

## **STATEMENT**

**For dissertation for awarding educational and scientific degree "DOCTOR" on:**  
**"ECHOCARDIOGRAPHIC PREOPERATIVE ASSESSMENT OF**  
**PATIENTS WITH COMPLETE ATRIOVENTRICULAR**  
**SEPTAL DEFECT"**

**To Dr. Zornitsa Nikolova Vasileva,**

doctor at the Clinic of Pediatric Cardiology of the National Cardiology Hospital, PhD student of independent training, PhD program Pediatric Cardiology, professional field 7.1. medicine, in the field of higher education "Health and Sport", with training facilities Clinic of Pediatric Cardiology at the National Cardiology Hospital, Sofia.

### **Scientific supervisor**

Prof. Anna Kaneva, MD, PhD

### **Prepared the opinion**

Prof. Dr. Elena Todorova Kinova, MD, PhD, University Hospital "Tsaritsa Yoanna – ISUL", MU-Sofia, member of the Scientific Jury by order of the Executive Director of National Cardiology Hospital, No343/21.10.2022.

The set of materials and documents presented by Dr. Zornitsa Vassileva complies with the requirements of the Law on the Development of Academic Staff in the Republic of Bulgaria and the Regulations for its implementation and with the rules for acquiring the NSA "Doctor" of the National Cardiology Hospital. When reviewing the submitted dissertation, abstract and included publications, I find no evidence of plagiarism.

### **Structure of the dissertation**

The presented dissertation contains 148 pages. It is illustrated with 38 figures and 36 tables. The references includes 142 literary sources, of which 9 are by Bulgarian authors. Over 25% of the cited sources are from the last 10 years. All of them are directly related to the topic being developed.

### **Actuality of the topic**

Complete atrioventricular septal defect (CAVSD) is a complex congenital cardiac malformation with a wide range of pathomorphological changes with variable anatomy and a number of associated abnormalities. Echocardiographic diagnosis, assessment of all elements of abnormalities and differentiation between balanced and unbalanced forms of CAVSD are the basis for determining the operational approach in each case. For this purpose, various measurements are still used in practice, without having developed an algorithm.

All this determines the importance and underlies the choice of the topic "Echocardiographic preoperative assessment of patients with complete atrioventricular septal defect", which makes it of utmost importance.

### **Literature review**

The literature review was prepared in detail and systematically with a presentation of the different forms of CAVSD and the echocardiographic indicators used so far for the accurate diagnosis of malformation. The review draws conclusions and outlines the need for further clarification in the assessment and precise determination of the balance of the CAVSD to select an appropriate surgical intervention.

### **Purpose and objectives**

The purpose of the dissertation is defined clearly and concretely - to prepare an algorithm for reliably distinguishing the balanced and unbalanced forms of the CAVSD. To achieve it, five tasks have been set, which include covering patients with CAVSD who had been admitted at the Clinic of Pediatric Cardiology in a period of 8 years, in terms of demographic and echocardiographic characteristics; clinical outcome; analyzing the indicators separately in the retrospective and prospective groups, as well as a general analysis of the entire group of patients to build an echocardiographic algorithm and assessing it to distinguish between different forms of CAVSD.

### **Material and methods**

The dissertation included a total of 100 patients with CAVSD, who had passed through the clinic with an average age of 31 days for the period from the beginning of 2014 to the end of 2021. Sixty-four of them were studied retrospectively and the rest prospectively. In operated patients, the clinical outcome was followed up to day 30. Echocardiographic indicators and their measurement are described in detail and presented by figures. The statistical analysis

used descriptive analysis, parametric and non-parametric tests for comparison of quantitative indicators between independent samples, tests for comparison of qualitative indicators, correlation analysis, discriminant analysis for selection of indicators for the production of diagnostic score, C-statistics with presentation of ROC-curves for indicators and their sensitivity and specificity to distinguish balanced from unbalanced forms of CAVSD. The statistical analysis used descriptive analysis, parametric and non-parametric tests for comparison of quantitative indicators between independent samples, tests for comparison of qualitative indicators, correlation analysis, discriminant analysis for selection of indicators for the production of diagnostic score, C-statistics with presentation of ROC-curves for indicators and their sensitivity and specificity to distinguish balanced from unbalanced forms of CAVSD.

## **Results**

The results obtained from the study are detailed and presented with tables and figures. Anatomical features of the defect and associated abnormalities were evaluated. 86 patients had balanced CAVSD and 14 with unbalanced CAVSD.

A fatal outcome occurred in 15 children. Ten were with balanced CAVSD and 2 of them died in the early postoperative approach, two after auxiliary operations and 6 before surgery. Of the 5 who died with unbalanced CAVSD, two had incorrectly indicated for 2-ventricle correction and three after auxiliary operations in the neonatal period.

From the analysis of echocardiographic indicators in the retrospective group, three parameters were selected – angle of the incoming blood flow of RV/LV, z-score for the size of the left AV-valve and the ratio of the dimensions of LV/RV in diastole. Based on their linear discriminant function coefficients, models for the diagnosis of each of the two forms of CAVSD were obtained, with the relationship between the values for the first and second diagnosis  $>1$  or  $<1$  categorizing the patient to the balanced or unbalanced form, respectively. The analysis of the indicators in the prospective group allows model adaptation with calculation of scores  $>-1.273$  and  $<-1.273$ , distinguishing the balanced from the unbalanced form of the CAVSD. This algorithm includes 4 parameters. In addition to the RV/LV angle of the incoming blood flow, the ratio of the long axes of LV/RV, the ratio of the incoming parts of both chambers and the incoming blood flow through the left AV-valve are included. The difficult diagnostic cases and deceased patients were examined in detail and assessed by linear discriminant function and by score-model. The score model showed an advantage in its sensitivity and

specificity to distinguish between the two forms of CAVSD, which is explained by the addition of the parameter of incoming blood flow through the left half of the AV-valve. The difficulties in the assessment of the CAVSD were also investigated, and it was recommended that the score-model to be used in combination with the anatomical details and associated malformation abnormalities.

The results of the dissertation complement and enrich the information on the exact diagnosis of CAVSD, which is important for management strategy in these patients.

### **Conclusions**

5 conclusions were drawn:

1. CAVSD as a complex malformation requires a systematic approach to echocardiographic assessment.
2. At this stage, there is no standardized protocol for echocardiographic assessment.
3. Incorrect assessment of the form of the defect and undertaking an inappropriate surgical correction are the cause of a fatal outcome.
4. Echocardiographic examination by protocol minimizes inconsistencies in diagnosis.
5. The application of a complex of echocardiographic measurements in an algorithm gives an accurate identification of the form of the defect in 97% of cases.

### **Research contributions**

The dissertation has not only scientific-theoretical contribution, but also can be applied in clinical practice.

Two of the contributions are of original significance:

1. The developed algorithm, which is based on a small number of echocardiographic parameters, is easily feasible and reproducible in practice, therefore it would be of great benefit to pediatric cardiologists and cardiac surgeons in classifying CAVSD as balanced or unbalanced.
2. The predictive model is at the base for prospective validation in a larger number of patients.

Confirmatory contributions:

1. This is the first systematized study of patients with CAVSD in Bulgaria.
2. Anatomical, echocardiographic characteristics of malformation and the outcome of surgical treatment are discussed.
3. Detailed echocardiographic measurements of a number of parameters are performed, with a thorough statistical analysis.

#### **Sciencemetric indicators related to dissertation**

In association with her dissertation, Dr. Zornitsa Vasileva has presented a list of three full-text publications in "Bulgarian Cardiology" journal. They correspond to the different stages of the research carried out.

#### **Autoabstract**

The dissertation autoabstract consist of 78 pages, 23 figures and 35 tables and includes the main content of the dissertation and the results obtained.

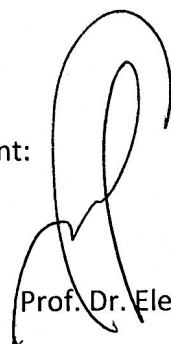
#### **Conclusion**

The dissertation of Dr. Zornitsa Vassileva is dedicated to a modern and actual topic of echocardiographic preoperative assessment of patients with complete AV-septal defect. The purpose of the dissertation is fulfilled through the set tasks. Conclusions and contributions definitely have a place in science and practice. The dissertation meets all the criteria for acquiring a scientific and educational degree "Doctor".

All this gives me a reason to vote positively and I propose to the honorable scientific jury to vote for awarding of scientific and educational degree "DOCTOR" to Dr. Zornitsa Vasileva in the scientific specialty "Pediatric Cardiology".

Jan 12, 2023

Prepared the statement:



Prof. Dr. Elena Kinova