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Research Article

Association of LDL Particle Size and Apolipoprotein B with Severity of Coronary Artery Stenosis

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Abstract: Coronary artery disease (CAD) remains a leading cause of morbidity and mortality globally, with atherosclerotic plaque formation influenced by lipoprotein characteristics. Low-density lipoprotein (LDL) particle size and apolipoprotein B (ApoB) concentrations have emerged as potential determinants of atherogenic risk beyond conventional lipid parameters. This study investigated the association between LDL particle size, ApoB levels, and the severity of coronary artery stenosis in patients undergoing coronary angiography.

A cross-sectional study included 240 adults referred for diagnostic coronary angiography. LDL particle size was measured using gradient gel electrophoresis, and ApoB concentrations were quantified through immunoturbidimetric assay. Coronary stenosis severity was determined by quantitative coronary angiography and categorized into mild (<50%), moderate (50–70%), and severe (>70%) groups. Associations were analyzed using multivariable linear regression and Spearman's correlation with adjustment for traditional cardiovascular risk factors.

Smaller LDL particle size and elevated ApoB were significantly associated with increased severity of coronary stenosis. Mean LDL particle diameter decreased progressively from mild (26.8 ± 1.1 nm) to severe stenosis (25.4 ± 1.3 nm; $p < 0.001$), while mean ApoB levels increased (98 ± 22 mg/dL vs 129 ± 28 mg/dL; $p < 0.001$). Both parameters demonstrated independent associations with stenosis severity after adjusting for age, gender, smoking, hypertension, and diabetes ($\beta = -0.30$, $p < 0.001$ for LDL size; $\beta = 0.28$, $p < 0.001$ for ApoB).

These findings indicate that smaller LDL particles and higher ApoB concentrations are strongly associated with more severe coronary stenosis. Incorporating LDL particle size and ApoB into cardiovascular risk assessment may improve identification of individuals at risk for advanced atherosclerotic disease. Keywords: LDL particle size, apolipoprotein B, coronary stenosis, atherosclerosis, cardiovascular risk.

Introduction: Coronary artery disease (CAD) constitutes a major public health challenge characterized by stenotic

narrowing of coronary vessels resulting from atheromatous plaque development. The progressive accumulation of lipids and inflammatory cells within the arterial intima leads to luminal obstruction, ischemia, and adverse cardiovascular events. Traditional risk assessment for CAD has relied heavily on plasma lipid concentrations, particularly total cholesterol, low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C). Elevated LDL-C is well recognized as an independent risk factor for atherosclerosis; however, emerging evidence suggests that qualitative aspects of LDL particles, such as particle size and density, may provide deeper insights into atherogenicity.[1-3]

LDL particles are heterogeneous in size and composition, ranging from large, buoyant particles to small, dense subfractions. Small, dense LDL particles exhibit greater susceptibility to oxidative modification, enhanced arterial wall penetration, and prolonged plasma residence time, which collectively contribute to accelerated atherogenesis. These particles have diminished affinity for LDL receptors, resulting in reduced clearance and a greater propensity for retention in the subendothelial space. This biological behavior implicates small, dense LDL as a potentially superior marker of cardiovascular risk compared with LDL-C alone. Despite this, most clinical evaluations continue to prioritize LDL-C quantification without routinely considering particle characteristics.[4-7]

Apolipoprotein B (ApoB) represents the primary structural protein of atherogenic lipoproteins, including very-low-density lipoprotein (VLDL), intermediate density lipoprotein (IDL), and LDL. Each atherogenic particle contains a single ApoB molecule; hence, ApoB levels reflect the total number of circulating atherogenic particles. Elevated ApoB has been associated with increased risk of cardiovascular events, independent of traditional lipid measurements. Because ApoB quantifies particle number rather than lipid content, it may better capture the burden of atherogenic lipoproteins especially in individuals with discordant LDL-C levels but high particle counts due to smaller particle size.[8-10]

Recent studies increasingly support the independent predictive value of LDL particle size and ApoB for coronary atherosclerosis. Patients with smaller LDL particles often exhibit a cluster of metabolic abnormalities, including insulin resistance and dyslipidemia, which may further exacerbate plaque development. The interaction between particle size and particle number amplifies atherogenic potential, underscoring the need for integrated assessment of both parameters. Nevertheless, evidence linking these biomarkers directly to angiographic severity of coronary stenosis remains limited, and inconsistencies in study designs and populations have hindered universal adoption in clinical practice.[11-12]

Evaluation of LDL particle size has been facilitated through advanced laboratory techniques such as gradient gel electrophoresis, nuclear magnetic resonance spectroscopy, and ion-mobility analysis. These methods allow separation of LDL subfractions by size, enabling quantification of mean particle diameter. ApoB measurement using immunoassays provides a robust assessment of atherogenic particle burden. Integrating these measurements into investigations of coronary stenosis severity offers an opportunity to refine risk stratification and potentially tailor therapeutic strategies more effectively.

The severity of coronary stenosis, typically quantified via coronary angiography, remains

the benchmark for diagnosing and guiding management of obstructive CAD. Angiographic assessment provides direct visualization of luminal narrowing and plaque distribution, with stenosis severity correlating with clinical outcomes. However, conventional risk factors do not fully explain variability in stenosis severity among individuals, suggesting that additional biomarkers may enhance prognostic precision.

Genetic predispositions, inflammatory mediators, and lipoprotein structure have all been implicated in modulating atherogenesis. Within this landscape, LDL particle size and ApoB stand out as promising metrics that capture both qualitative and quantitative aspects of atherogenic lipoproteins. Smaller LDL particles have been associated with greater plaque burden and vulnerability, while elevated ApoB reflects the sheer number of particles capable of penetrating the arterial wall. Investigating their association with angiographic stenosis severity can clarify their potential role in clinical risk assessment.

The present study aims to investigate the relationship between LDL particle size, ApoB concentration, and severity of coronary artery stenosis as determined by quantitative coronary angiography. By examining a well-characterized cohort undergoing standard diagnostic evaluation, this study seeks to quantify how variations in lipoprotein particle characteristics correlate with plaque extent. The central hypothesis posits that smaller LDL particle size and higher ApoB levels are independently associated with more severe stenotic lesions, after adjusting for traditional cardiovascular risk factors.

Understanding these associations has implications for both risk stratification and therapeutic decision-making. While LDL-C remains a cornerstone of lipid management, it does not fully capture the complexity of atherogenic lipid profiles. Incorporating metrics that reflect particle number and qualitative features may identify high-risk individuals who could benefit from more aggressive interventions. Moreover, elucidating the relationship between these biomarkers and angiographic findings may support their integration into routine clinical practice and guidelines.

In summary, the heterogeneity of LDL particles and the quantification of atherogenic burden through ApoB measurement represent promising avenues for advancing cardiovascular risk assessment. This study's findings are anticipated to clarify the extent to which these biomarkers correlate with anatomical severity of coronary lesions, thereby contributing to a more nuanced understanding of atherosclerotic disease progression.

Methodology: A cross-sectional observational design was implemented to evaluate associations between LDL particle size, apolipoprotein B concentrations, and severity of coronary artery stenosis among adults referred for clinically indicated coronary angiography at CMH, Sialkot. Eligible participants were adults aged 35–75 years with suspected or established CAD presenting with anginal symptoms or positive non-invasive testing. Exclusion criteria included acute myocardial infarction within the preceding 30 days, active systemic inflammatory or infectious disorders, known hepatic or renal insufficiency, autoimmune diseases, use of lipid-modifying therapies within 12 weeks prior to enrollment, and any condition that could influence lipoprotein metabolism independent of atherosclerotic disease. Sample size was determined using

Epi Info software, targeting 80% power to detect a moderate effect size (Cohen's d = 0.5) between biomarkers and stenosis severity with a two-sided α of 0.05, resulting in a calculated requirement of 234 subjects; recruitment was set at 240 to account for potential missing data. After obtaining verbal informed consent in accordance with institutional ethical standards, fasting blood samples were collected prior to angiography for measurement of lipid profile, LDL particle size, and ApoB. LDL particle size was determined through standardized gradient gel electrophoresis, and mean particle diameter was recorded. ApoB levels were quantified using an immunoturbidimetric assay calibrated to reference standards. Coronary angiograms were interpreted by cardiologists blinded to biochemical results, with quantitative assessment of stenosis severity in major epicardial vessels. Stenosis was categorized into mild (<50%), moderate (50–70%), and severe (>70%) based on percentage luminal narrowing. Traditional risk factors were documented, including age, gender, smoking status, blood pressure, diabetes status, and body mass index. Data analysis involved Spearman's correlation to assess relationships between LDL particle size, ApoB, and stenosis severity. Multivariable linear regression models were constructed to evaluate independent associations after adjustment for confounders. Statistical significance was defined as $p < 0.05$, and all analyses were performed using statistical software to ensure robust evaluation of observed associations.

Results

Table 1. Baseline Demographic and Clinical Characteristics (n=240)

Variable	Mild (n=72)	Moderate (n=88)	Severe (n=80)	p-value
Age (yrs), mean ± SD	56.2 ± 9.1	57.8 ± 8.6	59.3 ± 7.9	0.08
Male, n (%)	48 (66.7)	62 (70.5)	58 (72.5)	0.72
Smoking, n (%)	28 (38.9)	40 (45.5)	42 (52.5)	0.12
Diabetes, n (%)	18 (25.0)	30 (34.1)	36 (45.0)	0.03*
Hypertension, n (%)	32 (44.4)	46 (52.3)	50 (62.5)	0.05

*Significant at $p < 0.05$

Table 2. Lipoprotein Metrics by Stenosis Severity

Parameter	Mild	Moderate	Severe	p-value
LDL Particle Size (nm), mean ± SD	26.8 ± 1.1	26.0 ± 1.2	25.4 ± 1.3	<0.001*
ApoB (mg/dL), mean ± SD	98 ± 22	112 ± 24	129 ± 28	<0.001*

Parameter	Mild	Moderate	Severe	p-value
LDL-C (mg/dL), mean ± SD	130 ± 30	136 ± 32	142 ± 35	0.09

*Significant at $p < 0.001$

Table 3. Correlation between Biomarkers and Stenosis Severity

Variable	Spearman's ρ	p-value
LDL Particle Size	−0.42	<0.001*
ApoB	0.39	<0.001*

*Significant correlation

Smaller LDL particle size and higher ApoB levels were significantly associated with greater severity of coronary stenosis. Conventional LDL-C did not show significant association. These data suggest particle quality and number are more reflective of stenotic burden than LDL cholesterol concentration alone.

Discussion : This study demonstrates a robust association between smaller LDL particle size, elevated apolipoprotein B, and increased severity of coronary artery stenosis. The progressive decrease in mean LDL particle diameter from mild to severe stenosis groups indicates that particle size may reflect atherogenic potential more precisely than conventional lipid measurements. These findings support the concept that qualitative lipoprotein characteristics contribute significantly to the anatomical burden of coronary atherosclerosis.[13-15]

ApoB concentration emerged as a strong positive correlate of stenosis severity, underscoring the relevance of atherogenic particle number in plaque development. Because each ApoB molecule represents a single atherogenic lipoprotein particle, higher ApoB levels denote a greater number of LDL and remnant particles capable of infiltrating the arterial wall. This aligns with mechanistic evidence that particle number, rather than cholesterol content alone, drives retention and subsequent atheroma progression.[16-17]

Conventional LDL-C did not show a statistically significant association with stenosis severity in this cohort, highlighting the limitations of relying solely on cholesterol content to estimate atherogenic risk. While LDL-C remains a pivotal target for therapeutic intervention, its quantitative focus may overlook individuals with smaller, more numerous particles, who harbor a greater propensity for plaque buildup despite LDL-C values within traditional targets.

The inverse correlation between LDL particle size and stenosis severity reinforces the pathogenic role of small, dense LDL. These particles exhibit increased susceptibility to oxidative modification, reduced receptor-mediated clearance, and enhanced arterial retention, all of which accelerate foam cell formation and plaque expansion. This study's data corroborate experimental models of

atherogenesis and extend these observations to clinically meaningful stenotic outcomes.

Adjusting for traditional risk factors did not attenuate the associations of LDL particle size and ApoB with stenosis severity, suggesting that these biomarkers provide additive value beyond established risk profiles. This underscores their potential utility in comprehensive cardiovascular risk assessment models, particularly for individuals with discordant lipid patterns. Participants with metabolic abnormalities, such as insulin resistance, often exhibit both small LDL particles and elevated ApoB, further emphasizing metabolic influences on lipoprotein structure and atherogenicity.[18-20]

These findings have potential clinical implications for risk stratification and personalized therapeutic strategies. Incorporating LDL particle characterization and ApoB measurement into standard clinical workflows could identify high-risk individuals who might benefit from intensified lipid-lowering or targeted interventions, even when LDL-C is within acceptable ranges. Such an approach may refine preventive cardiology paradigms and improve outcomes.

In conclusion, the present evidence affirms that LDL particle size and apolipoprotein B are independently associated with the severity of coronary artery stenosis. These biomarkers capture dimensions of lipoprotein biology that conventional cholesterol metrics do not fully explain, offering enhanced insight into atherosclerotic disease burden.

Conclusion: Smaller LDL particle size and higher apolipoprotein B are strongly associated with greater coronary stenosis severity. These biomarkers offer incremental risk information beyond traditional lipid measures. Integrating them into cardiovascular assessment could improve stratification and guide targeted interventions.

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