Hemostasis is a complex of processes that aim to keep the blood in the fluid state in the vascular bed and, in the case of damage to the blood vessel, to prevent blood loss. These processes involve plasma coagulation factors, platelets, the wall of blood vessels and endothelial cells.

The main objective of the study is to assess the mechanisms leading to thrombin generation disorders in adult patients after the Fontan surgery. **The secondary objective** is to evaluate fibrin clots properties and the role of polyhydrocytes in the structure and function of blood clots in adults after Fontan surgery. **The tertiary aim** of the study is to assess the incidence of thromboembolic complications and factors affecting their occurrence during the two-year follow-up period in adults after Fontan surgery.

Fontan surgery is the method of choice in the treatment of patients with single ventricle. . Heart defects with single ventricle pathology are included into the group of rare diseases. The number of patients after Fontan surgery is increasing each year and about 85% of them reach adulthood. Thromboembolic complications are among the most common negative events in long-term follow-up, occurring in 20%-33% of patients. Currently, there are no guidelines addressing anticoagulant treatment in this group of patients. Thrombi can be detected in the systemic venous pathway, systemic ventricle or ligated pulmonary artery. Asymptomatic pulmonary emboli have been reported in 17% of Fontan patients. Recurrent pulmonary embolisms significantly impair blood flow in the lung and may aggravate cyanosis and lead to Fontan circulation failure. Mechanisms leading to thromboembolism in patients with FC are still not clear and remain to be elucidated. Taking into consideration that hemostasis is regulated by plasma coagulation/fibrinolysis proteins and platelet and endothelial function, all of them could contribute to the increased thrombotic risk in patients after FS. Indeed, changes in plasma activity of coagulation factors and inhibitors, endothelial dysfunction and enhanced platelet activation were demonstrated in children after the Fontan surgery. There are, however, only a few studies reporting hemostatic abnormalities in adult patients, occurring late after the Fontan surgery and even experts hold controversial views as to the optimal antithrombotic treatment. While some authors reported that Fontan patients taking either aspirin (ASA) or warfarin had lower thromboembolic rates than those not on antithrombotic therapy, others concluded that there was no benefit of antithrombotic therapy.

Our preliminary study has indicated that there are complex hemostatic disturbances in adult FC patients. On the one hand, such complications seem to favor bleeding by reduction of coagulation factor production and on the other, they promote thrombosis through reduced protein S, hypofibrinolysis, impaired endothelial function and increased platelet activation. However, the net effect of all the hemostatic disturbances in FC patients tilts the balance towards prothrombotic tendency. Nevertheless, bleedings are fairly uncommon in FC patients, which suggests that despite a lower platelet count and coagulation factors, other potent mechanisms can overcome these alterations, leading to a prothrombotic state as evidenced by heightened thrombin generation reflected by increased F1.2.

Previous studies have shown that markers of platelet activation were elevated in spite of lower platelet count in adults after Fontan procedure. The primary mechanism leading to decreased platelet count in this group of patients is complex and unclear. One explanation of this phenomenon may be increased platelet destruction. Splenomegaly, liver cirrhosis and portal hypertension is a frequent finding in Fontan circulation. The other reasons of thrombocytopenia might include a possible right to left shunt, delivering megakaryocytes into the system arterial circulation, bypassing the lungs where megakaryocytic cytoplasm is fragmented into platelets.

Microparticles are generated to extracellular environment during cells activation and apoptosis. Enhanced production of microparticles due to e.g platelet activation and increased destruction since splenomegaly might exist in Fontan patients and have prothrombotic effect however there are no studies regarding this subject in Fontan patients. The project was divided into three main tasks:

1. Evaluation of the influence of plasma coagulation factors, platelets and microparticles on the thrombin generation.
2. In vitro studies will provide a comprehensive overview of the properties of fibrin clots and the efficiency of their fibrinolysis. In addition, the role of polyhedrocytes in the structure and function of blood clots in adults will be assessed.
3. Evaluation of risk factors for thromboembolic complications in a two-year follow-up in adult patients after OF.