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POTENTIAL ROLE AS BOTH A BIOMARKER AND A MEDIATOR OF CARDIOMETABOLIC DISEASE

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Annotation. Cardiometabolic diseases remain the leading cause of morbidity and mortality worldwide. Arterial hypertension, dyslipidemia, obesity, and type 2 diabetes mellitus represent the most prevalent and modifiable risk factors contributing to cardiovascular disease development. Importantly, growing epidemiological evidence suggests that the clustering of these risk factors often begins in early adulthood. Abdominal obesity is a key driver of early metabolic disturbances and plays a central role in the development of insulin resistance and cardiometabolic diseases. Increasing evidence indicates that these pathological processes begin at a young age, long before the clinical manifestation of cardiovascular disease. C-peptide, traditionally considered a marker of endogenous insulin secretion, has emerged as an important indicator of insulin resistance and metabolic stress[1]. This narrative review summarizes current evidence on the associations between abdominal obesity, C-peptide, insulin resistance, and inflammatory mechanisms in young adults. Particular attention is given to the role of low-grade inflammation and gut-derived hormones in the early stages of cardiometabolic risk formation. Understanding these mechanisms may facilitate the identification of early biomarkers and support the development of preventive strategies targeting young populations. Insulin resistance represents a central mechanism linking abdominal obesity to cardiometabolic disorders[2]. Visceral adiposity promotes macrophage infiltration of adipose tissue and increased secretion of proinflammatory cytokines, including IL-6 and TNF-α. These cytokines interfere with insulin receptor signaling and exacerbate metabolic dysregulation.

Keywords: arterial hypertension; dyslipidemia; cardiometabolic risk; abdominal obesity; visceral adipose tissue; insulin resistance; C-peptide; atherosclerosis;

Low-grade chronic inflammation has been consistently observed in young individuals with obesity and insulin resistance, even in the absence of overt cardiovascular disease. This inflammatory state may contribute to the early onset of endothelial dysfunction and atherosclerotic changesFrom a clinical perspective, arterial hypertension and dyslipidemia interact at multiple levels to accelerate vascular damage. Elevated blood pressure induces endothelial dysfunction and arterial wall stress, facilitating lipid infiltration and plaque instability. Dyslipidemia further exacerbates vascular injury through lipid oxidation and inflammatory activation, leading to faster progression of atherosclerosis.In everyday clinical practice, this combination is commonly observed in patients with obesity, metabolic syndrome, and type 2 diabetes mellitus. Recognizing this clustering is essential for individualized cardiovascular risk assessment and therapeutic decision-making. Abdominal obesity is increasingly recognized as a superior predictor of cardiometabolic risk compared with body mass index. Excess visceral

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adipose tissue contributes to insulin resistance, low-grade inflammation, and adverse lipid profiles, all of which are directly relevant to clinical outcomes. Markers of insulin resistance, including C-peptide, may provide additional information for early identification of high-risk individuals, even before the onset of overt diabetes. Incorporating these parameters into clinical evaluation may improve risk stratification and guide preventive strategies. In clinical settings, achieving simultaneous control of blood pressure and lipid levels remains a major challenge due to polypharmacy and suboptimal adherence. Fixed-dose combination therapies offer a practical solution by simplifying treatment regimens and improving long-term adherence[4]. Clinical trials and real-world evidence support the use of fixed-dose combinations in reducing cardiovascular events and mortality. Their implementation aligns with contemporary guideline recommendations emphasizing comprehensive risk factor management. For clinical practice, arterial hypertension and dyslipidemia should be addressed as interconnected conditions rather than isolated entities. Early identification of abdominal obesity and insulin resistance, combined with the use of fixed-dose combination therapy, represents an effective strategy for reducing cardiovascular risk and improving patient outcomes. Cardiometabolic disorders constitute a complex network of interrelated pathophysiological processes that culminate in atherosclerotic cardiovascular disease. Arterial hypertension and dyslipidemia are central components of this network and frequently coexist due to shared genetic, metabolic, and environmental determinants[6].Accumulating epidemiological evidence demonstrates that their coexistence dramatically amplifies cardiovascular risk, suggesting synergistic rather than additive effects. Understanding the underlying mechanisms of this interaction is essential for the development of targeted preventive and therapeutic strategies.

Determination of total cholesterol and lipoprotein(a) [Lp(a)] is considered optimal for every adult individual [2]. In this context, the identification of cardiovascular risk factors (RFs), including dyslipidemia (DLP), should be performed in all adults or from the age of 18 years. Measurement of blood lipid levels is indicated in patients with cardiovascular disease (CVD), as well as in all clinical conditions associated with increased cardiovascular risk (CVR), such as arterial hypertension (AH), chronic kidney disease (CKD), and type 2 diabetes mellitus (T2DM).Attention should be paid to the presence of tendon and cutaneous xanthomas, xanthelasma of the eyelids, or corneal arcus in individuals younger than 45 years. These clinical signs indicate severe lipid metabolism disorders, such as familial hypercholesterolemia (FH), the most common monogenic disease associated with early development of atherosclerotic cardiovascular disease (ASCVD).Blood samples for lipid analysis are usually obtained in the fasting state; however, fluctuations in plasma lipid concentrations, with the exception of triglycerides (TG), are not significantly affected by food intake. Therefore, for screening purposes, blood sampling may be performed in the non-fasting state [3], with determination of total cholesterol (TC), TG, and high-density lipoprotein cholesterol (HDL-C).Non–HDL cholesterol (non–HDL-C) reflects the total burden of atherogenic lipoproteins and is calculated using the formula:

non–HDL-C = TC − HDL-C.Low-density lipoprotein cholesterol (LDL-C) is calculated using the Friedewald formula:

LDL-C (mg/dL) = TC − HDL-C − TG/5

LDL-C (mmol/L) = TC − HDL-C − TG/2.2

The formula is based on two assumptions:

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1. the majority of plasma TGs are contained in very-low-density lipoproteins (VLDL) and chylomicrons (CM);
2. the mass ratio of TG to cholesterol in VLDL is 5:1 in mg and 2.2:1 in molar units.

Use of the Friedewald formula in cases of TG concentrations >4.5 mmol/L, presence of chylomicrons, or type III dyslipidemia leads to overestimation of VLDL cholesterol and underestimation of LDL-C. In such situations, direct methods for LDL-C determination should be used. In individuals with known TG concentrations >4.5 mmol/L and type 2 diabetes mellitus, blood samples for lipid analysis should be obtained in the fasting state.

At the vascular level, arterial hypertension induces mechanical stress, endothelial shear alterations, and vascular smooth muscle cell remodeling. These changes increase endothelial permeability to atherogenic lipoproteins and promote oxidative modification of low-density lipoprotein cholesterol[5].Dyslipidemia further amplifies these processes by activating inflammatory signaling pathways, macrophage recruitment, and foam cell formation.[7] The convergence of hemodynamic stress and lipid-driven inflammation accelerates plaque development and destabilization. Visceral adipose tissue plays a pivotal role in cardiometabolic dysfunction through its endocrine and paracrine activity. It secretes adipokines, cytokines, and bioactive lipids that modulate insulin sensitivity, vascular tone, and inflammatory responses.Excess visceral fat is associated with increased release of free fatty acids and pro-inflammatory mediators, leading to hepatic insulin resistance, dyslipidemia, and systemic inflammation. These mechanisms establish a direct link between abdominal obesity and cardiovascular pathology.Insulin resistance represents a unifying mechanism connecting obesity, hypertension, and dyslipidemia. C-peptide, co-secreted with insulin, has emerged as a valuable marker of endogenous insulin secretion and metabolic stress. Recent studies suggest that elevated C-peptide levels may exert direct biological effects on the vasculature, including modulation of endothelial function and inflammatory responses[8].

These findings support its potential role as both a biomarker and a mediator of cardiometabolic disease.A deeper understanding of the shared molecular pathways linking hypertension, dyslipidemia, visceral obesity, and insulin resistance may facilitate the identification of novel therapeutic targets. Translational approaches bridging experimental research and clinical application are essential for addressing the growing global burden of cardiometabolic disease.From a mechanistic standpoint, arterial hypertension and dyslipidemia represent interconnected components of a broader cardiometabolic continuum. Visceral adipose tissue dysfunction and insulin resistance serve as central drivers of this process, highlighting the need for integrative research strategies that transcend traditional disease classifications.

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