

EXPERT OPINION
ON A DISSERTATION PAPER
FOR AWARDING A DOCTORAL DEGREE

Topic of the PhD thesis: "Interventional treatment in patients with left main stenosis and concomitant complex coronary pathology".

By Prof. Dr. Asen Rachev Gudev, MD, ScD

**Member of the Jury for awarding the scientific and educational degree "PhD" in
Cardiology, designated by order №355/21.07 2021 by the Executive Director of Acibadem
City Clinic Tokuda Hospital**

Author of the dissertation: Dr. Ivayla Zhivkova Zheleva-Kyuchukova – PhD student on a self-study basis, Clinic of Cardiology, Acibadem City Clinic Tokuda Hospital, Sofia

Scientific tutor: Prof. Dr. Milena Staneva, MD, PhD

1. General presentation of the procedure and the doctoral candidate

The set of materials and documents presented by Dr. Ivayla Zheleva in electronic format complies with the requirements of the Law of Academic Staff Development in the Republic of Bulgaria and the Regulations for its implementation, the Law on Higher education, as well as the regulations of Acibadem City Clinic UMBAL Tokuda, on the terms and conditions for the acquisition of educational and scientific degree "Doctor of Medicine".

2. Brief biographical data about the candidate

Dr. Ivayla Zheleva was born in 1974 in Stara Zagora, where she graduated from the Language High School with a degree in English. She graduated from the Medical University of Sofia with a degree in Medicine. Since 1999 Dr. Zheleva has been working as an intern at the Cardiology Clinic of UNSBAL "St. Ekatherine", Sofia. In 2002 she was enrolled in the specialization in internal medicine at the Alexandrovska Hospital, MU Sofia. The specialization in internal medicine was

completed in 2009 and the same year she was enrolled in the specialization in cardiology, which she completed in 2013. From 2009-2013. works in the Department of Invasive Cardiology at Pirogov Hospital, after which she has been an invasive cardiologist at the Cardiology Clinic of Acibadem City Clinic Tokuda. Dr. Zheleva has been practicing invasive cardiology since 2004. In 2016 she completed a master's degree in public health and health management. She has passed many training courses at home and abroad. He is a member of the Bulgarian Society of Cardiology, the Bulgarian Society of Interventional Cardiology and the European Society of Cardiology. From the presented data it is clear that the doctoral student has the necessary competencies and skills for successful development and completion of a dissertation on this topic, in the doctoral program "Cardiology", professional field 7.1 Medicine, higher education 7. Health and Sports.

3. Relevance of the topic

The topic of the dissertation is actual and innovative. LM stenosis is found in 4-9% of patients referred for coronary angiography and in approximately 15% of patients with symptomatic ischemic heart disease (CHD). It is associated with over 20% risk of death up to one year and over 50% up to 3 years. Revascularization of these patients significantly improves their prognosis. Bypass surgery has long been accepted as the standard of care. In recent years, percutaneous revascularization has been established as a method in patients with LM stenosis with low and moderate complexity of coronary lesions, but patients with high complexity are still under discussion. With the development of technology and the routine entry of new generations of DESs, the present study is a step forward in determining the location of percutaneous coronary interventions in patients with LM stenosis and accompanying complex coronary pathology, which determines its significant value for real clinical practice. In Bulgaria so far there are no systematic data on percutaneous revascularization of patients with LM stenosis.

4. Structure of the dissertation paper

The dissertation and the abstract are well structured and meet the generally accepted criteria. The dissertation is written on 158 pages, divided into 5 chapters and includes an introduction and literature review, purpose and tasks, material and methods, results, discussion and conclusions. The individual sections are well balanced. The dissertation contains 62 figures and 19 tables, which are informative and clearly present the results of the work. The abstract is 78 pages long and presents the main data in the dissertation. Materials presented by the doctoral student show a

completed and competently written dissertation. The goal is specific, well-structured, corresponding to the problem under consideration. The tasks are 6 well-structured according to the set goal.

5. Knowledge of the issue

The literature review is presented on 33 pages and is well structured, covering the knowledge on the topic so far. The doctoral student demonstrates competence in the problems related to the topic and the need to develop the dissertation. The conclusion made and the conclusions at the end of the literature review summarizes the problem and indicates unresolved issues on the topic. This gives grounds for the doctoral student to formulate precisely and clearly the purpose of his research.

6. Methodology of research and evaluation of the dissertation paper

The study is prospective by examining a sufficient number of patients divided into 2 groups, with well-formulated inclusion and exclusion criteria. The material and methods are described in detail and informatively. The statistical methods used are adequate and allow appropriate illustration of the obtained results. The results are presented on 37 pages, consistently and exactly in accordance with the set goal, well-illustrated with figures and tables. The discussion is analytical and its main value is in the comparative consideration of own results compared to the published data of other authors, where possible. An algorithm for management of patients with LM stenosis has been developed. The conclusions are presented accurately, correspond to the set goals and objectives and reflect in detail the results. The topic of the thesis has undergone serious development in recent years and is still the subject of active discussion. Patients with a high risk profile (typical for our country), with complex coronary anatomy of LM lesions and subsequent successful percutaneous interventional procedure, with a low percentage of procedural complications and comparable, with a number of publications rate of MACE in the two-year follow-up period were analyzed. One of the remarkable results of the study was the finding of no significant difference in the incidence of major cardiovascular events between groups, regardless of SS value. In analyzing the probable reasons for this, Dr. Zheleva discusses the application of a number of modern technologies such as the use of only second-generation DES; established stenting techniques; achievement of complete/maximal revascularization in patients, which is rare in most studies involving patients with $SS \geq 32$ and last but not least the widespread use of intravascular ultrasound (IVUS) in order

to optimize the final result and achieve the recommended minimal stented area (MSA) in these patients.

7. Contributions to and significance for science and practice

The contributions of the dissertation are original, reflected in the Abstract - 6 with scientifically applied and original character and 3 with confirmatory character. The algorithm for management of patients with LM stenosis created for the first time in Bulgaria is of significant scientific and scientific-practical value.

8. Publications related to the dissertation

In relation to the dissertation paper, Dr. Zheleva presents 2 publications in national journals and 4 scientific reports of which 1 presented at international (Euro PCR - 2019) and 3 at Bulgarian national forums. There are no citations in Bulgarian and international magazines.

Conclusion

I highly appreciate the work of Dr. Zheleva due to the relevance of the study and mainly regarding the attempt to solve a serious problem in cardiac practice related to the treatment of high-risk patients with LM stenosis and the development of an algorithm for management, based on the proposed model not only the assessment of the anatomical features, the clinical condition, the opinion of the patients, but also the accumulated experience and training of the team and hospital.

The presented dissertation is valuable and fully meets the requirements of the Law for the development of the academic staff in the Republic of Bulgaria and the Regulations for the development of the academic staff at Acibadem City Clinic Tokuda Hospital EAD.

I recommend the members of the honorable Scientific Jury to vote positively and award the scientific and educational degree "DOCTOR" to Ivayla Zheleva in the doctoral program in cardiology.

12.08.2021

Sofia

Author:

Prof. Dr. Asen Gudev