

## ACADEMIC REVIEW

**From:** Assoc. Prof. Dr. Deyan Zdravkov Neychev, DM, Department of Oral Surgery, Faculty of Dental Medicine, Medical University – Plovdiv, member of the Scientific Jury, appointed by Order No. R-109-313/21.07.2025 of the Rector of Medical University "Prof. Dr. Paraskev Stoyanov" - Varna

**On the dissertation** entitled "**Association between periodontal status and periodontal infection with coronary artery disease**" for the award of the educational and scientific degree of '**Doctor**' (PhD) in the doctoral program in "**Therapeutic Dentistry**", professional field 7.2 Dental Medicine, field of higher education 7. Healthcare and Sport

Author: Dr. Atanaska Atanasova Nyagolova, full-time doctoral candidate at the Department of "Periodontology and Dental Implantology" of the Faculty of Dental Medicine at Medical University - Varna.

Scientific Supervisor: Prof. Dr. Stefan Vasilev Peev, DMD, DSc.

### 1. General Presentation of the Procedure and the Doctoral Candidate

The presented set of materials for the procedure on electronic media has been prepared correctly, complying with the requirements of the *Act on the Development of Academic Staff in the Republic of Bulgaria* (ADASRB) and the *Regulations for the Development of Academic Staff* of Medical University–Varna from 14 April 2025. The materials include: an abstract, the dissertation, publications, and documents of the doctoral candidate, including copies of publications related to the dissertation topic, an autobiography, a copy of her diploma for the completed Master's degree, the order of enrolment, the order of graduation with the right to defend, the protocol from the Academic Council with a positive decision for readiness for defence, and a list of publications related to the topic.

Dr. Atanaska Atanasova Nyagolova completed her secondary education in 2006. In 2013, she graduated from the Faculty of Dental Medicine at MU-Varna. Since 2020, she has been a full-time doctoral candidate at the Department of "Periodontology and Dental Implantology" at FDM at MU-Varna. She has an excellent command of English and a good command of Russian.

### 2. Relevance of the Topic

The presented dissertation by Dr. Atanaska Atanasova Nyagolova addresses one of the most pressing problems in contemporary medicine – the interrelationship between chronic inflammatory diseases of the periodontium and coronary artery disease. The relevance of the topic is exceptionally high, due to several fundamental factors that are of key importance for both public health and clinical practice.

Cardiovascular diseases are the leading cause of morbidity and mortality worldwide. In Bulgaria, according to data from the National Statistical Institute (NSI), nearly one-third of all deaths result from ischemic heart disease and cerebrovascular diseases. This statistic

underscores the social significance of the problem and the necessity for in-depth investigation of all possible risk factors.

On the other hand, periodontitis is one of the most widespread chronic diseases, affecting approximately 11% of the global population in its severe forms. Beyond tooth loss and impaired oral function, it leads to systemic exposure to pathogens and inflammatory mediators that can have a substantial influence on general health.

In this light, the dissertation is positioned at the intersection of these two socially significant diseases, investigating the pathogenetic mechanisms that connect them. The author correctly emphasizes the necessity of an interdisciplinary approach that integrates the expertise of dental medicine, cardiology, microbiology, and clinical laboratory medicine to achieve a comprehensive understanding of the problem.

### **3. Knowledge of the Problem**

In her dissertation, Dr. Atanaska Nyagolova demonstrates profound knowledge of the topic under investigation. The literature review spans 38 pages. The doctoral candidate has conducted a thorough review of the literature related to the connection between periodontitis and cardiovascular diseases (CVD), particularly coronary artery disease (CAD). The review presents periodontitis as a non-communicable disease with high prevalence, characterized by tissue destruction in response to pathogens in the dental biofilm. The review describes the main periodontal pathogens from the red complex (*Tannerella forsythia*, *Porphyromonas gingivalis*, *Treponema denticola*) and *Aggregatibacter actinomycetemcomitans*, as well as their virulence factors. The conclusion emphasizes that despite extensive evidence, a definitive causal relationship between periodontitis and CAD in humans has not yet been categorically established. The literature review provides current data on the examined problem, with 117 of the cited sources being published within the last 10 years. This demonstrates the doctoral candidate's knowledge of the problem and guided the research in the correct direction.

Following the critical analysis of the literature, the doctoral candidate has formulated conclusions and generalizations based on the literature review.

### **4. Aim and Objectives of the Dissertation**

The aim of the dissertation is clearly and precisely formulated: "To investigate the association between periodontal status, microbiological profile of periodontal infection, and the presence and severity of coronary artery disease". This aim is ambitious and adequately reflects the relevance of the topic.

To achieve this aim, Dr. Nyagolova has set and successfully addressed the following four objectives:

1. **Assessment of clinical periodontal status:** Detailed and systematic evaluation of clinical periodontal parameters (periodontal pocket depth, clinical attachment loss, bleeding on probing, plaque index, etc.) in patients with varying degrees of coronary disease.

2. **Investigation of the microbiological profile:** Identification of key periodontal pathogens in subgingival plaque using contemporary methods.
3. **Analysis of laboratory parameters:** Monitoring of key laboratory indicators of systemic inflammation (C-reactive protein (CRP), interleukin-6 (IL-6), etc.) and analysis of their relationship with the severity of periodontal and coronary changes.
4. **Comparison of the obtained data:** Identifying potential pathophysiological mechanisms underlying the connection between periodontitis and coronary disease, based on a comparison of all obtained results.

These objectives are logically structured and sequentially build upon one another to form a comprehensive study that leads to achieving the main aim.

## 5. Research Methodology

The dissertation is characterized by a complex, contemporary, and adequate methodological approach. To achieve the set objectives, Dr. Nyagolova has employed a suite of methods that cover different aspects of the investigated diseases:

- **Clinical assessment of periodontal status:** Standardized clinical protocols were applied for measuring periodontal pocket depth, clinical attachment loss, and bleeding on probing, as well as other indices.
- **Cardiological diagnostics:** The severity of coronary disease was assessed through selective coronary angiography, using validated indices such as the SYNTAX score I for assessing the severity of the damage.
- **Microbiological and molecular methods:** Contemporary methods for the identification of key periodontal pathogens were used, ensuring precise data on the microbiological profile of the periodontal infection.
- **Laboratory parameters:** Analyses of systemic inflammation markers were conducted, such as high-sensitivity CRP (hs-CRP) and interleukin-6 (IL-6), which are important indicators of inflammatory processes in the organism.
- **Statistical analysis:** Adequate statistical methods were used for data processing, including correlation analysis and regression models, ensuring the reliability of the obtained results.

The methodology is precise, aligned with the dissertation's aims, and reflects the candidate's ability to apply contemporary scientific approaches in her research work.

## 6. Characteristics and Evaluation of the Dissertation

Dr. Nyagolova's dissertation is properly structured, containing all the required elements for a dissertation: contents, abbreviations used, introduction, literature review, aim and objectives, materials and methods, results, discussion, conclusions, findings, contributions, bibliography, and appendices. The presented dissertation is 173 pages in length. It is illustrated with 28 tables,

44 figures, and 5 appendices. The bibliography includes 392 literature sources, of which 3 are in Cyrillic and 389 in Latin script. The presentation is accessible and concise.

The presentation of the original research and discussion comprises 58 pages. The results are accurately and correctly described, comprehensively analyzed with subsequent interpretation, and illustrated through tables and diagrams. The critical analysis conducted allows Dr. Nyagolova to evaluate the methods used and formulate eight main conclusions. The formulated conclusions correspond to the set aim and objectives.

Analysis of the presented data leads to several important conclusions that are thoroughly described and discussed in the dissertation:

- A direct relationship was observed between the severity of periodontal disease and the degree of coronary damage. Patients with more severe periodontitis tended to have more pronounced coronary artery changes, supporting the hypothesis of an interrelationship between the two diseases.
- A higher frequency of isolation of key periodontal pathogens was found in patients with coronary disease compared to control groups.
- Laboratory parameters of systemic inflammation, such as CRP and IL-6, showed a tendency toward elevated values in patients with combined pathology, indicating the role of systemic inflammation as a connecting link.

### **Discussion and Critical Remarks**

These results align with global scientific efforts to clarify the role of periodontal infection in the pathogenesis of atherosclerosis. They provide grounds for considering periodontitis not only as a local disease but as an independent risk factor contributing to the development and progression of coronary disease.

At the same time, the following critical remark is worth noting:

- Systemic inflammation has specific characteristics – chronicity, persistence, a multifactorial nature, and the involvement of multiple biomarkers. The dissertation analyzed some of them (CRP, IL-6), but the question remains whether these parameters fully characterize systemic inflammation or merely reflect it partially. This aspect could be the subject of future in-depth investigations.

Another remark relates to the number of patients studied. Although sufficient for statistical processing, it does not allow for extensive subgroup analyses that would further enrich the conclusions.

These remarks, however, do not diminish the value of the work but, on the contrary, emphasize its potential for future development.

### **7. Contributions and Significance of the Development for Science and Practice**

The dissertation offers both substantial scientific and significant practical contributions:

**Scientific contributions:**

- A direct correlation between periodontal disease severity and the degree of coronary damage, assessed with validated clinical indices, was demonstrated.
- Specific periodontal pathogens that are more frequently identified in patients with coronary disease have been identified, opening new pathways for investigating pathophysiological mechanisms.
- An in-depth analysis of inflammatory markers and their relationship with cardiovascular pathology was conducted, contributing to a better understanding of systemic inflammation.

**Practical contributions:**

- The necessity of a comprehensive medical approach to the patient is emphasized, including collaboration between dentists and cardiologists.
- The dissertation provides a scientific basis for improving preventive strategies, with early diagnosis and treatment of periodontal diseases considered as part of cardiovascular risk prevention.
- The work creates opportunities for integrating dental and cardiological care in clinical practice, which may lead to better health outcomes for patients.

**8. Evaluation of Publications Related to the Dissertation**

Dr. Nyagolova has authored three publications related to the dissertation.

**9. Personal Participation of the Doctoral Candidate**

The research, patient observations, and the resulting outcomes, conclusions, and contributions in the dissertation are the original work of the candidate.

**10. Abstract**

The content and quality of the abstract correspond to the dissertation. It contains the following sections: introduction, aim and objectives, materials and methods, results and discussion, conclusions, contributions, and publications related to the dissertation. It reflects the main results achieved in the dissertation, the conclusions drawn, the contributions, and the associated publications.

**Conclusion**

The dissertation submitted for my review meets the requirements of the *Act on the Development of Academic Staff in the Republic of Bulgaria* (ADASRB) and its implementing regulations. The dissertation by Dr. Atanaska Atanasova Nyagolova is original, scientifically grounded, and practically significant. The author has demonstrated profound knowledge in the field of periodontology, an ability to work interdisciplinarily, and to apply a comprehensive scientific approach.

The dissertation demonstrates that the doctoral candidate, Dr. Atanaska Atanasova Nyagolova, possesses the required theoretical knowledge and professional skills in the scientific specialty "Therapeutic Dentistry". Based on this thorough analysis, I consider that the dissertation by Dr. Atanaska Atanasova Nyagolova fully meets all requirements for awarding the educational and scientific degree of '**Doctor**' (PhD), and I give a **positive** evaluation to the dissertation entitled "**Association between periodontal status and periodontal infection with coronary artery disease**". Based on the above, I recommend that the Honourable Scientific Jury vote positively for awarding the educational and scientific degree of '**Doctor**' (PhD) to **Dr. Atanaska Atanasova Nyagolova**.

Plovdiv

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