### **STATEMENT**

# By Prof. Dr. Plamen Marinov Gatsov, MD, DSc

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

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

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

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

### 1. Paper Relevance

In recent decades, interventional techniques have become a major method of treating coronary heart disease. Numerous studies have proven the benefits of this treatment in the entire spectrum of ischemic heart disease - both in chronic coronary syndrome (stable angina) and in patients with acute coronary syndrome, including acute myocardial infarction with ST-elevation. Along with the treatment of chronic coronary occlusions, interventional treatment of left main coronary artery with stenting has emerged in recent decades as a treatment that is not inferior to cardiac surgery, and in many cases is preferable in these patients.

### 2. Structure of the dissertation paper

The dissertation is presented on 158 pages, illustrated with 62 figures and 19 tables. The bibliography includes 276 titles, of which 6 in Cyrillic and 270 in Latin. The literary review is 38 pages and provides a comprehensive overview of the current state of the problem. The aim is formulated as follows: to analyze the clinical, anatomical and procedural characteristics of patients with unprotected left main stenosis and concomitant complex coronary pathology, who underwent coronary intervention with implantation of second-generation DES, in order to

determine the effectiveness and safety of the procedure early and distant (2-year prognosis), as well as the establishment of predictors of adverse major events. To fulfill this goal, Dr. Zheleva sets 6 tasks.

#### 3. Material and methods

The dissertation work includes 136 patients with catheter intervention of unprotected left main stenosis, according to the respective inclusion and exclusion criteria. The patients are divided in 2 groups - 1. Study group - patients with SYNTAX Score ≥ 32 and 2. Control group - those with SYNTAX Score <32. The criteria for significance of stenoses are described in detail. One- and two-stent techniques are also described in detail. The endpoints of follow-up are defined: the primary endpoint is the combined MACE (all-cause mortality/ cardiac death / stroke / revascularization of the target lesion) at 2-year follow-up. The predictors for MACE after PCI of LM are defined as a secondary endpoint. 13 statistical methods were used.

### 4. Results

In both groups predominate patients with acute coronary syndrome /unstable angina. Patients with SS  $\geq$  32 have lower LVEF. Calcium antagonists are more commonly used in the same group. Ticagrelor is preferred in the complex anatomy group over clopidogrel. The value of the Euro Score is also higher in the studied group. Logically, SYNTAX Score is higher in the study group, the same is the result in terms of distal LM involvement. Regarding the applied interventions, in the studied group there is a more frequent treatment of a vessel other than the LM (100%). In the study group, compared with the control, femoral access is used more often than radial. Two-stent techniques are used more often in the study group. They also have a larger number and total length of implanted stents. In the study group with SS  $\geq$  32, predilation of the stenosis is performed more often. Only in this group rotablation is used - in 4.4%. Postidilation is performed in every case in both groups. The technique of proximal optimization is more often used in the studied group. Regarding the application of the kissing technique, there is no difference between the groups. In the study group, the procedures were longer, with more fluoroscopic time, more contrast agent used, more radiation for the patient, and more heparin used. Procedural success is 100% for both groups. In the follow-up for adverse events, there was no difference between the groups both in terms of the combined MACE and its separate components for each point in the follow-up and at the end of the follow-up. Among the factors determining the risk of adverse events, statistical significance have reached the previous myocardial infarction, GFR <40 ml/min/1,75 m2 and the use of a double-stent technique. Adverse events occur earlier in patients with MI, renal failure and dual stent technique. Based on the results obtained, Dr. Zheleva proposes a practical and understandable "Algorithm for management of patients with LM stenosis."

# 5. Conclusions and contributions

The conclusions, Dr. Zheleva grouped into 17 points, described in detail and with repetition of the data from the results. In my opinion, the most important concern the differences in the two groups in terms of a number of indicators, such as the features and severity of the procedure, the measured characteristics of coronary lesions, the materials and techniques used, and the differences in procedural times, contrast agent, radiation and drug loading. Overall, the procedural success is excellent and complications are rare. The incidence of adverse events during the follow-up period are comparable to that of other large studies, with only overall mortality being higher. The most important predictors of adverse events are previous myocardial infarction, advanced renal failure and double stent technique. In general, PCI in patients with LM stenosis and complex coronary anatomy is a procedure with minimal risks and favorable results. Dr. Zheleva divided the contributions into those with scientifically-applied and original character - 6, and those with confirmatory character - 4.

In relation to the dissertation paper, Dr. I. Zheleva has 2 full-text publications in Bulgarian journals and 4 scientific reports of which 1 presented at international (Euro PCR - 2019) and 3 at Bulgarian national congresses.

### 6. Critical remarks

The conclusions are presented in unnecessarily detailed form. For me, they are too numerous. The aim of this part of the dissertation for the author is to present concisely, clearly and systematically the main findings of its research, as well as the most important conclusions. Repetition of large parts of the results, together with the digital material, is unnecessary and makes this extremely important part of the dissertation cumbersome. On the other hand, the contributions are clear and straightforward.

## 7. Conclusion

The dissertation of Dr. Ivayla Zheleva - Kyuchukova is the first completed work in Bulgaria, analyzing the interventional treatment of patients with stem stenosis of the left coronary artery and complex anatomy. She methodically examines the clinical, anatomical and technical side of the study and treatment of this difficult group of patients. Follows them for a 2-year period and assess outcomes. Based on this knowledge, the dissertation proposes a structured and practical algorithm for diagnostic - therapeutic approach to them. I believe that the dissertation of Dr. Zheleva has all the necessary qualities and I call on the honorable members of the Scientific Jury to vote positively and to award Dr I. Zheleva the educational and scientific degree "PhD", and I also join my positive vote.

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Sofia

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