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## **Dyslipidemia and thrombosis: Causal relationship or epiphenomenon of sedentary lifestyle? Response**

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## Dyslipidemia and Thrombosis: Causal Relationship or Epiphenomenon of Sedentary Lifestyle?

To the Editor:

Doggen et al report that low HDL cholesterol and high triglyceride levels are associated with an increased risk for venous thrombosis in a population-based case-control study. The authors explain their results with an interaction of triglycerides with different coagulant factors as activated protein C (APC), factor VIIc, factor VIII, factor IX, and fibrinogen.<sup>1</sup> However, low HDL cholesterol and high triglycerides are found frequently in subjects with a predominantly sedentary lifestyle and are key features of the metabolic syndrome.<sup>2</sup> Individuals with the metabolic syndrome are characterized by prothrombotic hemostatic abnormalities such as elevated plasma fibrinogen, elevated factor VIIc, and raised concentrations of plasminogen activator inhibitor (PAI).<sup>3</sup> Regular aerobic exercise leads to an improved metabolism of serum lipids with increased levels of HDL cholesterol and decreased plasma triglycerides, resulting in a lower risk of atherothrombotic events.<sup>4</sup> Moreover, a recent publication shows that moderate-intensity aerobic exercise leads to a decreased platelet coagulation, hematocrit and blood viscosity, and PAI I antigen.<sup>5</sup> All these factors are beneficial to hemostatic balance and presumably reduce the risk for thromboembolic events. However, Doggen et al provide no data on physical activity and basic hematologic parameters such as hematocrit.

We suggest that the reported association of low HDL cholesterol and hypertriglyceridemia with thrombosis might be explained, besides the pathomechanisms discussed by Doggen et al,<sup>1</sup> in part by lower physical activity resulting in a procoagulant state with increased coagulant factors and higher blood viscosity.

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viscosity, platelet aggregation and fibrinolytic balance in young and middle-aged sedentary subjects. *Blood Coagul Fibrinolysis.* 2004;15: 31–37.

### In response:

We thank the authors for their interest in our study, in which we describe an increased risk of venous thrombosis in the presence of low HDL cholesterol and high triglyceride levels.<sup>1</sup> Adjustment for potential confounders, such as weight and height, could only partly explain the associations. Elevated triglyceride levels in women are associated with a low activated protein C (APC) ratio and increased coagulant factors, both of which are known risk factors for venous thrombosis, therefore potentially clarifying the increased risk with triglycerides. Unfortunately, we were unable to measure (anti)coagulation or fibrinolytic factors in our study. Besides these mechanisms, Sturm and Sandhofer describe the possibility that lower physical activity results in a “bad lipid profile,” and suggest that a procoagulant state and a higher blood viscosity may be additional explanations. This may indeed be true. However, the role of platelets, hematocrit, blood viscosity, and the fibrinolytic system in causing a venous thrombosis has not yet been extensively investigated. One recent study indicates that plasma hypofibrinolysis constitutes a risk factor for venous thrombosis.<sup>2</sup> We must also keep in mind that circumstances for a thrombus occurring in an arterial system are different from those in a venous system, and different risk factors play a role in both diseases. Although many studies have investigated the role of physical activity in arterial diseases, the risk of venous thrombosis has not been studied. The latter is currently under investigation in a large population-based case-control study, the “Multiple Environmental and Genetic Assessment of risk factors for venous thrombosis (MEGA-) Study.”

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