

ABSTRACT

The habilitation thesis "**Fundamental research and clinical studies for the assessment of periodontal status**" includes in the first part the results of the scientific research activity, carried out since obtaining the title of Doctor of Medical Sciences until now. Starting from these achievements, the second part presents the directions of professional, scientific, and academic career development, which I wish to approach in the future.

The first section includes, in three chapters, the main research directions approached over the years and the results of the most relevant studies.

The preoccupation during the doctoral studies regarding the evaluation of the periodontal status continued using new research techniques and methods.

The first part of this thesis presents the main fundamental research carried out for diagnostic purposes, but also for evaluating the results of periodontal therapy. The assessment of periodontal status by determining some inflammatory markers has been one of the research directions addressed in recent years. In one study we aimed to determine if there is a correlation between the level of cyclooxygenase-2 (COX-2) and matrix metalloproteinase (MMP - 9) in the gingival tissue and its degree of damage. COX-2 and MMP-9, as active biomarkers of chronic inflammation, angiogenesis, and extracellular matrix degradation, can be used in clinical practice to detect patients at high risk for periodontitis. Given the high expression of these two enzymes in patients with periodontal disease, treatment with COX-2 inhibitors versus nonselective nonsteroidal anti-inflammatory drugs (NSAIDS) and MMP inhibitors—chemically modified tetracyclines—can be considered. Pathological changes at the periodontal tissue level are determined by the presence of periodontal pathogens, therefore their identification and quantification has been a permanent concern over the years. Unlike the means used during my doctoral studies, the technique of polymerization in the chain reaction (PCR), presents a high specificity and allows the identification of periodontal pathogens by their DNA, thus being more sensitive than the bacterial culture. By using this technique, we managed to evaluate the subgingival flora and the results of these studies demonstrated that a knowledge of the bacterial composition and load can bring a series of advantages related to an early and correct diagnosis, it allows the choice of a targeted, local and/or general medication and it also prevents relapses. Qualitative and quantitative determination of the level of pro-inflammatory cytokines in gingival crevicular fluid (GCF) can be a useful tool for assessing the severity and evolution of periodontal disease. Based on these observations we performed a study in which we evaluated the levels of interleukin-1 α (IL-1 α) and interleukin-1 β (IL-1 β) in the GCF of patients with periodontal disease and hepatitis C and compared them with those of patients with periodontal disease but systemically healthy. The results of the study revealed a much worse situation of the periodontal status and much higher levels of IL-1 α and IL-1 β in patients with both conditions compared to patients with periodontitis but systemically healthy.

Recently, there is more and more talk about the existence of a strong link between periodontal disease and systemic conditions, a reason to approach new research directions. In an effort to find the correlations between periodontal disease and cardiovascular conditions, I participated in the ATHERODENT study. The aim

of this study was to evaluate the correlation between the severity of the periodontal disease and the degree of vulnerability of atheromatous coronary plaques, assessed by CCTA, in patients with unstable angina. The results of this study show an association between the severity of the periodontal disease, the severity of atherosclerosis and the vulnerability of coronary plaques in patients with unstable angina, probably due to systemic inflammation as a common substrate for all these conditions. This study has great practical applicability and led us to formulate certain recommendations for all categories of patients. Following the emergence of SARS-CoV-2 virus infection, we have expanded research in this area, with the aim of providing a better understanding of the inflammatory triangle underlying acute myocardial infarction (MI), periodontal disease (PD) and COVID- 19.

The fact that there are only a few studies on the link between periodontal disease and organs of the digestive system, led us to investigate the link between periodontal disease and liver disease. The aim of an ex vivo study was to illustrate the changes that occur in the gingival tissue, by using optical coherence tomography (OCT), allowing the determination of the pixel density of the cross-sectional images. Based on the hypothesis that a lower pixel density could be associated with a higher degree of inflammation, we aimed to highlight the possible influence that non-alcoholic fatty liver disease could have on local inflammatory gingival changes, in patients suffering from these two conditions. With all the limitations of this study, given the small number of patients, analyzing the images obtained by the OCT technique, we could conclude that non-alcoholic fatty liver disease can have a negative effect of worsening the local periodontal inflammatory reaction in patients with periodontal disease, by increasing inflammation of the gingival tissues. Patients with chronic hepatitis C (CHC) can very often manifest important oral health problems, which can have a negative impact on the quality of life, because they add to the pathological manifestations of the liver disease and its complications. To establish these correlations, we assessed the levels of the NLRP3 inflammasome and its components in GCF, in patients with periodontitis and CHC. We aimed to determine whether the regulation of the NLRP3 inflammasome is influenced by the overlap of the two pathologies, periodontitis, and chronic hepatitis C, which could thus lead to a more exacerbated manifestation of periodontal disease in CHC patients. The results of this study show that CHC and periodontitis patients showed severe changes in clinical periodontal status. Considering that these patients also showed the highest levels of NLRP3 in GCF, the negative character of their periodontal status could be related to the upregulation of this mediator.

Another area of interest was the effects of laser therapy on periodontal structures. Controversies in the literature led us to design a series of clinical and laboratory investigations to provide additional data on the effects of laser therapy on periodontal structures. Numerous studies have observed that orthodontic treatment with fixed appliances, by creating retention sites, can cause the accumulation of bacterial plaque, which can lead to the development of dental or periodontal lesions. Starting from these observations, we carried out a study in which we aimed to evaluate the advantages and limitations of using laser therapy, on periodontal status, during orthodontic treatment. This study led us to a series of conclusions with practical applicability regarding the maintenance of a healthy periodontal status, in adult patients with orthodontic treatment. It has been proven that laser therapy, used as an adjunct to mechanical treatment, can cause a reduction of

subgingival bacterial flora and thus of gingival inflammatory phenomena. In order to better understand the mechanisms that take place at the cellular level, we continued this direction of research and aimed to evaluate the effects of laser application on osteoblast cultures, by assessing cell viability, proliferation and activity. This study demonstrated that laser application on osteoblast cultures contributes to increasing the proliferation rate and the intensification of their cellular activity, having as a practical implication the acceleration of the rhythm of dental movements. Regarding the use of laser therapy as an adjuvant in the treatment of peri-implant mucositis, the reported results are controversial. Therefore, we conducted a study in which we aimed to evaluate the effectiveness of this modern therapeutic method, on the peri-implant status, in the treatment of peri-implant mucositis. Analyzing the results of this study, we came to the conclusion that the state of peri-implant health is directly correlated with the maintenance of oral hygiene; therefore, the clinician must give special importance to supportive therapy, in order to increase the success rate of dental implants. In our study, laser therapy as an adjunct to conventional treatment of peri-implant mucositis led to a statistically significant reduction in probing bleeding at 3-month and 6-month re-evaluations. The findings of this study should be considered preliminary and interpreted with caution, as further clinical trials are needed to draw strong conclusions.

The second section of the habilitation thesis presents the proposals for professional, scientific, and academic career development. Based on the experience gained, my concerns for the coming years will focus on finding new directions for basic and clinical research. The tools used in fulfilling the development plans will be both maintaining and increasing the standards of academic and professional excellence, as well as permanent collaboration with students, residents, PhD students and my colleagues, the teaching staff.