REVIEW from

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External member of Scientific Jury from Medical University - Sofia on the basis of order № 2 / 29.06.2022 of the Chairman of the Supervisory Board at "NKB" EAD-Sofia

Regarding the dissertation on the topic: "Invasive evaluation of hemodynamics in patients after Fontan operation" for awarding the educational and scientific degree "Doctor" in the scientific specialty "Pediatric Cardiology" to Dr. Elisaveta Dimitrova Levunlieva at "NKB" EAD – Sofia.

As an appointed member of the jury for this competition, I have no conflicts of interest to be declared.

The dissertation is written on 155 standard pages and includes 39 figures and 57 tables. The bibliography contains 297 literature sources, of which 11 in Cyrillic and 286 in Latin.

Relevance of the topic

Many of the health problems of Fontan patients are related to the biophysics and physiology of their cardiac anatomy and the consequences of the serial surgical corrections necessary for their survival. These patients pose multiple health challenges in addition to purely organic ones that are yet to be recognized and appreciated. Postoperative follow-up of Fontan patients is of utmost importance to recognize and possibly prevent the adverse evolutionary complications of this "unnatural" circulation. There is no consensus on when to catheterize patients after Fontan surgery. There is no consensus on the definition of "routine follow-up" and it varies widely and is a matter of institutional conception. Fenestration during the Fontan operation is performed with the aim of favorably influencing the early postoperative adaptation, but its effect is not unambiguous, especially in the long postoperative period. It has a beneficial effect on hemodynamics in the early postoperative period, but its effect on the development of Fontan-circulation failure and prognosis is not specified with certainty until 2021. The effect of phosphodiesterase inhibitors in Fontan-patients has been evaluated in only nine studies out of which studies with invasive hemodynamic assessment of long-term sildenafil use in children are extremely few and the number of patients included in the studies is also very limited. Therefore, the assessment of postoperative hemodynamics in patients with

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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 makes the topic very relevant.

Structure of the dissertation

The dissertation is in accordance with the standards for the preparation of scientific work for the acquisition of the scientific and educational degree "Doctor". It includes the following separate parts: literature review – 39 pages, aim and tasks – 1 page, material and methods – 6 pages, results – 35 pages, discussion – 27 pages, conclusions – 2 pages, contributions – 1 page, appendices – 21 pages, bibliography – 12 pages and publications related to the dissertation work – 1 page.

The proportion between the structuring departments of the work is according to the requirements.

Knowledge of the problem and scientific formulation

The literature review done is very well structured, detailed and comprehensive. It covers in depth the different aspects of the subject: epidemiology, morphological classification of congenital heart malformations with single chamber physiology, morphological diagnosis in patients with common chamber physiology and Fontan type surgical correction, hemodynamics in native single chamber circulation, preoperative behavior and surgical treatment, and late problems and complications after Fontan. The results of other publications on the topic are correctly cited. Appropriate visualization with 3 tables and 4 figures contribute to the clarity of the presentation.

The conclusions of the literature review are meaningfully formulated and logically argued upon the purpose and tasks of the dissertation work.

The aim is clearly and specifically defined: "To evaluate the 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."

Fully in accordance with the formulated goal, 8 specific tasks are correctly identified.

The dissertation included 71 children who met the inclusion criteria for the study for the period 2000-2020 from a total of 159 patients with a completed stage of Fontan palliation.

The inclusion and exclusion criteria are clear and fully aligned with the set goals and objectives.

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The results of the dissertation work are described in detail on 59 standard pages and very well illustrated with overview figures and tables. They strictly follow the goal and the tasks of the dissertation work. The results are thoroughly and competently discussed and compared with those of other collectives.

In accordance with the obtained results, 6 contributions were formulated - 3 original and 3 confirmatory, two of the original ones being of a scientific-theoretical and a scientific-applied nature. They are meaningfully and factually argued by the results and the discussion and prove the scientific and clinical-applied value of Dr. Ivanova's work.

The summary report is designed according to the requirements and reflects the main results, the discussion, the conclusions and the scientific contributions of the dissertation.

The required publications on the topic are correctly cited. The forms used to provide the information about the patients participating in the study are included in a separate appendix No. 11.

Conclusion

Doctoral student Dr. Elisaveta Dimitrova Levunlieva-Ivanova has mastered important research, methodological and clinical skills. Her work proves that she is able to independently formulate a scientific statement, correctly conduct scientific research, choose and use appropriate statistical methods and adequately interpret scientific results.

The dissertation shows that the doctoral student Dr. Elisaveta Dimitrova Levunlieva - Ivanova has in-depth theoretical knowledge and professional skills in the scientific specialty of pediatric cardiology demonstrating qualities and skills for independent research.

Due to the above, I **CONVINCEDLY** give my **POSITIVE** assessment of the study, presented by the above reviewed dissertation, abstract, results and contributions, and I offer the esteemed JURY to award the educational and scientific degree "**DOCTOR**" to **Dr.** Elisaveta Dimitrova Levunlieva - Ivanova in the scientific specialty of pediatric cardiology, to the primary unit of the Children's Cardiology Clinic of the NKB - EAD, Sofia.

15.09.2022

Review prepared by:

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