ACADEMIC REVIEW

From: Associate Professor Dr. Deyan Zdravkov Neychev, DMD, Department of Dental, Oral and Maxillofacial Surgery, Faculty of Dental Medicine, Medical University – Plovdiv, Member of the Scientific Jury, appointed by Order No. R 109-312/21.07.2025 of the Rector of MU-Varna

Regarding: Dissertation thesis entitled **"Coronary Artery Pathology in Patients with Peri-implantitis"** for the award of educational and scientific degree **"Doctor"** in doctoral program **"Therapeutic Dentistry"**, professional field **7.2 Dental Medicine**, area of higher education **7. Healthcare and Sports**

Author: Dr. Velislava Deyanovna Slavova, regular doctoral student at the Department of Periodontology and Dental Implantology, Faculty of Dental Medicine, Medical University - Varna.

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

1. General Characteristics and Relevance of the Dissertation

The presented dissertation is devoted to an extremely topical and socially significant problem at the intersection of dental medicine and cardiology – the investigation of the relationship between inflammatory diseases around dental implants (peri-implantitis) and coronary artery pathology. The relevance of the topic is indisputable and is determined by two main factors. First, with the continuous improvement of implantological methods and their increasingly widespread application in daily dental practice, the frequency of associated complications is also increasing, among which biological complications such as peri-implant mucositis and peri-implantitis occupy a central place. Second, cardiovascular diseases (CVD), and in particular coronary atherosclerosis, remain a leading cause of morbidity and mortality globally and in Bulgaria. In this context, the investigation of the potential role of local oral infection as a risk factor for the occurrence and progression of systemic vascular diseases is of key scientific and clinical significance.

The dissertation is developed in a volume of 121 pages and is structured in a classical and logical order, including all necessary sections: introduction, literature review, aims and objectives, original research (materials and methods, results and analysis), discussion, conclusion, conclusions, contributions, bibliography, and appendices. The work is illustrated with 61 tables and 10 figures that present the obtained data in a clear and accessible manner. The language used is scientific, precise, and fully corresponds to the standards for this type of academic work. The bibliographic reference includes 179 literary sources, predominantly in English, which testifies to an in-depth knowledge of contemporary achievements in the investigated field.

2. Literature Review

The literature review, presented on 27 pages, demonstrates the doctoral candidate's profound theoretical knowledge and ability to navigate through a vast amount of scientific information,

systematize it, and analyze it critically. The review is logically structured, sequentially introducing the reader to the problem area.

Initially, peri-implant diseases – peri-implant mucositis and peri-implantitis – are defined and thoroughly characterized according to the latest 2017 classification. An extremely important and detailed comparison between peri-implant and periodontal infection at histological, immunological, and microbiological levels has been made, highlighting both similarities and essential differences, such as faster progression and the lower microbial threshold necessary to trigger inflammation around implants.

A central place in the review is occupied by a detailed analysis of microbiological aspects. Microbiological complexes are examined, and special attention is given to key periodontal pathogens from the **"red complex"** and ***Aggregatibacter actinomycetemcomitans***. For each of these, virulent factors and mechanisms through which they contribute to tissue destruction are described.

The final part of the review is devoted to coronary artery pathology and the pathogenesis of atherosclerosis. Here, the doctoral candidate convincingly presents the contemporary "response to injury" hypothesis and the role of inflammation. Data on the two main mechanisms through which oral pathogens can contribute to atherogenesis are systematized: **direct** (hematogenous spread and invasion into atheroma plaque) and **indirect** (systemic elevation of pro-inflammatory mediators).

The literature review is comprehensive, current, and logically prepares the ground for the original investigation, clearly outlining existing gaps in scientific knowledge that the dissertation aims to fill.

3. Aims, Objectives, and Research Methodology

The aim of the dissertation is formulated clearly, specifically, and ambitiously:

"To investigate the role of periodontal pathogens in the etiology of coronary stenosis in patients with dental implants." For its achievement, four sequential and logically connected objectives are defined, encompassing comprehensive analysis of patients' health and peri-implant status, investigation of the relationship between specific microorganisms and peri-implant inflammation, establishing correlation with the severity of coronary disease (Syntax Score), and comparison with patients with periodontitis.

The chosen methodology is of exceptionally high scientific level and is fully adequate to the set aims and objectives. The study is prospective, observational, conducted in the period 2021-2024 after obtaining permission (No. 108 / 25.11.2021) from the Ethics Committee for Scientific Research at MU-Varna. Two groups of patients undergoing coronary angiography were formed: a main group of 37 patients with implants and a control group of 51 patients with natural teeth, with clear inclusion and exclusion criteria applied.

The study design is impressive with its multidisciplinary approach and scope of collected data:

- **Clinical methods:** Taking detailed anamnesis, anthropometric data, and complete periodontal/peri-implant status through standardized and generally accepted indices (gingival index by Ainamo & Bay, plaque index by O'Leary, probing depth, mobility, etc.).
- **Instrumental methods:** Selective coronary angiography was performed to assess coronary anatomy. The use of **SYNTAX score I** for quantitative assessment of anatomical complexity and severity of coronary artery disease is an extremely valuable element of the methodology, allowing objective and standardized comparison of data.
- **Laboratory methods:** Blood samples were taken for a complete set of biochemical and hematological parameters, including lipid profile and markers of inflammation (CRP) and myocardial injury (TnI).
- **Microbiological methods:** A contemporary and highly sensitive **real-time PCR test** was used for quantitative determination of three key periodontal pathogens (*P. gingivalis, T. denticola, A. actinomycetemcomitans*) and total number of microorganisms in samples from peri-implant/periodontal tissues.
- **Statistical methods:** A rich and data-appropriate arsenal of statistical methods was applied, including descriptive analysis, parametric and non-parametric hypothesis testing (t-test, Mann-Whitney U test, χ^2-test, Fisher's exact test), and correlation analyses (Pearson, Spearman, Kendall's Tau). Data processing with specialized software (IBM SPSS, Jamovi) guarantees the objectivity and reliability of the drawn conclusions.

The overall research methodology is impeccably planned and executed, which is a prerequisite for achieving scientifically reliable and significant results.

4. Results and Discussion

The results section is the most extensive in the dissertation and presents the enormous amount of collected information in an extremely detailed and systematized manner. The data are presented in 61 tables and 10 figures, allowing for in-depth and multifaceted analysis.

From the analysis of **Objective 1**, the profile of patients with implants and coronary pathology emerges: male gender, average age 60 years, with above-normal weight (BMI 29.22 kg/m^2). All patients (100%) suffer from arterial hypertension, which in most cases is well controlled with medication. Their lipid profile is within reference ranges, which is due to the fact that 75.7% of them take statins. Concerning is the finding of early-stage kidney disease (eGFR 79.7 ml/min/1.73 m^3). The oral status of these patients is characterized by generalized, plaque-induced inflammatory process (GI=95%, PII=74%), with 86.5% of them diagnosed with peri-implantitis.

Results from **Objective 2** reveal a strong positive correlation between clinical signs of inflammation (bleeding, plaque) and total number of microorganisms (Spearman's ρ=0.837, $p<0.001$). It is established that in milder forms (peri-mucositis, PPD≤3mm), *T. denticola* contamination dominates, while in moderate peri-implantitis (PPD 4-5mm), *P. gingivalis* plays

the leading role. In advanced lesions (PPD>5mm), both microorganisms are isolated in high quantities.

The key and most significant result is from **Objective 3**. The study establishes a **very high, positive, statistically significant relationship between the degree of *T. denticola* contamination and SYNTAX score I values** (Spearman's $\rho=0.551$, $p<0.001$) and a moderate one for *P. gingivalis* (Spearman's $\rho=0.487$, $p=0.002$). This result is direct evidence that the presence and quantity of specific microorganisms in the peri-implant sulcus correlates with the anatomical complexity and severity of atherosclerotic lesions in coronary arteries.

The comparative analysis from **Objective 4** between the implant group (peri-implantitis) and the control group with natural teeth (periodontitis) reveals extremely interesting and important data. Despite patients with periodontitis showing higher total microbial counts, higher plaque index values, and greater probing depths, **patients with implants demonstrate more severe coronary artery involvement**, especially of the right coronaries (RCx 80% stenosis in group 1 versus 20% in group 2; RCA 75% versus 20%). SYNTAX score I is also higher in the periodontitis group, although the difference does not reach statistical significance ($p=0.182$). These results suggest that either the immune-inflammatory response around the implant biomaterial or the specific microbiome associated with peri-implantitis has a more pronounced systemic pro-atherogenic effect, even with lower total microbial load.

The discussion of results is in-depth, with the author demonstrating maturity and ability to interpret their own data in the context of world scientific literature. Both confirmatory and contradictory results from other studies are correctly cited, with possible explanations proposed.

5. Critical Remarks and Recommendations

Overall, the dissertation is of very high scientific level. Nevertheless, in the spirit of well-intentioned academic debate, I would like to make one critical remark that in no way diminishes the significance of what has been achieved, but rather outlines directions for future research.

The main remark is related to the study design, which is **cross-sectional**. This design is excellent for establishing associations and correlations between different factors at a specific point in time, which the dissertation accomplishes brilliantly. The established strong relationship between peri-implant infection and the severity of coronary atherosclerosis is an indisputable fact. However, the cross-sectional design does not allow for categorical conclusions about **cause-and-effect relationships**. The possibility cannot be completely excluded that the presence of severe systemic vascular pathology and associated risk factors and immune changes predispose to the development of more severe peri-implantitis, rather than just the reverse. To prove causality, it would be necessary to conduct a **longitudinal study** in which a cohort of patients would be followed over time from the moment of implant placement to see whether the development of peri-implantitis precedes and contributes to the progression of coronary disease. Of course, conducting such a study is extremely difficult, expensive, and time-consuming, and falls outside the scope of a doctoral project. Therefore, this remark should be viewed not as criticism of the work performed, but as a recommendation for the author's future scientific development in this promising field.

6. Contributions of the Dissertation

The dissertation contains indisputable and significant scientific and applied contributions, which are correctly formulated by the author.

Original contributions:

1. For the first time in world literature, the **correlation between specific microorganisms (*P. gingivalis, T. denticola*) isolated from peri-implant tissues and SYNTAX score I** – an objective indicator of coronary disease severity – is investigated and proven.
2. For the first time, a **direct comparison of coronary pathology severity** in patients with peri-implantitis versus patients with periodontitis is performed, establishing more severe involvement in the implant group.
3. For the first time, an **association between peri-implantitis and early-stage kidney disease** is established.

Original contributions for the country:

1. This is the **first study in Bulgaria** devoted to coronary artery pathology in patients with peri-implantitis, laying the foundations of this important interdisciplinary field in the country.

Confirmatory contributions: The work confirms and enriches with original data several important hypotheses, including the general relationship between peri-implantitis and CVD, the leading role of *T. denticola* and *P. gingivalis*, the lower total microbial count around implants compared to natural teeth, and the most frequent involvement of the molar region.

7. Assessment of Publications Related to the Dissertation

Dr. Velislava Slavova presents three publications related to the dissertation.

8. Personal Participation of the Doctoral Candidate

The conducted research and patient observations and subsequent results, conclusions, and contributions in the dissertation are the personal work of the author.

9. Abstract

The content and quality of the abstract correspond to the developed work. It contains the following parts: introduction, aims 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, conclusions drawn, contributions, and publications.

10. Conclusion

The dissertation of Dr. Velislava Deyanovna Slavova entitled "Coronary Artery Pathology in Patients with Peri-implantitis" represents a completed, in-depth, and original scientific investigation of an extremely topical interdisciplinary problem. It is distinguished by precisely

planned and executed methodology, rich factual material, correct and in-depth statistical analysis, and significant scientific contributions of international importance. The obtained results have not only theoretical but also great practical value, emphasizing the need for close collaboration between dental practitioners and cardiologists, and highlighting the importance of prevention and treatment of oral diseases as part of the overall strategy for reducing the risk of severe systemic complications.

The qualities of the dissertation, the research skills demonstrated by the doctoral candidate, erudition, and capacity for scientific analysis give me full grounds to provide my **CATEGORICALLY POSITIVE** assessment and to propose to the esteemed Scientific Jury to award **Dr. Velislava Deyanovna Slavova** the educational and scientific degree of **"Doctor"** in the scientific specialty "Therapeutic Dentistry."

Plovdiv
16.09.2025

Associate Professor Dr. Deyan Neychev, DMD