

REVIEW

In connection with the procedure for occupying the academic position of "professor" in the field of Higher Education 7. Health care and sports by professional direction 7.1 "Medicine" and scientific specialty "Cardiology", for the needs of the First Department of Internal Medicine, Department of Cardiology and the first clinic in cardiology at UMBAL Sveta Marina, Varna

Member of the Scientific Jury, who prepared the review - Prof. Dr. Arman Shnork Postajian, PhD

The competition for "professor" in the scientific specialty of cardiology for the needs of the needs of the First Department of Internal Diseases, Department of Cardiology and the first cardiology clinic of UMBAL Sveta Marina, Varna is announced in the "State Gazette" no. 28 of 28.03.2023

The scientific jury for the competition was appointed by order of the Rector of the Varna Medical University No. R-109-269/25.05.2023.

The review was prepared in accordance with the Law on the Development of the Academic Staff (LAD), the Regulations for the Application of the LAD (PRDLA) and the Regulations for the Terms and Procedures for Acquiring Scientific Degrees and Holding Academic Positions (PURPNSZAD) at MU-Varna.

The presented set of materials on paper / electronic media is in accordance with the procedure for acquiring the academic position of "professor" and the regulations of the MU - Varna.

The only candidate is Assoc. Dr. Maria Negrinova Negreva, MD, Associate Professor at the Department of Internal Medicine, Department of Cardiology and Rheumatology, Head of the Department of Cardiology, First Department of Internal Medicine, Varna University of Medical Sciences

I declare the absence of conflict of interest in preparing the review.

I have not detected any plagiarism in the papers submitted to me for peer review

Biographical data

Prof. Dr. Maria Negrinova Negreva, MD, was born in 1981. In 2000, she graduated from the First Language High School with the main profile "English Language", Varna. He completed his higher medical education in 2006 at the Medical University - Varna. Since 2006, he has been working as a resident physician, and subsequently as an assistant physician in the First Clinic of Cardiology with an intensive cardiology department, UMBAL "St. Marina"-Varna. She began his academic career at the Department of Internal Diseases, University of Cardiology and Rheumatology, University of Varna in 2008, initially as an assistant, and since 2016, associate professor in the same department, diploma of University of Varna. Since 2018, he is the Head of the Department of Cardiology, First Department of Internal Medicine, Varna Medical University.

In 2015, Dr. Negreva obtained the educational and scientific degree "Doctor of Medicine" after a defended dissertation on the topic: ""Dynamics in the oxidative status in patients with paroxysmal atrial fibrillation" (diploma of MU-Varna). After specialization at Medical University-Varna, he acquired a clinical specialty in cardiology in 2013. In the course of his professional development, he participated in

numerous national and international courses directly related to the scientific specialty and its practical application, as well as an additional qualification in the field of non-invasive cardiology and echocardiographic examination – I Medizinische Klinik, Universitätsklinikum Augsburg, Ospedale Niguarda Ca' Granda di Milano, Milano. Has a professional qualification certificate - echocardiography expert level since 2017.

Since 2016, after participating in a competition and decision of the AC, Dr. Negreva is an associate professor of cardiology at the Medical University - Varna.

In 2022, after a successfully defended thesis on PAROXISMAL Atrial ventricular fibrillation - EARLY DEVIATIONS IN THE COAGULATION AND FIBRINOLYTIC SYSTEM, he obtained the scientific degree of Doctor of Sciences, diploma of MU-Varna

At the moment, Associate Professor Negreva has a total of 16 and a half years of work experience and has held the academic position of Associate Professor for 7 years. Prof. Negreva is a member of the European Society of Cardiology (ESC) and the Society of Cardiologists in Bulgaria, as well as EACVI, EAPCI, ACVC. He is a member of the editorial board of journals Thrombosis and hemostasis: Research, Journal of blood disorders, Merit Res. J Med. Med. Sci., Journal reviewer Clinical and applied thrombosis and hemostasis, Scripta Scientifica Medica

Research activity

In the course of her scientific and research activity, Prof. Maria Negreva has made numerous scientific participations in international and national forums, directly related to the scientific specialty and its practical application, 17 of which were in European congresses, where she presented the results of her own studies - 6 oral presentations and 11 poster presentations. 12 of the participations at European congresses were published as full-text articles or abstracts in journals referenced in the world databases (WOS/Scopus), and 3 - in non-refereed journals with scientific review.

She participated in two national scientific projects: "Investigation of the application of new mathematical methods for the analysis of cardiac data", financed by the "Scientific Research" Fund, MES (KP-06-H22/5 of 07.12.2018) and "Circulating Histone Proteins as Biomarkers of Disease (CHIP-BiD)", financed by the "Scientific Research" Fund, MES (KP-06-DV/4 of 15.12.2021)

Assoc. Dr. Maria Negreva is a co-author in a total of 71 scientific publications, of which 53 were published in foreign journals and 18 in Bulgarian journals. He is the first author in 42 publications, and second author in 16. 21 publications are referenced in the world databases (WOS/Scopus). A total of 51 publications have been submitted for ONS "Doctor", JSC "Associate" and NS "Doctor of Sciences". A dissertation was defended for the ONS "Doctor" on the topic "Dynamics in the oxidative status in patients with paroxysmal atrial fibrillation" (2014) and a dissertation for the National Academy of Sciences "Doctor of Sciences" on the topic "Paroxysmal atrial fibrillation - early deviations in coagulation and fibrinolytic system" (2022).

The following are presented for this competition:

- 20 publications (14 publications in foreign journals, 4 of which are referenced in the world databases WOS/Scopus), some of which are closely related to the dissertation work for the National Doctor of Sciences;

- habilitation work - a monograph on the topic "Platelets - fundamental and clinical projections", which could conditionally be divided into two parts: a modern view of the morphology and hemostasis functions of platelets; importance of platelet pathomorphology in clinical cardiology practice, where own results regarding platelet activity in paroxysmal atrial fibrillation are also presented;
- textbook "Clinical Echocardiography", in which Prof. Negreva is a co-author.

A report on the Impact Factor of the journals in which Prof. Negreva's publications and their citations are found is presented. 60 citations were found (37 in WOS/Scopus worldwide databases). The total impact factor of Assoc. Prof. Negreva is 79.913, from full-text articles published after the defense of the National Doctor of Sciences - 3.577.

Main emphases in research activity

Assoc. Prof. Negreva's research activity is directed in several main directions - the study of coagulation and fibrinolytic indicators, as well as indicators of platelet activity, in patients with paroxysmal atrial fibrillation, the application of mathematical methods for the analysis of cardiac data, the study of echocardiographic indicators and serum NT-proBNP levels in patients with an implanted dual-cavity pacemaker and others. In this aspect, the combination in most of the publications of imaging methodology together with in-depth clinical characterization and biomarkers represents an original and thorough approach

The following contributions can be derived from the scientific output:

- Direct and convincing evidence is presented for the development of early significant systemic hypercoagulability in the course of short (≤ 24 hours) episodes of paroxysmal atrial fibrillation, present in both very low-risk patients (CHA₂DS₂-VASc score = 0 regardless of gender) and in those with increased thromboembolic risk (CHA₂DS₂-VASc score ≥ 1 regardless of gender) in the absence of significant differences in the hemostatic profile between the two groups of patients in these early hours of the arrhythmia. The identified abnormalities predispose to an increased periprocedural thromboembolic risk in both groups of patients (Publication Nos. 1 and 3, Indicator D7; Indicator E13).
- The principled approaches to periprocedural anticoagulation presented in the latest recommendations of the European Society of Cardiology for the treatment of atrial fibrillation (2020) are confirmed and expanded: a clear need for timely periprocedural anticoagulation therapy until full recovery of the hemostatic profile is outlined in all patients with a short (≤ 24 hours) episode of paroxysmal atrial fibrillation, incl. in the case of very low-risk patients (CHA₂DS₂-VASc score = 0 outside gender characteristics) according to the hemorrhagic risk; presented a reasoned need for the earliest possible attempt to restore sinus rhythm in paroxysmal atrial fibrillation and in this sense it was shown that the "wait and watch" approach during the first 24 hours of the disease is inappropriate (Publication no. 1 and 3, Indicator D7; Indicator E13).
- An objective premise has been given for the clinical search for effective anticoagulation by influencing the activity of FXI and FXII with an expected, defined by their role in the coagulation cascade, greatly reduced hemorrhagic risk compared to established anti-FIIa and anti-FXa drugs (Publication No. 1 and 3, Indicator D7; Indicator E13).

- It has been established that the plasma activity of FVIII provides a good diagnostic opportunity to identify the occurrence of paroxysmal episodes of atrial fibrillation. Clinical validation of the results will allow detection of patients at increased thromboembolic risk, optimization of prevention and reduction of the frequency of thromboembolic events associated with paroxysmal atrial fibrillation (Publication No. 1, indicator D7; Indicator E13).
- The possibility of prediction of ischemic stroke in patients with paroxysmal atrial fibrillation, the main complication of the rhythm disorder, by the plasma levels of TF, FVIII and vitronectin has been outlined. The predictive value of the CHA2DS2-VASc score and the patient's age for the occurrence of an ischemic stroke was confirmed (Publication No. 3, indicator D7; Indicator E13).
- Significantly increased platelet activity in the first 24 hours of the clinical manifestation of paroxysmal atrial fibrillation was shown by the established increased plasma levels of β -thromboglobulin and platelet factor-4 (Publication No. 4, indicator G7). It is a serious and necessary prerequisite for the development of a hypercoagulable state, represented by the results of (Publication No. 1 and 3, Indicator D7; Indicator E13; Indicator B3).
- A modern view of megakaryopoiesis and thrombopoiesis, morphology and hemostatic functions of platelets is presented. The importance of platelet pathomorphology in clinical cardiology practice is clearly outlined, and own results regarding platelet activity in paroxysmal atrial fibrillation are also presented (Indicator B3).
- The possibility of distinguishing patients with heart failure by non-linear methods of heart rate variability analysis has been shown, which in clinical practice will improve the diagnosis and early detection of the disease (Publication No. 5, Indicator D8).
- Early left atrial remodeling after DDDR dual-chamber pacemaker implantation (up to week 24) was demonstrated, with a significant increase in left atrial volume index as well as an increase in serum NT-proBNP levels. Dimensions and pump function do not undergo significant early changes.
- Contributions related to assessment of the hemodynamic characteristics at high normal arterial pressure by impedance-cardiography and capillaroscopy (Publication No. 7, Indicator D8) - Evidence material was received confirming that in persons with high normal arterial pressure there are more pronounced changes (compared to normal arterial pressure) in the vessel wall at the macro- and micro level, which can be assessed using non-invasive methods.

Teaching and learning activity

Prof. Negreva's educational and teaching activity is related to teaching cardiology and echocardiography to: medical students (Bulgarian and English speaking), cardiology specialists. The total classroom occupancy, according to a report provided by MU-Varna, exceeds 100 study hours per year for the last 4 years.

In addition, Associate Professor Negreva is a Scientific Consultant of 1 graduate student with a thesis topic: "Application of logistic regression in modeling data from atrial fibrillation" / 07.2015, TU - Sofia, as well as a scientific supervisor of 4 doctoral students - 3 doctoral students program "Cardiology", 1 doctoral student in the doctoral program "Health Care Management"

Diagnostic and therapeutic activity

Prof. Negreva has over 16 years of work experience and extensive experience in clinical cardiology, non-invasive cardiovascular diagnostics and treatment. What characterizes the candidate's diagnostic and therapeutic activity is the accumulated experience and practical knowledge in all aspects of modern cardiology - emergency, outpatient, with knowledge and mastery of all methods of non-invasive functional and imaging cardiology. From the impressive number of studies and publications, it is evident that he has a taste for scientific research work and systematic analysis of the obtained data

As a result of his professional realization, Prof. Negreva is a member of a number of scientific organizations in the country and abroad - the Society of Cardiologists in Bulgaria and the European Society of Cardiology.

Compliance with minimum national requirements

Assoc. Negreva presented a completed table in accordance with PPZRASRB. The fulfillment of the minimum requirements by groups of indicators is as follows:

- Group A - completed 50t.
- Group B - not required for JSC "professor"
- Group B - the candidate has included a published monograph, which covers the required minimum of 100t.
- Group D- filled with 202 t with a minimum of 200 t

Indicator D7 Publications and reports published in scientific publications, refereed and indexed in world-renowned databases of scientific information*mandatory minimum for clinical specialties - 80 points. The candidate gains 135 points.

- Group D- completed. The candidate presents 37 citations in foreign sources, 2 - in Bulgarian monographs and 21 citations in Bulgarian magazines, with which he collects 680 points. Thus, the actual number of points many times exceeds the required minimum.

Group E - The candidate gains 116 points by meeting the requirements in each direction - scientific projects, training of doctoral students, participation in the preparation of teaching aids, specialties

In conclusion

In the competition, Prof. Negreva presents himself as an exceptional specialist with sufficient medical, research and teaching experience. She has a recognized specialty in cardiology, received the educational and scientific degrees of Doctor of Medicine and Doctor of Science. She moved up the academic ladder to associate professor and has significant teaching and clinical experience, as well as administrative experience as the Head of the Board of Cardiology, First Department of Internal Medicine in a prestigious institution in our country. Prof. Negreva is an established cardiologist who knows and applies practically all modern methods of functional and non-invasive cardiology. The candidate's scientific interests are broad, his scientific production is completely sufficient in terms of volume and content, and in terms of its significance, degree of novelty and justification of scientific achievements, it meets the requirements of the Regulations on the terms and conditions for acquiring scientific degrees and holding academic positions and conditions and procedure for awarding the academic position "professor" First Department

of Internal Medicine, Department of Cardiology, Medical University Varna and first clinic of cardiology of UMBAL Sveta Marina, Varna. The contribution of scientific production is substantial, proof of which is the positive citations in medical periodicals. The candidate is a member of prestigious national and international societies in the field of cardiology.

On these grounds, I support the candidacy and propose to the respected members of the Scientific Jury to vote positively for Assoc. Dr. Maria Negrinova Negreva, MD, to take the academic position of "professor" in the scientific specialty of Cardiology, for the needs of the First Department of Internal Medicine, Department of Cardiology, Varna University of Medical Sciences and the first cardiology clinic of Sveta Marina UMBAL, Varna

29/07/2023

A handwritten signature in blue ink, appearing to read 'Arman Postajian', with a large, stylized initial 'A' on the left.

Prof. Dr. Arman Postajian, MD

Head of the Department of Cardiology at the Cardiology Clinic of St. Anna Sofia UMBAL,

MU – Sofia

Member of the Scientific Jury