

TO
THE CHAIRMAN OF THE SCIENTIFIC JURY,
APPOINTED BY ORDER NO 15-01-516 /23.11.2023
THE EXECUTIVE DIRECTOR AND THE PROCURATOR
OF "ACIBADEM CITY CLINIC UMHAT TOKUDA" EAD

OPINION

**From Assoc.Prof. Dr. Svetlin Nedkov Tsonev, PhD
University "Prof. dr. Asen Zlatarov", Burgas**

Regarding a dissertation thesis for the acquisition of the educational and scientific degree "PhD" in the field of higher education 7. Health care and sports, professional direction 7.1. Medicine, PhD program "Angiology".

Topic: „ATHEROSCLEROSIS OF CAROTID, CORONARY AND PERIPHERAL ARTERIES IN PATIENTS WITH DEGENERATIVE AORTIC STENOSIS"

Author: Dr. Desislava Bojdarova Bojadgieva-Marincheva

Form of doctoral studies: Independent preparation

Scientific unit: Clinic of angiology

Research supervisor: Prof. Dr. Milena Staneva Staneva, PhD.

Prof. Dr. Sotir Todorov Marchev, DSc

1. General presentation of the procedure and the PhD student

The dissertation is constructed and written in compliance with the requirements of the procedure in terms of thesis topic, internal defense and selection of the Scientific Jury.

Dr. Desislava Bojadgieva was enrolled in a PhD program on an independent basis by Order No. 464 of 13.12.2019 of the Executive Director and the Procurator of "Acibadem City Clinic UMHAT Tokuda" EAD. The requirements for the type of doctoral studies have been fulfilled, namely: the individual doctoral plan and a successful completion of the doctoral examination. On 24.10.2023. the completed dissertation was presented and successfully defended in front of an extended Scientific Board of the Clinic of Angiology, after which, at a meeting of the Scientific Board (Minutes 49/03.11.2023), she was discharged with the right to defend. By Order No. 15-01-516/24.11.2023 of the Executive Director and the Procurator of the Hospital, I have been appointed as an external member of the Scientific Jury in connection with the dissertation of Dr. Desislava Bojadgieva.

I am determined to prepare an Opinion.

The dissertation, the abstract and the set of documents and materials related to the formal defense provided by the doctoral candidate fully comply with the legal requirements of the above mentioned regulatory framework.

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I declare that I have no conflict of interest with the author of the thesis.

Dr. Desislava Bojadjeva was born on 03.09.1978 in Pleven. In 1997 she graduated the Foreign Languages High School in Pleven. In 2003 she graduated in medicine at the University of Medical Sciences in Pleven. From 2008 to 2012 she was a specialist and assistant professor in Cardiology at the University Hospital "Dr. Georgi Stranski" in Pleven. In 2012 she acquired a specialty in Cardiology. From 2017 to 2020 she specializes Angiology at Ajibadem City Clinic Tokuda Hospital, Sofia and in December 2020 she acquired a specialty in Angiology. In 2019 she obtained a certificate for HSW "Ultrasound Vascular Diagnostics" from MU - Sofia. From 2017 to 2020 she worked at the Heart and Brain Hospital in Pleven as an angiologist and cardiologist at the Vascular Surgery Clinic. From 2020 to the present, she has worked in an ambulatory practice.

She annually attends and participates in national and international scientific forums, and successfully masters and practices instrumental techniques in the field of Angiology.

2. Topical relevance

The topic of the thesis is carefully selected and topical, combining a multidisciplinary approach- cardiological-angiological. The incidence of aortic stenosis is increasing and is the most common valvular disease in adults, and atherosclerosis is the leading cause of arterial vascular disease. The combined morbidity and mortality of the two diseases is extremely high. Scientific researches are found in the literature that testify to a common etiopathogenesis of the both conditions. Based on the literature review, the dissertation attempts to answer some unresolved questions in this topic.

3. Knowledge of the problem

The PhD student has studied the problem in detail and critically evaluates the literature.

4. Methodology of the study

The chosen methodology is well implemented in clinical practice with a good level of reproducibility and is well mastered by the dissertant, which is important for achieving the objectives under the scientific hypothesis thus developed in the dissertation.

5. Characteristics and evaluation of the thesis and contributions

The dissertation of Dr. Bojadjeva is written in 117 pages, illustrated with 20 figures and 59 tables. It is properly structured and includes 9 sections:

Abbreviations and symbols used - 1 page;

1. Introduction - 1 page;
2. Literature review - 26 pages;
3. Aim and objectives - 1 page;

4. Material and Methods - 11 pages;
5. Own results - 41 pages;
6. Discussion - 11 pages;
7. Conclusion - 1 page
8. Inferences - 1 page;
9. Bibliography - 19 pages; The bibliography contains 182 references, of which 3 in Cyrillic and 179 in Latin.

In the introduction the problem is formulated in detail and the aim of the thesis is justified.

The literature review is competently and critically written and demonstrates a reasonably good knowledge of the problem at hand. There is a substantial body of literature regarding the general mechanisms, risk profile for degenerative aortic stenosis, and previous evidence of similarity with atherosclerosis of different localizations.

The aim of the dissertation is properly formulated in accordance with the dissertation topic and the unsolved problems arising from the literature review. Dr. Bojadjeva aims to assess the presence and severity of atherosclerosis with different localization, including combined, in patients with degenerative aortic stenosis and after analyzing the results to develop an algorithm for management for prevention and improved prognosis.

There are six main tasks and they are well formulated in line with the stated objective.

In the section "**Materials and methods**" are described in detail the 132 patients, men and women, aged from 48 to 92 years, studied in the period 2018 - 2019. The studied patients are divided into two main groups: Group I - Patients with aortic stenosis - 91 (average age 73 years), divided into 3 subgroups: 1. High grade AS - 46 patients, 2. Mid-stage AS - 16 patients. 3. Low-grade AS - 29 patients; Group II - control - 41 patients (mean age 72 years) - patients with risk factors and clinical manifestation of atherosclerosis but without congenital or acquired aortic malformation. The study was prospective in design for the period, with an analysis of total mortality after the second year of completion.

For the statistical processing of the data were used appropriate methods and specialized statistical package SPSS (Statistical Package for the Social Sciences) version 16.0, as well as consulting with a statistician, which ensures the reliability and correct interpretation of the obtained

Results: The results obtained by Dr. Bojadjeva are well illustrated numerically and graphically and meet the objectives of the study.

Discussion of the results

A sufficient amount of the dissertation is devoted to analysis and discussion of the data obtained.

Conclusions and contributions: based on the results obtained, Dr. Bojadgieva logically draws 9 conclusions, which correspond to the set tasks.

1. The most common clinical manifestation of atherosclerosis is in patients with mild aortic stenosis.
2. Patients with a more severe form of aortic stenosis have a smaller number of arterial pools affected by atherosclerosis compared with patients with mild aortic stenosis.
3. Patients with mild aortic stenosis were found to have more severe coronary pathology and fewer realized myocardial infarctions, and those with high-grade aortic stenosis, milder coronary pathology with more realized coronary events.
4. There was no statistically significant association between the presence of a specific risk factor and aortic stenosis.
5. Risk factors for atherosclerosis are similar to those for aortic stenosis, but have no relationship to disease progression and the degree of valvular stenosis.
7. High-grade AS is protective for MSDs - the presence of severe AS reduces the risk of developing MSDs by 2.9 times.
8. Patients with AS resemble patients with atherosclerotic disease in their involvement of the abdominal aorta.
9. Despite identical conditions and risk factors for the occurrence, we have two different pathways of development of the pathological condition: to AS or to atherosclerotic vascular disease

The construction of the scientific work expresses thoroughness and consistency, and a sufficient part of the data are personal merit of Dr. Bojadgieva. The 6 contributions are of original scientific and clinical significance.

1. For the first time in Bulgaria, a detailed assessment of the relationship between aortic stenosis and atherosclerosis was performed.
2. An algorithm for the management of patients affected by atherosclerotic disease and aortic stenosis was developed.
3. Telephone interview was used to check the current status of patients, which is a convenient and safe method in a pandemic setting.
4. The results of the present work clarify that, although not completely mutually exclusive, degenerative aortic stenosis and atherosclerosis of the coronary and carotid arteries are largely opposite conditions. Ultrasound evaluation of the vessels should not be used as a screening method for aortic stenosis.
5. With known atherosclerotic disease of the aorta, it is appropriate to look for aortic valve stenosis, and also vice versa: with known aortic stenosis, the condition of the aorta should also be checked.
6. In compiling the present work, a large amount of data has been collected and processed, which can serve as a starting point for further research on the problem

6. **The abstract** is written in 58 pages, meets the requirements and fully reflects the results presented in the thesis. In a clear and summarized manner, it gives an overview of the overall design of the work, methods, results and main conclusions.

7. Assessment of publications and personal contribution of the PhD student

The PhD student has applied 2 publications in national journals and 7 scientific participations at national scientific forums. In all the attached publications Dr Bojadieva is the first author, and in 1 she is an independent author. This research activity meets the criteria for the national minimum requirements for the educational and scientific degree "PhD".

CONCLUSION

The thesis contains scientifically substantiated results of theoretical and applied nature, which represent an original contribution, expanding our knowledge in the field of multifocal atherosclerosis and cardiology. It has been created in a strictly scientific style. It meets all the requirements of the Law on the Development of the Academic Staff in the Republic of Bulgaria (_DASRB), the Regulations for the Implementation of LDRASRB and the Regulations of "Acibadem City Clinic UMHAT Tokuda" EAD. The presented materials and dissertation results completely meet the specific requirements adopted in regard with the Regulations of "Acibadem City Clinic UMHAT Tokuda" EAD for the application of LDASRB.

Dr. Desislava Boyadjieva is a specialist in cardiology with 11 years of experience and in angiology with 3 years of experience. She is actively involved in research and is certified to perform highly specialized activities in both areas. The PhD student demonstrates the qualities and skills to independently conduct scientific research.

Due to the above, I give my positive assessment and strongly recommend to the members of the Scientific Jury to positively evaluate the dissertation work "Atherosclerosis of carotid, coronary and peripheral vessels in patients with degenerative aortic stenosis" and to award Dr. Desislava Bojidarova Bojadgieva - Marincheva Scientific and educational degree "PhD" in the field of Higher Education 7. Health care and sports, professional direction 7.1. Medicine, doctoral "Angiology".

10.01.2024

Assoc.Prof. Svetlin Tsonev, PhD

Sofia