Obesity is a major determinant of the association of C-reactive protein levels and the metabolic syndrome in type 2 diabetes.

Kahn, Steven E. Zinman, Bernard. Haffner, Steven M. O'Neill, M Colleen. Kravitz, Barbara G. Yu, Dahong. Freed, Martin I. Herman, William H. Holman, Rury R. Jones, Nigel P. Lachin, John M. Viberti, Giancarlo C. ADOPT Study Group.

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The inflammatory factor C-reactive protein (CRP) and the fibrinolytic variables fibrinogen and plasminogen activator-1 (PAI-1) are associated with long-term cardiovascular morbidity. To determine the contribution of body adiposity (BMI), insulin sensitivity (homeostasis model assessment of insulin resistance [HOMA-IR], and glycemia (HbA(1c) [A1C]) to the levels of these inflammatory and fibrinolytic variables in recently diagnosed (<or=3 years), drug-naive, type 2 diabetic subjects (fasting plasma glucose <or=10 mmol/l), we examined a representative subgroup (n = 921) of the U.S. cohort in ADOPT (A Diabetes Outcome Progression Trial). The relationship between levels of CRP, fibrinogen, PAI-1 antigen and PAI-1 activity, and baseline variables including National Cholesterol Education Program Adult Treatment Panel III metabolic syndrome phenotype were explored. All four factors increased significantly with increasing numbers of metabolic syndrome components (P = 0.0136 to P < 0.0001). BMI (P < 0.0001) and HOMA-IR (P < 0.0001) but not A1C (P = 0.65) increased with increasing numbers of metabolic syndrome components. Adjustment of CRP levels for BMI eliminated the association between CRP and the number of metabolic syndrome components, while adjusting for HOMA-IR did not (P = 0.0028). The relationships of PAI-1 antigen and PAI-1 activity with the number of metabolic syndrome components were maintained after adjusting for BMI (P = 0.0002 and P = <0.0001, respectively) or HOMA-IR (P = 0.0008 and P = <0.0001, respectively), whereas that with fibrinogen was eliminated after adjusting for BMI but not after adjusting for HOMA-IR (P = 0.013). Adjustment for A1C had no effect on any of the relationships between the inflammatory and fibrinolytic factors and the metabolic syndrome. We conclude that in recently diagnosed, drug-naive type 2 diabetic subjects, markers of inflammation and fibrinolysis are strongly related to the number of metabolic syndrome components. Further, for CRP and fibrinogen this relationship is determined by body adiposity and not by insulin sensitivity or glucose control.