# Dissertation Abstract

Abdominalaortic aneurysm (AAA) is a serious disease. Its prevalence is in the developed countries about 3%. As an aneurysm is considered a dilatation of all layers of a vessel wall over 3 cm. Majority of AAA are small and asymptomatic, and although the risk of rupture increases with the size of aneurysm sack, even the small aneurysms rupture. The rupture mortaliry ranges about 70 %. Surgical treatment is indicated in the asymptomatic patients in diameter of AAA over 5 cm. The average speed of growth of AAA is 0.3 cm per year, e.g. in the early diagnosed patients there is a several years interval for a pharmacolocical influencing of the progression of this disease. Knowledge of pathogenesis is essential for any targeted pharmacological treatment. Our prospective, non-randomised studies are based on the application of the stereological methods for the histopathological assessment of the AAA samples. The acquired data enable the statistical analysis, including the null hypothesis testing.

In our study analyzing the histopathology of AAA aortae of 65 patients (65 walls and 55 thrombi) and 6 normal abdominal aortae from the organ donors we assessed the following parameters: the area fractions of collagen and elastin, and the length density of elastin in intima and media, the area fraction of actin, desmin and vimentin in the same reference space. In the intima, media, and adventitia we estimated the number of microvessel profiles, the area fractions of granulocytes and macrophages, area fraction of uPA, tPA and PAI-1. The mean area fractions of macrophages and granulocytes were assessed in the thrombus. In thrombus and wall the levels of interleukins IL-6, -8, and -10; matrix metalloproteinases MMP-1, -2, -7, and -9 were measured with the use of the multiplex immunoanalysis. The tissue inhibitor of matrix metalloproteinases TIMP-1, and -2 were measured in the same samples by ELISA. Comparing with the aneurysmatic aorta, the normal aorta contained more elastin, more contractile elements, more microvessels and more PAI-1-positive elements. AAA samples contained more collagen. Microvessel density was lower in AAA samples than in normal aortae, it grew with the size of aneurysm, big AAAs (> 7 cm) appeared to be the most vasculated. Asymptomatic AAAs had more abundant inflammatory infiltrates, they showed the increased fibrinolysis. In thrombus of the asymptomatic patients, expression of MMP-2 and VCAM-1 was increased. In general, thrombus was less inflammatory infiltrated than the adjacent wall. In thrombus of big AAAs (diameter >7 cm) expression of VCAM--1 and ICAM-1 was increased. Results of our study did not comfirm some of the generally accepted principles of AAA pathogenesis – the amount of collagen and elastin, also the inflammatory infiltrate did not change with the AAA size. Our results show that asymptomatic AAA walls often have more potentially deleterious histopathological alterations than symptomatic AAA walls. This result indicates that a progression from an asymptomatic AAA to rupture can be expected and screening patients who are at-risk for rupture could be beneficial. Normal aorta is the most vasculated. Microvessel density grew with the size of AAA, which indicates its importance in the progression of this disease.

In the study focused on the influence of atorvastatin on the experimental porcine AAA we assessed samples of 14 AAA influenced by statin, non-statin AAA group (n=13) and 6 normal abdominal aortae. Aortae of the statin group contained, comparing with the non-statin group, more elastin, more contractile elements, less vimentin. Microvessesel density was higher in the statin group, microvessels were predominantly found in the outer layer of aorta. Atorvastatin prevented the thickening of intima and media and enlargement of AAA.

Inflammatory infiltrate did not change with the statin treatment. In conclusion, most of the effects of atorvastatin seem to prevent the histopathological progression of AAA. Our study indicates also the differences between the human and porcine experimental AAA histopathology. The area fraction of collagen in intima and media was lower in porcine AAA than in healthy animals, on the other hand area fraction of granulocytes, macrophages and smooth muscle cells of the synthetic phenotype was higher here. We did not notice any presence of thrombus in the porcine experimental AAA, which is very featuring for the human AAAs. Both in the human and in the porcine experimental AAA there was a lower content of elastin, actin and desmin in intima and media, the wall of AAA was less vasculated comparing with the healthy samples.

The results of both of our studies indicate the importance of vasa vasorum in AAA progression. That is why the proceedings of corrosion microvascular casts are also being presented. Micro-CT scans allow the 3D reconstruction, particular scans may be, under conditions stereology principles, used for the needs of quantification.