Fabry disease is an X-linked glycosphingolipid storage disorder caused by deficient activity of the lysosomal enzyme α-galactosidase A. This leads to progressive intracellular accumulation of neutral glycosphingolipids, mainly globotriaosylceramide. Besides various extracardiac disease-related abnormalities, cardiovascular involvement represents a typical manifestation of Fabry disease. The primary underlying mechanism relies on pathological substrate accumulation in cardiomyocytes, conduction system cells, valvular fibroblasts, endothelial cells and vascular smooth muscle cells. The development of cardiac and vascular hypertrophy represents a characteristic cardiovascular feature of Fabry disease.

The aim of our studies was to describe in detail cardiovascular abnormalities in patients with Fabry disease using ultrasonography, which currently represents basic noninvasive imaging modality in cardiology. We focused on structural and functional abnormalities of ventricles, valvular apparatus and their relationship to vascular involvement expressed on common carotid arteries. We also compared the diagnostic accuracy of the two novel echocardiographic methods used for the left ventricular diastolic function assessment. The possible existence of circulating proliferative factor, which might be associated with the progression of cardiac and vascular hypertrophy, was studied in *in vitro* study.

We showed that the hypertrophy of both ventricles is frequent in patients with Fabry disease and is associated with age of affected subjects. Concentric geometry represents a dominant morphological left ventricular abnormality. Structural changes of both ventricles do not lead any apparent global systolic dysfunction. However, mild to moderate diastolic dysfunction associated with the severity of myocardial hypertrophy is frequently present. Nevertheless, severe restrictive impairment of ventricular filling is a rare finding. In comparison with color M-mode mapping of left ventricular inflow, tissue Doppler echocardiography seems to be more accurate in differentiation of normal and abnormal left ventricular diastolic function in Fabry disease. This is due to the dependence of color M-mode parameters on systolic function and geometrical alterations of left ventricle together with preload conditions.

We found a high prevalence of aortic and mitral valve abnormalities in subjects with Fabry disease. Nevertheless, they do not lead to hemodynamically significant lesions.

Diffuse carotid wall hypertrophy in Fabry patients is associated with age and severity of left ventricular hypertrophy. This vascular hypertrophy is probably reflecting a specific disease-related manifestation as we did not find apparent atherosclerotic lesions in affected subjects. The correlation between carotid wall and left ventricular hypertrophy suggests their common pathogenesis. This hypothesis was confirmed in experimental settings. We demonstrated a proliferative effect of plasma of Fabry patients on animal cardiomyocytes and vascular smooth muscle cells. The presence of specific, growth-stimulating factors in the circulation might explain pathogenesis of myocardial and vascular hypertrophy, in which intracellular glycosphingolipid deposition plays a minor role.