

# Lower Androgenicity is Associated With Higher Plasma Levels of Prothrombotic Factors Irrespective of Age, Obesity, Body Fat Distribution and Related Metabolic Parameters in Men

Giovanni De Pergola, Vito De Mitrio, Marcello Sciaraffia, Nicola Pannacchiulli, Antonio Minenna, Francesco Giorgino, Mariella Petronelli, Ester Laudadio and Riccardo Giorgino

Institute of Medical Clinic, Endocrinology and Metabolic Diseases, and Centro Emostasi e Trombosi, University of Bari, School of Medicine, Bari, Italy

Received 22 October 1996; accepted 28 April 1997. Available online 31 August 2004.

## Abstract

The purpose of this study was to examine the relationships between androgenic status and plasma levels of both prothrombotic and antithrombotic factors in men, irrespective of obesity, body fat distribution, and metabolic parameters. Sixty-four apparently healthy men, 40 with a body mass index (BMI) greater than 25 kg/m<sup>2</sup> (overweight and obese [OO]) and 24 non-obese controls with a BMI less than 25, were selected and evaluated for (1) plasma concentrations of plasminogen activator inhibitor-1 (PAI-1) antigen, PAI-1 activity, fibrinogen, von Willebrand factor (vWF) antigen, vWF activity, and factor VII (FVII) as the prothrombotic factors; (2) plasma levels of tissue plasminogen activator (TPA) antigen, protein C, and antithrombin III as the antithrombotic factors; (3) fasting plasma concentrations of insulin and glucose and the lipid pattern (triglycerides [TG] and total and high-density lipoprotein [HDL] cholesterol) as the metabolic parameters; and (4) free testosterone (FT), dehydroepiandrosterone sulfate (DHEAS), and sex hormone-binding globulin (SHBG) serum levels as the parameters of androgenicity. Body fat distribution was evaluated by the waist to hip ratio (WHR). In OO and non-obese subjects taken together, plasma levels of PAI-1 antigen, fibrinogen, and FVII were inversely associated with FT ( $r = .255$ ,  $P < 0.5$ ,  $R = -3.14$ ,  $P < .05$ , and  $r = -.278$ ,  $P < .05$ , respectively), and the negative relationships of both fibrinogen and FVII with FT were maintained after stepwise multiple regression analysis. Plasma concentrations of PAI-1 antigen and PAI-1 activity were also negatively correlated with SHBG ( $r = -.315$ ,  $P < .05$  and  $r = -.362$ ,  $P < 0.01$ , respectively), and these associations held irrespective of the other parameters investigated. None of the antithrombotic and fibrinolytic factors were independently related to serum androgen levels. Subjects with a BMI higher than 25 kg/m<sup>2</sup> had higher plasma concentrations of PAI-1 antigen, PAI-1 activity, and fibrinogen as compared with non-obese controls ( $P < .001$ ,  $P < .001$ , and  $P < .01$ , respectively). In addition, in OO and control subjects as a whole, multiple stepwise regression analysis showed that the associations of BMI with PAI-1 activity, fibrinogen, vWF antigen, and vWF activity were independent of any other metabolic and hormonal parameters. Plasma concentrations

of PAI-1 antigen, PAI-1 activity, and fibrinogen were also directly correlated with WHR in all subjects taken together, irrespective of the other parameters investigated. Evaluation of antithrombotic factors showed that OO subjects had higher TPA plasma concentrations than non-obese controls ( $P < .001$ ), whereas protein C and antithrombin III did not differ in the two groups. TPA was also directly correlated with BMI ( $r = .415$ ,  $P < .001$ ) and WHR ( $r = .393$ ,  $P < .001$ ) in all subjects. The results of this study indicate that (1) men with lower FT serum levels have higher fibrinogen and FVII plasma concentrations, and those with lower SHBG serum levels also have higher levels of PAI-1 antigen and activity; (2) irrespective of other factors, obesity per se may account for higher concentrations of PAI-1, fibrinogen, and vWF; (3) plasma levels of PAI-1 (antigen and activity) and fibrinogen correlate independently with WHR; and (4) among the investigated antithrombotic factors (TPA antigen, protein C, antithrombin III), only TPA antigen plasma concentrations are higher in men with abdominal obesity. Thus, because of the increase in several prothrombotic factors, men with central obesity, particularly those with lower androgenicity, seem to be at greater risk for coronary heart disease (CHD). Apparently, this risk is not counteracted by a parallel increase in plasma concentrations of antithrombotic factors.