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The role of periodontal treatment in comprehensive cardiac rehabilitation

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Abstract: (1) Background: Periodontitis is a chronic infectious, inflammatory disease associated with significant local disastrous effects due to alveolar bone destruction and systemic morbidities. Some associations between periodontitis and coronary and cerebrovascular diseases have been highlighted in the literature. The present study investigated a group of patients with atherosclerotic cardiovascular diseases and periodontitis and aimed to as-sess the comprehensive effects of nonsurgical periodontitis treatment. (2) Methods: The present study included 11 patients with atherosclerotic cardiovascular disease and perio-dontitis, that were diagnosed after a complete and a complex periodontal evaluation. These patients received periodontal treatment and periodontal reevaluation after 2 months from initial therapy. (3) Results: A significant improvement of the oral hygiene and gingival bleeding scores was recorded at two months follow-up. For moderate pockets of 5 mm, there was a significant reduction of their median values at two months follow-up moment (p=0.021). (4) Conclusion: The nonsurgical periodontal treatment significantly improves the clinical-related parameters of the periodontal tissues, as revealed by gingival bleeding and pocket closure.

Keywords: periodontitis, cardiovascular disease, inflammation, probing depth, treatment

Introduction

Periodontitis is a chronic infectious, inflammatory disease affecting more than 50% of the population worldwide [1]. Periodontitis has been associated with significant local disastrous effects due to alveolar bone destruction and tooth loss, systemic morbidities through the enormous subgingival bacterial loads and inflammatory components [2] as well as with an increased mortality rate [3]. Although most inflammatory reactions develop locally, it has been established that the inflammatory mediators generated by periodontitis lesions, as well as some periodontal pathogens can disseminate from the oral cavity contributing to the development of systemic conditions [4]. Moreover, periodontitis may indirectly generate an increased synthesis of proinflammatory mediators in the systemic circulation augmenting the impact on other organs [5]. Untreated periodontitis is a potential risk factor for a large group of systemic diseases, including diabetes, atherosclerotic cardiovascular diseases (CVDs) and their acute accidents, rheumatic diseases, or some pregnancy complications [6].

Some associations between periodontitis on the one hand and coronary heart and cerebrovascular diseases on the other hand have been highlighted [7, 8, 9]. These associative relationships are even more important considering the enormous burn represented by CVDs. In 2017, the European Heart Network reported that CVDs

represented the leading cause of mortality in Europe, responsible for more than 3.9 million deaths. Moreover, approximately 34.9 million cases of ischemic heart disease, 20.4 million strokes, 25.8 million cases of peripheral vascular disease, and 10 million cases of atrial fibrillation were reported [10]. Periodontitis has been associated with an increased risk of acute coronary events in patients with preexisting coronary disease [11]. Peripheral arterial disease was more prevalent in patients with periodontitis than non-periodontitis patients [12].

The direct association between periodontitis and CVD is underpinned by two primary biological mechanisms that have gained considerable attention. One theory posits that periodontal bacteria and their byproducts disseminate via the bloodstream, directly colonizing endothelial cells or atheroma plaques, thereby triggering CVD [13, 14, 15]. The second theory suggests that inflammatory pathways may connect both conditions, with locally produced pro-inflammatory mediators, matrix metalloproteinases, and elevated nitric oxide potentially entering the bloodstream, alongside alterations in lipid profiles and thrombotic/hemostatic markers, collectively contributing to systemic inflammation [14, 16, 17]Additionally, another hypothesis implicates an aberrant immune-inflammatory response shared by periodontitis and CVDs, potentially influenced by specific genetic profiles and epigenetic risk factors, thereby predisposing individuals to both conditions [18, 19].

However, no causal role of periodontitis in the development of CVDs has been established until now, and other studies should be carried out to clarify this issue [20, 21]. The most recently updated review on the effects of periodontitis treatment on CVDs [22] reported uncertain evidence about whether conventional periodontal treatment could prevent CVDs or its fatal consequences in periodontitis patients.

The nonsurgical treatment (subgingival mechanical instrumentation) of periodontitis targets to dramatically reduce local infection, and inflammation and thus to decrease the general deleterious effects of periodontitis and improve CVD parameters as some studies reported [23, 24, 25]. Based on actual information, the present paper narrowed the group of cardiovascular diseases to atherosclerotic cardiovascular diseases (ACVDs). It aimed to investigate the comprehensive effects of nonsurgical periodontitis treatment in a group of patients with ACVDs and periodontitis.

2. Results

From the total number of 13 patients with cardiovascular disease and periodontitis included in the study, only the medical records of 11 patients with a mean age of 59.45 (SD 8.813) years and a mean BMI of 26.477 (SD 4.464) kg/m^2 were available for final analysis (Figure 1). From the 11 patients, 5 patients (45.45%) were female and 3 patients (37.053%) were current smokers.

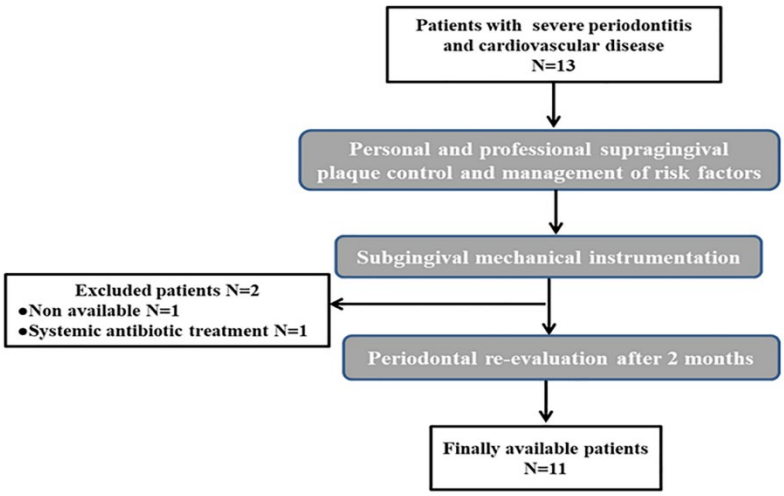

Figure 1. Flowchart of the patients.

The periodontal evaluation of the study group found a mean number of 20.73 (SD 5.255) teeth and recorded periodontal parameters from 124.36 (SD 31.532) surfaces.

The periodontal healing after the two-step therapy developed uneventfully in all patients. The patients did not report any important adverse effects excepting for a local gingival sensibility on the first day after the intervention.

Table 1 shows periodontal patients' characteristics at baseline and two months' reexamination moment.

TABLE 1. Periodontal parameters of the study group

Parameter:	Baseline (n1=11)	Reevaluation (n2=11)	p-value
IHI (%), mean (SD)	54.4 ±17.5	34.2|±13.4	0.000
GBI (%), mean (SD)	33.8±21.8	19.9±9.6	0.011
CAL (mm), mean (SD)	4.0±1.7	3.9±1.7	0.135
PD (mm), mean (SD)	3.0± 0.9	2.6±0.8	0.059
CAL, median (SD)	3.9±1.9	3.7±1.9	0.096
PD, median (SD)	2.6±1.4	2.1±1.1	0.138
Sites with PD=5 mm, median (IQR)	22 (10-26)	16 (4-24)	0.021
Sites with PD≥5mm, median (IQR)	8 (4-19)	1 (0-9)	0.240
Sites with PD ≥ 6 mm, median (IQR)	8 (4-19)	1 (0-9)	1.0

Abbreviations: CAL, clinical attachment loss; GBI, gingival bleeding index; OHI, oral hygiene index; IQR, interquartile range (25-75); n1, n2, number of subjects in the analysis,; PD, probing depth;

A significant amelioration of the oral hygiene (IHI) (p=0.000) and gingival bleeding (GBI) (p=0.011) scores was recorded at two months follow-up. Objective ameliorations in the aspect of superficial periodontal tissues were observed including diminution of the local eritema and gingival edema (Fig.2). Moreover, during the two months period, most of the patients managed to maintain an acceptable hygiene status after the professional removal of deposits (Fig.3, 4). Tooth splinting with fiber-reinforced resin composite in the first step of therapy did not accentuate local heavy and soft tooth deposits (Fig.3, 4).

Periodontal treatment including supragingival hygiene and subgingival instrumentation did not induce significant modifications of the mean attachment level (CAL) (p=0.135) or periodontal pocket dimensions (PD) (p=0.059).

For moderate pockets (PD=5 mm), there was a significant decrease in of their median values at two months follow-up moment (p=0.021). Although a reduction of median values of deep pockets (PD ≥ 6 mm) was also reccorded after two months after the treatment, the modifications were not statistically significant (p=1.0).

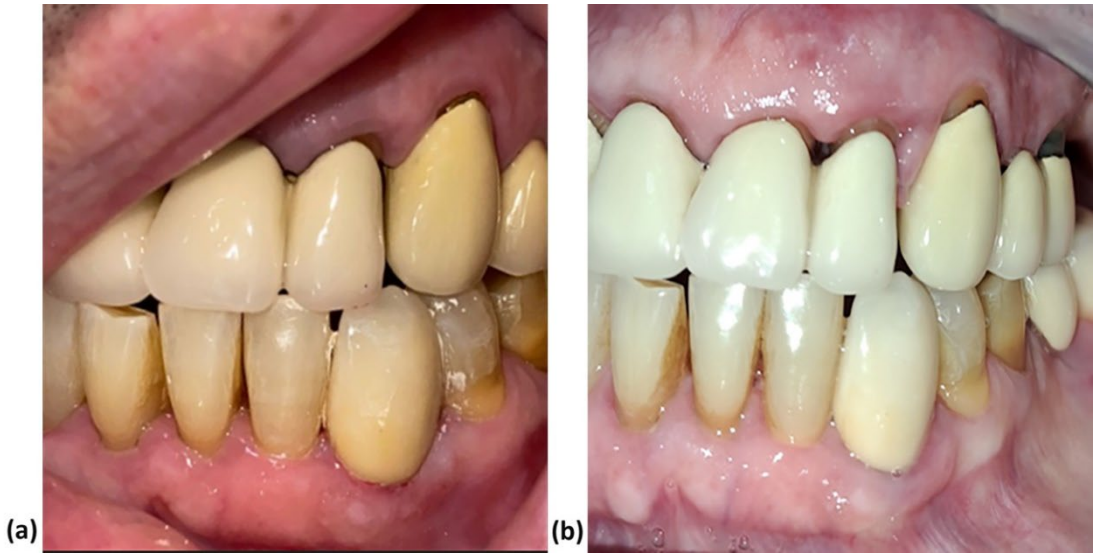

Figure 2. A 58-year-old patient with cardiovascular disease (hypertension, ischemic heart disease, stable angina, positive stress test) and generalized stage IV, grade B periodontitis. **A.** Intra-oral view at baseline. **B.** Intra-oral view two months after the periodontal treatment.

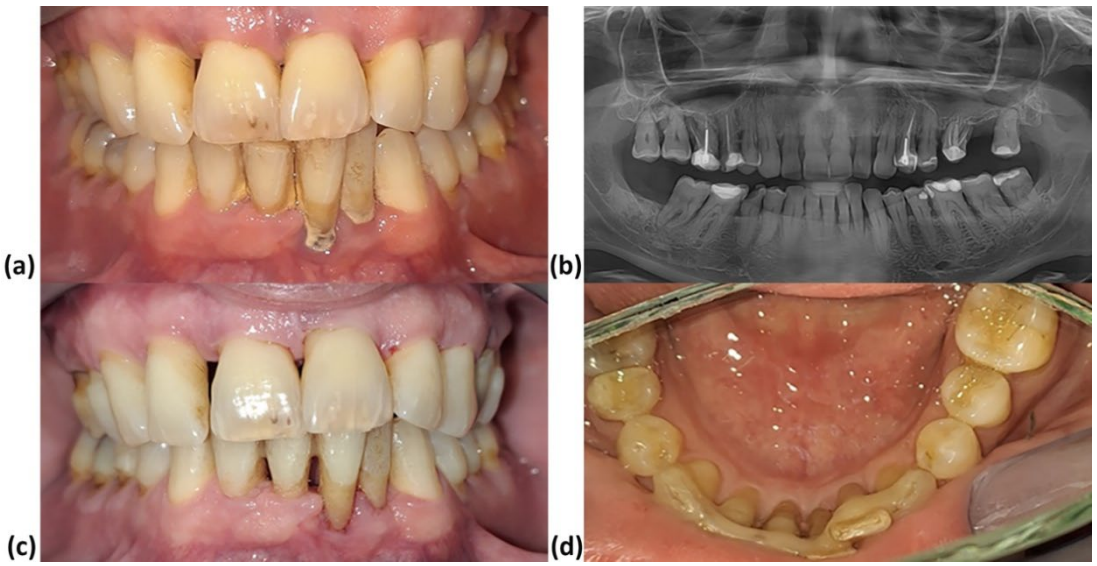

Figure 3. A 46-year-old patient with cardiovascular disease (hypertension, peripheric arterial disease stage 2b, claudication at 100m, asimptomatic atherosclerosis of the left internal carotid artery) and generalized stage IV, grade C periodontitis. **A.**Intra-oral view at baseline -havy deposits in the mandible. **B.**Panoramic radiography. **C.**Intra-oral view at two months follow-up moment revealing a good dental hygiene. **D.** Fiber-reinforced composite splint at inferior incisors.

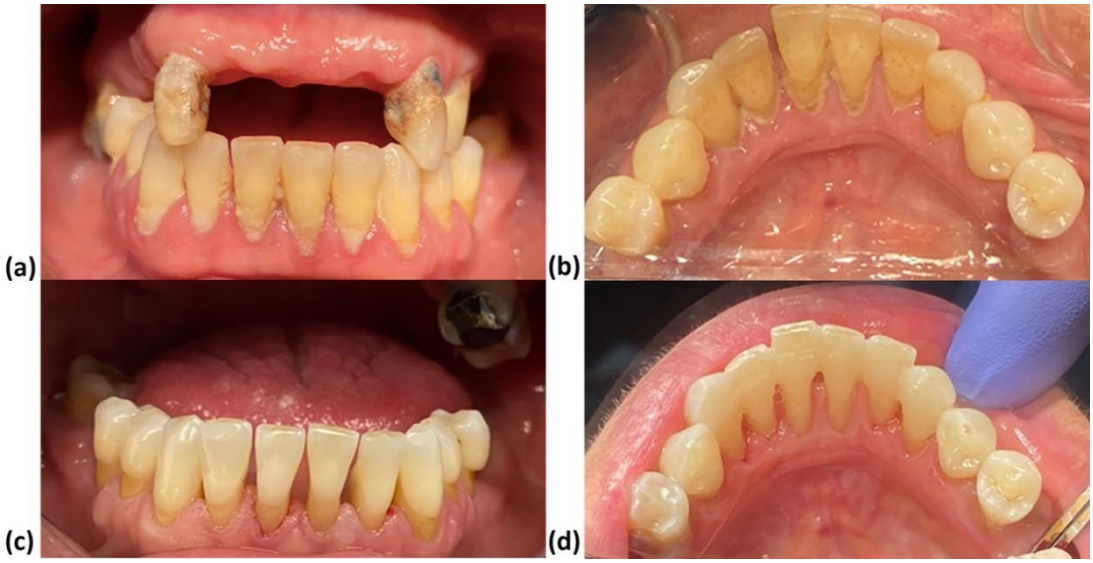

Figure 4. A 52-year-old patient with cardiovascular disease (hypertension, atrial fibrilattion, moderate mitral regurgitation, heart failure with preserved ejection fraction) and generalized stage IV, grade C periodontitis. **A.**Intra-oral view at baseline – sub-total maxilla edentoulism and havy deposits on buccal mandibular surfaces. **B.** Heavy deposits on the oral surfaces of the mandibular incisors. **C.**Intra-oral view at two months follow-up moment. **D.** Fiber-reinforced composite splint at inferior incisors and good dental hygiene

3. Discussion

The limited evidence provided by a recent systematic review [22] on the preventive effects of periodontitis therapy in relation with CVDs incited to the initiation of the present study.

In our study group formed by patients suffering from ACVD and severe periodontitis, significant improvements of the oral hygiene (p=0.000) and reduction of gingival bleeding (p=0.011) were calculated. The important reduction in gingival inflammation would not have been possible without optimizing the plaque index [7]. Our results are in agreement with the data reported by other studies. In periodontitis CVD patients, the subgingival mechanical instrumentation (nonsurgical therapy) resulted in an important improvement of all periodontal variables: a mean reduction of PD of 0.02 mm, bleeding on probing score of 25.8%, and plaque index of 0.28%. Changes were statistically significant for all the above-mentioned variables [26]. Other authors reported a reduction of gingival bleeding score by 40% after subgingival mechanical instrumentation at the end of 6 months [27].

In our group of patients, the reduction of the mean PD was at the limit of statistical significance (p=0.059) possible due to the small sample size. On the other side, other authors reported a mean PD reduction of 1.7 mm and a statistically significant mean clinical attachment gain of 0.35 mm and 0.3 mm [28].

No significant modifications of attachment levels (CAL) were found by the present study. Other authors also highlighted a non significant reduction of CAL of 0.07 mm after nonsurgical treatment in periodontitis CVD patients [26].

Comprehensive cardiac recovery considers, in addition to specific cardiac therapy, the approach to associated risk factors. Periodontitis has been listed as a risk factor for CVD [6] through disseminated subgingival infection and inflammation that trigger the formation of atherosclerotic plaques [29]. The most recent systematic review [22] provided inconsistent information on the effect of periodontitis treatment on the prevention of CVDs in terms of acute accidents or death. The authors of this review [22] maintained the term 'chronic periodontitis' as the reviewed articles used former case definition systems. However, a new multidimensional staging and grading system for periodontal disease

has been published [30]. From this perspective, our study adds value to this topic because it is based on the 2018 periodontitis classification and definition system, in case a standardized framework of reports should be developed to facilitate comparisons and analyses of further data.

Although there have been no new completed clinical trials on this topic since the last publication targeting this theme [31], the recent review [22] included in the analysis two RCTs and reported very low certainty, inconclusive evidence on the role of subgingival periodontal treatment plus antibiotics over supragingival hygiene on the primary prevention of CVD. One study reported only one death in the scaling and root planning plus antibiotic group. Still, it could not confirm that this periodontitis treatment is able to reduce the incidence of all-cause deaths, and all CVD-related deaths, and neither can it rule out that the reported treatment could increase cardiovascular events compared with supragingival plaque control, after 12 months [32]. Also, no reliable evidence was identified to sustain the effect of subgingival mechanical treatment of periodontitis for the secondary prevention of CVD [22, 33].

The amelioration of clinical parameters in periodontitis patients after subgingival mechanical instrumentation as our study provided is expected to ameliorate systemic markers influencing the cardiac status. Increased levels of C-reactive protein (CRP) have been identified in periodontitis patients [34]. CRP concentrations above 10mg/L has been related with an augmented cardiovascular risk [35]. Increased count of white blood cells has been identified in both CVDs and periodontitis [36] and it represents a strong independent predictor for future coronary heart disease [37]. Nonsurgical periodontal treatment has been reported to improve cardiovascular risk markers and outcomes, including the reduction of CRP, fibrinogen, and white blood cell levels [38, 26, 39]. Some authors reported a reduction of CRP concentrations after subgingival instrumentation periodontitis systemically healthy individuals to a degree equivalent to that obtained through traditional lifestyle modifications [40] or medication [41]. However, attention should be paid in clinical practice on the possible acute-phase response in the first day after one-stage full-mouth instrumentation in severe periodontitis patients [42, 28]. The significant decrease in white blood cell levels induced by subgingival mechanical instrumentation recorded after two months was maintained at six months follow-up moment [26]. Although nonsurgical periodontitis treatment triggers short-term systemic inflammation, it is followed by a progressive and important diminution of systemic negative consequences and an amelioration of endothelial function [7]. However, the long-term systemic changes induced by periodontitis therapy and its impact on CVD burden are inconsistent [27].

An important consideration from the present study is that it provides the evolution of standard periodontal parameters after periodontitis therapy and some ones considered as markers of intense local inflammation (eg. number of deep pockets). In some patients from our study group important reductions of the number of moderate as well as deep periodontal pocktes were calculated. It is known that the impact of periodontitis treatment on ACVD evolution should be appreciated from the perspective of inflammation control. In other words, without observing an effective restraining of the periodontal inflammation in terms of periodontal pocket closure and gingival bleeding reduction, it is impossible to appreciate the contribution of local inflammation to the CVD risk and of the periodontitis treatment on CVD outcomes [22, 23].

The important reduction of gingival inflammation after standard periodontal therapy can represent a premise for the improvement of the systemic disease. Closing some moderate periodontal pockets and reducing the number of deep pockets through periodontal treatment would decreases the periodontal microbial and inflammatory load.

Our interventional clinical study constitutes the departure point for implementing a RCTs treating patients with both periodontitis and CVD in order to reach conclusions about the local and systemic effects of nonsurgical periodontitis treatment as recommended by the literature [22].

Integrating periodontal treatment into cardiac rehabilitation programs offers a promising multidisciplinary approach to improving patient outcomes for individuals with both ACVD and periodontitis. This integrated approach has the potential to enhance cardiovascular health and improve quality of life. However, the crucial factor in this synergy lies in the collaboration between periodontologists and cardiologists, facilitating the screening of periodontitis cases and the implementation of therapeutic interventions through integrated care planning. This includes customized periodontal interventions and regular monitoring to optimize patient care.

One limitation of the present research is related to the small sample size, which may limit the generalizability of our findings. Due to scarce and inconsistent information on the the outcomes of periodontal therapy in ACVD patients with periodontitis, the group was selected based on specific inclusion criteria to isolate the effects of nonsurgical periodontitis treatment on patients with co-existing ACVDs and periodontitis with the aim of contributing more knowledge to this area. Our study also considered the restricted data on this topic when considering periodontis case definition based on recent acknowledged classification of periodontal conditions [30]. The lack of a control group may weaken the power of the results. However, the challenge in recruiting periodontitis patients with healthy systemic status made it difficult to include such a control group. Despite this limitation, we plan to conduct further investigations using a case-control design to better elucidate the local and systemic effects of periodontal therapy in ACVD patients.

Medical and dental communities must raise awareness and promote multidisciplinary collaboration to refer patients with cardiovascular diseases to dental practitioners for periodontal diagnosis and treatment.

4. Materials and Methods

Study design and population

The study included patients with both severe periodontitis and ACVDs, which were addressed to the Periodontology Department of "Iuliu Haţieganu" University of Medicine and Pharmacy by cardiologists. This study was approved by the Ethical Board of „Iuliu Haţieganu" University of Medicine and Pharmacy, Cluj-Napoca (No. 249/30.06.2021) and by the Ethical Board of Rehabilitation Hospital of Cluj-Napoca (No.4048/23.04.2021). It was performed in conformity with the guidelines of the Declaration of Helsinki and EU regulations. The participants signed a written informed consent before periodontal evaluation and treatment.

The study included patients with ●stable ACVDs including atherosclerotic coronary artery, cerebrovascular, and peripheral vascular diseases as provided in the medial letter (stable symptoms for at least 60 days), ●no evidence of recent myocardial damage, ●severe periodontal damage (clinical attachment loss CAL≥5 mm) not treated in the last 12 months, ●presence of ≥ 10 teeth (excluding third molars). Patients were excluded if the following conditions were present: ●they did not fulfill criteria of the defined stable CVD cases, ●pregnancy, ●taking systemic antibiotic therapy in the last 3 months, ●<10 teeth (excluding third molars), ●suffering from other forms of periodontal diseases.

All periodontitis patients received supra- and subgingival mechanical instrumentation based on the recommendations of current guidelines [7]. All patients underwent a reevaluation after a two-month period, aligning with the standard timeframe recommended for assessing periodontal healing following etiological therapy according to current guidelines and numerous prior studies [7, 43-45]. Subsequently, all patients continued with additional therapy approaches as necessitated by their individualized treatment plans, which included lifelong supportive periodontal care. This ongoing care is aimed at maintaining periodontal stability and preventing recurrences [7].

Demographic Characteristics of the Population and Cardiovascular Diagnosis

The following general parameters were recorded: age, gender, and smoking status.

All patients included in the study had a medical history of cardiovascular diseases. Their diagnosis was confirmed or revised by a cardiologist from Clinical Rehabilitation Hospital Cluj-Napoca (DP, BC). The patients were evaluated by clinical exam, ECG analysis and cardiac ultrasound. Patients with palpitations or a history of arrhythmias were monitored by Holter ECG for 24 hours, and those who complained of typical angina pectoris performed an exercise test. The positive diagnosis of atrial fibrilattion was established when the ahrrythmia was present on a 12-lead electrocardiogram or lasted for more than 30 seconds during the Holter ECG monitorization. The stress test was considered to be positive for miocardial ischemia if an ST depression of at least 1mm in amplitude was recorded in two contiguos leads during physical exercise compared to the resting electrocardiogram. In cases of peripheral arterial disease, vascular ultrasound was performed, and plaques that caused at least 50% vascular stenosis were considered to be clinically relevant. The diagnosis was established according to the latest clinical guidelines of the European Society of Cardiology [46-50].

Periodontal Evaluation and Periodontitis Case Definition

All patients benefited from a full-mouth periodontal examination (baseline) and at two months after completing mechanical subgingival instrumentation, which was performed by two calibrated examiners (AC and CC), who attended two training meetings supervised by the senior periodontist (AR) and examined four patients not included in the study. The periodontal examinations were done in the clinical setting with a standard equipment (dental mirror, 1 mm marking periodontal probe—UNC-15 periodontal probe, Hu-Friedy, Chicago, IL, USA). Probing depth (PD), gingival recession (GR), and clinical attachment loss (CAL) were evaluated in six sites per tooth based on a standard methodology [51]. Bleeding on probing was appreciated, and the Gingival Bleeding Index (GBI) was calculated as a percentage of the total number of bleeding sites reported to the total number of evaluated sites [52]. Oral hygiene was quantified with the Oral Hygiene Score (IHI) [53]. The number of missing teeth was also recorded.

Severe (stage III and IV) periodontitis was diagnosed according to the 2018 European Federation of Periodontology (EFP)/American Academy of Periodontology (AAP) case definition system [54, 55] as follows: presence of interdental CAL at two non-adjacent teeth with at least one CAL≥ 5mm, or presence of two buccal or oral CAL≥ 3 mm associated with PD > 3 mm with at least one CAL≥ 5mm, the absence of gingival necrotic signs or severe debilitating systemic diseases [30, 54].

Periodontal Treatment and Study Outcomes

Each patient was provided with a structured treatment plan in accordance with current guidelines [28]. This approach involved two main initial steps [28]. The first focused on modifying patient behaviors and risk factors as well as managing supragingival deposits through a supervised personal oral hygiene and professional approaches. In the second step, the subgingival pocket instrumentation was done as part of cause-related therapy, following a full-mouth design and using conventional instruments (Unit-P5 Booster Suprasson-Satelec, Acteon, Mount Laurel, NJ, USA and Gracey curettes- Hu-Friedy, Chicago, IL, USA) . The results were re-evaluated after two months. After treatment, patients were instructed to use 0.2% chlorhexidine-based mouthwash, to potentially tackle the extrasulcular colonization of periodontopathogenic bacteria.

The primary outcome was the PD and the secondary outcomes were the CAL, count of total probing depths of 5 mm, and ≥ 6 mm, IHI and GBI scores.

Statistical Analysis

Statistical analysis was carried out using the MedCalc® Statistical Software version 22.016 (MedCalc Software Ltd, Ostend, Belgium; https://www.medcalc.org; 2023). In cases where the data were normally distributed and exhibited symmetric patterns, the central tendency was expressed using the mean and the dispersion around the mean was described using the standard deviation. For variables that displayed skewed distributions or contained outliers, the median and interquartile range (IQR) were employed as more robust measures of central tendency and dispersion, respectively. For comparing measurements between groups, we utilized appropriate statistical tests based on the nature of the data. Specifically, we employed the paired t-test when assumptions of normality and homogeneity of variance were met. Alternatively, when these assumptions were violated, we applied the Mann-Whitney test, a non-parametric method, to ensure robustness of our analysis. A p value <0.05 was considered statistically significant.

5. Conclusions

The nonsurgical periodontal tratement improved the aspect of superficial periodontal tissues including diminution of the local eritema, gingival edema, and bleeding on probing. A significant reduction of the median values at two months follow-up moment for moderate pockets was highlighted, constituting a premise for the diminution of the systemic inflammatory impact.

Author Contributions: Conceptualization, Caloian Carmen Silvia, Roman Alexandra and Pop Dana; methodology, Roman Alexandra, Ciurea Andreea, Soanca Andrada; software, Caloian Carmen Silvia, Micu Cristina Iulia; validation, Roman Alexandra, Soanca Andrada, Caloian Bogdan; investigation, Caloian Carmen Silvia, Ciurea Andrea and Stanomir Alina; resources, Caloian Carmen Silvia.; data curation, Caloian Carmen Silvia and Caloian Bogdan.; writing—original draft preparation, Caloian Carmen Silvia, Roman Alexandra; writing—review and editing, Roman Alexandra, Soanca Andrada.; visualization, Roman Alexandra.; supervision, Roman Alexandra, Soanca Andrada, Pop Dana; project administration, Caloian Carmen Silvia, Caloian Bogdan, Ciurea Andreea.; funding acquisition, Caloian Carmen Silvia. All authors have read and agreed to the published version of the manuscript.

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Conflict of interest: none declared

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