To the Chairman
of the Scientific Jury,
appointed by Order № R-109-101/28.01.2025
of the Rector
of the Medical University – Varna

REVIEW

Of a thesis on **Cardiotoxicity in Conventional and Contemporary Cancer Treatment Protocols**,

submitted for public defence before a scientific jury for awarding the educational and scientific degree of Philosophy Doctor, professional field 7.1. Medicine, scientific speciality Cardiology

Author of the thesis: Dr. Svetoslava Elefterova Slavcheva, full-time doctoral student in the doctoral program Cardiology, professional field 7.1. Medicine, enrolled by order № P-100-35/28.01.2019 at the Medical University – Varna;

Reviewer: Prof. Zhaneta Georgieva Tyaneva, MD, PhD, Medical University - Varna, external member of the Scientific Jury,
appointed by Rector's Order № R-109-101/28.01.2025

Biographical data

Dr. Slavcheva completed her medical education at the Medical University of Varna, where she graduated in 1999. In 2009, she acquired a specialty in Internal Medicine, and in 2014, a speciality in Cardiology. During 2006–2007, she worked at St. Marina University Hospital – Varna in the Emergency Department for adults. Since 2007, she has been a resident physician in the First Cardiology Clinic with ICU. In 2014, she obtained a qualification in Echocardiography – basic level, and in 2017, she was certified at the Expert level in Echocardiography – transthoracic, transesophageal, and stress-echocardiography. Dr. Slavcheva specialised at the National Cardiology Hospital in the *Analysis of myocardial*

deformation and *Transesophageal echocardiography*. In 2020–2021, she specialised at Stanford University, Center for Professional Development, in Medical Statistics Parts I, II, III.

Since 2019, she has held the position of assistant professor in cardiology at the First Department of Diseases, Educational Section Cardiology, at the Medical University "Prof. Dr. P. Stoyanov" – Varna.

From February 2019 to February 2024, she was a doctoral student in Cardiology, Medical University "Prof. Dr. P. Stoyanov" – Varna. Her research thesis is on Cardiotoxicity in Conventional and Contemporary Cancer Treatment Protocols.

Research activity

The thesis *Cardiotoxicity in Conventional and Contemporary Cancer Treatment Protocols* explores current issues in the field of cardio-oncology, focusing on the links between malignant conditions and cardiovascular diseases.

Thesis structure

The thesis is 222 pages long and is designed with a clear and systematic structure. The results are presented in 41 tables and visualised in 83 figures. The bibliography contains 262 reference sources, of which 258 are in Latin. The sources from the last 7 years predominate.

The doctoral student has 2 thesis-related papers published in a specialised journal. She has 5 presentations at scientific forums in Bulgaria.

The literature review showcases a strong understanding of literary references and the ability to derive comprehensive information from those sources. The author emphasises the importance of systemic antitumour therapy associated with the development of cardiac dysfunction (cardiomyopathy), as well as structural abnormalities in the myocardium when using individual antitumor medications. The literature review focuses on cancer therapy-induced cardiac dysfunction (cardiomyopathy) and heart failure. Cardiac dysfunction associated with oncological therapy (CD–OT) is presented according to the definition of the European Society of Cardio-Oncology from 2022. The review examines cardiotoxicity associated with radiation therapy for tumor diseases and its cardiovascular consequences, as well as changes in the right ventricle. In the literature, there is insufficient clarity about the clinical significance of right

ventricular damage. There is also little clinical evidence regarding diastolic left ventricular dysfunction.

Aim of the study: To prospectively examine the change in systolic and diastolic function of the RV (right ventricle) in various chemotherapeutic therapies and to propose an easy-to-apply algorithm for echocardiographic assessment. The aim is clearly formulated and specific.

The Tasks are precisely formulated and defined, aimed at reaching the selected objective: Dynamic monitoring of echocardiographic parameters for LV and RV systolic and diastolic function through 2D echocardiography and tissue Doppler in patients on antitumor therapies. Searching for correlational relationships between echocardiographic parameters. Sixty patients were followed-up. The following indicators were recorded: ECG, laboratory parameters – hsTroponin T (hsTnT). Echocardiographic parameters include assessment of LV and RV function, tricuspid valve and regurgitation, systolic pressure in the pulmonary artery, and the area and volume of the RA (right atrium).

Statistical methods: Modern statistical methods were used, enabling assessment of the interaction of the observed indicators. The study is complex, representative, and comprehensive. A wide range of modern, diverse, and adequate statistical methods appropriate to the research were used, allowing for clear and specific conclusions to be drawn.

The results and conclusions drawn from them are convincing and precise, have scientific value and contributory character. The discussion of the results presents a connection between the author's own results and data from the literature review.

I agree with the conclusions and the statement of contributions made by the doctoral candidate. Conventional echocardiographic indicators register early deviations in the systolic and diastolic function of the LV as a result of oncological therapy (OT). Right ventricular echocardiographic indicators show statistically significant deviations in the first 1–3 months from the beginning of OT. Oncological therapy affects the RV systolic and diastolic function. Examining hsTnT can aid in diagnosing OT-induced myocardial damage. The early changes in the right ventricular conventional indicators and their functional and prognostic predictive value are arguments for monitoring during OT. The correlational and prognostic associations involving echocardiographic metrics for RV and LV from tissue Doppler provide grounds for their routine monitoring in the conditions of OT. According to the study, a mandatory

minimum in echocardiographic cardiac assessment during and after OT is the measurement of tissue velocities in the right ventricle.

SCIENTIFIC CONTRIBUTIONS: The first of its kind study in Bulgaria was conducted, tracking changes in the systolic function of the RV through conventional echocardiographic indicators in the conditions of systemic OT for an 18-month period. An assessment of the diastolic function of the RV during and after OT was performed. For the first time in Bulgaria, changes in the systolic and diastolic function of the LV were monitored through conventional echocardiographic indicators in conditions of systemic OT for 18 months after its initiation. For the first time in the country, the prognostic significance of various echocardiographic indicators for the occurrence of cardiac dysfunction (left ventricular and right ventricular) within 18 months after starting OT was studied. The impact of OT revealed changes in the conventional echocardiographic systolic indicators of the right ventricle, consistent with existing scientific research. Deviations in the echocardiographic diastolic conventional indicators of the RV under the influence of OT were registered.

In Conclusion

The presented thesis by Dr. Slavcheva is relevant to modern cardiology and oncology. It precisely combines in-depth analysis of literature data with original research and conclusions. The doctoral candidate contributes to a substantial clarification of cardiovascular changes occurring in patients after oncological therapy.

The thesis and scientific publications meet all the necessary scientometric criteria for awarding the scientific and educational degree of Philosophy Doctor according to DASRBA and the Rules and Regulations at the Medical University-Varna. The thesis offers significant original and confirmatory contributions.

I vote positive for awarding the scientific degree of Philosophy Doctor to Dr. Svetoslava Elefterova Slavcheva.

10/03/2025
Varna

Reviewer:
Prof. Zh. Georgieva, MD, PhD