

To the Chairman
of the Scientific Jury, appointed
by the Rector of the Medical University,
Varna "Prof. Dr. Paraskev Stoyanov",
by order № R-109-99/28. 01. 2025

REVIEW

By Prof. Dr. Borislav Georgiev Georgiev, PhD
Head of the Cardiology Clinic at the National Heart Hospital,
Member of the Jury for awarding the scientific and educational degree "PhD", designated by
order by the Rector of the Medical university of Varna
№ R-109-99/28. 01. 2025

Regarding: Dissertation of Simona Nikolaeva Yankova, MD, PhD student on a part-time, Medical
University Varna with a topic of the PhD thesis:

"Acute coronary syndrome in patients with chronic obstructive pulmonary disease"

Scientific supervisor: Assoc. Prof. Dr. Atanas Angelov, PhD and scientific consultant:

Prof. Diana Petkova, MD, PhD

in the field of higher education 7. "Health and sports", professional direction 7.1. "Medicine" and
scientific specialty "Cardiology"

The documents presented by Dr. Simona Nikolaeva Yankova —dissertation, abstract, and
additional documents - are in accordance with the requirements of the regulation for the
acquisition of the educational and scientific degree "PhD" and the rules of the Medical University
of Varna. I do not find any omissions in the submitted documentation.

I declare that I have no conflict of interest with the candidate.

All presented materials are precisely arranged and described.

No evidence of plagiarism.

Brief CV data of the applicant

Dr. Simona Nikolaeva Yankova was born in 1991 in the city of Harmanli. She completed
high school at Neofit Rilski's Language Parallel in 2010, where she studied intense English and
German as a second language. She graduated from the Medical University "Prof. Dr. Paraskev
Stoyanov" - Varna, in 2016. In the same year, she started working as a doctor at the emergency
medical center at Dolni Chiflik. From February 2017 to June 2021, she was appointed as an
honorary assistant in the Department of Internal Diseases of English-speaking students at the
Medical University of Varna. Since November 2017, Dr. Simona Yankova has been working as a
cardiologist in the Department of Cardiology at MBAL Dobrich AD, in the city of Dobrich.

Since 01.02.2019 she has been a part-time doctoral student at the First Department of
Internal Diseases with the scientific supervisor Assoc. Prof. dr. Atanas Angelov.

She obtained a specialty in Cardiology in 2022, and in 2023 and a certificate of
professional qualification – Echocardiography – fundamental level.

Significance of the topic

The topic of the dissertation is contemporary and relevant.

Acute coronary syndrome (ACS) and chronic obstructive pulmonary disease (COPD) are
the leading causes of mortality and disability in the world. COPD is a complex multi-component

disease. Patients with pulmonary obstruction have up to five times higher risk of developing cardiovascular disease (CVD). This is explained by the systemic inflammation that is characteristic of COPD. Patients with ACS and COPD are a high-risk group for whom a comprehensive approach is needed both in treatment and during follow-up. CVDs are responsible for 20-30% of deaths in COPD patients, and CVD mortality is twice as high in these patients as in the general population. Patients with COPD and accompanying CVD consume more resources in primary and secondary medical care - consultations, emergency department visits, hospitalizations, hospital stays, and respectively for these patients there are higher healthcare costs. The incidence of ACS in COPD patients is 16%. The main mechanisms that determine the increased cardiovascular risk in COPD patients are chronic inflammation, oxidative stress, obesity, decreased physical activity, smoking, and dyslipidemia. This turns this cohort of patients into a high-risk group with high morbidity and mortality. In combination with ACS, it continues to be a diagnostic and therapeutic challenge for physicians in the 21st century. The peculiarities of ACS in patients with COPD are the subject of major studies in the world literature, but data in this direction are lacking in Bulgaria. Patients with ACS and accompanying COPD consume more resources in primary and secondary medical care - consultations, emergency room visits, hospitalizations, and hospital stays. Healthcare costs for these patients are correspondingly higher. Creating an algorithm to track patients with ACS and COPD after their dehospitalization could reduce risk factors and control adherence to their prescribed therapy. This would significantly reduce healthcare costs and, most importantly, lower mortality rates for this high-risk group of patients.

Structure of the dissertation work:

The scientific work of Dr. Simona Nikolaeva Yankova is structured on 174 pages according to the requirements and contains an introduction, a literature review, objectives and tasks of the study, materials and methods, results and discussion, conclusion, contributions, 4 appendices, and bibliography. The dissertation material is presented with 43 figures and 20 tables.

The introduction is on 2 pages. **The literature review** is presented on 40 pages and shows the good knowledge of the author regarding ischemic heart disease, chronic obstructive pulmonary disease, acute coronary syndrome in patients with COPD - pathophysiological mechanism in acute coronary syndrome and COPD, and treatment of patients with acute coronary syndrome and COPD. A very good impression is made by the figures, which are the author's illustrations and show the attitude of the dissertator to the layout of the dissertation work. Based on the literature review, Dr. Simona Yankova draws some conclusions on which her study is based.

The bibliography contains 501 cited languages, 18 of which are in Cyrillic, and 469 in Latin. There are 14 references to web pages. All citations are spelled correctly.

Dr. Simona Yankova **aims** to analyze the clinical and demographic characteristics, adherence to the prescribed therapy, the causes of rehospitalizations, and mortality in patients with ACS and COPD.

To achieve this goal, it sets the following **tasks**:

1. To investigate the risk characteristics, clinical presentation, and therapeutic behavior in persons with acute coronary syndrome and accompanying COPD.
2. To make a comparison with a control group of patients with acute coronary syndrome with similar demographic and clinical characteristics, but without data on COPD.
3. To evaluate adherence to the prescribed therapy after hospitalization and in particular to treatment with beta-blockers.
4. To assess the quality of life in patients with ACS and COPD compared to the control group.
5. To determine the causes of hospitalizations.
6. To analyze the clinical and demographic characteristics of deceased patients with ACS.

Methodical approach: A total of 140 consecutive patients were diagnosed with ACS and hospitalized in the intensive care unit of the Department of Cardiology at MBAL Dobrich AD, city Dobrich. The subjects studied were divided into two groups depending on the presence or not of previously outpatient diagnosed COPD: **Group A** - 70 patients with ACS and known COPD and **Group B** - 65 individuals with ACS without COPD.

The statistical analysis of the data was done with the software product IBM SPSS MAC v. 29.0.1.0 (208) and for their graphical analysis was used Microsoft Excel for Mac Version 16.69.1, 2019. To evaluate the statistical veracity, the value or level of significance (R) for the found value of hi-square is used. This is the probability of rejection of the null hypothesis (H_0) when it is true. Significant differences at the level of significance $p < 0.05$ are considered.

The following statistical methods were used: descriptive statistics, Analysis of variance (ANOVA), parametric, nonparametric, correlational, logistic regression analysis, and proportional regression method.

Results: The results obtained by Dr. Simona Yankova are presented carefully. The results are well observed. The obtained results meet the objectives of the study.

Some of the results are interesting and differ from the accepted concepts. For example, in the *Risk Characteristics*, there is a difference in the distribution of hypertension, smoking, and dyslipidemia in the patients analyzed in the study and in epidemiological studies, which is reported by the author, but this may be due to the peculiarities of the sample for the study. It would be nice, especially in the context of the topic of the thesis, to analyze also risk modifiers. The Framingham risk calculator was used in the thesis, which is basically for the United States, in Europe there are others, but probably used for comparison with other studies that use this calculator. In CRP analysis, it would be good to analyze in hsCRP where possible. A little more in-depth analysis of anemia should be done.

Overall, the results indicate a desire for a comprehensive analysis of the complex interrelationships between acute coronary syndrome and chronic obstructive pulmonary disease. The thesis shows the need for an interdisciplinary approach in polymorbid patients with ACS and the need for general internistic training of staff in cardiology departments.

The discussion of the results is included in the chapter "Results and discussion" and is compared, where possible, with other publications on the subject.

Each of the results is interesting in terms of clinical benefit and should be further developed in a separate publication. Due to the small groups of patients, there are different results from the literature, but it should be borne in mind that this is a single-center study.

There is also an algorithm for behavior in patients with ACS and COPD in 15 points, which significantly increases the quality of the thesis. I think that item 11 has no place in the algorithm, but it can be proposed to improve the knowledge of doctors and the introduction of the tracking algorithm. Perhaps it is appropriate, given the changing European recommendations, to mention that the tracking of some risk parameters is according to the currently available recommendations. It would also be good if the algorithm is presented graphically.

Interesting and important for the practice are the results related to the applied therapy and it would be good to link, where possible, the results for achieving target values of risk parameters – blood pressure, lipid control, etc.

The dissertator is also aware of some limitations of the study, which shows criticality to the obtained results.

Conclusions: Dr. Simona Yankova offers 8 conclusions. They come from the tasks set and from the research conducted.

1. Patients with ACS and COPD have a more pronounced risk profile for IHD compared to patients with ACS without COPD.
2. The incidence of anemia, CKD, and stroke is higher in the COPD group.
3. Patients with ACS and COPD have poorer lipid profile control and are slower to achieve the target blood sugar values in the presence of DM. They are less motivated to quit smoking in the long term and are less physically active.
4. Patients with COPD are more likely to present with a clinical sign of ACS without ST elevation. Because of their high-risk profile, they are less frequently referred for invasive diagnosis and subsequent treatment. According to their coronary pathology, people with ACS and COPD have a dominating single-vessel CAD, with RCA being the most typically impacted.
5. The population with ACS and COPD studied by us shows weaker adherence to the prescribed main classes of medications – BB, ACE/ARBs/ARNI, lipid-lowering agents, and antiplatelet therapy.
6. ACS, in combination with COPD, has a multifactorial effect on all aspects of patients' lives, with health status remaining permanently reduced within one year after ACS compared to the control group.
7. Patients with concomitant COPD are at greater risk of hospitalization for CVD up to twelve months after the acute coronary event. The most common cause is HF, followed by IHD.
8. Higher BMI, smoking, lower physical activity, and higher baseline CRP values are associated with higher mortality in COPD patients one year after ACS.

Contributions: The contributions are 13, divided into two groups - with original nature (5) and with confirmatory character (8).

Contributions of an original nature

1. For the first time in Bulgaria, a study has been conducted on the risk and clinical characteristics of patients with ACS and COPD. The merit of the study is the monitoring of the spirometric parameters of pulmonary obstruction.
2. For the first time in Bulgaria, the quality of life of patients with ACS and COPD is being studied.
3. For the first time in Bulgaria, adherence to the prescribed drug therapy for the region of Northeastern Bulgaria is objectively monitored.
4. For the first time in Bulgaria, the causes of hospitalizations in patients with ACS and COPD for one year after the acute coronary event are being tracked.
5. For the first time in Bulgaria, mortality in patients with ACS and COPD is monitored.

Confirmatory contributions

1. The risk characteristic for CAD in patients with COPD is confirmed.
2. The need for patients with COPD to be treated as a high-risk population for the manifestation of ACS is confirmed.
3. The need for functional testing after ACS in patients with established COPD is confirmed.
4. The poorer quality of life in patients with ACS and COPD is confirmed;
5. The more frequent occurrence of ACS without ST elevation in patients with COPD is confirmed.
6. The less frequent referral for SCA in patients with ACS and COPD is confirmed.
7. The thesis, defended by an increasing number of authors, about the lack of contraindications to the use of cardioselective BB and the need for control for adherence to therapy is confirmed.
8. The role of CVD as a cause of more frequent hospitalizations in patients with COPD has been confirmed.

The abstract is presented in Bulgarian and English, the Bulgarian version contains 84 pages, the English - 77 pages and reflects what was written in the dissertation work. It has been published according to the requirements.

Publications: In connection with the dissertation the author presents 2 publications in journals and 3 presentations at scientific forums.

Conclusion: Dr. Yankova's dissertation was written based on a study conducted entirely in the Department of Cardiology of MBAL Dobrich AD and despite the non-academic environment the study meets all the criteria for conducting a scientific study. I assess Dr. Simona Nikolaeva Yankova's work on the topic "*Acute coronary syndrome in patients with chronic obstructive pulmonary disease*" as interesting in scientific terms and important for clinical practice. I consider this dissertation to meet the requirements for awarding an educational and scientific degree "PhD" according to the Academic Staff Development Act in the Republic of Bulgaria and the Rules for the Academic Staff Development at the Medical University of Varna. Based on the above-mentioned merits of the dissertation of Dr. Simona Yankova's dissertation work, I strongly recommend the honorable members of the Scientific Jury to vote positively and to award Dr. Simona Nikolaeva Yankova the educational and scientific degree "PhD".

16.02.2025
Sofia

Заличено на основание чл. 5,
§1, б. „В“ от Регламент (ЕС)
2016/679

Prof. Borislav Georgiev Georgiev, MD, PhD

