

OPINION

of a thesis and an abstract on a topic "Invasive evaluation of hemodynamics in patients after Fontan operation"

Presented by the National Cardiology Hospital for public defense to a scientific jury for awarding the scientific and educational degree "Doctor" in the doctoral program "Pediatric Cardiology", professional direction "Medicine", field of higher education - "Health and Sports".

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Prepared the statement: Prof. Elina Trendafilova, MD, PhD, National Cardiology Hospital. Elected as a member of the Scientific Jury by order № 228/04.07.2022 and for preparing a statement on the thesis submitted on 02.08.2022 by the members of the Scientific Jury, before which the public defense will be held. Office address: Prof. Elina Trendafilova, MD, PhD, National Cardiology Hospital, Sofia.

I have not found any violations in the documents attached by Dr. Levunlieva, the requirements of the Law on Scientific Research and Development of the Republic of Bulgaria have been met. I do not have a conflict of interest caused by my participation in the current scientific jury. I do not have shared scientific papers with the doctoral student among those presented for the thesis.

Data from the professional biography: Dr. Levunlieva graduated in medicine in 1991, since 2002 and currently works as an assistant at the National Cardiology Hospital - Sofia, has over 30 years of experience as a doctor and is board certified in pediatrics and pediatric cardiology, as well as certificates in invasive cardiology and pediatric echocardiography. Since 2018, he is a doctoral student in self-study in the specialty "Pediatric cardiology". Dr. Levunlieva is a respected and erudite pediatric cardiologist, with diverse interests and extensive clinical, organizational and teaching experience.

Assessment of the presented thesis: The problem presented for research by the doctoral student is extremely relevant for modern theory and practice in pediatric cardiology in the context of constantly improving diagnostic non-invasive and invasive diagnostic methods, operative and interventional techniques, and modern drug therapy of pulmonary arterial hypertension and increased life expectancy of children with congenital heart malformations.

The dissertation is presented on 155 standard pages, includes 25 tables and 39 figures, and an additional 32 tables are included in the appendices. The bibliography is complete and up-to-date, contains 297 sources, of which 11 are in Cyrillic. The abstract is presented on 58 pages and meets the requirements of the scientific organization at National Cardiology Hospital. The dissertation was discussed and approved for public defense at a meeting of the Primary Scientific Unit at the Pediatric Cardiology Clinic on June 20, 2022.

The review is modern, detailed, logically constructed and presented on 39 pages, it describes the main changes in hemodynamics after Fontan surgery, a review of the world literature on the subject is made, and the questions that await their answer are clearly defined.

The aim of the thesis is defined as the assessment of postoperative hemodynamics in patients with congenital heart malformations of the "common chamber" type and completed stages of surgical treatment with an extracardiac conduit and the influence of anatomical and functional factors on the long-term postoperative evolution. The eight main tasks are well formulated and meet the set objective.

Statistical methods are modern and correctly used, a large number of parameters are analyzed, which allows clear and specific conclusions to be drawn.

The material and methods correspond to the set goals and tasks and are correctly selected. The data of 71 children with total cavo-pulmonary anastomosis, operated in the Pediatric Cardiology Clinic of National Cardiology Hospital from 2000 to 2020, were analyzed retrospectively and prospectively, the inclusion and exclusion criteria were clearly selected. Numerous epidemiological and hemodynamic parameters were analyzed, and an original score was compiled to evaluate the prognosis, which is based on hemodynamic indicators registered during catheterization: cavo-pulmonary pressure, transpulmonary gradient, pulmonary vascular resistance, oxygen saturation, as well as the development of pulmonary stenosis and protein-losing enteropathy. The material is well arranged and illustrated.

The results are presented on 35 pages. Changes in the main hemodynamic parameters assessed during cardiac catheterization were analyzed, depending on the postoperative morphology - left ventricular or right ventricular, depending on the previous postoperative interventions, according to the interventional data from the fenestra occlusion test and after sildenafil was administered.

Especially valuable is the long-term follow-up (over 10 years) in these children and the identification of the most frequent complications, which, in combination with the valuable hemodynamic parameters, allows:

1. to define an original protocol for follow-up with cardiac catheterization with the justification of the moment of catheterization and the analyzed parameters;
 2. to define modified Bulgarian criteria for definitive fenestration closure;
 3. to create a prognostic model with very good sensitivity and specificity.
- The conclusions drawn are 9, logically and correctly formulated and follow from the results of the clinical and statistical analysis.

Scientific contributions: The dissertation clearly defines the importance of hemodynamic parameters for the follow-up of children after Fontan operation. The author divides the contributions into two groups: original and confirmatory. I agree with both their scientific value and their content. For the first time in Bulgaria, hemodynamic data are systematically recorded during the long-term follow-up of operated children and it is proven that Fontan operation with an extracardiac conduit increases the saturation, improves the

pulmonary/systemic blood flow ratio, lowers the ventricular end-diastolic pressure, without registering changes in the cavo-pulmonary pressure, pulmonary vascular resistance and systemic blood flow. The early benefit and its late risks of fenestration are demonstrated. Hemodynamic criteria in test occlusion have been defined to select patients in whom defenestration can be "safely" performed. The author proves that the morphologically left type of common ventricle shows more favorable hemodynamics. The benefit of selective pulmonary vasodilators has been shown, which significantly lower cavo-pulmonary pressure, pulmonary vascular resistance, improve transpulmonary blood flow and systemic oxygen saturation, thereby affecting increased pulmonary vascular resistance as a key factor for adverse postoperative evolution.

Particularly valuable is the proposed score for predicting the late prognosis, including invasive hemodynamic indicators, which allows proactive management.

Publications related to the thesis: Dr. Levunlieva presents 3 full-text publications in peer-reviewed journals in Bulgarian.

Critical notes: Abstracts presented at congresses at home and abroad are not presented. This will prove the scientific community's positive assessment of the thesis.

Conclusion: The presented thesis of Dr. Levunlieva "Invasive assessment of hemodynamics in patients after Fontan surgery" is an up-to-date and scientifically supported study of the possibilities of cardiac catheterization with hemodynamic parameters for monitoring of children after cavo-caval anastomosis with single-chamber circulation. For the first time in Bulgaria, a systematic analysis of the invasively assessed hemodynamic indicators in patients with a functional single-chamber heart with completed stages of Fontan circulation was performed. A unified follow-up protocol was created, Bulgarian criteria for definitive closure of the fenestration were defined, and a prognostic model with hemodynamic parameters was created to assess the long-term prognosis with very good sensitivity and specificity.

I strongly recommend the members of the Scientific Jury to positively evaluate the thesis "Invasive assessment of hemodynamics in patients after Fontan surgery" and award Dr. Elina Levunlieva and educational degree "Doctor" in doctoral program - "Pediatric Cardiology", professional field - "Medicine", field of high education - "Health and Sports".

2019, 2020

Prepared the statement:

Signed

/ prof. Dr. Elina Trendafilova, MD, PhD /