Fabry disease (FD) is an X-linked genetic disorder of glycosphingolipid metabolism due to deficiency of lysosomal enzyme a-galactosidase A. The disease is characterized by the progressive intracellular accumulation of neutral glycosphingolipids throughout the body, including the cardiovascular system. Myocardial abnormalities are characterized mainly by parietal thickening, the most frequent abnormal structural pattern being concentric left ventricular (LV) hypertrophy. In some patients the disease mimics a typical hypertrophic obstructive cardiomyopathy. It has been reported that in some patients the cardiac involvement could be a sole manifestation of the disease. Systolic function is largely preserved in most affected individuals. In contrast, mild to moderate diastolic filling impairment is a relatively common finding. Valvular structural abnormalities are frequent due to valvular infiltration. Valvular regurgitation seems to be relatively frequent but mostly nonsignificant. Electrocardiographic changes in Fabry disease are multiple and include AV conduction abnormalities (PQ interval shortening or AV blockades), signs of LV hypertrophy and repolarization abnormalities. Cardiac symptoms in Fabry disease patients include shortness of breath on effort, vasospastic and/or exertional angina pectoris, endothelial dysfunction and/or fixed coronary artery stenosis and syncope.

• The aim of our work was to assess the prevalence of cardiac involvement and the extent of cardiac organ damage in patients with Fabry disease and to determine the effect of enzyme replacement therapy on cardiac structure and function. This reasearch is conducted on an unique cohort of 63 heterozygous females and 34 hemizygous males with confirmed Fabry disease.

• The predominant finding was high prevalence of left ventricular hypertrophy, most frequently as concentric left ventricular hypertrophy. Furthermore, concentric remodeling was present among patients with normal LV mass. We think that the predominant type of LV structural abnormality in Fabry disease is concentric LV geometry.

• In Fabry disease patients some traditional voltage criteria correlate with echocardiographically assessed LV mass (Cornell index, Romhilt-Estes score) and some do not (Sokolow-Lyon index). The cut-off values for LVH detection for these indexes are much lower than that reported in hypertensive LVH.

• Severe left ventricular hypertrophy mimicking hypertrophic cardiomyopathy is found in patients with Fabry disease. However LVH in females was milder and there was a 10 yrs delay in occurrence of significant LVH.

• Terminal heart failure was the dominant cause of death. In the natural course of the disease untreated patients die relatively young and their management is quite demanding..

• Despite a certain role of ventilation impairment, the exertional dyspnea in Fabry disease patients is mainly due to diastolic dysfunction.

• Cardiovascular involvement in heterozygous women with Fabry disease is frequent. But its prognosis is widely variable. The exact mechanism of this involvement is not clear yet although it seems to be related in our opinion to the random inactivation of X chromosome during early embryogenesis.

• ERT with Agalsidase beta even in reduced dose has stabilising effects on left ventricular structure and function. Significant thinning of the posterior wall and improvement in midwall fiber shortening suggests a real functional improvement.

In conclusion our study confirms the high prevalence of cardiac morbidity associated wiht FD. The presence of LVH is associated with higher frequency of cardiac signs and symptoms. The cardiac involvement, in particular LV mass assessment, represent an ideal surrogate endpoint for the evaluation of the efficacy of a specific treatment.