

To The of Scientific Jury
designated by Order No. R-109-239 / July 26, 2019
by the Rector of the Medical University-Varna

Review

by Prof. Zhaneta Tianeva Georgieva, MD, Ph.D

Chairman of the Scientific Jury for the competition for the occupation of the academic position Associate Professor in the field of higher education Health and Sports, in the professional field Medicine and scientific specialty "Cardiology" for the needs of the Department of Propaedeutics of Internal Medicine, Faculty of Medicine at the Medical University of Varna and for the Clinic of Internal Medicine at the University Hospital "St. Marina "- Varna,

Brief information about the competition

The competition was announced in the State Gazette no. 43 / 31.05.2019

By order No. R-109-239/26.07.2019 of the Rector of the Medical University-Varna I was appointed to prepare a review. Dr. Maria Stoyanova Dimova-Mileva is the only candidate. The procedure for announcing the competition is in accordance with the requirements of the Law for the Development of the Academic Staff in the Republic of Bulgaria / 05.05.2018 and with the Rules for the Development of the Academic Staff in the Medical University-Varna / 29.10.2018.

Brief CV data of the applicant:

Dr. Maria Stoyanova Dimova-Mileva completed her secondary education in 1995 at the Language High School, Silistra, with main language English and second language French. She graduated in medicine in 2001 at the Medical University – Varna. Part of her pre-graduate internship she spent at the University Hospital in Besançon, France.

She started working as a resident intern at the hospital of Silistra in 2001, next she worked as a medical representative at a French pharmaceutical company,

at the Cardiology Clinic of the Hospital “St. Marina, Varna, in outpatient endocrinology practice and since 2008 as a physician at the Clinic for Internal Medicine

at the University Hospital "St. Marina. " Dr. Dimova is fluent in English, French and Russian.

Specialties acquired

Dr. Maria Dimova-Mileva has acquired specialties in Internal Medicine - 2014 and Cardiology – 2018.

Postgraduate qualifications

1. Abdominal Echoscapy - 2014
2. Certificate of Transthoracic Echocardiography in Adults of the European Association of Cardiovascular Imaging - 2016.(ESC/EACVI) – 2016 r.
3. Expert activities in Echocardiography - 2018
4. Ultrasound diagnostics of vessels – 2019r.

Professional Experience

Dr. Maria Dimova started working in the field of internal diseases and more specifically in the field of cardiology as soon as she completed her medical education. She has two acquired specialties in medicine. Her professional interest and development is focused on imaging, and in particular ultrasound diagnostics. She has qualifications and certificates for highly specialized activity in three different fields of internal diseases and cardiology - abdominal echoscapy, echocardiography and ultrasound diagnostics of vessels, which make her a highly qualified and trained doctor and teacher.

In terms of professional qualification, she fulfills the requirements for habilitation.

Research activity

Dr. Maria Dimova-Mileva received her PhD degree in 2017 after successfully defending her dissertation on the topic: "Prospective Follow-up Of Patients With Beta-Thalassemia Major For Cardio-vascular Status And Cardio-vascular Pathology"

In this competition, the applicant presented the following scientific data

1. Monograph in Bulgarian with the title "*Anemia and cardiovascular changes*", 2019, edition of Medical University-Varna

2. Full-text articles in scientific publications, referenced or indexed by WOS or Scopus databases - 3, abstracts of reports in scientific publications, referenced or indexed by world-famous WOS or Scopus databases - 5
3. Full-text publications in non-refereed peer-review journals and editing of collective volumes - 19 issues.
4. Chapter in a collective monograph - 1.
5. Full-text publications in non-refereed journals with scientific review beyond the required minimum state requirements - 3 issues.
6. Participation in European Cardiology Congresses 4 issues, participation in an international conference on Thalassemia 1 issue; participation in the European Congress on Oncology-1 issue;
7. Participation in national congresses in cardiology and hematology -3 issues
8. Participation in student international and national forums as an academic mentor -10 issues
9. Number of citations: 10 in Bulgarian literature in non-refereed journals with scientific review

Dr. Dimova is the individual author in 1 publication, first author in 16, second author in 10 and third and subsequent in 16 scientific papers.

From the submitted publications and the citations Dr. Maria Dimova-Mileva covers the minimum state requirements of the Law and of the Regulations of the Medical University of Varna for acquiring the academic position of Associate Professor.

Scientific achievements and contributions

I. Scientific contributions to cardiovascular damage and cardiac function assessment in patients with anemia.

Dr. Maria Dimova's main scientific work is in the field of cardiovascular involvement in patients with various types of anemia and thalassemia. Her PhD work is one of the few in our country dedicated to patients with this rare monogenic disease and the onset of cardiovascular complications. The contribution is to the establishment and presentation of an early diagnosis algorithm based on echocardiographic indices and a biomarker approved for the diagnosis of heart failure. She is one of the first researchers

in the cardiology community to address this issue, both in Bulgaria and in the global scientific community in general.

Her monograph work is a wide-ranging material devoted to cardiovascular changes occurring in anemic syndromes. The knowledge so far known about the lesions that occur in the most common congenital anemia, such as thalassemia and sickle cell anemia, has been reviewed and presented. So far, sickle cell anemia and cardiac involvement have not been reported in our cardiology literature, and in this respect the information provided in Dr. Dimov's monograph is of high scientific and theoretical value.

Much of the monograph is devoted to cardiovascular damage in iron deficiency anemia without the presence of prior cardiac damage, the effect of iron deficiency anemia in heart failure, and the current problem of iron deficiency without anemia in patients failure. The effects of renal failure and erythropoietin treatment in patients with heart failure, as well as the impact of other aetiologically known anemias such as vitB12 anemia on prognosis in patients with heart failure, have also been discussed. Anemia, as a concomitant condition and determinant of the course of the disease in patients with coronary heart disease, be it acute or chronic, in patients with arterial hypertension and rhythm disorders, is also a thoroughly discussed spectrum in monograph work.

1. Scientific contributions to cardiovascular damage and assessment of cardiac function in patients with Thalassemia

Several articles are dedicated to the spread of patients with thalassemia major - the most common monogeneous disease in Bulgaria and the world, the injuries that occur not only from the disease itself, but also as a consequence of treatment. Cardiovascular damage is a leading cause of morbidity and mortality in patients with thalassemia, with iron deposition in the myocardium being considered to be a major pathophysiological cause. Data on the Bulgarian population of patients with thalassemia have been presented, from the prospective observation of 38 patients with thalassemia major in the Center for Thrombocytopenia and Rare Anemia of the University Hospital St. Marina.

The cardiovascular changes of these patients were examined and compared with those in healthy controls. Early changes in hemodynamics and cardiac function have been found to correlate with NT-proBNP levels. Correlation between echocardiographic, biochemical, and NMR indices was also made.

Other articles are devoted to rhythmic disorders in patients with thalassemia. The onset of conduction and rhythmic changes is by a pathogenetic mechanism different from that of the other patients.

The article presents data on the epidemiology of these disorders, from the most harmless to life-threatening, pathophysiological pathways for the onset of rhythmic changes at the cellular and molecular levels are discussed; methods of diagnosis, follow-up, treatment and prevention, presenting data from state-of-the-art research in the field as well as guidance from recent recommendations for the treatment of transfusion-dependent thalassemia.

Other articles address renal changes in thalassemic patients. Not much has been written about these changes as they are not among the most common and determining factors for diagnosis. For the first time in Bulgaria, an article is published specifically on renal changes in patients with thalassemia, useful methods and biochemical measurements for early diagnosis of the oncoming changes.

Treatment of heart failure in patients with thalassemia differs from that in the other population of patients with heart failure. An article on the subject provides guidance on the administration of chelation medications, intensive care regimens for severe cardiac function impairment, use of other commonly used medications using guidelines for cardiovascular behavior in patients with thalassemia of the American Heart Association and the International Thalassemia Federation.

It is noted that the treatment is led by a special team in the relevant centers for rare anemia.

Pulmonary hypertension is a specific cardiovascular involvement in thalassemia intermedia (TI), also referred to as nontransfusion-dependent thalassemia, as indicated in the guidelines. TI is about 20–25% of thalassemia cases, and pulmonary hypertension is a major cause of heart failure.

An article that details the epidemiology, risk factors, etiology, and pathophysiology of pulmonary hypertension in patients with beta-thalassemia, as well as the latest data on the use of specific treatment is presented.

2. Scientific contributions in the field of heart failure and iron deficiency

The issue of iron deficiency and heart failure is extremely relevant nowadays, when the diagnosis and treatment of iron deficiency is included in the latest guidelines for the management of patients with reduced ejection fraction of the European Society of Cardiology. A review article on the topic presents current diagnostic methods and the prognostic value of iron deficiency and since this is a common condition - up to 50% of

patients with heart failure have iron deficiency as well, the article has a great practical application.

3. Scientific contributions to the field of cardiovascular involvement in thyroid pathology

Hyperthyroidism and cardiac impairment have always been in the scientific interest of both endocrinologists and cardiologists. One of the articles, in which Dr. Dimova is a co-author, presents recent scientific findings at the level of cardiomyocytes and molecular mechanisms of cardiac disfunction in hyperthyroidism.

Another article addresses the less frequently discussed issue of pulmonary hypertension in hypo- and hyperthyroidism which mechanisms of onset have been poorly understood.

Also interesting is the relationship between thyroid pathology and diabetes mellitus, which can be bidirectional and was considered in the clinical context of a patient with newly diagnosed diabetes mellitus, Hashimoto's thyroiditis, in connection with elevated BP.

4. *Scientific contributions in the field of heart failure, diabetes mellitus and comorbidities.*

With the introduction of the new class of medicaments for the treatment of patients with type 2 diabetes mellitus, SGLT2 inhibitors, and the positive results in patients with heart failure, the interest of the cardiology community in them has increased.

The article shares the personal clinical experience of a small team with the use of empagliflozin in patients with heart failure with preserved ejection fraction and diabetes mellitus.

In another article on patients with heart failure and kidney failure, addresses the use of erythropoietin stimulating agents in these patients and recommendations from the American Kidney Federation, the American Heart Association, and the European Society of Cardiology for the treatment of heart failure.

Article presenting a complex case of a patient with a mechanical valve prosthesis, advanced heart failure and necrotizing vasculitis discuss the challenges facing the treating team of options to influence the condition in a truly complicated case.

The collective monograph "Biomarkers in cardiovascular disease. From pathogenesis to prognosis ", Arbilis 2016, chapter " Progress in the application of biomarkers in diagnostics, risk stratification, treatment and prognosis for heart failure ',

discusses the biomarkers known to date for the diagnosis, prognostic evaluation and follow-up of treatment outcome in patients with heart failure.

5. Scientific contributions in the field of Cardio Oncology

Cardiooncology is a newly emerging specialty at a rapid pace. Knowledge of the mechanisms of cardiotoxicity of cancer drugs is of paramount importance in the follow-up of cancer patients. The cardiotoxicity article discusses the mechanisms of cardiomyocyte damage, molecular interactions and biochemical pathways of involvement. In another article, a clinical case of rare myocardial metastases resulting from light cell sarcoma is presented.

6. Scientific contributions in the field of Congenital heart diseases

Congenital heart diseases are rarely diagnosed in adulthood.

Two cases of late diagnosed coarctation of the aorta and an atrial defect have been presented and described.

Opportunities for surgical or interventional correction of relevant cardiac malformations and monitoring methods are discussed.

7. Scientific contributions to other fields of medicine

Ferroptosis is a newly discovered form of cell death that has been described for the first time in our literature.

Its difference from apoptosis and necrosis is that it results from the accumulation of iron-dependent lipid peroxidase in the cell. During oxidative phosphorylation in the mitochondria, a process that requires the presence of iron, reactive oxygen radicals are also synthesized, but if they exceed the potential for neutralization by reductase systems, damage to various molecules, including nucleic acids, and ultimately death.

Kidney damage in diabetes continues to be the focus of scientific attention.

Several articles address the application of state-of-the-art biochemical markers and Doppler ultrasound features for early diagnosis of renal involvement. Introduced and own team experience in measuring pulsatile and resistive index in patients with diabetes mellitus and renal impairment.

Educational and teaching activities:

Dr. Maria Dimova-Mileva was selected as a full-time assistant Professor at the Department of Propaedeutics of Internal Medicine of the Medical University of Varna, in 2012, and since June 2018 she has been a senior Assistant Professor at the same department.

The workload for the last 5 years with English-language medical students is as follows:

2014/2015 - 180 academic hours

2015/2016 r. – 174 academic hours

2016/2017 r. – 180 academic hours

2017/2018 r. – 156 academic hours

2018/2019 r. - 168 academic hours

According to this indicator, she fulfills and exceeds the required minimum according to the Law and the Regulations for Academic Development of MU-Varna. Dr. Dimova was selected by graduating international medical students as their most favorite teacher in 2016 and 2018. She also serves as administrative officer for the 5th and 6th year English speaking students.

Dr. Maria Dimova-Mileva is a member of the following national and international scientific organizations:

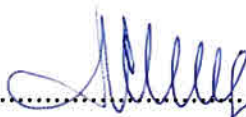
1. Bulgarian Society of Cardiology
2. European Society of Cardiology
3. Bulgarian Heart and Vessel Association

In conclusion: According to the requirements of the Academic Staff Development Act in the Republic of Bulgaria and the Rules for the Academic Staff Development in the Medical University of Varna Dr. Maria Dimova-Mileva meets more than the minimum requirements

Dr. Dimova is a cardiologist with extensive knowledge and skills, especially in the fields of internal diseases, abdominal ultrasound and echocardiography, with excellent professional training and proven teaching skills. Her scientific output is sufficient in volume, covers more than the minimum state requirements and shows a variety of interests. She complies with the requirements of the Academic Staff Development Act in the Republic of Bulgaria and the Rules for the Academic Staff Development at the Medical University of Varna, which gives me reason to recommend to the honorable

members of the scientific jury to vote positively for the academic position of Associate Professor to Dr. Maria Stoyanova Dimova-Mileva, MD.

7.09.2019


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(Prof. Zh. Georgieva, MD, PhD)