Clinical research in pediatric cardiology and fetal echocardiography

SUMMARY

The habilitation thesis represents the most important part of my research activity, the results of which brought a benefit not only to my clinical activity, but also resulted in the publication of 23 ISI articles.

Having the chance to work at the Institute of Cardiovascular Diseases and Transplantation, I understand the importance of the developement of fetal diagnostics of congenital heart diseases. The activity we carried out as a team with obstetricians has led to a significant increase in the rate of fetal diagnosis. Our first study included 44 fetuses. Fetal echocardiography was performed according to a protocol based on the main sections of fetal screening and the sections used in the postnatal diagnosis of cardiac malformations. The number of fetuses diagnosed has reached 259. In this group we evaluated the diagnostic significance of a persistent left vena cava. We also conducted a retrospective study, which included 60 fetuses with conotruncal anomalies with the aim to evaluate the echocardiographic appearance of the thymus. We concluded that the association of a hypoplastic thymus with a cardiac malformation is suggestive of the existence of microdeletion. I had the chance to contribute to the diagnosis of cardiac malformations that are difficult to assess in the intrauterine period: total anomalous pulmonary venous return, common arterial trunk, or extremely rare pathologies such as Cantrell syndrome. These particular clinical situations were presented in "case report and literature review" type articles.

The knowledge acquired from the field of pediatric arrhythmology allowed me to combine them with the acquisitions made in the domain of fetal echocardiography, thus managing to develop a diagnostic protocol for fetal tachyarrhythmias. We completed the diagnostic protocol with the evaluation of the response of fetal tachyarrhythmias to vagal maneuvers. This allowed us to differentiate the two types of supraventricular tachycardias with long ventriculo-atrial interval. We diagnosed and treated 29 fetuses with various types of supraventricular tachycardia. Considering the lack of treatment guidelines for fetal tachycardias, we conducted an extensive review of the data available in the specialized literature regarding the efficacy and safety of antiarrhythmic drugs used for this pathology. We followed fetuses with atrioventricular block, respectively developed a diagnostic protocol for their evaluation. In addition to classic echocardiography, we also used speckle tracking for the evaluation of cardiac function, method that has brought useful informations in therapeutic decision making.

Coarctation of the aorta in the newborn is one of the critical cardiac malformations. Fetal diagnosis has improved the detection rate of this malformation. We conducted several studies on this pathology. The first study addressed fetal disproportion, an aspect in the intrauterine period that raises diagnostic suspicion. We concluded that ventricular disproportion in the third trimester of pregnancy is associated with a positive diagnosis in a percentage of 28.12%. We developed a multiparametric score that can exclude this

pathology with high probability. We studied this pathology in newborns. We used speckle tracking echocardiography, with the aim of integrating new parameters into the diagnostic algorithm. We were able to demonstrate that the longitudinal strain parameter can be used in the evaluation of newborns with diagnostic suspicion of critical CoAo. In this research topic we reported the case of a newborn with infantile calcification, CAGI, an autosomal recessive condition characterized by extensive calcification and intimal proliferation. The reported case mimicked a severe coarctation of the aorta. Whole-exome analysis was performed using the Illumina HiSeq PE 150 platform, which revealed the homozygous variant for the c.1896C>A(p.His632Gln) genotype in exon 15 of the ABCC6 gene. This case contributed to the enrichment of the scientific literature with data on a new mutation of the ABCC6 gene.

We researched the contribution that the speckle tracking method can bring in the field of neonatal cardiology. We performed a study including 127 healthy newborns, in which we performed longitudinal strain analysis, the aim being to obtain reference values for certain strain parameters and to test reproducibility. The reference values obtained were as follows: VSpGLS [-24.65 and -14.62], RVFWSL [-28.69 and -10.68], respectively RV4CSL [-22.30 and -11.37]. These parameters can be used in the clinical practice, the method being reproducible. Knowing the reference values, we can apply this method of assessing cardiac function to newborns with cardiac malformations. The first study applied in the pathology of cardiac malformations was performed on a group of newborns with severe valvular pulmonary stenosis. Following this study, we identified the RV4CSL parameter as being sensitive for the evaluation of the longitudinal deformation of the right ventricle.

We continued the application of longitudinal strain in the quantification of cardiac function in newborns with transposition of the great arteries. In this malformation, the afterload of the left ventricle is low, which leads to its deconditioning. The assessment of the myocardial performance of the future systemic ventricle is extremely important. In this study we included 90 newborns, the main objective being the identification of strain parameters with great sensitivity for the detection of myocardial dysfunction. The obtained results demonstrate that LVpGLS is a sensitive parameter with statistical significance.

Considering the fact that during the intrauterine period the right ventricle is the dominant one, and with the transition to neonatal circulation important changes occur, we considered it necessary to standardize the evaluation of the left ventricle beginning from the intrauterine period. Volumetric determination of left ventricular ejection fraction is not performed during routine echocardiography, and reference values for fetuses are less well known. In order to implement a correct assessment, we conducted a prospective study. 103 fetuses were included in the study. With the help of a rigorous statistical analysis, reference values were determined: AP4pLG (-16.02 ± 4.48SD) and EF (59.67 ± 8.75SD) with excellent interobserver reproducibility.

As the director of a project obtained through the competition, I managed to materialize only an important part of my research ideas in the field of fetal and neonatal cardiology, but the purchase obtained from this project allow continuation of my research, respectively with the evaluation of the fetal and neonatal heart , including by 3D echocardiography and atrial speckle. I wish to get involved in the training of resident

doctors from the field of pediatric cardiology, trying to share with them, in particular, my experience in the field of fetal cardiology.