

OPINION

By Assoc. Prof. Dr. Maria Ivanova Dimitrova, MD, UMHATEM "N.I.Pirogov"

Regarding the dissertation for educational and scientific degree "PhD", developed by Dr. Paola Nikolay Kulicheva

Title: Predictive factors for mortality in patients with ischemic stroke in young and middle-aged people

Field of higher education: "Health and Sports"

Professional field: 7.1 Medicine

Doctoral program: "nervous diseases"

Specialty code: 03.01.19

Scientific supervisor: Assoc. Prof. Dr. Darina Kirilova Georgieva-Hristova, MD

Brief biographical information about the candidate

Dr. Paola Nikolay Kulicheva was born in 1993. She graduated from the 23rd High School "Frederic Joliot Curie", after which she graduated with a degree in Medicine from the Medical University of Varna in 2017. She acquired a specialty in nervous diseases after specialization at the University Hospital "St. Marina" Varna. In 2023, she acquired a certificate for highly specialized activity in neurology "Ultrasound diagnostics of the nervous system". She speaks English and French.

From the submitted required and mandatory documents, it is evident that the procedure for enrollment, taking the doctoral minimum exam, expulsion, and scheduling a public defense complies with the legal provisions and the regulations for the Development of the Academic Staff of MU-Varna.

Dr. Paola Nikolay Kulicheva was enrolled with Enrollment Order No. R-109-479 dated 4.11.2020 by Prof. Dr. Valentin Ignatov, Rector of the Medical University "Prof. Dr. Paraskev Stoyanov" - Varna.

By order No. R-109-476 of 20.11.2025 of Prof. Dr. Dimitar Raykov - Rector of MU-Varna, on the basis of Art. 24, para. 6 and Art. 30, para. 3 of the Regulations for the Implementation of the Law on the Development of the Academic Staff and Art. 68, para. 1 of the Regulations of MU-Varna, Dr. Paola Kulicheva is dismissed with the right to defense and the composition of the scientific jury is determined, in which I am appointed as an external member with the preparation of an opinion.

Characteristics and evaluation of the dissertation work

Descriptive characteristics The presented dissertation work "Predictive factors for mortality in patients with ischemic stroke in young and middle-aged people" by Dr. Paola Nikolay Kulicheva contains 178 pages and is illustrated with 46 figures, 41 tables, two appendices. 259 sources are cited, of which 6 sources are in Cyrillic, most of the titles are from the last 5 years. The presentation is written in a scientific style, presented in a well-organized and concise manner. The dissertation work is properly structured, contains all the main parts for presenting a dissertation work: introduction, literature review, aim and

objectives, material and methods, results and discussion, summary and conclusions, contributions, bibliography and appendices.

Relevance of the topic

The topic of ischemic stroke is extremely relevant and constantly evolving in medicine, as it remains a leading cause of disability and mortality.

Ischemic stroke is the most common type of stroke, affecting millions of people worldwide, making it a global health priority. Unfortunately, the trend is for an increasing incidence of cerebrovascular accidents at a young age. This creates a need for research interest in this group of patients in order to identify risk factors and prognostic factors for the outcome of the disease.

The introduction of the dissertation work well justifies the relevance of the problem. **The literature review** is in-depth, well-structured, and reflects the doctoral student's knowledge of the topic. A significant place is given to Bulgarian authors in developing the topic, and global studies in the field are also examined in detail. The risk factors for ischemic stroke in young and middle-aged patients and their role in mortality in this population are presented in detail. After each section, an analysis of the literature data is made and debatable issues are identified. The relevance of the dissertation work becomes categorically clear from the literature review. Based on the summaries drawn from the literature review, the doctoral student defines a clear **goal** and sets herself eight **tasks** for its implementation. **The design** of the study is well described with a detailed examination of the clinical **material**, the inclusion and exclusion criteria are defined. The scientific study was approved by the Research Ethics Committee of MU-Varna. The text contains a detailed description of **the methods used**: clinical, laboratory, determination of risk factors, neuroimaging, used assessment scales and the methodology of statistical processing. The methods used are adequate to the set goals and tasks. The statistical analysis is distinguished by the application of a wide range of modern statistical methods for processing data from the studies performed, which provide the necessary credibility. In **the Own Results section**, all analyses of the examined material are presented. The diagrams and figures are properly structured and clear. An interpretation and discussion of the obtained results is made in the light of identifying prognostic factors for mortality in young patients with ischemic stroke. In **the discussion**, the obtained results are skillfully compared with the data of foreign and our authors. The applied methods for processing and presenting the results clearly demonstrate what the doctoral student has achieved. **The conclusions** completely accurately and generally reflect the obtained data and are well formulated. 6 conclusions are drawn, of which the first one identifies the predictors with the greatest weight. The main conclusion is that low systolic blood pressure (≤ 120 mmHg), severity of neurological deficit (NIHSS > 15 points), and chronic left-sided heart failure are the most powerful and independent predictors of mortality in young patients with ischemic stroke.

Contributions of the dissertation work

The contributions of the dissertation are divided into two groups: original and confirmatory. There are four original contributions: 1. It presents a specific analysis of a young and middle-aged cohort, as the work presents a detailed descriptive and comparative analysis of the demographic, clinical and imaging characteristics of patients up to 59 years of age. The analysis allows for a more accurate identification of factors specific to this group, which is of key importance for improving the prognosis. 2. Independent prognostic factors are identified. 3. A comprehensive analysis of prognostic markers is performed. The study combines and analyzes the influence of a wide range of potential prognostic factors, including clinical indicators (such as NIHSS and vital parameters), imaging findings (localization, ASPECTS), laboratory parameters (inflammatory and metabolic) and etiological subtypes (TOAST classification). The integration of these data into a single study provides a comprehensive view of the mechanisms leading to an adverse outcome. 4. The work contributes to local clinical practice, as the results of the study conducted on patients hospitalized at the University Hospital "St. Marina" - Varna provide valuable epidemiological data for the region. They can serve as a basis for the development of local protocols for earlier recognition of high-risk young patients and the implementation of intensive therapeutic strategies. The confirmatory contributions are aimed at strengthening the role of chronic left-sided heart failure (CHF) described in the literature as a powerful independent predictor of fatal outcome following ischemic stroke; confirmation of NIHSS as the main predictor of fatal outcome following ischemic stroke; prognostic value of hemodynamic indicators; prognostic value of laboratory markers, among which both elevated CRP values and elevated leukocyte counts are independent predictors of death from ischemic stroke.

Publication activity and personal contribution of the doctoral student

The doctoral student presents two publications related to the dissertation, one in Neurology Asia, where she is a co-author, and one publication on the topic, of which she is the first author and which was published in Scripta Scientifica Medica.

More active publication activity is needed and this dissertation is a good start for subsequent scientific materials in national and foreign periodicals and participation in forums.

The results obtained and the conclusions, recommendations and contributions formulated are the personal merit of the doctoral student.

Abstract

The abstract fully reproduces the content of the dissertation work and is formatted according to the requirements. It reflects the structure of the methodology, the main results achieved in the dissertation, the conclusions and contributions made. The abstract contains 64 pages and is illustrated with 31 figures and 26 tables.

Conclusion

The dissertation "Predictive factors for mortality in patients with ischemic stroke in young and middle-aged people" is distinguished by its relevance, contains scientific and applied scientific results that represent an original contribution to science and meets all the requirements of the Act on the Development of Academic Staff in the Republic of Bulgaria (ADSRB), the Regulations for its implementation and the Regulations of MU - Varna. The dissertation shows that the doctoral student possesses in-depth theoretical knowledge and professional skills for independent conduct of scientific research.

Due to the above, **I confidently give my positive assessment of the conducted research**, presented by the above-reviewed dissertation, abstract, achieved results and contributions, and I recommend to the esteemed members of the Scientific Jury to vote positively and award Dr. Paola Nikolay Kulicheva the educational and scientific degree "Doctor" in the scientific specialty "Nervous Diseases".

29.12.2025

Заличено на основание чл. 5,
§1, б. „В“ от Регламент (ЕС)
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Assoc. Prof. Mariya Dimitrova, MD