OPINION

Subject: dissertation work for awarding the educational and scientific degree " PHILOSOPHY DOCTOR" on the topic: „Echocardiographic preoperative evaluation of patients with complete atrioventricular septal defect".

Author of the dissertation: Dr. Zornitza Nikolova Vasileva, doctor in the Clinic of Pediatric Cardiology at the MHAT "National Heart Hospital"- Sofia, doctoral student of independent training, professional direction 7.1. Medicine, specialty "Pediatric cardiology" in the field of higher education 7. "Health care and sports".

Research supervisor: Prof. Dr. Anna Kaneva-Nencheva, M.D. PhD

Prepared the opinion: Assoc. Prof. Lachezar Radoslavov Marinov, MD, PhD, pediatric cardiologist, external member of the Scientific Jury determined by order of the Executive director of the MHAT "National Heart Hospital"- Sofia No. 356/26.10.2022.

At the first absent meeting of the Scientific Jury, I have been appointed to prepare a opinion.

A opinion has been prepared in accordance with the Academic Staff Development Act (ACAS), the Regulations for the Application of the Academic Staff (PRAS) and the Regulations on the Terms and Conditions for Acquisition of Scientific Degrees and Occupation of Academic Positions (PURPNSZAD) in MHAT "NHH" EAD.

The presented set of materials on paper/electronic media is in accordance with the procedure for acquiring the scientific and educational degree "Doctor" and the regulations of MHAT "NHH" EAD.

I do not find plagiarism in the review of the dissertation, abstract and publications submitted to me for review, related to the dissertation development.

I declare the absence of joint scientific developments with the doctoral student and a potential conflict of interest.

Brief biographical data:

Dr. Zornitsa Vasileva graduated from "Medicine" in 2005 at MU - Sofia. From 2005 to 2011, he specialized in Children's Diseases at SBALDB "Prof. Ivan Mitev" - Sofia. Acquired a specialty in Children's Diseases in 2011. He specializes in Children's Cardiology at the Children's Cardiology Clinic of "NHH"-EAD - Sofia and at the University Hospital of Ghent - Belgium. In 2017, he acquired a specialty in Pediatric Cardiology. He has certificates for "Fetal echocardiography", "Echocardiography in childhood - fundamental level, transthoracic echocardiography (1R EchoKG, 2R EchoKG), pulse, continuous and color Doppler", European certificate "Echocardiography in Congenital Heart Disease" (European Association of Cardiovascular Imaging certification in Congenital Heart Disease Echocardiography), "Advanced fetal echocardiography" certificate, Fetal Medicine - Barcelona. From July 2020 to September 2022, he is a doctoral student of independent training at the Children's Cardiology Clinic at the NKB. Excellent command of English and Dutch, basic knowledge of Russian, German and French languages.

Member of the Bulgarian Medical Union (BLS), Orde der Geneesheren – Flemish Medical Union, Belgium, Society of Cardiologists in Bulgaria, European Society of Cardiology (ESC),

European Association of Pediatric Cardiology (AEPC), Fetal Heart Society, European Association of Cardiovascular Imaging (EACVI).

Relevance of the topic:

Complete atrioventricular septal defect (CAVSD) is a complex congenital heart malformation that accounts for about 7% of all CHD and occurs in 3.5 per 10,000 live births. The diagnosis is entirely echocardiographic. The treatment is surgical, with the main goal being double-chamber correction (2CC). Depending on the location of the common AV valve in relation to the chambers, there is a balanced form (CbAVSD), in which the valve is evenly distributed between the two chambers, and an unbalanced form (CuAVSD), in which the common AV valve is primarily connected to one of the chambers. while the other chamber remains hypoperfused and, accordingly, hypoplastic. In CuAVSD there may be a dominant right ventricle - the so-called right-dominant, which is more common, or left-ventricular dominant - left-dominant, which is less common. Severe forms of CuAVSD exclude the performance of bichamber correction and patients are indicated for unichamber circulation. A serious problem in determining the optimal surgical strategy is represented by forms with a borderline degree of imbalance and, in particular, with borderline dimensions of the LV, when there are doubts as to whether it is able to maintain systemic circulation after 2CK. There is still no algorithm on which to base the diagnosis and the choice of the most appropriate surgical strategy. Detailed preoperative visualization of all elements of the anomaly, making precise measurements and determining whether the defect is balanced or unbalanced is of utmost importance. The problem of determining the balance has not yet been resolved, there is no developed algorithm that would allow reliable differentiation of balanced from unbalanced forms of CAVSD.

CAVSD is combined with a number of other cardiac anomalies, which can be summarized in three groups: affecting the left half of the common AV valve; of the left ventricular outflow tract (LVOT) - subaortic stenosis and combination with other CHD.

Determining the balance in CAVSD poses serious diagnostic and therapeutic challenges. The most important question to answer is whether the patient will be able to tolerate bicameral correction. It is necessary to use a complex of echocardiographic measurements in an algorithm, which allow correct determination of the shape of the defect and the selection of the most appropriate surgical strategy.

Structure of the dissertation

The dissertation work of Dr. Zornitsa Vasileva is presented on 148 standard pages, includes 38 figures, 36 tables and two appendices. The bibliography includes 142 sources, of which 9 are in Cyrillic and 133 are in Latin. Most of the cited sources are from the last 10 years.

It is written in the literary Bulgarian language, well structured in accordance with the accepted standards for the preparation of a scientific work for the acquisition of a scientific and educational degree "Doctor". Contains the following pages: Title page – 1 page; Abbreviations used – 1 page; Introduction – 2 pages; Literature review - 49 pages; Purpose and tasks - 1 page; Material and methods – 11 pages; Results – 53 pages; Discussion – 6 pages; Conclusions – 1 page; Conclusion – 1 page; Contributions – 1 page; Literature – 15 pages; Appendices – 4 pages; Publications related to the dissertation - 1 page.

The proportional distribution between the individual sections is respected.

The introduction is on 2 pages and points to the essence of the scientific work.

Review of the literature

Presented in 49 pages, extremely detailed and informative, it shows the good awareness of the dissertation in terms of frequency, embryology, anatomy, classification of PAVSD, associated anomalies, combination with other CHD. Special attention is paid to the diagnostic approach with the use of clinical, instrumental, imaging and invasive methods. The review examines in detail the possibilities of echocardiography for determining the shape of the defect - balanced or unbalanced, which is of strategic importance for surgical behavior. The echocardiographic assessment for determining the balance between the chambers using different echocardiographic parameters is described in detail: Minor index, Atrioventricular septal angle, Atrioventricular valve index (AVCI, AVVI), Modified atrioventricular valve index (mAVCI, mAVVI), Left ventricular inflow index, Inflow Angle of DC/LV, Indexed Interventricular Defect.

In the last part of the review, the therapeutic behavior in CAVSD is considered. The natural evolution of complete balanced AVSD leads to premature death due to the serious complications - congestive heart failure and/or pulmonary vascular obstructive disease (PVOD). Surgical correction in infancy is recommended for all patients. In recent decades, there has been a decrease in the age for planned correction - from 1 year a few decades ago to 3 to 6 months nowadays, improvement of the postoperative outcome due to the improvement of surgical techniques and postoperative care. The goal of early correction is to minimize the risk of premature death.

The author shows a very good and thorough knowledge of the subject of the dissertation. The conclusions of the literature review are meaningfully formulated and logically argue the purpose and tasks of the dissertation work.

Purpose and tasks

The aim of this dissertation is: Based on a detailed and standardized preoperative echocardiographic evaluation of CAVSD, including systematic measurements of preset parameters, to develop an algorithm for reliably distinguishing balanced from unbalanced forms.

To achieve the set goal, 5 specific tasks have been correctly formulated.

Material and methods

The study is ambispective and covers 100 patients with PAVSD who have passed through the Children's Cardiology Clinic at the National Cardiology Hospital for the period 01.12.2014 - 31.12.2021.

The period from January 2014 to December 2018 was a retrospective study of the available documentation and stored echocardiographic images of the patients with this cardiac malformation and included 64 patients. During the period from January 2019 to December 2021, echocardiographic measurements were prospectively performed in 36 children with PAVSD (26 of them operated), and the clinical outcome in both groups was followed up to the 30th day after the last surgical intervention. The diagnosis of CAVSD was established echocardiographically, based on the characteristic morphological features of this CHD. Measurements in the prospective group were performed according to a predetermined protocol, including 2D echocardiography, M-mode echocardiography, color Doppler, pulsed and continuous Doppler. In the retrospective group, the static echocardiographic images and videos stored in the SyngoPlaza system of the

NHH were found and measurements were carried out according to the offline protocol. The average value of three consecutive measurements was taken to determine the various echocardiographic parameters. Additionally, from the operative protocols of the patients, data were obtained on intraoperative finding, inconsistency with the echographic finding and surgical strategy - double chamber correction, single chamber circulation, inoperable and fatal outcome. Information about the intracardiac anatomy was obtained from the autopsy reports of the autopsied children.

The statistical package IBM SPSS Statistics was used for the statistical processing of the data. The applied modern statistical methods give grounds for the reliability of the obtained results.

Results

The results obtained by Dr. Zornitsa Vasileva are presented correctly on 53 pages of the dissertation work, illustrated with sufficiently informative tables and figures. They strictly follow the goal and set tasks. The developed score system for preoperative echocardiographic assessment allows a reliable distinction between balanced and unbalanced forms of CAVSD.

Discussion

The discussion of the obtained results is presented on 6 pages. Own results are thoroughly discussed and competently compared with those of other authors.

Of particular importance for the preoperative echocardiographic diagnosis of CAVSD is the standardized approach to the examination of patients, mandatory measurements, their general assessment, determination of the shape of the defect by its anatomical characteristics, associated anomalies. Of the 9 separate echocardiographic measurements used, it was found that 4 differed significantly in the balanced and unbalanced forms of AVSD. An important advantage of the model proposed by the author is that, based on a small number of relatively easy to perform echocardiographic measurements, the shape of CAVSD is determined. This is a prerequisite for the correct choice of surgical strategy and for a favorable outcome for the patient.

Conclusions

The 5 conclusions made are clearly formulated in the context of the set tasks.

Contributions

The contributions of the dissertation, 5 in number, are of an original, scientific - applied and confirmatory in nature, well formulated and are the result of the study.

For the first time in Bulgaria, a systematic study of patients with CAVSD in Bulgaria was carried out. The anatomical and echocardiographic characteristics of the malformation and their significance for the operative strategy and the outcome of the surgical treatment were evaluated. Precise echocardiographic measurements of a number of parameters were performed. The developed algorithm is easily implemented in clinical practice, which is of great benefit to pediatric cardiologists and cardiac surgeons in classifying CAVSD as balanced or unbalanced, especially in borderline forms. The developed predictive model is the basis for prospective validation in a larger number of patients.

The abstract in a volume of 92 pages reflects the main results and discussion, conclusions and scientific contributions of the dissertation work.

Publications

The author presents 3 full-text publications related to the dissertation work in renowned Bulgarian medical journals, that meet the requirements, as well as other publications and contributions with fragments of the dissertation.

Dr. Zornitsa Vasileva presents a list with an impressive number, a total of 81 scientific publications, of which 11 are in publications with IF, 70 without IF.

Recommendations

Given the high scientific value of the dissertation work and its relevance, I recommend the author to continue monitoring patients with CAVSD and collecting more data to optimize proactive behavior and adequate treatment of these children. To publish the obtained data in the foreign scientific periodical.

CONCLUSION

The dissertation presented to me by Dr. Zornitsa Nikolova Vasileva contains data of an original, scientifically - applied and confirmatory nature and is a contribution to the development of pediatric cardiology.

For the first time in Bulgaria, a systematic study of patients with CAVSD in Bulgaria was carried out. The anatomical and echocardiographic characteristics of the malformation and their significance for the operative strategy and the outcome of the surgical treatment were evaluated. Precise echocardiographic measurements of a number of parameters were performed. The developed algorithm is easily implemented in clinical practice, which is of great benefit to pediatric cardiologists and cardiac surgeons in classifying PAVSD as balanced or unbalanced, especially in borderline forms. The dissertation work shows that the doctoral student has in-depth theoretical knowledge and professional skills in the scientific specialty, demonstrates qualities and the ability to independently conduct and discuss scientific research.

The dissertation meets the requirements for the award of the educational and scientific degree "Doctor" laid down in the Law on the Development of the Academic Staff in the Republic of Bulgaria and the Rules for the Development of the Academic Staff of the MHAT "National Heart Hospital"- Sofia.

This gives me reason to vote with a positive vote and I strongly recommend to the respected members of the Scientific Jury to vote for awarding Dr. Zornitsa Nikolova Vasileva the educational and scientific degree " Philosophy Doctor" in the scientific specialty "Pediatric Cardiology", professional direction 7.1. Medicine, field of higher education 7. "Health care and sports".

29.12.2022

Prepared the opinion:

Assoc. Prof. Lachezar Radoslavov Marinov MD, PhD