

REVIEW

by Prof. Stoyanka Georgieva Vladeva, Ph.D., M.Sc.

Faculty of Medicine, Trakia University, Stara Zagora,

of a dissertation for awarding the educational and scientific degree '**doctor**'

professional direction **7.1. Medicine**

doctoral program in Rheumatology

Author: Dr. Lilly Edward Meckenian

Form of doctoral study: full-time

Department: "Propaedeutics of internal diseases" Prof. Dr. Anton Mitov"

Topic: "High-frequency ultrasonography in polymyalgia rheumatica"

Scientific supervisors:

Associate Professor Rositsa Valerieva Karalilova, D.Sc., Faculty of Medicine, Medical University - Plovdiv

and Prof. Dr. Ilian Yordanov Doikov, Ph.d, Faculty of Medicine, Medical University - Plovdiv

(academic title, name, surname, last name, scientific organization)

1. General presentation of the procedure and the doctoral student

The presented materials on paper and electronic media are in accordance with Art. 70 (1) of I. Section, Acquisition of the educational and scientific degree "DOCTOR" at MU-Plovdiv; Regulations of MU-Plovdiv dated 28.01.2021 and include the entire package of required documents.

2. Brief biographical data for the doctoral student

Dr. Lily Edward Mekenyan was born on 26.11.1992 in Plovdiv. In 2012, she graduated from the Plovdiv Language High School, and in 2018 - his higher education in medicine (master's degree)

at the Medical University of Plovdiv with excellent results. Since 2019, she has been enrolled with a competition for a full-time doctoral student in rheumatology at the CPVB "Prof. Dr. Anton Mitov", MF, MU- Plovdiv. Starting in 2020, residence in the clinical specialty of Rheumatology at the Clinic of Rheumatology, UMBAL Kaspela, city of Plovdiv. Dr. Mekenyan was appointed after a competition as an assistant for teaching the discipline Propedeutics of internal diseases, including foreign language training at KPVB, MF, MU-Plovdiv from 2022.

3. Relevance of the topic

Polymyalgia rheumatica (PMR) is an inflammatory rheumatological disease with unclear etiology and complex pathogenesis. Specific clinical, laboratory and imaging biomarkers for diagnosis are currently lacking. There is a wide range of diseases that can mask PMR. This leads to non-recognition of the disease, delayed or ineffective treatment.

PMR can present as an independent disease or is often associated with giant cell arteritis (GCA). In recent years, the increasing incidence of subclinical GCA in PMR has been the subject of intense scientific interest. Early diagnosis of emerging vascular changes in patients with PMR without clinical evidence of GCA is of great importance to prevent potential ischemic complications.

The efforts of scientists worldwide are focused on studying the pathoanatomical morphological change of the musculoskeletal system in PMR by means of modern imaging methods. High-frequency ultrasonography (HFUS) is a non-invasive imaging method for visualization of intra-articular and peri-articular structures, as well as for the assessment of joint inflammation using PowerDoppler and Color Doppler modalities. USG is the preferred imaging study in daily rheumatology practice due to its easy availability and cost/quality ratio.

An important foundation for the implementation of the present study is the scientific team in which the doctoral student works. This team is one of the few in Europe, which for the first time in our country investigated the diagnostic possibilities of VUSG in patients with PMR. Thus, he managed to bring together various possible applications of this rapidly developing technique in the studied disease. The obtained results are summarized as modern theoretical and practical contributions in rheumatology.

4. Knowing the problem

The PhD student shows good theoretical preparation by presenting a thorough and well-structured literature review in 64 pages. The advantages and disadvantages of individual imaging methods in the diagnosis of PMR are examined in detail and analytically. Thanks to imaging methods, it becomes possible to assess the joint, peri-articular and vascular involvement in this disease. Literary data present evidence for the importance and place of VUSG. The possibility of the early and timely diagnosis of PMR by means of modern ultrasonographic techniques continues to be relevant. Usually, ultrasonographic studies examine the shoulder and hip joints and, less commonly, other joint areas in PMR. There are relatively few data in the literature that present the degree of involvement of articular and peri-articular structures (tendons, bursae, entheses) in PMR by means of Gray Scale and Power Doppler US. An innovation in the diagnosis of PMR is the US study of vessels. To date, there are insufficient data on the use of SC for the evaluation of subclinical vasculitis in PMR. In addition, there is no information on the diagnostic value of measuring the thickness of the intima-media complex (IMT), the so-called intima-media thickness (IMT) of cranial and extracranial vessels. Determining cut-off values of IMT enables timely diagnosis of the occurring changes in the vascular wall in patients with PMR without clinical evidence of GCA.

The analysis of the literature review ends with several critical, summarizing and well-argued conclusions regarding the need for a more in-depth study of the issues raised.

The bibliographic reference contains 309 titles, of which 10 are in Bulgarian and 299 in English, and a large part of them are from recent years. This once again emphasizes the relevance of the problem under consideration and the need to conduct the present scientific study.

5. Characterization and evaluation of the dissertation work

The dissertation is written on 251 standard typewritten pages and contains, according to the requirements of the MU - Plovdiv, the generally accepted sections: Contents - 3 pages, Abbreviations used - 3 pages, Literature review - 64 pages, Aim and tasks - 1 page, Materials and methods - 20 pages, Results - 79 pages, Discussion - 14 pages, Conclusions -1 page,

Contributions - 2 pages, Appendices -31 pages, Bibliography - 31 pages. Abbreviations used are correctly reflected. 43 figures, 36 tables and 27 appendices were used for illustration.

In her dissertation, the doctoral student sets herself a clear goal related to the assessment of joint, peri-articular and vascular involvement in patients with PMR by means of VUSG.

To fulfill the set goal, Dr. Mekenyan defines six research tasks. The tasks are specific, doable and meet the demand in the dissertation work.

The "Materials and Methods" section is described in 20 pages. The study included 74 participants, of which 37 were patients with PMD and 37 were healthy controls. The demographic and clinical characteristics of the diseased and healthy controls are described in detail and comprehensively. Inclusion and exclusion criteria are well chosen and clearly defined. Up-to-date, Modern and generally accepted classification criteria for PMR are used.

Dr. Lili Mekenyan describes in detail the conducted VUSG. Three US modalities were used - Two-dimensional US for examination of joints, extra-articular structures (tendons, bursae, entheses) and vessels (determination of intima-media thickness (IMT)); Power Doppler ultrasound for evaluation of synovitis, tenosynovitis, bursitis and enthesitis; Color Doppler US to assess vascular involvement. the statistical processing of the data was carried out with the modern program SPSS v. 27.0 and was illustrated with the relevant tables, figures and graphs.

The results are presented logically and consistently and correspond to the set goals and objectives. They are well interpreted using modern statistical methods and illustrated with a sufficient number of tables and figures. Each analysis is followed by a detailed discussion of the results obtained.

The discussion is critical, summarizing and comparing the results obtained by the PhD student with those worldwide and looking for the reasons for these differences.

The doctoral student has formulated ten conclusions that are properly argued and correspond to the set goal and the completed tasks. They synthesize the analysis of the survey data and their own research.

The work includes 27 appendices that supplement and enrich the dissertation work.

6. Contributions and significance of the development for science and practice

The contributions are respectively - 4 of an original nature, 4 of a scientific-applied nature and 2 of a confirmatory nature, which objectively reflect the significance of the obtained results in scientific terms and their applicability in real clinical practice. They put the national rheumatology school on a new, higher level. Behind the valuable conclusions and the extensive author's work of Dr. Mekenyan, one can see the competence and skillful guidance of the scientific supervisors. This is what allows the correct validation of the received scientific data for PMR.

7. Evaluation of publications on the dissertation work

In connection with the dissertation work, 3 full-text publications (3 articles referenced in global databases) and 4 publications from participation in Bulgarian scientific forums have been made. The major publication related to the dissertation has already been cited in the prestigious journal *Lancet*. The number of scientific works fulfills the quantitative criteria in the Regulations of the MU - Plovdiv.

8. Personal participation of the doctoral student

In the conducted dissertation research, including the presented publications, the obtained results are obviously the personal contribution of the doctoral student.

9. Abstract

The abstract presents the objectives, tasks, results and discussion, conclusions and contributions of the dissertation work in a concise, summarized form. The results are displayed graphically for greater demonstrability. The abstract gives an overall idea of the obtained results and contributions of the dissertation work. It consists of 64 pages.

10. Critical remarks and recommendations

I have no critical remarks and recommendations.

CONCLUSION

The dissertation contains scientific, scientific-applied and applied results, which represent an original contribution to science and meet all requirements of the Law on the Development of the Academic Staff in the Republic of Bulgaria (ZRASRB), the Regulations for the Implementation of ZRASRB and the relevant Regulations of the Ministry of Education - Plovdiv. The presented materials and dissertation results fully correspond to the specific requirements of the MU - Plovdiv.

The dissertation shows that the doctoral student Dr. Lili Edward Mekenyan possesses in-depth theoretical knowledge and professional skills in the scientific specialty of rheumatology, demonstrating the qualities and 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 work, abstract, achieved results and contributions, and I propose to the honorable scientific jury to award the educational and scientific degree "doctor" to Dr. Lily Edward Mekenyan in the PhD program in Rheumatology

06.11. 2023

Reviewer:

A small rectangular stamp with a white background and a thin black border. At the top, there is a small blue triangle. Below it, the text "Затворено на основание" is written in red. Underneath that, "Чл. 5, Ст. 6, 'б' Регламент (ЕС) 2016/679" is written in red. A blue handwritten signature is written over the stamp.

Prof. Dr. Stoyanka Vladeva, Ph.D.