**A comprehensive assessment of fibrin clot properties in patients with aortic stenosis - involvement of fibrinogen oxidation in the severity of aortic stenosis**

Aortic stenosis (AS) is one of the most common heart valvular disease, and its prevalence increases with the aging. Several studies suggested an active role of blood coagulation proteins in the regulation and progression of AS. It was demonstrated that within stenotic valve leaflets the area of tissue factor (TF) expression co-localized with the areas of fibrin deposits, suggesting that conversion of fibrinogen to fibrin takes place within stenotic valves. Natorska *et al.* showed that the amounts of fibrin within stenotic valves positively correlated with prolonged clot lysis time in severe AS patients, indicating an impaired fibrinolysis. Moreover, TF expression was observed at the sites of macrophage infiltration, pointing out the inflammatory role of TF within the aortic valves. Thus, it is reasonable that factors influencing the coagulation cascade or fibrinolysis, such as an oxidative stress might be responsible for activation of several signaling pathways connected with aortic valve damage. Oxidative stress is significantly increased in stenotic aortic valves as a result of inflammation, and might be linked to *in loco* fibrinogen/fibrin oxidation. Since the reactive oxygen species (ROS) can alter the fibrinogen structure not only in acute myocardial infarction, but also in stable coronary patients, it is likely that similar processes could occur in AS leading to enhanced fibrosis and inflammation within valvular leaflets.

We intend to enroll 150 consecutive patients with documented isolated AS (including at least 50 patients scheduled for aortic valve replacement), which will be divided into three equal groups matched for sex and age according to the severity of the disease. Subsequently we will determinate the fibrin clot properties, including the factors affecting them. In next step the effect of oxidation of fibrinogen/fibrin on fibrin clot properties will be assessed. Finally, *in loco* study will show whether oxidative stress in AS is increased in regions of fibrin deposition and regions of extensive fibrosis within stenotic valvular leaflets.

This project will allow us to get more insights into the issue as to whether subjects with a prothrombotic fibrin clot phenotype are more likely to develop severe forms of AS, and if the fibrinogen oxidation could contribute to a larger fibrin deposition within valve leaflets, and thus lead to excessive fibrosis and aortic valve stiffness in severe AS. This might lead to development of potential new therapeutic targets in the treatment of AS that interfere with fibrin-related mechanisms enhancing thickening of aortic valves in humans.