

**To the President of the  
Scientific jury designated by  
Order of the Executive Director of  
the National heart hospital  
No 139/02.04.2021**

## **Statement**

From Prof . Borislav Georgiev Georgiev, MD PhD,  
Head of the Cardiology Clinics, MHAT "National Heart Hospital" Sofia,  
Member of the scientific jury for awarding the educational and scientific degree "Philosophy  
doctor" on the basis of order No-139/02.04.2021 by the Executive director of the National heart  
hospital

**Subject:** Dissertation of Dr. Iskra Hristova Bayraktarova, PhD student in independent training in the  
Doctoral Program "Cardiology" on  
*"Clinical results in interventional revascularised patients with myocardial infarction"*  
Scientific adviser – Prof. Elina Trendafilova

For the competition Iskra Hristova Bayraktarova, MD has submitted all necessary documents -  
dissertation work, abstract and additional documents, in accordance of the Academic Staff  
Development Act in the Republic of Bulgaria and the Regulations of the Ministry of education and  
MHAT "National Heart Hospital" for its implementation. I do not find any gaps in the submitted  
documentation.

I declare that I have no conflict of interest with the candidate.

All presented materials are precisely arranged and described.

No evidence of plagiarism.

### **Importance of the topic**

The topic of the dissertation is contemporary and relevant. In Europe, more than 1.8 million  
people die each year from ischemic heart disease and its overall incidence increases. At present,  
maximum rapid and complete reperfusion of the infarct-related artery is the recommended and widely  
accepted model of therapeutic approach and can significantly reduce overall morbidity and mortality.  
When monitoring the effects of late revascularization, it was found that the patenal infarction artery  
resulted in improved cicatrice tissue formation and stabilization of the post-infarction zone, a decrease  
in post-infarction expansion and favorable remodeling, reduced electrical instability and improved  
collateral blood flow to adjacent areas, which further improved the remote prognosis. The clinical  
significance of multivessel disease (MVD) a STEMI patient has been investigated and it is clear that patients  
with MVD have a significantly higher risk of cardiovascular disease and mortality compared to patients with 1VD.  
The importance of complete revascularization with PCIs is somewhat controversial because it is difficult  
to be proven especially by survival. On the basis of the reported results of the surgical series, the

question of management of patients with MVD who are subject to invasive treatment, and especially the higher risk of them, namely patients with ACS, is raised. Especially in the Bulgarian patient population there are presented series of optimally treated patients with STEMI, in which the presence of multivessel coronary disease is undoubtedly confirmed as a risk factor for delayed survival. The aim of best treatment on the world trends, on the one hand, and the available rules for reimbursement of interventional procedures carried out, on the other hand, are the reason for the increasing frequency of planned invasive revascularization procedures of patients with multivessel coronary disease after MI, to the extent that they are routine practice, especially in big centers and in lower-risk subgroups of patients. However, there are no institutional and systematic follow-up of the criteria for planning such step-by-step procedures, their frequency and success rate. There is also no data on the effect of phased treatment on the delayed prognosis of patients.

**Structure of the dissertation work:**

The scientific work of Dr. Iskra Bayraktarova is formed on 162 pages. according to the requirements and contains an introduction with a literary overview, objectives, tasks, materials and methods, results, discussion, and publications, contributions and bibliography.

**The literary** review presented on 33 pages shows very good awareness of the author regarding the management of patients with myocardial infarction (with and without ST segment elevation) and their prognosis.

The bibliography contains 203 cited titles, 4 in Cyrillic and 199 in English.

Dr. Iskra Bayraktarova aims **to** track patients with myocardial infarction (with and without ST segment elevation) with optimal medical and invasive treatment conducted according to international guidelines and internal protocols in a single highly specialized center in terms of their long-term prognosis, assessing the effect of the additional invasive revascularization undertaken on survival, frequency and time until new ischemic events occur.

To achieve this goal the author sets itself the following **tasks**:

1. Based on a set of clinical and instrumental inclusion and exclusion criteria to select a group of patients who have been treated for myocardial infarction with and without ST-elevation in the Clinic of Cardiology and the Department of Emergency Cardiology of the National Heart Hospital – Sofia for the period 2014 (for patients with STEMI) and 2013-2015 (for those with NSTEMI).
2. To analyze the treatment carried out in the acute phase, in the context of the demographic characteristics of patients, the coronary anatomy, the complications occurring during the hospital phase and the additional therapeutic interventions carried out, as well as the achieved early (within the hospital stay) therapeutic effect and survival.
3. To establish the additional therapeutic procedures in the short term (up to 3 months from the index event) with regard to revascularization of coronary artery stenosis not associated with the heart attack.
4. To conduct prospective follow-up of the patient group in relation to adverse events (death by any cause, new heart attack, new angiography, new revascularization, new ischemic stroke) in patients after the end of the active therapeutic period.

5. To assess survival in the individual subgroups (STEMI/NSTEMI, one-, two- and three-vessel patients) according to revascularization and to analyze the predictors for the delayed prognosis.

6. Assess mortality indicators, the frequency of adverse events and the time until they occur in the formed subgroups.

7. To assess mortality indicators, the frequency of adverse events in the three time periods followed – in-hospital, short-term (up to 3 months after the primary event) and delayed (from 3 months to the end of follow-up).

**Methodological approach:** The scientific study included 403 patients with elevated troponin and ACS, of which 265 with STEMI and 138 with NSTEMI.

The statistical analysis includes various analyses which are consistent with the hypothesis and the objectives. The data collected was processed on SPSS version 22. The results were analysed using the Kolmogorov-Smirnov method, for mean values, a T-criterion and a Wilcoxon test were used for related samples, the score between the individual indicators was measured with the Spearman correlation factor, the survival analysis was done using the Kaplan-Meier method, and the individual groups were compared with the Log-Rank (Mantel-Cox) test.

**Results:** The obtained results of Dr. Iskra Bayraktarova are diligently presented on 55 pages of the dissertation work. The results are well illustrated. They include an analysis of the patient profile survival without events and time to events in general and according to the type of MI, analysis of patients according to the type of coronary anatomy and the final result achieved, regression analysis of factors influencing the survival of multivessel patients.

**Discussion** of the results is presented on 27 pp. In Bulgaria so far there has been no follow-up of the delayed effects in patient populations that have received various interventional therapies in multivessel coronary disease. The dissertation compares its results with other studies conducted in Bulgaria and with international studies. The patient group had a significantly more severe risk profile than the patient groups in the randomised STEMI clinical trials. The data are well matched with data from previous observational and cohort studies involving a mixed STEMI/NSTEMI population or a population of patients with acute coronary syndrome. In the presented patient series, a significantly higher incidence of new ischemic events was recorded in the presented patient series compared to data from large randomised studies. The author argues that the leading for the prognosis are possible differences in therapeutic approach and the risk profile of patients for all types of ACS, with publications in modern treated patient groups. Following a multi-variant regression analysis involving all factors of the single P below 0,1 variant, nine significant prognostic characteristics remained significant for survival, with eight of them associated with an poor prognosis and one being protective. There are also several factors of the angiographic finding that are determinative – the presence of left main stenosis, the CTO (chronic total occlusion of the coronary vessel) and the failure to achieve complete revascularization. A higher value of 0,846 vs. 0,702 to 0,737 was obtained when comparing the pre-calculated value of the analysis combination against the GRACE reference risk scale with the C-statistics method (equivalent to an area calculation under the curve). Such a finding is very interesting.

**Conclusions:** Dr. Iskra Bayraktarova offers 8 conclusions. They come from the survey and are trying to follow the tasks.

1. The patient population studied was baseline higher risk relative to similar populations described in the literature. The rates of recorded new ischemic events and deaths during the follow-up period were significantly higher in all three patient subgroups compared to those found in randomised clinical trials worldwide.

2. Adherence to the established current European Guidelines for the treatment of ACS during in-hospital treatment is at a very high level in the studied Bulgarian patient population.

3. A small proportion of multivessel patients are referred to try for planned complete revascularisation, despite the absence of systemic limitations. The proportion of those who actually achieve complete revascularization is even lower. Long-term therapeutic approach strategies in the individual patient are taken at an early stage at the acute phase and are not discussed subsequently.

4. The rate of complete step-by-step revascularisation within 3 months after the index event is effective and safe for patients.

5. Patients with the most severe baseline risk profile were relatively less likely to experience complete step-by-step interventional revascularisation, of which they would potentially benefit most.

6. Fully revascularised multivessel patients have a long-term prognosis comparable to that of single-vessel patients used as a reference group, along the line of new ischemic events and death for any reason.

7. Fully revascularized multivessel patients have a significantly better prognosis than incomplete revascularized multivessel patients through tracked new ischemic events and death for any reason.

8. When analysing the factors influencing survival in the group of patients with established multivessel coronary disease, it was found that the age, the presence of cerebrovascular disease, of atrial fibrillation in the current hospitalisation, left main stenosis or CTO from the invasive assessment, the deterioration of the Killip class during the stay, the haemodialysis treatment and the presence of incomplete revascularisation by the 90th day are associated with an increased risk of death in follow-up, while the absence of anaemia has a protective effect. A model including these essential survival factors has a better predictive ability in the described population than standard widely applicable risk groups.

**Contributions :** Contributions are 5 but are not grouped as scientifically theoretical and scientifically applied.

1. For the first time in Bulgaria, the characteristics of a general population of patients with ACS (STEMI and NSTEMS) – demographic and general risk profile, interventional finding and in-hospital treatment outcomes based on current European guidelines are examined and described.

2. For the first time in Bulgaria, a detailed comparison of Bulgarian patients with STEMI and NSTEMS is made on the basis of baseline characteristics, complex in-hospital treatment in the acute phase and achieved results.

3. For the first time in Bulgaria, the standard therapeutic strategy for the invasive treatment of multivessel patients with ACS in a single highly specialized center is described, and the delayed results are compared with the world's literature.

4. For the first time in Bulgaria, a comparison is made between baseline characteristics, in-hospital treatment in the acute phase and delayed outcomes in patients with ACS and single-vessel and

multivessel coronary disease, taking into account the effect of the degree of interventional revascularization on survival and cardiovascular events.

5. For the first time in Bulgaria, predictors for the delayed survival of Bulgarian patients with ACS are determined.

**Publications:** Related to the dissertation work, the author presents 2 full-text publications and participation in scientific forums in Bulgaria and abroad.

**The abstract** is in Bulgarian and contains 76 pages and reflects what is written in the dissertation. It is precise as required.

**Recommendations to the PhD student:**

➤ Continue work on the topic and publish some of the results of the study in scientific journals, if possible with an impact factor.

According to the minimum requirements of NACID for awarding educational and scientific degree "Philosophy doctor" Dr. Iskra Bayraktarova meets the requirements as follows:

<b>District 7. Health and sport</b>			
<b>Professional department 7.1. Medicine</b> <input checked="" type="checkbox"/> , <b>7.4. Public health</b> <input type="checkbox"/> , <b>7.5. Health care</b> <input type="checkbox"/>			
<b>Name, surname, surname:</b>		Dr. Iskra Bayraktarova	
<b>Applies for:</b> "Philosophy doctor" <input checked="" type="checkbox"/> ; Doctor of Sciences <input type="checkbox"/>			
<b>Academic position:</b> assistant <input type="checkbox"/> ; Assistant Professor <input type="checkbox"/> ; Associate Professor <input type="checkbox"/> ; Professor <input type="checkbox"/>			
<b>Number of points by metrics</b>			
<b>Scoreboard of indicators</b>	<b>minimum number of points</b>	<b>indicator</b>	<b>Points</b>
<b>A</b>	50	1. Dissertation on the award of an educational and scientific degree " Philosophy doctor"	<b>50</b>
	"Clinical results in interventional revascularised patients with myocardial infarction"		
<b>B</b>	30/n or distributed in proportion on the basis of a contribution protocol	8. Publications and lectures published in unrefered journals with scientific review or published in edited collective volumes	
	1.I. Bayraktarova, E. Naseva, E. Trendafilova, A. Alexandrov, A. Banka, I. Bogov, S. Georgieva, V. Grigorov, E. Dimitrova, H. Yordanova, E. Kostova, H. Mateev, I. Petrova, G. Hristova, P. Tasovska, N. Gocheva. Differences in the risk profile of patients with NSTEMS compared to patients with STEMI in the Bulgarian population, Bulgarian cardiology, volume XXIV, 2018, Annex 5, pp. 19-20 (BULG)		<b>1,875</b>
	2.I. Bayraktarova, E. Naseva, E. Trendafilova, A. Alexandrov, A. Bank, I. Bogov, S. Georgieva, V. Grigorov, E. Dimitrova, H. Yordanova, E. Kostova, H. Mateev, I. Petrova, G. Hristova, P. Tasovska and N. Gocheva. Admission anemia - a risk factor for the near and distant prognosis in patients with acute myocardial infarction without st-elevation (NSTEMI). BULGARIAN CARDIOLOGY Volume XXIV, 2018, Appendix 5, p. 37 (BULG)		<b>1,875</b>
	3.I. Bayraktarova, E. Naseva, E. Trendafilova, A. Alexandrov, A. Banka, I. Bogov, S. Georgieva, V. Grigorov, E. Dimitrova, H. Yordanova, E. Kostova, H. Mateev, I. Petrova, G. Hristova, P. Tasovska		<b>1,875</b>

and N. Gocheva. Influence of blood sugar values at reception (kz) on the near and distant prognosis in patients with acute coronary syndrome (ACS). BULGARIAN CARDIOLOGY Volume XXIV, 2016, Appendix 5, pp. 37-38 (BULG)	
4.I. Bayraktarova and E. Trendafilova. Complete interventional revascularization or revascularization of the infarction artery in patients with STEMI – Part I. Bulgarian cardiology, 2020, 26(3): 17-25. DOI: 10.3897/bgcardio.26.e51199 (BULG)	<b>15</b>
5.I. Bayraktarova, E. Naseva, E. Trendafilova. Blood sugar at reception – a factor for the prognosis of patients with acute coronary syndrome. General medicine, 2020, 22 (2):14-20 (BULG)	<b>10</b>
<b>Total: 80,625</b>	

**Conclusion:** I evaluate the work of Dr. Iskra Hristova Bayraktarova on the topic "Clinical results in interventionally revised patients with myocardial infarction" as interesting in scientific terms and important for clinical practice.

Based on the above merits of the dissertation of Dr. Iskra Bayraktarova, I recommend to the members of the esteemed Scientific Jury to vote positively and to award to Dr. Iskra Hristova Bayraktarova the educational and scientific degree "Philosophy doctor" in the scientific specialty "Cardiology", professional field 7.1 Medicine, field of higher education 7 Health and Sport.

27.05.2021



(Prof. Borislav Georgiev, MD PhD)