

REPORT

Of

Assoc. Prof. D-r. Dimitar Stefanov Karastatev, M.D.

Elected as a member of the scientific jury according to order No. R-109-187/15.03.2023 under the procedure for acquiring the educational and scientific degree "Doctor" with candidate Dr Kalina Binkova Ganeva at the Medical University – Varna

Dr Ganeva's dissertation, "Possibilities of some echocardiographic techniques and microRNA to detect subclinical myocardial damage in children and young adults with beta-thalassemia major", is dedicated to the possible changes in cardiac function in young patients with beta-thalassemia major (BTM). A thorough literature analysis of this problem suggests that in addition to the methods for assessing cardiac function, biomarkers - particularly micro RNAs - can be included in the pathogenesis of heart failure, myocyte hypertrophy, interstitial fibrosis, and cardiac remodelling.

The tasks set by Dr Ganeva are clearly formulated and aim to detect as early as possible signs of changes in the systolic and diastolic function of the left ventricle (LV) in asymptomatic children and young patients with BTM and the correlation between the echocardiographic assessment of cardiac function and myocardial iron accumulation.

The dissertation is a single-phase controlled study of 27 pediatric and adolescent BTM patients and 51 age- and sex-matched healthy controls. The Material and Methods section shows that Dr Ganeva is well versed in the assessment of cardiac function, but a significantly original element is the search for a link between changes in cardiac function and small RNAs.

Dr Ganeva has selected optimal statistical methods for the study. The author expectedly found a statistically insignificant higher heart rate in the BTM group and lower systolic and diastolic pressure. Hemodynamic expectations in patients with BTM (chronic high flow state) reflect the average muscle mass, as well as the indexed left ventricular muscle mass in 25 of 27 patients with BTM.

Another important indicator for the prospective assessment is the indexed left atrial volume to body surface area. Dr Ganeva, based on literature data and

her own results, shows that the indexed left atrial volume could be accepted as a risk arrhythmogenic factor.

The author found that average GLS (global longitudinal strain) values in children with BTM were within the age range, but suggested that this indicator should be controlled, as it becomes significantly lower with iron overload.

At this point, Dr Ganeva does not find a complete set of criteria for diastolic dysfunction, but it is a fact that the volume of the left atrium indexed to the body surface area in 56% of patients, and the tendency of the left ventricular end-diastolic pressure increment, depict a risk for deterioration of the diastolic left ventricular function.

The dissertation suggests monitoring ferritin levels as an indicator of adequate treatment and a predictor of reduced cardiac risk.

The microRNAs in patients with BTM researched for the first time in Bulgaria, display a moderate or weak correlation with the indexed left atrial volume (conclusion no. 9). These markers could reveal their reliability in a larger number of studies.

I believe that Dr Ganeva has the ambition to create an algorithm for long-term systematic monitoring of young patients with BTM, which will support the work of pediatric cardiologists.

The publications in conjunction with the dissertation work are sufficient and confirm the creative atmosphere in which Dr Ganeva works.

With complete conviction, I believe that the dissertation presented by Dr Kalina Binkova Ganeva meets all the requirements for awarding the educational and scientific degree "Doctor".

I believe that what has been said so far will be shared by the other members of the respected scientific jury.

05/03/2023 Associate Professor Dr. Dimitar Karastatev

