

**TO**  
**THE CHAIRPERSON 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**

## **REVIEW**

By Prof. Dr. Kiril Karamfilov Karamfilov, PhD  
Head of the Clinic of Cardiology at the University Hospital "Alexandrovska",  
MU-Sofia

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 Bojidarova 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**

In writing the dissertation, the requirements for the procedure in terms of thesis ability, choice of the topic, internal defense and selection of the Scientific Jury were followed.

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 Tokuda University Hospital" EAD. She has completed the individual doctoral plan and has passed the PhD 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 (Protocol 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

Prosecutor of the Hospital, I have been appointed as an external member of the Scientific Jury in connection with the dissertation of Dr. Bojadgieva.

I am determined to prepare a Review. 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.

No plagiarism was detected from the submitted StrikePlagiarism.com Metadata reference.

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

Dr. Desislava Bojadgieva 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 Acibadem 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.

## **2. Topical relevance**

The dissertation topic is well chosen and relevant. Degenerative aortic stenosis is the most common valvular disease in adults in industrialized countries, and atherosclerosis is the most common vascular disease. Both diseases have a high incidence of morbidity and mortality and lead to high healthcare costs. Many researchers are looking for similarities between the two diseases and the mechanisms that cause them, with the aim of improving their prevention and treatment. The present dissertation attempts to answer some unresolved and controversial questions about the relationship between aortic stenosis and atherosclerosis and this makes it extremely relevant.

## **3. Knowledge of the problem**

The PhD student knows the state of the problem and evaluates the literature creatively.

## **4. Methodology of the study**

The chosen research methodology allows achieving the set goal and obtaining an adequate answer to the problems solved in the dissertation.

## 5. Characteristics and evaluation of the thesis and contributions

The dissertation of Dr. Bojadgieva 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 well formulated and the aim of the thesis is justified.

The literature review is competently written and demonstrates a good knowledge of the problem at hand in its various aspects. The underlying mechanisms and risk factors for degenerative aortic stenosis are well reviewed, as are its similarities with atherosclerosis of different localization.

**The aim** of the dissertation is formulated in accordance with the dissertation topic and the presented literature review. Dr. Bojadgieva aims her research work to assess the presence and severity of atherosclerosis of carotid, coronary and peripheral arteries in patients with degenerative aortic stenosis in order to develop an algorithm for management for prevention and improved prognosis.

In order to achieve the set goal, the following **tasks** are set:

1. To determine which localization of atherosclerosis is more commonly associated with degenerative aortic stenosis.
2. To establish the relative importance of RF for atherosclerosis in the development of CAD.
3. How the presence of AS affects mortality.
4. To determine whether there is a correlation between the severity of the atherosclerotic process and the degree of AC.

5. To answer the question whether all patients with AS should be actively screened for peripheral, coronary and carotid atherosclerosis

6. To establish an algorithm for the management of patients with DAS with a view to prevention and improved prognosis.

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 (AS) - 91 (average age 73 years), who are divided into 3 subgroups: 1. High grade AS - 46 patients, 2. Mid-stage grade 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 for the period indicated, and an analysis of mortality among the patients studied was performed after the second year of its completion. For the statistical processing of the data appropriate methods and specialized statistical package SPSS (Statistical Package for the Social Sciences) version 16.0 were used, which guarantees the reliability of the results obtained.

**Results:** The results obtained by Dr. Bojadgieva are well illustrated and meet the objectives of the study.

**The discussion of the results** analyses the data obtained and compares, where possible, with other publications on the subject.

**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.

6. The number of risk factors in patients with aortic stenosis does not change the average number of arterial basins affected by atherosclerosis.

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 scientific development expresses thoroughness and consistency. The contributions are **6 original, scientifically applied.**

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 communications in national and international scientific forums, 2 of which in journals with IF. In all the attached publications Dr Bojadgieva is the first author, and in 1 she is an independent author. This scientific activity is sufficient to show that the PhD student is consistent in his/her scientific activity and meets the national minimum requirements for the educational and scientific degree "PhD".

## CONCLUSION

In the PhD Thesis there are scientific-theoretical and scientific-applied results representing an original contribution to science, 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 (ZRASRB), the Regulations for the Implementation of ZRASRB and the Regulations of "Ajibadem City Clinic UMBA\_ Tokuda" EAD. The presented materials and dissertation results completely meet the specific requirements adopted in regard with the Regulations of "Ajibadem City Clinic UMBAL Tokuda" EAD for the application of ZRASRB.

Dr. Desislava Boyadzhieva is a specialist in cardiology with extensive 11 years of experience and in the area of angiology 3 years of experience. Actively participates in research work. She demonstrates qualities and skills for independent conduction of 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 Bozhidarova Boyadzhieva - Marincheva Scientific and educational degree "DOCTOR" in the field of Higher Education 7. Health care and sports, professional direction 7.1. Medicine, doctoral "Angiology".**

12/12/2023

Prof. Dr. Kiril Karamfiloff, M.D, PhD, FESC.

Sofia

