REVIEW

by

ASSOC. PROF. MIGLENA ILIEVA BALCHEVA-ENEVA, DMD, PHD

Medical University "Prof. Dr. Paraskev Stoyanov" – Varna
Vice Dean of the Faculty of Dental Medicine
Head of EU of Oral Pathology, Dental Allergology and Physical Therapy
at Department of Conservative Dentistry and Oral Pathology

Member of the scientific jury by order № R-109-313 / 21/07/2025 of the Rector of MU – Varna

On dissertation for awarding the educational and scientific degree

"Doctor of Philosophy"

Topic: Association of periodontal status and periodontal infection with coronary heart disease

Sphere of higher education: 7. Health and sports

Professional field: 7.2. Dental Medicine

Scientific specialty: Therapeutic Dentistry

Author: Atanaska Atanasova Nyagolova

Form of doctorate programme: regular

Department: Periodontology and dental implantology, FDM, MU – Varna

Scientific supervisor: Prof. Stefan Vasilev Peev, DMD, PhD, DSc

GENERAL PRESENTATION OF THE PROCEDURE AND THE PHD STUDENT

The presented set of documents and materials is prepared in compliance with the requirements of the LDASRB, the Regulations for its implementation, art. 69 of the Regulations for the development of the academic staff at the MU – Varna, and includes:

1. Enrollment order № R-109-466 / 03/11/2020 and order for the change of topic № R-109-369 / 04/11/2024;
2. European form of CV signed by the author;
3. Copy of the diploma of completed Master's degree;
4. Doctoral minimum exam reports – in the specialty and in foreign language;
5. Protocol from the Department's Council №123 / 15/07/2025 with positive decision on the readiness for defense;
6. Deduction order № R-109-313 / 21/07/2025 for the right to defense;
7. Declaration of originality;
8. List of publications related to the topic of the dissertation;
9. Copies of the same publications;
10. Dissertation;
11. Abstract;
12. Declaration of credibility of data and of registered scientific profiles;
13. Declaration of registered scientific profiles;
14. Similarity reference;
15. Reference for registered scientific profiles.

Biographical data of the PhD student

Dr. Atanaska Atanasova Nyagolova is born on July 31st 1987 in Shumen. She graduated from high school in 2006 ("N. Y. Vaptsarov" FLHS – Shumen), and in 2013 she obtained a Master's degree in Dentistry at Medical University of Varna (diploma №003555). Since 2019 Dr. Nyagolova has been working as an assistant professor at the Department of Periodontology and dental implantology at the Faculty of Dental Medicine, MU – Varna, taking part in the educational course of the subject "Periodontology and oral diseases", both in Bulgarian and English.

CHARACTERISTICS AND EVALUATION OF THE DISSERTATION

Relevance of the topic

The dissertation under review addresses an interesting and timely topic of both scientific and practical significance. It explores two chronic diseases of major public health importance – coronary heart disease (CHD) and periodontitis – as well as the potential relationship between them. Cardiovascular diseases (CVDs) affect a large proportion of the population and remain the leading cause of mortality worldwide. At their core lies atherosclerosis, a progressive condition that may ultimately result in myocardial infarction, stroke, limb gangrene, and other complications. Periodontitis, on the other hand, is a plaque-induced inflammatory-destructive disease with high prevalence, responsible for recurrent daily episodes of transient bacteremia. Periodontopathogens may additionally translocate through the gastrointestinal tract or via neural pathways, thereby exerting systemic effects.

The concept of an association between periodontal infection and cardiovascular disease has long been debated. While some scholars remain skeptical, an increasing number of researchers consider periodontitis to be an independent risk factor for the development of atherosclerosis and, consequently, cardiovascular disease. Therefore, the findings of a dissertation that demonstrates a causal link between the two conditions could enrich our theoretical understanding and potentially reshape approaches to the prevention and management of both diseases.

Dissertation Structure

The dissertation of Dr. Nyagolova is organized in accordance with the requirements of the Regulations for Academic Development at the Medical University of Varna. It comprises 173 standard pages and is illustrated with 29 tables, 44 figures, and 5 appendices. The bibliography includes 392 references, of which 3 are in Cyrillic and 389 in Latin script; 90 (23%) of them have been published within the last ten years.

Knowledge of the Problem

The introduction is informative and comprehensive, providing a clear orientation to the research problem. **The literature review** summarizes the available evidence on the relationship between periodontal infection and coronary heart disease, with emphasis on the etiology and pathogenesis of periodontitis (bacterial complexes, the progression of periodontal inflammation, inflammatory cells, cytokines, and enzymes) and the pathophysiological alterations observed in coronary disease. Detailed descriptions are

provided of the main periodontopathogens from the red and orange complexes—*Porphyromonas gingivalis*, *Tannerella forsythia*, *Treponema denticola*, and *Aggregatibacter actinomycetemcomitans*. Special attention is devoted to the impact of periodontitis on various systemic conditions, including pregnancy, Alzheimer's disease, COPD, metabolic disorders, gastrointestinal cancers, and coronary heart disease. The analysis highlights the necessity of demonstrating a causal link between periodontitis and coronary artery disease in order to improve preventive and therapeutic approaches.

Aim and Objectives

The aim of the dissertation is to establish the relationship between periodontal infection and the severity of coronary symptoms in patients with coronary heart disease. **Three objectives** have been set, which are skillfully selected and fully adequate for achieving the research aim.

Materials and Methods

Dr. Nyagolova conducted her research on 199 patients aged 45 – 64 years, all with natural dentition and a history of selective coronary angiography. Patients with a diagnosis of rheumatoid arthritis were excluded from the study group.

The investigations were carried out at the Department of Invasive Cardiology (Second Clinic of Cardiology), University Hospital "St. Marina," Medical University "Prof. Dr. Paraskev Stoyanov," Varna.

For each eligible patient who signed informed consent, blood and urine samples were collected for standard laboratory tests, and ECG was performed. For Objective 1, a periodontal chart was completed, including data on O'Leary's plaque index, Ainamo & Bay's gingival index, and overall periodontal status. For Objective 2, pooled subgingival samples were collected from periodontal pockets to detect periodontopathogens using a PET test. For Objective 3, coronary angiography was performed, and SYNTAX Score I was calculated to evaluate the complexity of coronary artery lesions.

Data were processed using the Jamovi Statistical Software package.

Results and discussion

Regarding the first objective, Dr. Nyagolova found that the most common cardiovascular disease in the cohort – two-thirds of whom were men – was angina pectoris. In terms of general health, there was a marked trend toward overweight and obesity, nearly half of the patients were smokers, one-quarter had diabetes, and

dyslipidemia was moderately expressed. Periodontal status was significantly compromised, with the majority of patients exhibiting severe periodontitis and generalized gingival inflammation. The findings confirmed the role of male sex, hypertension, obesity, diabetes, and smoking as established risk factors for atherosclerotic changes. Consistent with current concepts, periodontitis – highly prevalent in Bulgaria and closely associated with these conditions – may also be considered an independent risk factor for cardiovascular disease.

The results for the second objective demonstrated a clear association between major periodontopathogens and indicators of periodontal destruction. *T. denticola* and *P. gingivalis* were detected in the majority of patients (88.9% and 80.9%, respectively), while *A. actinomycetemcomitans* was found in only 7.5%. The highest prevalence was observed for *P. gingivalis*. The findings showed that the intensity of local inflammation was determined by the overall microbial burden, while the increasing presence of highly virulent species such as *P. gingivalis* and *T. denticola* correlated with the progression of periodontitis. These results are consistent with previously published data.

The findings for the third objective established a correlation between the severity of periodontitis and coronary disease. Greater periodontal severity was associated with increased coronary artery stenosis and higher SYNTAX Score I values; however, no association was found with coronary thrombosis or diffuse disease. An interesting observation was the correlation between the severity of coronary stenosis and levels of CRP and Troponin I, as well as between CRP levels and *P. gingivalis*. These results align with other studies and underscore the possibility that *P. gingivalis* acts not only as a local pathogen but also as a systemic contributor.

Characteristics and Evaluation of the Dissertation

The stated aim and objectives were successfully achieved. The twelve conclusions drawn are a logical outcome of the obtained results.

Contributions and Significance for Science and Practice

Dr. Nyagolova classifies the contributions of her dissertation into two categories – original and confirmatory. This distinction, as well as the contributions themselves, may be considered well-founded.

Evaluation of Publications Related to the Dissertation

The results of the study have been promoted through three publications, with Dr. Nyagolova as first author of one of them.

Author's Abstract

The author's abstract consists of 81 pages, presented in appropriate length. It is well structured, clearly illustrated, and faithfully reflects the different sections of the dissertation.

Critical Remarks and Recommendations

Dr. Nyagolova has taken into account the recommendations I provided during an earlier stage of the review. I would raise only two observations: Figure 8 is not discussed in the text, and the data in Table 14 could be presented in percentages for greater clarity. Overall, the concise presentation of the material is commendable.

CONCLUSION

Dr. Atanaska Atanasova Nyagolova, doctoral student and an assistant professor at the Department of Periodontology and dental implantology at the Faculty of Dental Medicine – Varna has submitted for statement a completed dissertation, which meets the criteria for acquiring the educational and scientific degree "Doctor of Philosophy", set out in the Law for development of the academic staff in the Republic of Bulgaria, the Regulations for its implementation, and the Regulations for the development of the academic staff at MU – Varna.

This gives me grounds for **positive assessment and I propose to the esteemed Scientific Jury to award the educational and scientific degree "Doctor of Philosophy"** to Dr. Atanaska Atanasova Nyagolova in scientific specialty of Therapeutic Dentistry.

Varna .....

25/08/2025 (Assoc. Prof. Miglena Balcheva-Eneva, DMD, PhD)