mortality ($\text{HR} = 2.15$, 95% CI: 1.24–3.73) and incident atrial fibrillation ($\text{HR} = 2.10$, 95% CI: 1.21–3.65), compared to those with normal eGFR ($90\text{--}104 \text{ mL/min/1.73 m}^2$). Conversely, mild renal impairment ($\text{eGFR} 60\text{--}74 \text{ mL/min/1.73 m}^2$) was associated with a lower risk of heart failure ($\text{HR} = 0.45$, 95% CI: 0.21–0.96).³⁰ These findings support the role of renal function in cardiovascular risk stratification. However, in the present study, renal function showed only a modest association with cardiovascular risk and a negligible explained variance, indicating a limited contribution within this model.

From a clinical perspective, the AIP emerges as a practical and cost-effective biomarker for early cardiovascular risk detection. Compared with conventional lipid parameters, AIP better reflects the balance between protective and atherogenic lipoproteins and has been shown to predict both subclinical atherosclerosis and overt CVD. This makes AIP particularly useful for populations with increased visceral adiposity or reduced CSMM, where traditional lipid markers may underestimate cardiometabolic risk.

Complementary findings from Noels et al. (2025) further highlight the importance of renal function in cardiovascular risk stratification. In a large multicohort analysis, declining kidney function was associated with a marked increase in CVD prevalence, mortality, and heart failure incidence.²⁴ These findings underline the cardiorenal connection, where microvascular endothelial dysfunction, oxidative stress, and neurohormonal activation mediate the interaction between metabolic and vascular damage. Combining AIP and CKD-EPI with conventional scores such as the Framingham model could significantly enhance cardiovascular risk prediction.

Collectively, these findings highlight the importance of assessing body composition alongside traditional risk factors in cardiovascular risk prediction. Luo et al. (2024) demonstrated that higher Visceral Adiposity Index (VAI) was associated with increased risk of coronary heart disease and poorer overall survival, underscoring the prognostic value of visceral fat accumulation.¹⁹ These results indicate that higher visceral adiposity, reflected by an elevated VAI, significantly increases

coronary heart disease risk and is associated with poorer overall survival. Interventions aimed at reducing visceral fat and preserving CSMM may therefore provide dual cardiometabolic benefits. Integrating renal function measures such as CKD-EPI with adiposity indices like VAI could enhance cardiovascular risk stratification by capturing both metabolic and hemodynamic disturbances.¹⁹⁻²⁰

Although PLS-SEM was used to explore complex interrelationships among variables, complementary analyses using conventional regression models were not performed in this study. Future research incorporating traditional regression approaches may provide additional validation and improve the robustness of the findings.

Further research should explore the longitudinal implications of these associations and assess whether targeted interventions based on body composition can effectively reduce cardiovascular risk across diverse populations. In addition, sensitivity analyses or alternative analytical approaches to minimize mathematical dependency were not performed in this study and are recommended for future research to strengthen the validity and robustness of these findings.

Limitations

This study has several limitations that should be considered when interpreting the findings. First, due to the cross-sectional design, causal relationships between visceral adiposity, CSMM, AIP, renal function, and cardiovascular risk cannot be definitively established. While associations were observed, longitudinal studies are needed to confirm the temporal sequence and causality of these relationships.²⁵

Second, the study population and sample size may limit the generalizability of the findings. If the sample is not representative of wider populations in terms of age range, sex differences, ethnicity, or health status, caution must be exercised in extrapolating results to different demographic groups or clinical settings.²⁶ This study included a predominantly female population, which may limit the generalizability of the findings. Sex-specific analyses were not performed, and potential differences between males and females may not be fully captured. Future studies should consider stratified analyses or interaction testing to evaluate sex-specific effects better.

Third, potential confounding factors such as diet, physical activity levels, medication use, and socioeconomic status were not fully controlled or accounted for, which could influence the observed

associations between body composition variables and cardiovascular risk.²⁵

Fourth, measurement limitations related to assessing visceral fat and muscle mass through indirect methods or single time-point assessments may introduce variability or measurement bias. Advanced imaging techniques or repeated measurements could enhance accuracy in future research.^{25,27}

Fifth, the use of the FRS as the outcome may introduce methodological limitations due to shared lipid components with AIP, particularly HDL-cholesterol. This overlap may result in partial mathematical dependency and potential overestimation of associations. Therefore, the relationship between AIP and cardiovascular risk should be interpreted cautiously, and future studies using independent outcomes are needed to validate these findings.

A further limitation of this study is the use of the FRS, which was developed based on a Western population and may not be fully generalizable to the Indonesian setting. Differences in population characteristics may affect its predictive accuracy; therefore, the results should be interpreted cautiously. The use of regionally calibrated tools may provide more accurate risk assessment in future studies.

Finally, renal function's limited direct association with cardiovascular risk in this sample might be due to relatively preserved kidney function among participants or insufficient power to detect subtle effects. Broader studies with varied renal impairment levels may provide more insight.¹⁸

Addressing these limitations in future prospective studies with larger and more diverse cohorts, comprehensive confounder control, and improved measurement techniques will strengthen understanding of these complex interrelationships.

Larger, prospective cohorts with diverse populations are needed to validate and generalize findings, and to clarify causal pathways linking these markers with cardiovascular outcomes. Incorporating longitudinal measurements would allow evaluation of dynamic changes in these markers and their temporal relationship with cardiovascular events. Additionally, integration of emerging technologies such as machine learning and multi-omics data holds promise to refine risk stratification further, enabling precision prevention tailored to individual risk profiles. Standardization of measurement protocols and inclusive, multi-center collaborations will be crucial to translating

these advances into scalable, clinically actionable risk prediction tools for broader population health benefit.

Conclusion

This cross-sectional study demonstrates the significant associations of visceral adiposity, CSMM, and AIP with cardiovascular risk as measured by the FRS. Visceral fat is positively correlated with increased cardiovascular risk, underscoring its role as a critical modifiable factor in cardiometabolic health. Conversely, greater CSMM appears protective, inversely related to both atherogenic lipid profiles and cardiovascular risk, highlighting the importance of muscle preservation in reducing risk. While renal function showed limited direct association in this cohort, these findings collectively emphasize the need for integrated assessment of body composition in cardiovascular risk evaluation beyond traditional risk factors. Strategies aimed at reducing visceral fat and maintaining or increasing CSMM could be beneficial components of cardiovascular prevention programs. Accordingly, the findings of this study should be interpreted as exploratory, and the role of AIP and other body composition markers in enhancing cardiovascular risk prediction requires further validation using independent outcome measures. Future prospective studies should validate these findings and explore causal pathways. Additionally, incorporating muscle and fat composition metrics into clinical risk prediction models might enhance precision medicine approaches for CVD prevention.

List of Abbreviations

AIP	Atherogenic Index of Plasma
BIA	Bioelectrical Impedance Analyzer
BMI	Body Mass Index
CKD-EPI	Chronic Kidney Disease Epidemiology Collaboration
CSMM	Core Skeletal Muscle Mass
CVD	Cardiovascular Disease
eGFR	Estimated Glomerular Filtration Rate
f ²	Effect size
FRS	Framingham Cardiovascular Risk Score
HDL-C	High-Density Lipoprotein Cholesterol
LDL-C	Low-Density Lipoprotein Cholesterol
MACE	Major Adverse Cardiovascular

PLS-SEM	Events Partial Least Squares Structural Equation Modeling
Q ²	Predictive relevance
R ²	Coefficient of determination
SMI	Skeletal Muscle Index
SRMR	Standardized Root Mean Square Residual
TG	Triglycerides
VAI	Visceral Adiposity Index
VFA	Visceral Fat Area
WC	Waist Circumference

Ethical Clearance

This study was conducted in accordance with the ethical principles of the Declaration of Helsinki and was approved by the Universitas Tarumanagara Health Research Ethics Committee (011-UTH-REC/UNTAR/I/2026). Written informed consent was obtained from all individual participants included in the study.

Publication Approval

All authors consent to the publication of this manuscript.

Authors' Contributions

NRHW conceived and designed the study, performed data collection and processing, analyzed and interpreted the data, and drafted the initial manuscript. RWK contributed to the study design, supervised clinical assessments, and critically revised the manuscript for important intellectual content. AP provided expert cardiology guidance, contributed to the interpretation of cardiovascular risk stratification, and critically reviewed the manuscript. YF oversaw the physiological and statistical methodology, assisted with data analysis interpretation, and gave final approval of the version to be published. All authors read and approved the final manuscript.

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Conflict of Interest

None.

Availability of Data and Materials

Not applicable.

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Copyright/Permissions for Figures

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Generative AI and AI-Assisted Technologies in the Writing Process

The authors acknowledge that artificial intelligence (AI) tools were only used to assist in language editing, grammar refinement, and formatting, and did not generate or alter the scientific content, data analyses, or final conclusions presented in this manuscript.

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