

Visceral Fat, Atherosclerosis and Coronary Artery Disease

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Introduction

Metabolic Syndrome (MS) is currently considered to be a risk factor for atherothrombosis disease. Visceral Fat (VF) is one of the important factors in the diagnostic criteria of MS, and the increase of VF can cause arteriosclerotic diseases as a result of coronary risk factors such as diabetes mellitus, dyslipidemia, hypertension, endothelial dysfunction, inflammation, insulin resistance, glucose intolerance, and obesity (Figure 1). The VF has paracrine and systemic effects and is a source of adipocytokines and it has been implicated in the pathogenesis of Coronary Artery Disease (CAD) [1-9].

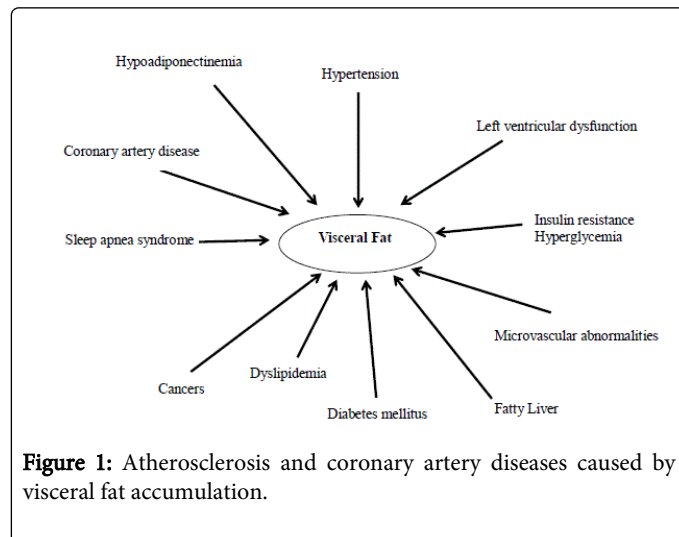


Figure 1: Atherosclerosis and coronary artery diseases caused by visceral fat accumulation.

The VF contributes to metabolic disorders by altering levels of adipocyte-derived cytokines. The increased of visceral fat lowers the concentration of adiponectin, and causes excessive secretion of cytokines and (TNF- α). The blood concentration of (PAI-1), a fibrinolytic regulation factor, and the amount of VF are both positively correlated [10-13].

Patients in the visceral obesity had several other coronary risk factors, indicating that they had a high risk of developing coronary arterial lesions. Several studies have shown that the accumulation of VF causes arteriosclerosis [10,14-16].

In a study the authors examined 216 consecutive patients suspected to have coronary artery disease. VF was greater in subjects with non-calcified plaque than in those with no plaque or with calcified plaque (126 ± 39 mL vs. 98 ± 34 mL and 97 ± 45 mL, respectively; $P=0.010$). VF was significantly correlated with BMI, triglycerides, and the triglyceride/high-density lipoprotein cholesterol ratio ($r=0.51, 0.19$, and 0.20 , respectively) but not with plasma levels of adipocytokines. Adiponectin and IL-6 concentration was significantly

correlated with abdominal visceral fat area in coronary plaque patients ($r=-0.49$ and 0.20) [17].

Analysis of VF on Computed Tomography (CT) scan, correlates with diabetes, atherosclerosis, state prothrombotic and proinflammatory, metabolic abnormalities, which is associated with increased risk of atherosclerotic cardiovascular disease [18,19].

Other investigators demonstrated that visceral adiposity measured by CT correlates with the ultrasound-measured carotid IMT, plaque area and total area (IMT area plus plaque area) after adjusting for demographics, family history, smoking and percent body fat [20].

The Framingham Heart study showed a significant correlation between visceral adiposity and cardiovascular diseases (HR=1.44; 95%CI: 1.08-1.92; $P=0.01$), even after adjustment for clinical risk factors and BMI [21-23]. In men and women the VF was significantly associated with blood pressure, fasting glucose, triglycerides, HDL-C and a higher risk of hypertension, impaired fasting glucose, diabetes mellitus, and metabolic syndrome ($P<0.01$). More consistent relationship between VF and the risk factors in women were observed. The VF was more strongly correlated with most of the metabolic risk factors than were both women and men, and was associated with increased odds of developing metabolic syndrome.

In a study the authors evaluated 607 consecutive patients who underwent VF examinations using computed tomography (CT) scans, the VF showed significant positive correlations with the age, BMI, WC, Subcutaneous Fat Area (SCFA), VF area/SCFA (v/s) ratio, systolic blood pressure, diastolic blood pressure, the fasting blood sugar (FBS), the Hemoglobin A1c (HbA1c), HDL-C, triglyceride, uric acid, HOMA-IR and ApoB and the ApoB/LDLc ratio and significant negative correlations with the levels of HDLC and adiponectin. The levels of the total cholesterol, LDL-C, non-HDLc and Lp(a) and the ApoB/ApoAI ratio were not correlated with the VF in either men or women. The RLP exhibited a significant positive correlation with the VF in women [24].

In a study the authors investigated the relationship between multiple risk factor accumulation and CAD in Japanese without and with visceral fat accumulation. The study subjects comprised 257 Japanese with suspected CAD (males/females=153/104), who underwent 64-row multi slice (CT) coronary angiography and VF area (VFA) measurement by CT. Subjects with VFA ≥ 100 cm² were much higher [6.46 (1.25-33.44, $p=0.0261$) and 20.42 (3.60-115.73, $p=0.0007$)] ($p<0.0001$ for trend). The multivariate adjusted model demonstrated a CAD risk of 1.08 ($p=0.0484$) and 5.01 ($p<0.0001$) for the interactions of 2 risk factors and VFA ≥ 100 cm², and 3 risk factors and VFA ≥ 100 cm², whereas multiple risk factor accumulation was not related with the increase of CAD risk in subjects with VFA <100 cm² [25].

In a case control study the VF was an excellent predictor of cardiovascular risk (area under ROC curve 0.915 cm²). Coronary artery disease was diagnosed by coronary angiography. The visceral fat area was significantly higher (122.58 ± 37.59 vs. 36.95 ± 88.4 cm²; P=0.003) in cases, and correlated with BMI, waist hip ratio, blood sugar, triglycerides, and C-reactive protein. The VF is associated with an increased risk of CAD and correlated risk markers [26]. In a retrospective cross-sectional study, the authors was measured the VF area at the level of the umbilicus using CT. Coronary stenosis and plaques were evaluated using coronary CT. Coronary stenosis <50% and non-calcified plaques increased steadily as the VF area increased (P<0.001). The 4th quartile of VF area was significantly associated with prevalence of coronary stenosis <50% and the presence of non-calcified plaques when compared with the first through third VAT quartiles in the cardiovascular risk factor-adjusted model (odds ratio (OR): 1.58, 95% confidence interval (CI): 1.09-2.30 and OR: 1.66; 95% CI: 1.02-2.68, respectively). The VF area was associated with coronary stenosis <50% and non-calcified plaques, independent of traditional cardiovascular risk factors [27].

In one study in which the VF area was examined using a hybrid SPECT/CT scanner the fatty acid binding protein A-FABP levels correlated significantly with adiponectin, hs-CRP<BMI, WC, and VF area. A-FABP was significantly associated with metabolic syndrome (OR 3.2, 95% CI 1.6-6.4, p=0.001), significant myocardial ischemia (OR 1.9, 95% CI 1.0-3.4, p=0.05), on SPECT. Chemerin was significantly associated with serum triglyceride levels but not with metabolic syndrome, significant ischemia [28].

In the MESA (Multi-Ethnic Study of Atherosclerosis) the authors studied 1,511 individuals with adiposity assessment by computed tomography (CT). The VF was associated with cardio-metabolic risk and coronary artery calcification, regardless of BMI, and more strongly associated with incident MetS than subcutaneous fat [29].

In the Jackson Heart Study (n=2477; 64% women; mean age, 58 years) underwent multi detector computed tomography, and the volumetric amounts of VF. Men had a higher mean volume of VF (873 vs.793 cm³) than women (P=0.0001). The effect size of VF in women was larger than that of subcutaneous adipose tissue (SAT), fasting plasma glucose, 5.51 ± 1.0 vs. 3.36 ± 0.9; triglyceride, 0.17 ± 0.01 vs. 0.05 ± 0.01; HDL-C, -5.36 ± 0.4 vs. -2.85 ± 0.4; and odds ratio for hypertension, 1.62 (1.4-1.9) vs.1.40 (1.2-1.6); diabetes, 1.82 (1.6-2.1) vs.1.58 (1.4-1.8); and metabolic syndrome, 3.34 (2.8-4.0) vs. 2.06 (1.8-2.4), respectively; P<0.0001 for difference between VAT and SAT [30].

The VF may be a cause of coronary risk factors, which may eventually develop into coronary stenosis. Diagnostic methods and treatment of VF may impact on morbidity and mortality of the population.

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