Opinion

by Assoc. Prof. Dr. Atanas Angelov Atanasov, Ph. D

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Member of the scientific jury for the competition (SG 17/26. 02. 2021) for the occupation of the academic position "Associate Professor" in the field of higher education 7. "Health and Sport", professional field 7. 1. " Medicine" and scientific specialty "Cardiology" for the needs of the Faculty of Medicine, the First Department of Internal Medicine and the Second Clinic of Cardiology - non-invasive at the University Hospital "St. Marina" Varna

By the order of the Rector of MU Varna R-109-175/23.04.2021, I was elected as a member of the scientific jury, and according to protocol N:1 of the first meeting of the scientific jury I was appointed to prepare an opinion on the procedure for the acquisition of the academic position "Associate Professor" for the needs of the Faculty of Medicine, First Department of Internal Medicine and Second Clinic of Cardiology - non-invasive at the University Hospital "St. Marina" Varna.

The procedure for announcing the competition complied with the legal requirements, no procedural violations were found. For the competition documents were submitted by one candidate - **Dr. Antoniya Rumenova Kisheva**, **Ph. D.** The academic review of the publication activity and citations established that the candidate meets the minimum requirements for the position of Associate Professor according to the Law for the Development of the Academic Staff in the Republic of Bulgaria and the Rules for the Development of the Academic Staff in the Medical University – Varna.

1. Short biographical data of the applicant

Dr. Antoniya Kisheva graduated from the Medical University of Varna in 1999. In 2007 she acquired a specialty in General Medicine. Since 2014 she is an assistant professor at the Educational Sector of Cardiology at the First Department of Internal Medicine at Medical University Varna. In 2014, she obtained a specialty in cardiology. Dr. Kisheva has additional professional qualifications in echocardiography - fundamental and expert level. Dr. Kisheva is a member of the Board of Directors of the Heart-Lung Association and is the responsible secretary of the Heart-Lung Journal.

In 2017, Dr. Antoniya Kisheva acquired the educational and scientific degree "Doctor" with the dissertation topic "Role of fibrosis and mineralocorticoid receptor blocking in atrial fibrillation"

2. Research activity of the candidate - assessment of quantitative and qualitative indicators

Dr. Antonia Kisheva has submitted the following scientific papers for review:

- 1. Monograph: Antonia Kisheva. The stroke Cardiologist' Point of View. ISBN 978-619-221-273-5, 192 pp.
- 2. Publications and reports in scientific journals, referenced and indexed in a global databases of scientific information 7 pcs.
- 3. Publications and reports in peer-reviewed scientific journals 9 pcs.
- 4. Full-text publications in scientific journals and collections, beyond the minimum science-metric requirements for the position of Associate Professor 1 pc.

Dr. Antonia Kisheva is an individual author in 4 scientific papers. First author in 14 (74%) In 16% of the publications, Dr. Kisheva was the third or subsequent author.

The total impact factor of Dr. Kisheva's publications is: 9,678.

Citations: Dr. Kisheva's scientific papers have been cited over 100 times in various scientific publications. Eight of these were used as evidence that met the minimum science-metric requirements for the position of Associate Professor. Two of the citations are in a refereed and indexed international journal in a global database of scientific information.

Dr. Kisheva has 40 participations in national and international scientific forums, and in two of her participations in national conferences she was awarded the prize for the best poster and the best clinical case.

3. Scientific fields in which the candidate has mainly worked and where the scientific publications are concentrated

- atrial fibrillation
- cardiac fibrosis
- neurology
- ultrasound diagnostics
- heart failure
- atherosclerosis

4. Scientific and applied contributions

Most of Dr. Kisheva's publications are in the field of atrial fibrillation. In her research, Dr. Kisheva investigated the role of fibrosis in the development and maintenance of atrial fibrillation using galectin-3 as a biomarker. Patients with atrial fibrillation were found to have higher galectin-3 levels compared to healthy controls. The role of age, female sex and arterial hypertension in the progression of this rhythm disorder has been confirmed. Patients with left ventricular hypertrophy, as assessed by left ventricular muscle mass, had a

higher incidence of atrial fibrillation recurrence at 1-year follow-up. In a separate publication, evidence is presented for the role of gout as an independent risk factor for atrial fibrillation recurrence and rehospitalizations in these patients. The administration of the aldosterone antagonist spironolactone in persons with atrial fibrillation has been prospectively studied to influence the fibrosis process responsible for the onset and recurrence of the rhythm disturbance. This study is pioneering for Bulgaria, and few studies have been conducted worldwide.

For the first time in our country and one of the first studies in the world, a correlation was sought between galectin-3 (a marker of fibrosis), coronary artery calcium scoring (a marker of the presence of subclinical coronary atherosclerosis) and the incidence of recurrent atrial fibrillation.

In other publications, Dr Kisheva presents data from a study searching a correlation between the marker of fibrosis and inflammation galectin-3 and the validated thromboembolic risk assessment tool CHA2DS2Vasc score. An association between galectin-3 levels and gout was found. Individuals with atrial fibrillation and gout have significantly higher levels of galectin-3. Similarly, the presence of arterial hypertension in patients with atrial fibrillation is a predictor of more pronounced fibrosis, expressed by higher galectin-3 values. The relationship between age and renal function and galectin-3 levels has been confirmed.

Dr. Kisheva's work on the problems of patients with atrial fibrillation raises her interest in neurology and ischemic stroke in particular. Dr. Kisheva presents her own experience with the use of contrast transcranial Doppler ultrasonography to detect persistent foramen ovale with right-to-left shunt in individuals with stroke of undeterminate source.

As a logical continuation of several years of work in the field of atrial fibrillation and cryptogenic stroke comes Dr. Kisheva's monograph "The stroke – Cardiologist' Point of View ". The monograph aims to clearly define the role of the cardiologist as an important member of the team that diagnoses and treats stroke. All the major risk factors and diseases that are associated with an increased risk of stroke, as well as those that are relevant to the course and consequences of stroke, are discussed in detail. In a separate chapter, the possible cardiac complications in stroke patients are discussed. The role of some cardiac biomarkers as an accessible diagnostic method for the diagnosis of stroke-heart syndrome is discussed. Both natriuretic peptides and troponin I are predictors of worse prognosis in both ischemic and hemorrhagic stroke.

Dr. Kisheva proposes a protocol for collaboration between cardiologists and neurologists in the diagnosis and treatment of stroke. Emphasis is placed on the problem of ischemic stroke of undeterminate source, which is of greatest

concern to the cardiologist. A diagnostic algorithm is proposed that can be followed by the cardiologist in such patients. The advantages and limitations of the different imaging methods used for the diagnosis of cardioembolic sources are discussed in detail. A special place is given to contrast transcranial ultrasonography as an affordable noninvasive method that may be an alternative to transesophageal echocardiography in individuals with suspected right-to-left shunt. The author's own experience in 177 individuals with ischemic stroke of undeterminate source is also presented. In 69 of them a persistent foramen ovale was detected using this method.

The last chapter of the monograph discusses the current views and recommendations for the treatment and prevention of stroke with emphasis on the involvement of the cardiologist in this process.

Dr. Kisheva is also involved in heart failure research. The importance of a common comorbid condition in individuals with heart failure has been investigated. Many patients have iron deficiency, which is not always accompanied by anemia. Both conditions are predictors of a worse prognosis. A screening test to detect iron deficiency is recommended for timely correction.

4. Participation in scientific projects

Dr. Kisheva is a leading participant in the scientific project "Randomized clinical trial to evaluate the efficacy and safety of adding an aldosterone antagonist to the therapy to reduce atrial fibrillation recurrences in patients with restored sinus rhythm" at the Medical Science Fund, Medical University - Varna 2012-2016.

5. Teaching

Dr. Antonia Kisheva conducts seminars and lectures on Internal Medicine with Bulgarian and English speaking medical students. Her teaching load for the last 5 years is:

2015/2016 - 180 hours

2016/2017 - 146 hours

2017/2018 - 212 hours

2018/2019 - 210 hours

2019/2020 - 189 hours

Dr. Antonia Kisheva participates in the examination committees in Internal Medicine for IV year medical students. She trains intern physicians during their state internship in Internal Medicine. Participates in the training of physicians in the specialty of "Cardiology".

In conclusion: The scientific production and teaching workload of Dr. Antoniya Kisheva, Ph. D. fully meet the requirements of the Rules for the Academic Staff Development in the Medical University – Varna and the Regulations on the conditions and procedure for the acquisition of scientific degrees and academic positions at MU Varna. This gives me the reason to confidently propose to the honoured scientific jury to vote positively for the award of the academic position of Associate Professor to Dr. Antoniya Kisheva in the scientific specialty "Cardiology" for the needs of the First Department of Internal Medicine at the Faculty of Medicine at Medical University Varna.

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