Standpoint

by **Prof. Dr. MARIYA PETKOVA TOKMAKOVA, MD, PhD**

Section of Cardiology, First Department of Internal Diseases

Medical University - Plovdiv

In connection with order No. R-2309/21.08.2023

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

Field of higher education: 7. Health care and sports

Professional direction: 7.1 Medicine

Scientific direction and doctoral program: Nephrology

Author: Dr. Reneta Yovcheva Koycheva

Form of doctoral studies: independent preparation

Department: Second Department of Internal Diseases, Nephrology Section

Topic: "Cardiac biomarkers and echocardiographic changes in patients with in-hospital failure of hemodialysis treatment"

Scientific supervisors:

Assoc. Prof. Eduard Tilkiyan, MD, PhD and Assoc.Prof. Margarit Penev,MD, PhD

1. General presentation of the procedure and the PhD student

The set of materials and documents presented by Dr. Reneta Koycheva complies with the requirements of the Law for the Development of the Academic Staff in Republic of Bulgaria and the Rules for its Application, as well as with the rules of MU-Plovdiv from the Procedure for the Acquisition of the educational and scientific degree "doctor".

The opinion is prepared on the basis of the dissertation and the abstract to it, which are well structured and meet the established criteria. The dissertation is presented on 159 pages, 9 chapters and contains 23 figures and 62 tables. The bibliography covers a total of 334 literary sources, of which 14 are in Cyrillic and 320 are in Latin. The abstract is 63 pages long

and represents the main data presented in the dissertation work. A comprehensive reading of the materials presented by the doctoral student indicates a completed dissertation work.

It is all concrete, well structured, responding to the problem at hand. The scientific tasks are five and are focused on the study objective.

2. Relevance of the aim and appropriateness of the set goals and tasks

The aim of the developed dissertation work is to analyze the relationship between hsTnT, TnI, NT-proBNP, hsCRP and left ventricular function in asymptomatic patients with renal failure treated with hemodialysis and to determine their prognostic role. CVDs are an important cause of CKD, but they are also a consequence of CKD. CVD is also the leading cause of death in dialysis patients. CV risk stratification in this population allows early detection of high-risk patients. Cardiac biomarkers - troponins and natriuretic peptides - are known to be predictors of death among dialysis patients.

3. Knowledge on the problem

The literature review is properly structured, up-to-date, analytical and contains sufficient information. It comprehensively represents the knowledge on the topic up to now. The doctoral student demonstrates competence in the issues related to the topic and the need for the development of the dissertation. Unsolved problems are analyzed and indicated, the purpose and tasks of the dissertation are convincingly motivated. In the process of developing her dissertation, the doctoral student has entered deeply into the researched issues. The conclusions drawn at the end of the literature review indicate the unresolved issues, which gives grounds to formulate precisely and concretely the purpose of the research.

4. Research methodology

A total of 140 patients in stage 5HD of CKD, undergoing renal replacement therapy for at least 3 months, with precisely formulated inclusion and exclusion criteria, were studied prospectively. The material and methods are described in detail and informatively. The choice of biomarkers is appropriate as they are validated for CV risk assessment. The assessment of LV function - systolic and diastolic is in accordance with international guidelines, and easily reproducible indicators have been selected. The selected main methods enable the

implementation of the goal set. The statistical methods are precise and allow appropriate visualization of the obtained results and the drawing of the main conclusions from the scientific research. The results and discussion are presented in 50 pages and are well illustrated. In the discussion, a logical and in-depth analysis of the results was made, which emphasizes the professional and competent approach of Dr. Koycheva to the developed problem. There are 14 conclusions.

5. Characterization and evaluation of the dissertation work

The dissertation as a complete scientific research, represents a substantive analysis of an important problem with certain theoretical and practical contributions. The results of the study are critically reviewed. The discussion is analytical and focused on the main goal and tasks. The conclusions drawn by the doctoral student are more, 14 in number, and to some extent overlap with the results.

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

I find the following main contributions of the dissertation mainly of a scientific-theoretical and scientific-applied nature:

- A well-designed study of the levels of the main cardiac biomarkers for myocardial damage and hemodynamic stress in asymptomatic patients with CKD and their influence on the hemodialysis procedure was carried out
- Echocardiographic findings in asymptomatic patients treated with hemodialysis were analyzed
- The diagnostic reliability and prognostic value of each of the biomarkers regarding total and cardiovascular mortality was determined.
- "Cut-off" values were determined for the investigated biomarkers, which identify a subgroup of asymptomatic patients subject to a more detailed assessment of LV function.
- It has been proven that the effective use of established biomarkers and echocardiographic indicators for CV risk stratification in asymptomatic hemodialysis patients is the basis of a timely personalized treatment and prevention approach

7. Assessment of the dissertation publications

In relation to the dissertation work, 3 scientific articles have been published, two of them in Bulgarian and one in an international periodical. There are no noted citations in our and international journals.

8. Personal contribution of the doctoral student

I appreciate the personal participation of the doctoral student in the preparation of the dissertation work, given the fact that she conducted the selection and follow-up of the patients related to the study, as well as the processing and analysis of the results. Dr. Koycheva is the first author in all three presented publications.

9. Abstract

It covers the content of the dissertation and the requirements for an abstract. It reflects the main points of the study, the most demonstrative figures and tables from the dissertation are included. The main scientific contributions of the doctoral student are also presented.

CONCLUSION

The dissertation work of Dr. Reneta Koycheva contains scientific-theoretical and scientific-applied results, which represent an original contribution to science and meet all the requirements of the Law on the Development of the Academic Staff in the Republic of Bulgaria, the Regulations for the Implementation of the law and the relevant Regulations of MU - Plovdiv.

The dissertation shows that the doctoral student Dr. Koycheva possesses sufficient theoretical knowledge and professional skills in the scientific specialty of nephrology and demonstrates qualities and skills for independent conduct of scientific research.

Given the above, I give a **positive assessment** of the conducted research and propose to the honorable scientific jury **to award** the educational and scientific degree "doctor" to Dr. Reneta Koycheva in the doctoral program in the scientific field of nephrology.

29.09.2023

(Prof. Mariya Lokmakova, MD, PhD)