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Relationship of periodontal status and periodontal infection with coronary disease

THESIS SUMMARY

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a thesis

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Prof. Dr. Stefan Vassilev Peev, DMD, PhD

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The dissertation contains 173 standard pages and is illustrated with 29 tables, 44 figures, and contains 5 appendices.

391 literary sources are cited, of which 3 in Cyrillic and 388 in Latin.

The dissertation has been admitted to public defense by the department council of the Department of Periodontology and Dental Implantology on 15.07.2025. The official defense of the dissertation will be held on 10.10.2025. in Auditorium 103 "Assoc. Prof. Dr. Dimitar Klisarov" of the Faculty of Dental Medicine at the Medical University "Prof. Dr. Paraskev Stoyanov" - Varna, at a meeting of the scientific jury.

The defense materials are available in the Scientific Department at MU-Varna and are published on the MU-Varna website.

CONTENTS:

LIST OF ABBREVIATIONS

Aa – Aggregatibacter actinomycetemcomitans

ACS – acute coronary syndrome

AS – atherosclerosis

BoP – bleeding on probing

CAD – coronary artery disease

CAL – clinical loss of attachment

CDT – cytolethal distending toxin

CRP – C-reactive protein

CVD – cardiovascular diseases

ECG – electrocardiogram

EFP – European Federation of Periodontology

IL- – interleukin

LAD – left anterior descending artery

LM – left main stem

LPS – lipopolysaccharide

MMP – matrix metalloproteinases

MO – microorganisms

OMV – outer membrane vesicles

PAD – peptidylarginine deaminase

PPAD – bacterial peptidylarginine deaminase

PCR – polymerase chain reaction

Pg – Porphyromonas gingivalis

PGE2 – prostaglandin E2

PPD – periodontal pocket depth

RA – rheumatoid arthritis

RANKL – receptor activator of nuclear factor kB ligand

RCA – right coronary artery

RCx – circumflex artery

SSI – SYNTAX score I (Synergy Between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery)

Td – Treponema denticola

Th – helper T-lymphocytes

TLR – toll-like receptors

TNFα – tumor necrosis factor alpha

TnI – troponin I

Treg – regulatory T-lymphocytes

UNC – University of North Carolina

UMBAL – university multiprofile hospital for active treatment

WHO – World Health Organization

I. INTRODUCTION

Cardiovascular diseases are a group of diseases of the heart and blood vessels, including coronary heart disease, cerebrovascular disease, rheumatic heart disease, etc. According to the World Health Organization, cardiovascular diseases are the leading cause of death worldwide, claiming nearly 17.9 million lives annually.

Atherosclerosis is the underlying cause of a large proportion of cardiovascular diseases. Depending on the area affected by atherosclerosis, it can lead to myocardial infarction and angina pectoris (atherosclerosis of the coronary arteries), transient cerebral ischemia and stroke (atherosclerosis of the arteries supplying the central nervous system), gangrene of the extremities (atherosclerosis of the peripheral arteries), ischemia of the internal organs.

Not all manifestations of atherosclerosis are the result of stenosis and occlusion of blood vessels. It can also manifest with ectasia and aneurysmal changes, which occur mainly when the aorta is affected.

Over 80% of deaths from cardiovascular diseases are due to heart attack or stroke, making atherosclerosis the most common cause of mortality in the world. One third of these deaths are in people under 70 years of age.

In Bulgaria, according to data from the National Statistical Institute, the mortality rate for 2022 due to ischemic heart disease (including acute myocardial infarction) and cerebrovascular diseases is 518.8 per 100,000 people. Against the background of the total mortality rate for the same period (1837.8 per 100,000), this is slightly over 28% of deaths in the country.

Periodontitis is a plaque-induced inflammatory-destructive disease involving periodontal tissues (gingiva, periodontal ligament, root cementum and alveolar bone), occurring with loss of clinical attachment level. With the progression of inflammation and destruction, a periodontal pocket is formed, which is the clinical characteristic of periodontitis. Over time, untreated periodontitis leads to increased tooth mobility and ultimately to tooth loss.

According to data from the European Federation of Periodontology, periodontitis is one of the most common diseases worldwide, affecting approximately 743 million people or about 11% of the world's population.

The oral microbiome contains over 1000 species of bacteria. Bacteria from dental plaque (biofilm) are grouped into bacterial complexes, according to their pathogenicity and the time of colonization of the tooth surface. Through the infected soft tissue wall of the pocket, bacteria from the dental biofilm pass into the systemic circulation, causing episodes of transient bacteremia. If the total area of the soft tissues affected by periodontitis is calculated, a wound surface measuring 8 - 20 cm2 is obtained, through which bacteria easily pass into the bloodstream. A patient with periodontitis goes through several episodes of bacteremia daily with a total duration of about 3 hours.

In addition to the bloodstream, periodontal pathogens can be dislocated in areas distant from the oral cavity directly through the digestive tract, as well as moving along the peripheral nerve endings to the central nervous system.

For decades, the relationship between periodontitis and systemic diseases has been discussed in scientific circles. For example, the pathogenetic mechanisms determining the reciprocal

relationship between the severity of periodontitis and glycemic control in diabetes mellitus have been established. Data are accumulating on the involvement of periodontal pathogens in the genesis and development of Alzheimer's disease, depression, rheumatoid arthritis, oral cancer, esophageal cancer, pancreatic cancer, chronic obstructive pulmonary disease, lung cancer, and complicated pregnancy.

It is almost universally believed that there is a relationship between periodontitis and cardiovascular diseases. The idea that periodontitis is an independent risk factor for the development of atherosclerosis and, accordingly, cardiovascular disease is increasingly being advocated. The results of a number of studies support this relationship. However, it has not yet been definitively proven that it is causal.

There are also opponents of this thesis, who unite around the fact that periodontitis and atherosclerosis share common risk factors - age, smoking, diabetes mellitus - which also determine shared comorbidity.

Given the widespread prevalence of periodontitis and atherosclerosis, as well as the high mortality rate due to the latter, proving a causal relationship between them could fundamentally change the approach to the prevention and treatment of atherosclerosis. In addition, it could increase the interest of the population in the prevention and treatment of periodontal diseases.

II. PURPOSE AND OBJECTIVES

The purpose of the dissertation is to establish the relationship between periodontal infection and the severity of coronary symptoms in patients with coronary heart disease.

To achieve this goal, the following tasks of the dissertation were set:

Task 1

To determine what proportion of the studied patients with cardiovascular diseases have periodontal inflammation.

Task 2

To investigate the correlation between infection with Porphyromonas gingivalis, Treponema denticola and Aggregatibacter actinomycetemcomitans and signs of periodontal inflammation.

Task 3

To determine whether the severity of periodontal infection affects the SYNTAX score.

III. OWN RESEARCH

1. Materials and methods

1.1. Materials and methods for task 1

This cross-sectional study was conducted after obtaining permission from the Research Ethics Committee at the Medical University "Prof. Dr. Paraskev Stoyanov", Varna (Appendix 1).

The study subjects were 199 patients, men and women, admitted for diagnosis and treatment at the Second Cardiology Clinic at the University Multi-profile Hospital for Active Treatment "St. Marina", Varna in the period December 2021 - January 2024.

The place of conduct of the study is the Second Cardiology Clinic at the University Hospital "St. Marina", Varna.

Criteria for inclusion in the study: patients aged between 45 and 64 years, who have undergone SKAG and have available natural teeth.

The selected age range was determined to capture the overlapping onset and progression of the conditions studied. The onset of periodontitis usually occurs around the age of 45, which coincides with the clinical manifestation of atherosclerosis in this population. The upper limit of 64 years was set to minimize the influence of additional systemic diseases, which are more common in older age and could affect the results of the study.

Exclusion criteria: age under 45 years; age over 64 years; lack of natural teeth; patients who have not undergone SCAG, anamnestic data for RA.

Upon admission to the clinic, each patient underwent standard blood and urine tests, ECG.

Patients who underwent SCAG were provided with an information leaflet about the purposes of the study and its expected results (Appendix 2). Patients who gave informed consent to participate in the study (Appendix 3) had their gingival index according to Ainamo & Bay, plaque index according to O'Leary and periodontal status recorded in a periodontal chart (Appendix 4)

Instruments used

UNC15 periodontal probe (Aesculap) (Fig. 1). The probe has a black working part and white markings every millimeter from 1 to 15, with white rings between 4 and 5, 9 and 10, 14 and 15 millimeters. The probe has a pressure limiter up to 0.20N.

Fig. 1 – Periodontal probe UNC 15 (Aesculap).

Nabers 1 furcation probe (MEDESY) (Fig. 2) for examining the furcation area of multi-rooted teeth in the upper jaw.

Fig. 2 – Nabers 1 furcation probe (MEDESY).

Nabers 2 furcation probe (MEDESY) (Fig. 3) for examining the furcation area of multi-rooted teeth in the lower jaw.

Fig. 3 – Nabers 2 furcation probe (MEDESY).

Methodology for registering the O'Leary plaque index:

For each tooth, the presence (+) or absence (-) of dental plaque is registered in six areas of the tooth surface:

MV – medio-vestibular;

CV – central-vestibular;

DV – disto-vestibular;

ML – medio-lingual/palatal;

CL – central-lingual/palatal;

DL – disto-lingual/palatal.

The presence of plaque is recorded by scraping the corresponding tooth surface with the tip of the periodontal probe. The index is calculated as a percentage ratio between the surfaces with plaque and the total number of surfaces examined. O'Leary index values above 10% are an indicator of unsatisfactory plaque control by the patient.

Methodology for recording the gingival index according to Ainamo & Bay:

To record the index, the sulcus around each tooth is probed, with the periodontal probe inserted parallel to the tooth surface in constant contact with the tooth until resistance is felt, then, without removing it completely from the sulcus, it is moved in steps of 1 mm medially/distal. After 20 seconds, the presence (+) or absence (-) in the six areas (MV, CV, DV, ML, CL, DL) is recorded. The index is calculated as a percentage ratio between the areas with bleeding and all areas examined. An Ainamo & Bay index value above 10% is considered an indicator of the presence of gingival inflammation.

Methodology for recording periodontal status:

The probing depth (PPD) is the distance measured with a periodontal probe from the edge of the gingiva to the bottom of the gingival sulcus/periodontal pocket. The measurement was performed by inserting the probe into the sulcus/pocket with the working part held parallel to the tooth surface and in constant contact with the latter until resistance was felt. The probe was advanced in a medio-distal direction with a step of 1 mm and a vertical amplitude of 1-2 mm without being completely removed from the sulcus/pocket. In the area of the interdental contacts, the probe was slightly angulated to probe the area below the interdental contact. It was probed around each tooth, and for each of the six areas (MV, CV, MD, ML, CL, DL) the highest measured value was recorded. Intermediate values (1.5 mm, 2.5 mm, etc.) were rounded to the higher number (respectively 2 mm, 3 mm, etc.).

The level of the gingival margin, margo gingivalis (MG), is the distance from the cementoenamel junction to the gingival margin, and was recorded for each of the six areas. Depending on whether the gingival margin is coronal or apical to the ECG, the MG value is recorded with a positive or negative sign, respectively, and 0 when the MG is at the level of the ECG.

Furcations of multi-rooted teeth were examined with furcation probes Nabers 1 for the upper jaw and Nabers 2 for the lower jaw (Fig. 3 and 4). Furcation damage in the horizontal direction was classified according to Hamp, as follows:

F1 – the probe enters up to 3 mm into the furcation;

F2 – the probe enters more than 3 mm without passing the furcation;

F3 – the probe passes through the entire width of the furcation.

Tooth mobility was assessed according to Miller's classification:

0 – physiological tooth mobility;

1 – pathological tooth mobility in the horizontal direction up to 1 mm;

2 – pathological tooth mobility in the horizontal direction more than 1 mm;

3 – tooth mobility in horizontal and vertical directions.

The presence of dental implants and their position was specified based on anamnestic data and findings from the clinical examination.

After registering the periodontal status of the patients, a diagnosis was made in accordance with the current classification of periodontal diseases and conditions.

1.2. Materials and methods for task 2

Object of the study: see Materials and methods for task 1.

Place of conduct: see Materials and methods for task 1.

Criteria for inclusion in the study: see Materials and methods for task 1.

Criteria for exclusion from the study: see Materials and methods for task 1.

To perform task 2, after registering periodontal status, material was taken from each patient for examination of the presence of periodontal pathogens by PET-test (MIP Pharma GmbH) (Fig. 4).

Fig. 4 – Diagnostic kit for periodontal pathogens (PET test).

The following procedure was followed when collecting the samples:

The patient rinses his mouth with clean water, as the presence of blood after probing may compromise the results of the study. Then, a sterile paper pin is inserted into the periodontal pocket, inserted to the bottom and held for 20 seconds. The pin is removed and placed in a sterile container included in the kit.

The areas from which the samples are collected were determined according to the measured probing depth – the areas with the highest PPD.

The sample is pooled – the paper pins from the five areas are collected in a common sterile container. In a form attached to the test (Appendix 5), the patient's data, the depth of the periodontal pockets, their location, the type of sample and the address for receiving the results are filled in.

The material prepared in this way is sent to the MIP Pharma laboratory, where it is tested for the presence of A. actinomycetemcomitans, T. denticola, P. gingivalis and the total number of microorganisms, by real-time polymerase chain reaction (real-time-PCR).

The results obtained for each of the indicated pathogens are expressed as the number of microorganisms and the percentage of the total number of microorganisms (Appendix 4).

The advantages of a PET test are the ability to qualitatively and quantitatively determine the causative agents in the sample, the high sensitivity, and the lack of the need for a special environment for storing and transporting the samples, which reduces the risk of compromising the results.

1.3. Materials and methods for task 3

Object of study: see Materials and methods for task 1.

Place of conduct: see Materials and methods for task 1.

Criteria for inclusion in the study: see Materials and methods for task 1.

Criteria for exclusion from the study: see Materials and methods for task 1.

To perform task 3, after anesthesia and catheter insertion, a contrast agent (Iomeron, Bracco S. p. A.) was injected for visualization of the coronary vessels (Fig. 5). After registration and recording, the angiographic images were analyzed by cardiologists (D. T., R. H. and R. A.) and a SYNTAX score I was calculated for each patient.

Fig. 5 – Angiograph in the Second Cardiology Clinic, Department of Invasive Cardiology at St. Marina University Hospital, Varna.

SYNTAX Score I is a digital tool used in cardiology to assess the complexity of coronary artery lesions (https://syntaxscore.org/calculator/start.htm).

Coronary anatomy is examined angiographically, examining both the left and right coronary arteries simultaneously. The assessment includes any lesion in an arterial vessel with a diameter of ≥ 1.5 mm, in which there is stenosis of the vascular lumen ≥ 50%. Each lesion can include one or more damaged segments. Ideally, the assessment is made by a team of three specialists to reduce the risk of subjectivity.

Depending on the value, the SYNTAX score I is defined as low (0 – 22), medium (23 – 32) and high (≥33). Higher values of the SYNTAX score I are indicative of more complex coronary artery lesions.

SYNTAX score II calculates the 4-year mortality rate after myocardial revascularization based on the SYNTAX score I and additional factors (age, gender, smoking, etc.).

The SYNTAX score (I and II) serves as a guide for choosing a method for myocardial revascularization in patients who are indicated for such.

For the purposes of this study, only the SYNTAX score I was used.

The collected data were analyzed with the statistical software jamovi. Spearman's statistical test was used for the correlation analysis due to the uneven distribution of the data.

2. RESULTS

2.1. Results and analysis of results for task 1

In carrying out task 1, we studied the indicators of general health and periodontal status of the sample.

Table 1 shows the distribution of the main indicators of physical parameters, and in table 2 the same indicators are divided by gender.

	Median	**Min.**	**Max.**	**Q1**	**Q3**
Age	58.0	45.0	64.0	52.0	62.0
Weight (kg)	83.0	43.0	144.0	74.0	95.0
Hight (m)	1.7	1.5	1.9	1.6	1.8
BMI (kg/m^2)	28.7	17.9	47.8	25.8	31.8

Table 1 – Distribution of physical indicators.

	Sex	**Median**	**Min.**	**Max.**	**Q1**	**Q3**
Age	Male	57	45	64	52	61
	Female	58	45	64	51.5	62
Weight (kg)	Male	88.5	57	144	78	100
	Female	74	43	125	65	82.5
Hight (m)	Male	1.75	1.56	1.93	1.7	1.8
	Female	1.62	1.45	1.75	1.57	1.65
BMI (kg/m^2)	Male	28.96	19.2	47.75	26.06	32.13
	Female	27.85	17.9	46.07	25.1	31.2

Table 2 – Distribution of physical indicators by gender.

The results of the study of biochemical indicators are presented in Table 3 and Table 4.

Indicator	**N**	**Missing**	**Median**	**Min.**	**Max.**	**Q1**	**Q3**
Total cholesterol, mmol/L	199	0	4.910	2.450	9.550	4.015	5.935
LDL-C, mmol/L	199	0	2.860	0.610	6.340	2.025	3.730
HDL-C, mmol/L	199	0	1.210	0.590	3.130	1.000	1.420
Triglycerides, mmol/L	199	0	1.500	0.430	17.750	1.035	2.375
CRP, mg/L	194	5	3.005	0.100	149.000	0.900	10.450
TnI, ng/ml	199	0	0.200	0.200	180.000	0.200	0.390
Creatinine,, mcmol/L	199	0	79.000	42.000	262.000	67.000	91.000
eGFR, ml/min/1.73m2	199	0	84.900	21.500	148.500	71.615	98.700

Table 3 – Biochemical indicators.

Indicator	Sex	N	Missing	Median	Min.	Max.	Q1	Q3
Total cholesterol, mmol/L	**Male**	132	0	4.675	2.450	9.55	3.950	5.793
	Female	67	0	5.330	3.010	8.14	4.190	6.140
LDL-C, mmol/L	**Male**	132	0	2.800	0.770	6.34	2.010	3.583
	Female	67	0	3.200	0.610	6.06	2.150	3.925
HDL-C, mmol/L	**Male**	132	0	1.140	0.590	3.13	0.970	1.348
	Female	67	0	1.330	0.820	2.26	1.140	1.510
Triglycerides, mmol/L	**Male**	132	0	1.510	0.430	17.75	1.048	2.368
	Female	67	0	1.440	0.460	9.87	1.025	2.335
CRP, mg/L	**Male**	129	3	3.120	0.120	149.00	0.800	9.800
	Female	65	2	2.870	0.100	51.60	1.300	10.500
TnI, ng/ml	**Male**	132	0	0.200	0.200	180.00	0.200	4.115
	Female	67	0	0.200	0.200	180.00	0.200	0.200
Creatinine, mcmol/L	**Male**	132	0	84.000	55.000	262.00	74.000	101.250
	Female	67	0	66.000	42.000	131.00	57.000	73.000
eGFR, ml/min/1.73m2	**Male**	132	0	85.380	21.500	148.50	67.950	98.882
	Female	67	0	84.220	37.680	140.00	74.300	98.200

Table 4 – Biochemical indicators by gender.

The distribution of patients according to indications for invasive diagnostics is presented in Table 5.

Indicator	**Count**	**Proportion**
Angina pectoris	96	48,2%
Non-ST ACS	50	25,1%
ACS with ST	37	18,6%
Valve prosthesis	14	7,0%
AP+VP	2	1,0%

Table 5 – Distribution of patients according to indications for invasive diagnostics.

Table 6 presents the distribution of patients by number and as a share of the total number depending on the stage of periodontitis. Table 7 presents the results of the study of PI, BoP and periodontal status.

Stage of periodontitis	Count	Total count	Proportion
1	4	199	2.0%
2	44	199	22.1%
3	41	199	20.6%
4	108	199	54.3%
0	2	199	1.0%

Table 6 – Grouping of patients depending on the stage of periodontitis.

Indicator	Count	Missing	Median	Min.	Max.	Q1	Q3
BoP, %	199	0	100.00	5.00	100.00	73.500	100.00
PI, %	199	0	100.00	10.00	100.00	98.000	100.00
Number of teeth with BoP & PPD over 5 mm	199	0	4.00	0.00	30.00	1.000	10.00
Number of multi-rooted teeth	199	0	4	0	12	2.000	7.00
Number of teeth available	199	0	21.00	1.00	32.00	14.000	26.00
Mean PPD, mm	199	0	4.50	1.83	11.50	3.833	5.50
Mean CAL, mm	199	0	-5.83	-18.33	-1.83	-7.833	-4.25

Table 7 – Results of PI, BoP and periodontal status examination.

A comparison between the mean CAL values by tooth groups is presented in Table 8.

Indicator		Patients N	Median	Min.	Max.	Q1	Q3
CAL,mm	Average value in the most affected area of the dentition	199	-5.83	-18.3	-1.83	-7.83	-4.25
	Anterior teeth	59	-6.0	-14.3	-1.83	-7.92	-4.67
	Premolars	31	-6.5	-11.0	-2.17	-9.25	-4.67
	Molars	97	-5.5	-18.3	-2.67	-6.83	-3.83
	3rd molars	12	-5.08	-12.3	-2.17	-8.38	-4.46

Table 8 – CAL values in the areas with the greatest involvement among patients and by tooth groups.

Tables 9 and 10 present the results of the study of multi-rooted teeth.

Presence of multi-rooted teeth	Patients N	Share
No	33	16,6%
Yes	166	83,4%

Table 9 – Presence of multi-rooted teeth among the patients in the sample.

Class of furcation involvement	Presence	Patients N	Patients with multi-rooted teeth	Share
F1	NO	137	166	82,5%
	YES	29		17,5%
F2	NO	144		86,7%
	YES	22		13,3%
F3	NO	152		91,6%
	YES	14		8,4%

Table 10 – Degree of furcation involvement among patients with multi-rooted teeth in the sample.

Analysis of the demographic characteristics of the study population showed that approximately two-thirds of the patients were male (Fig. 6). The study of Body Mass Index (BMI) revealed a trend towards overweight and obesity in both sexes (Fig. 7).

Fig. 6 – Distribution of patients by gender.

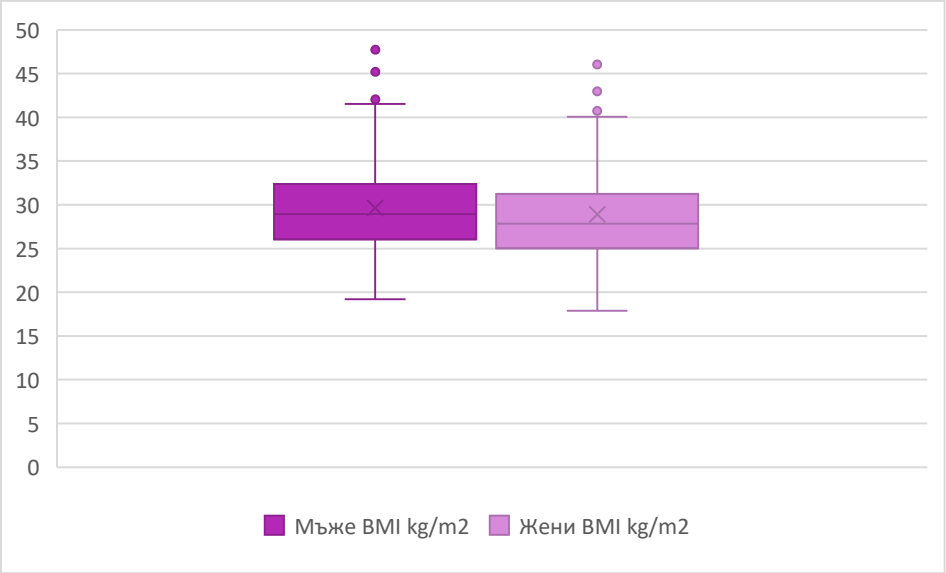

Fig. 7 – Comparison of body mass index (BMI) between men and women.

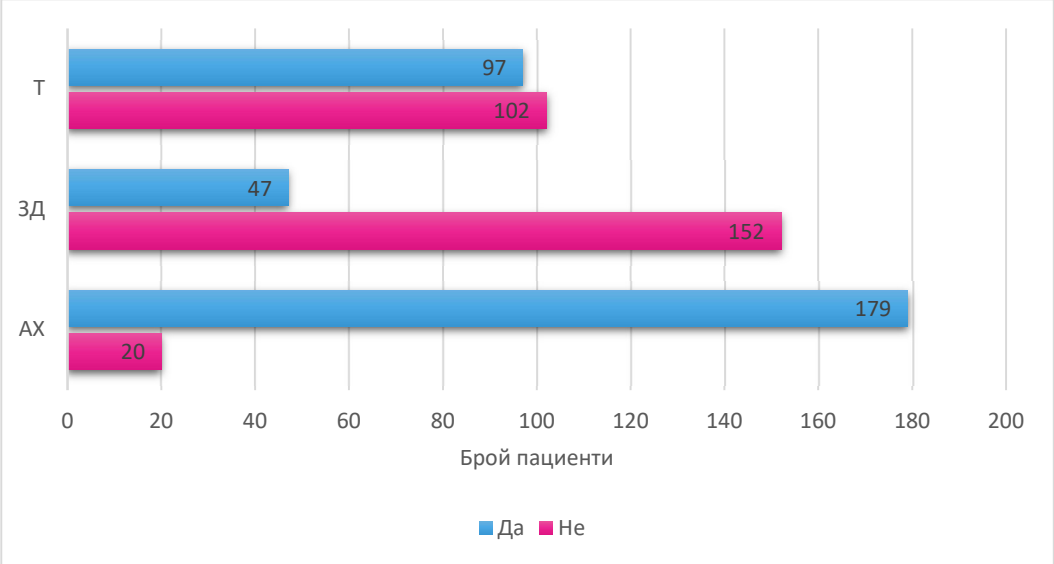

Fig. 8 – Distribution of smoking (T), diabetes mellitus (DM) and arterial hypertension (AH) among patients.

Special attention was paid to the lipid profile of the patients. In Fig. 9, individual values of total cholesterol (TC) are presented. The purple and blue lines indicate the upper limit of normal values (5.2 mmol/L) and the high-risk threshold (6.2 mmol/L), respectively. Most patients showed TC values within the reference range, suggesting that dyslipidemia is not a universally expressed risk factor in this population.

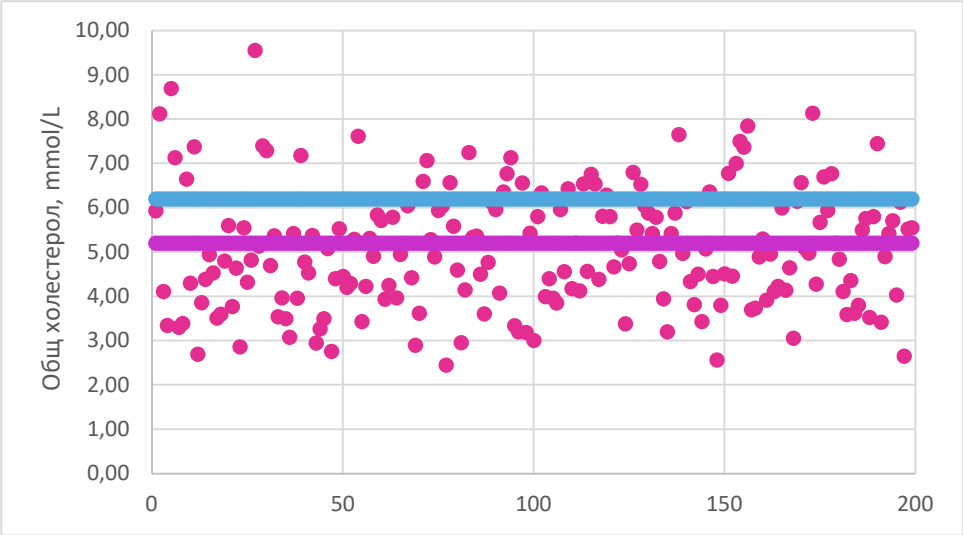

Fig. 9 – Total cholesterol values among patients.

A separate analysis was also performed on the levels of HDL-cholesterol (HDL-C), which has a protective effect on the cardiovascular system. For men, values below 1.0 mmol/L, and for women below 1.2 mmol/L, are considered unfavorable. The data presented in Fig. 10 and Fig. 11 show that the majority of patients of both sexes have HDL-C levels above the minimum acceptable values, which partly explains the moderate lipid risk in this group of patients.

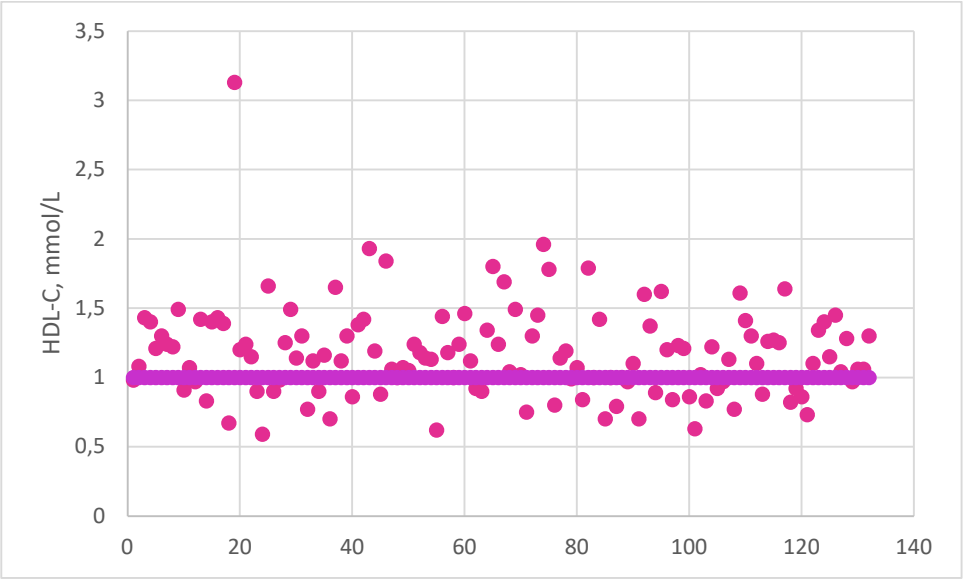

Fig. 10 – High-density cholesterol values in men in the sample.

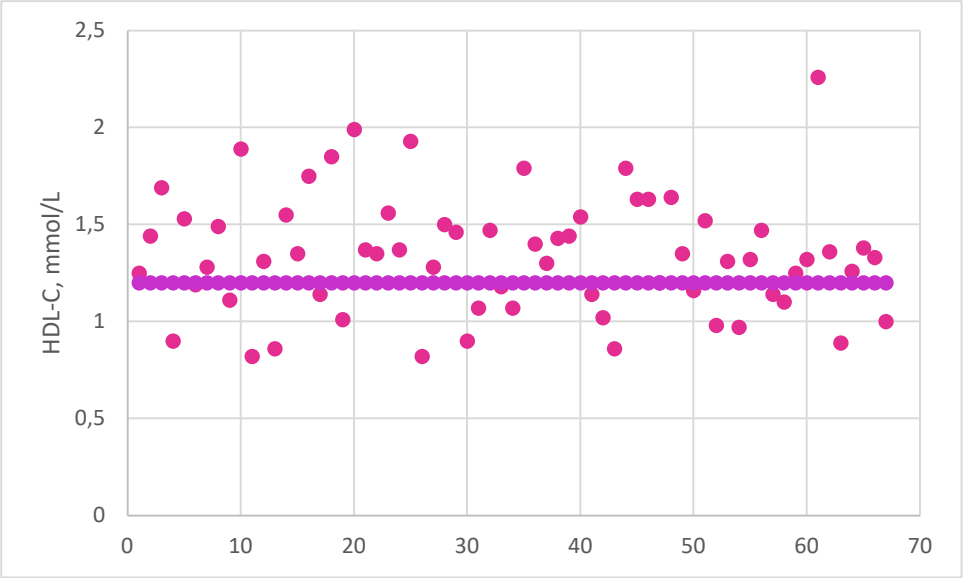

Fig. 11 – High-density cholesterol values among women in the sample.

The ratio of total cholesterol to HDL-C (TC/HDL-C) is considered a more reliable predictor of cardiovascular risk than the absolute values of individual lipid fractions. Individual values of this ratio are presented in Fig. 12. The reference value for low risk is < 3.5 (indicated by the purple line). The analysis shows that 60 of the patients fall into the low-risk category, while the rest show moderate to high risk, with only 24 patients demonstrating high values correlating with increased atherogenic risk.

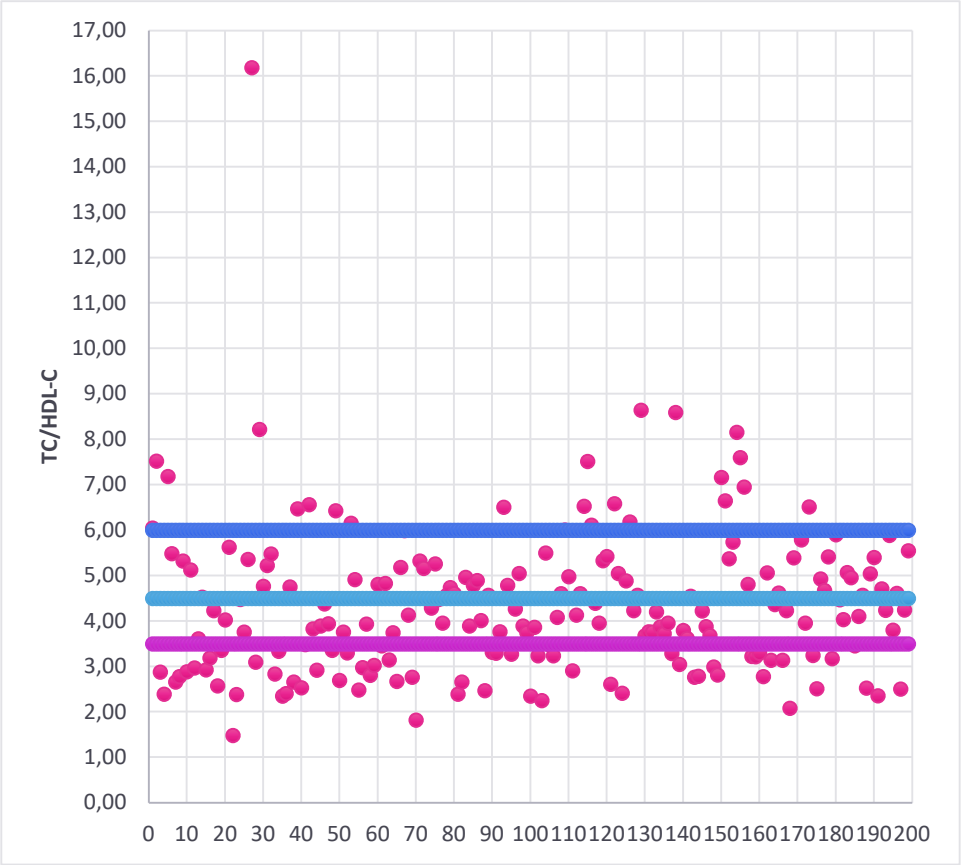

Fig. 12 – Relationship between total cholesterol and high-density cholesterol levels among patients.

The largest number of patients were admitted for diagnosis due to clinical symptoms related to stable angina pectoris, followed by acute coronary syndromes, respectively without and with ST-interval elevation on ECG. The smallest number among the cohort were patients with prosthetic valves (Fig. 13).

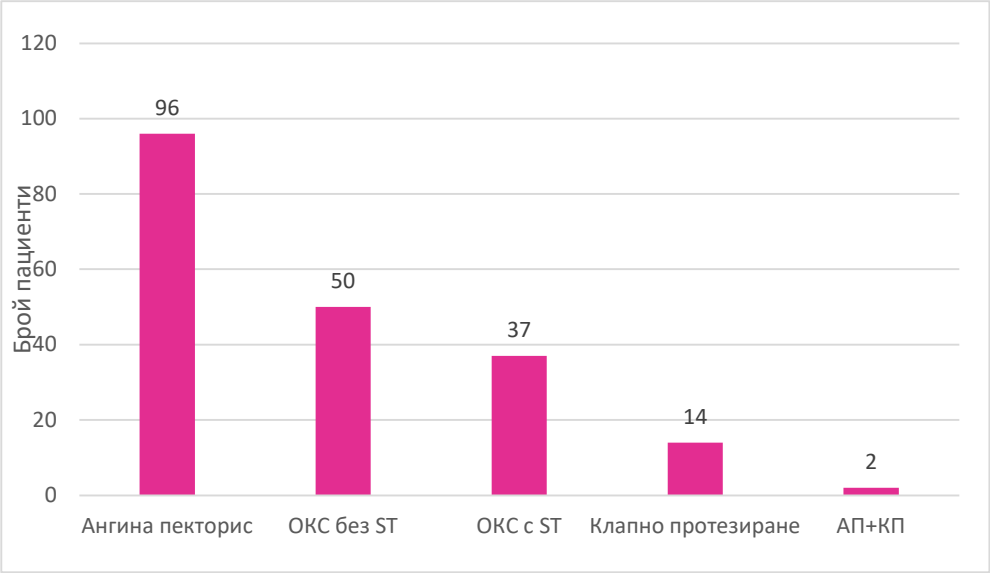

Fig. 13 – Indications for invasive diagnostics. ACS – acute coronary syndrome; ST – electrocardiogram segment; AP – angina pectoris; VP – prosthetic valve.

От изследваните 199 пациенти двама са без пародонтит, а 149 са с тежък пародонтит (приблизително 2/3 от изследваната корта) (Фиг. 14).

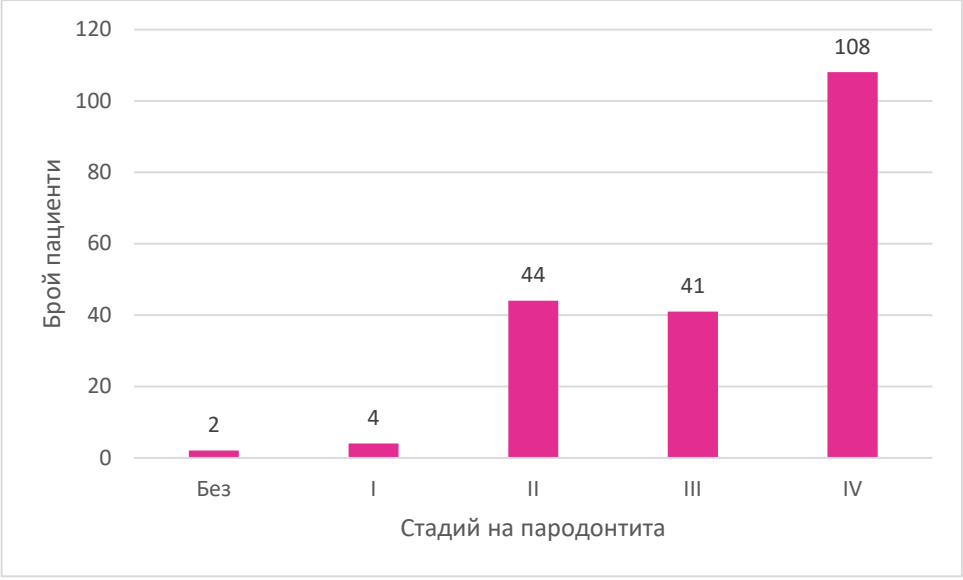

Fig. 14 – Number of patients depending on the stage of periodontitis.

Analysis of the results of the gingival and plaque index study showed generalized plaque-induced inflammation of the gingival tissues in almost all representatives of the sample (Fig. 15).

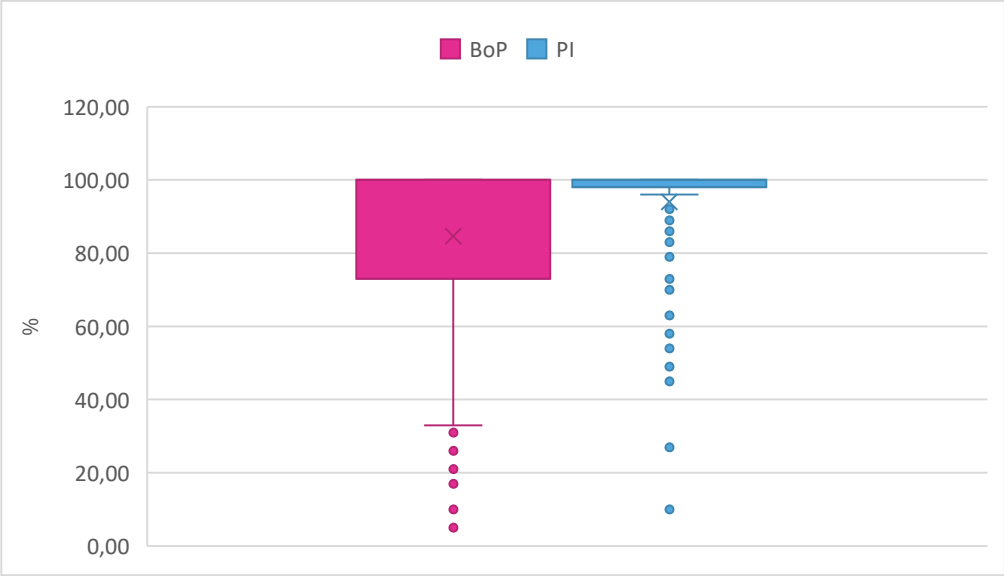

Fig. 15 – Boxplot diagram presenting the values of BoP – bleeding on probing and PI – plaque index among patients.

The study of CAL in groups of teeth showed the premolars to be most affected, with differences between groups not being statistically significant ($p > 0.05$) (Fig. 16).

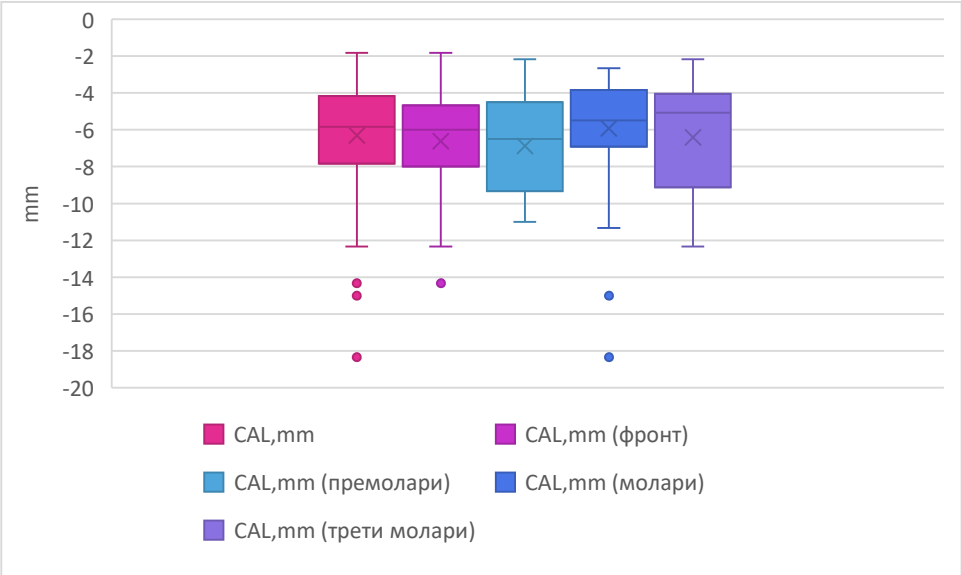

Fig. 16 – Box Plot diagram of the results of CA values by tooth groups.

Furcation involvement was observed in approximately 1/3 of patients with existing multi-rooted teeth (n = 166) (Fig. 17).

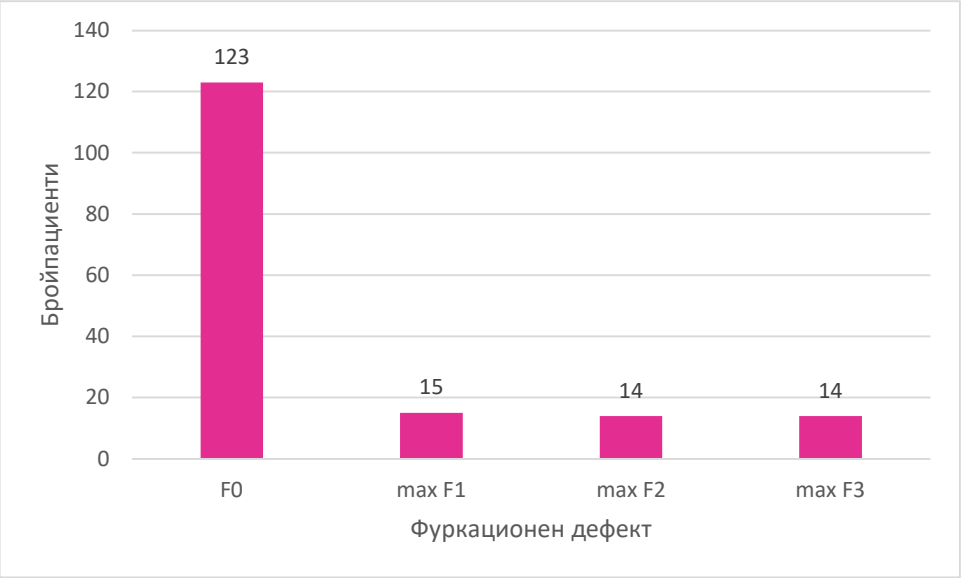

Fig. 17 – Number of patients depending on the highest recorded class of furcation involvement.

2.2. Results and analysis of the results of task 2

In carrying out task 2, we studied the presence of certain bacterial species, as well as the total microbial load among the patients in the sample, and what are the dependencies between the respective bacterial species and the individual indicators of periodontal destruction.

The results of the study on the presence of periodontal pathogens and their quantity are presented in Tables 11 and 12, respectively.

Indicator		**Patients N**	**Total number of patients**	**Proportion**
Presence of Aa	NO	184	199	92,5%
	YES	15		7,5%
Presence of Pg	NO	38		19,1%
	YES	161		80,9%
Presence of Td	NO	22		11,1%
	YES	177		88,9%

Table 11 – Presence of Aggregatibacter actinomycetemcomitans (Aa), Porphyromonas gingivalis (Pg) and Treponema denticola (Td) among the patients in the sample.

Species	Patients N	Median	Min.	Max.	Q1	Q3
Aggregatibacter actinomycetemcomitans	199	0.00	0.00	6.2×10^5	0.00	0.00
Porphyromonas gingivalis	199	7.5×10^4	0.00	1.4×10^7	9.95×10^2	4.2×10^5
Treponema denticola	199	1.5×10^5	0.00	4.1×10^6	2.55×10^4	4.7×10^5
Total microbial count	199	6.6×10^9	4.7×10^3	3.5×10^{14}	1.2×10^9	4.9×10^{10}

Table 12 – Quantity of microorganisms by type of periodontal pathogens studied and by total number of microorganisms among patients.

Table 13 presents the results of the study of the microbiological profile of the patients in the sample, and Table 14 presents the distribution of the microbiological profile among the patients depending on the stage of periodontitis.

Microbiological profile	**Patients N**	**Proportion**
None of the species investigated	12	6,03%
All of the investigated species	12	6,03%
Only Pg	8	4,02%
Only Aa	2	1,01%
Only Td	23	11,56%
Aa+Td	1	0,50%
Td+Pg	141	70,85%
Aa + Pg	0	0,00%

Table 13 – Microbiological profile of the studied patients.

Microbiological profile	**Stage of periodontits**					**Total**
	I	**II**	**III**	**IV**	**No periodontitis**	
None of the examined	1	4	1	6	0	12
All of the examined	0	0	4	8	0	12
Only Pg	0	4	1	3	0	8
Only Aa	0	0	0	2	0	2
Only Td	0	8	4	10	1	23
Aa+Td	0	0	1	0	0	1
Td+Pg	3	28	30	79	1	141
Total	4	44	41	108	2	199

Table 14 – Microbiological profile of patients depending on the stage of periodontitis.

Table 15 presents the results of the correlation study between individual microorganisms.

Species	**Aggregatibacter actinomycetemcomitans**	**Porphyromonas gingivalis**		**Treponema denticola**		**Total microbial count**	
Aggregatibacter actinomycetemcomitans		**Spearman's rho**	**p-value**	**Spearman's rho**	**p-value**	**Spearman's rho**	**p-value**
		0.023	0.745	-0.020	0.781	0.093	0.190
Porphyromonas gingivalis				0.479***	<.001	0.001	0.988
Treponema denticola						0.224**	0.001

Table 15 – Correlation between individual microorganisms (MO).

The average CAL value depending on the number of isolated periodontal pathogenic species is shown in Table 16.

Number of species	**Number of patients**	**Mean CAL, mm**	**Standard deviation**
None of the examined	12	-5,25	2,21
One of the examined	33	-5,35	2,04
Two of the examined	142	-6,53	2,84
All of the examined	12	-7,36	2,12

Table 16 – Average CAL value depending on the number of isolated periodontal pathogen species (N = number of patients).

The results of the study on the correlation between indicators of periodontitis severity and the amount of microorganisms are presented in Table 17.

Indicator	Aggregatibacter actinomycetemcomitans		Porphyromonas gingivalis		Treponema denticola		Total microbial count	
	Spearman's rho	p-value	Spearman's rho	p-value	Spearman's rho	p-value	Spearman's rho	p-value
BoP, %	0.016	0.827	0.076	0.289	0.210**	0.003	0.302***	<.001
Mean PPD, mm	0.100	0.160	0.186**	0.008	0.280***	<.001	0.031	0.659
Mean CAL, mm	-0.150*	0.035	-0.191**	0.007	-0.268***	<.001	-0.031	0.659
Number of teeth with Bop and PPD > 5 mm	0.118	0.097	0.192**	0.007	0.326***	<.001	0.110	0.120
Stage of pariodontitis	0.112	0.117	0.162*	0.022	0.259***	<.001	-0.055	0.443

Table 17 – Correlation analysis between periodontal disease indicators and the amount of microorganisms.

The most frequently isolated periodontal pathogen among patients was T. denticola, followed by P. gingivalis and A. actinomycetemcomitans (Fig. 18).

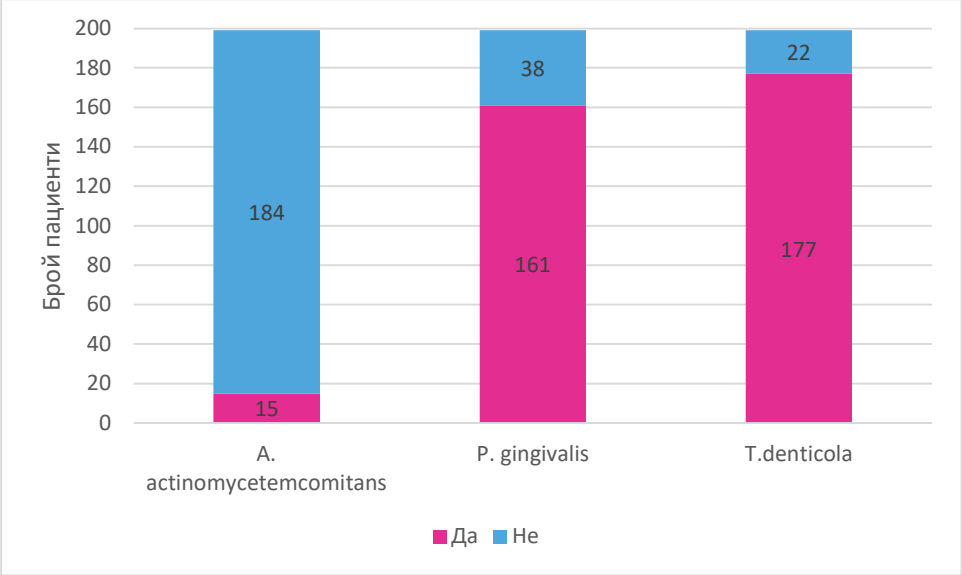

Fig. 18 – Presence of the studied periodontal pathogens among the patients.

Further analysis of the co-occurrence of these microorganisms showed that in the largest number of patients (n = 153) T. denticola was found together with P. gingivalis (Fig. 19), suggesting a functional and etiological relationship between the two pathogens. Of the 15 cases of isolation of A. actinomycetemcomitans, 13 were found to be co-infected with at least one member of the red complex, supporting the hypothesis of synergism between Aa and other key pathogens in advanced periodontal infection.

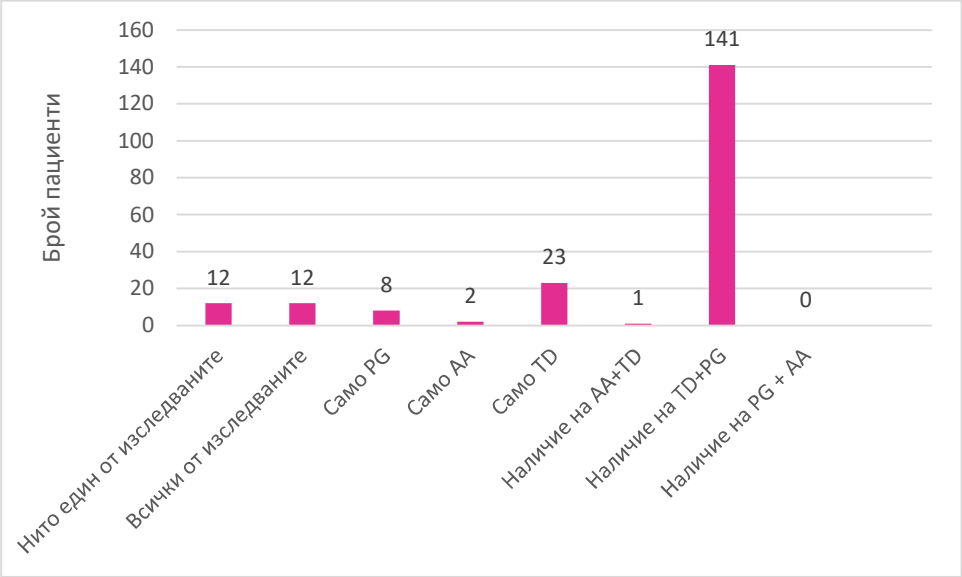

Fig. 19 – Combinations of periodontal pathogens isolated among the sample representatives (AA – Aggregatibacter actinomycetemcomitans, PG – Porphyromonas gingivalis, TD – Treponema denticola).

At the statistical analysis level, a moderate positive correlation was found between the presence of T. denticola and P. gingivalis ($\rho > 0.3$; $p < 0.001$), demonstrating a stable association between these two microorganisms within the oral microbiome (Fig. 20).

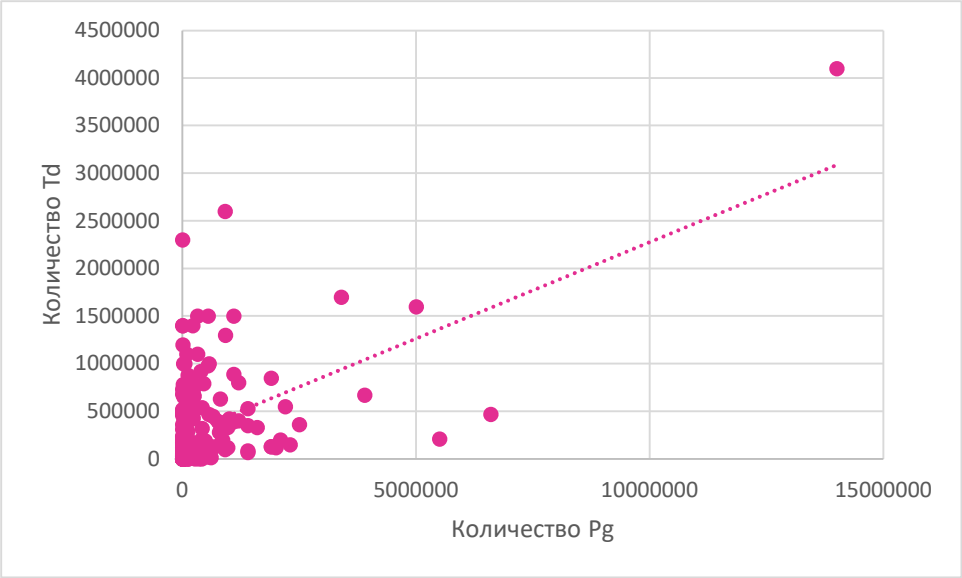

Fig. 20 – Correlation between the amount of P. gingivalis and T. denticola.

To investigate the clinical significance of the microbiological profile, the correlation between the amount of pathogens and clinical indicators of periodontal status, including the Bleeding on Probing (BoP) indicator, was analyzed. A significant positive correlation was found between the BoP value and the amount of T. denticola ($\rho = 0.210$, $p = 0.003$) as well as with the total amount of microorganisms ($\rho = 0.302$, $p < 0.001$) (Fig. 21 and 22).

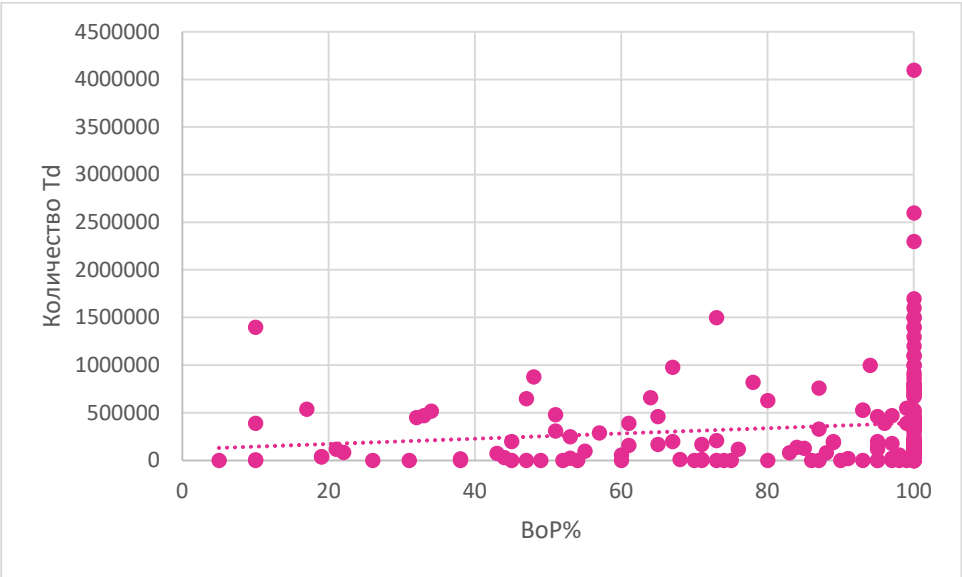

Fig. 21 – Correlation between the value of the Ainamo & Bay index and T. denticola.

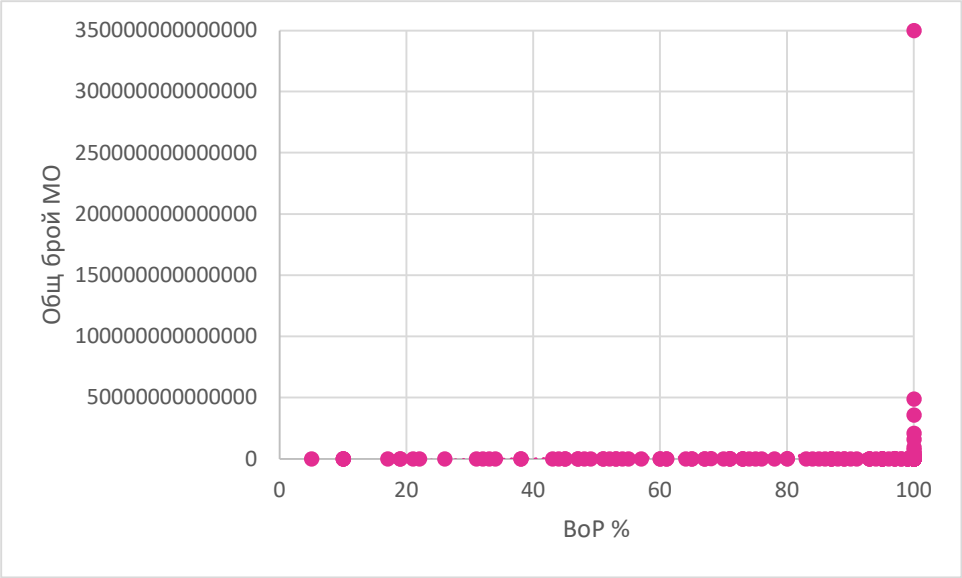

Fig. 22 – Correlation between the value of the Ainamo & Bay index and the total amount of microorganisms (MO).

Further analysis revealed a weak but statistically significant positive correlation between mean probing pocket depth (PPD) and the amount of P. gingivalis and T. denticola ($\rho = 0.186$, $p = 0.008$ and $\rho = 0.280$, $p < 0.001$ respectively) (Fig. 23 and 24).

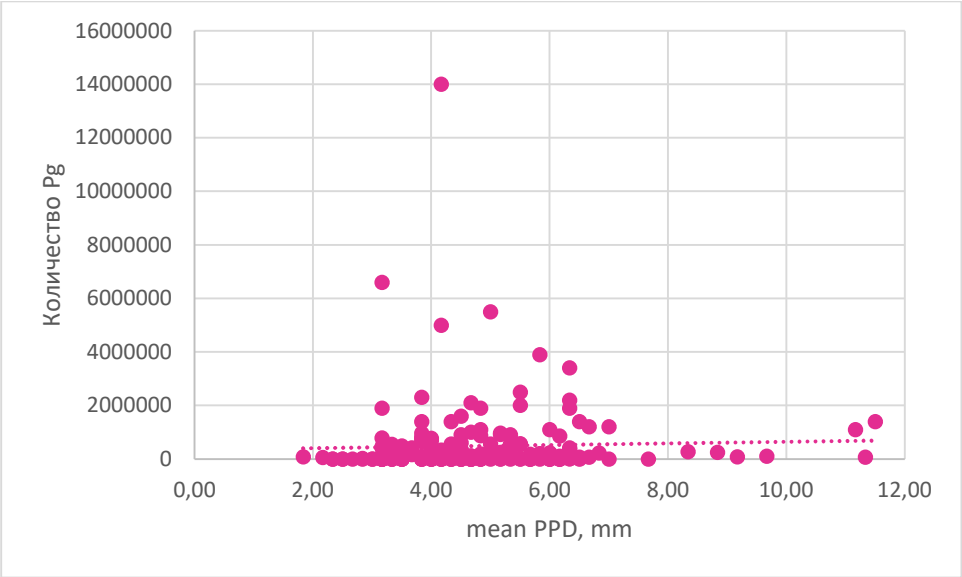

Fig. 23 – Correlation between the mean PPD value and the amount of P. gingivalis (Pg) in subgingival plaque.

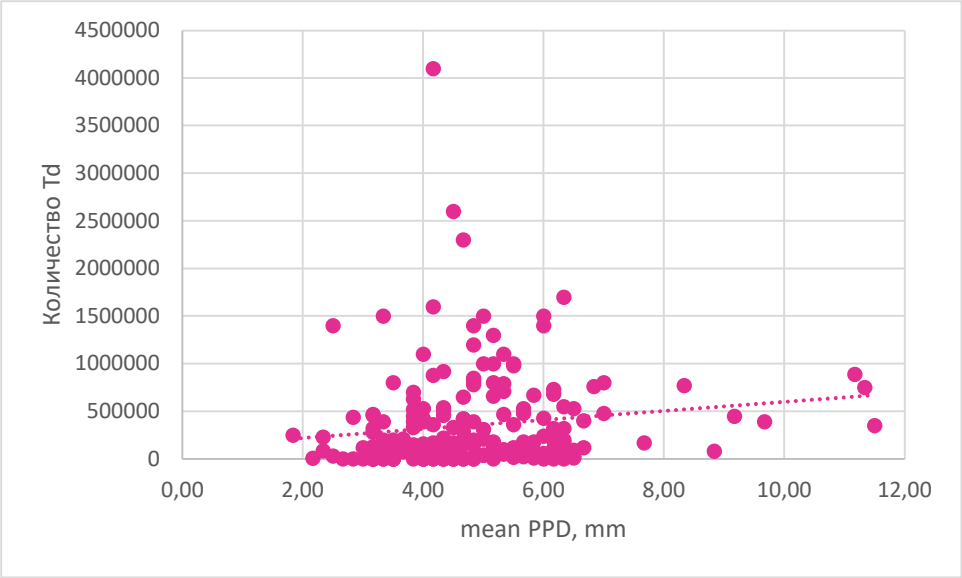

Fig. 24 – Correlation between the mean PPD value and the amount of Td in subgingival plaque.

The correlation analysis between the mean clinical attachment loss (CAL) and microbial parameters showed a negative statistically significant relationship between CAL and the amount of A. actinomycetemcomitans ($\rho = -0.150$, $p < 0.035$), P. gingivalis ($\rho = -0.191$, $p = 0.007$) and T. denticola ($\rho = -0.268$, $p < 0.001$) (Figure 25 – 27).

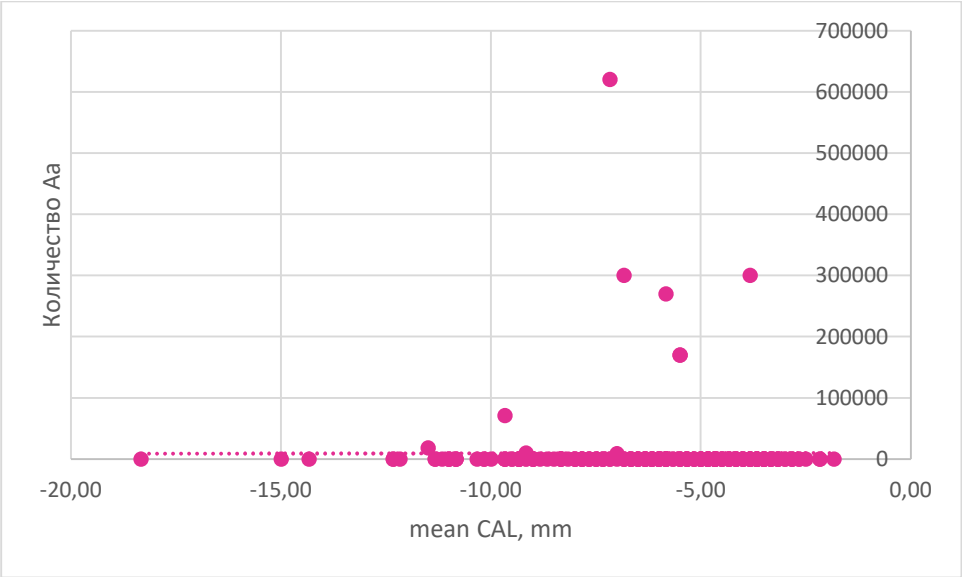

Fig. 25 – Correlation between the mean CAL value and the amount of Aa in subgingival plaque.

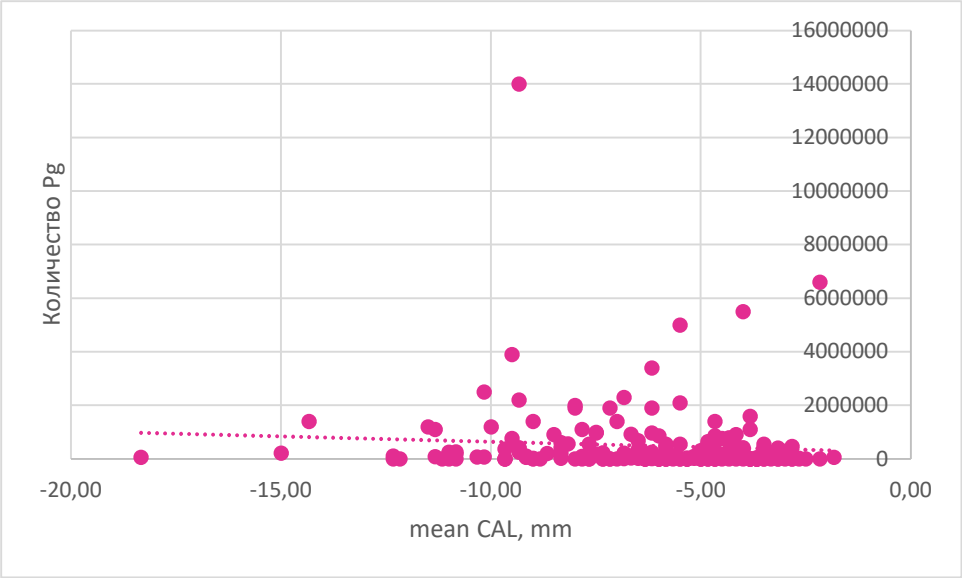

Fig. 26 – Correlation between the mean CAL value and the amount of Pg in subgingival plaque.

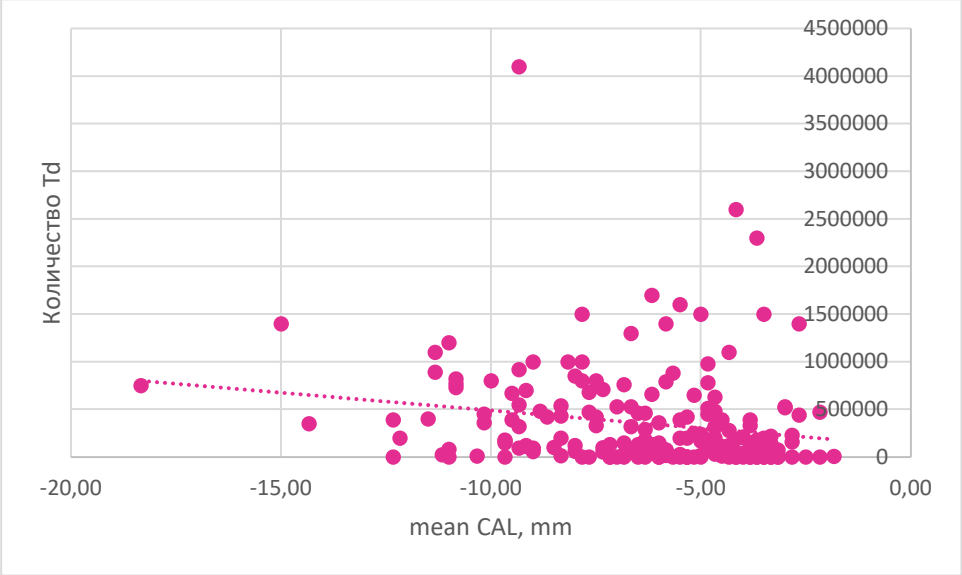

Fig. 27 – Correlation between the mean CAL value and the amount of Td in subgingival plaque.

This relationship means that higher levels of these pathogens are associated with greater attachment loss, which is a clinical marker of advanced periodontal destruction. No such correlation was found for total microbial counts, highlighting that in the presence of tissue-structural loss, the stage of periodontal progression is more closely related to the presence of specific, highly virulent species than to the total microbial mass.

The levels of T. denticola and P. gingivalis in subgingival plaque correlated positively with the number of teeth affected by deep periodontal pockets (PPD > 5 mm) as well as with the overall severity of the disease (Figure 28 – 31).

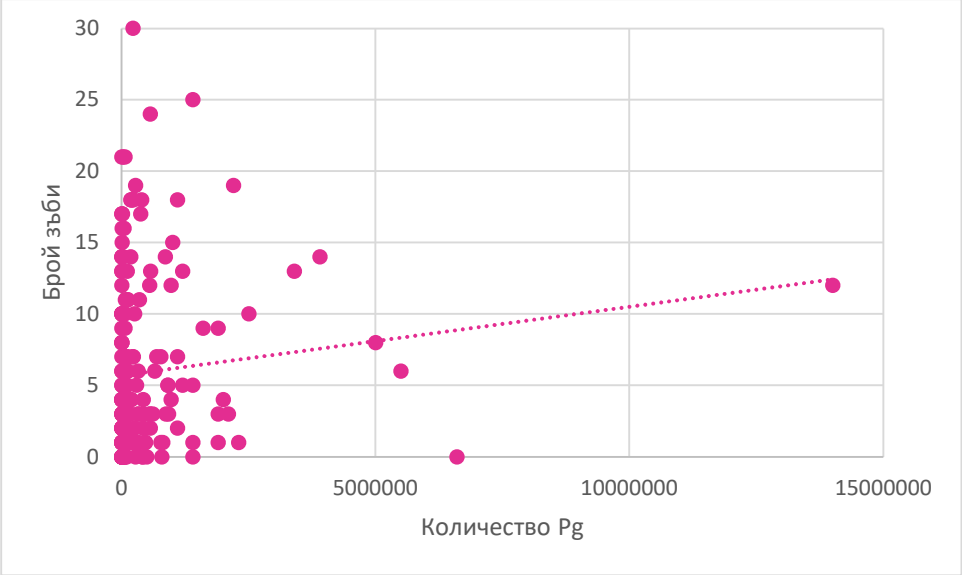

Fig. 28 – Correlation between the number of teeth with deep periodontitis and the amount of Pg in the subgingival plaque.

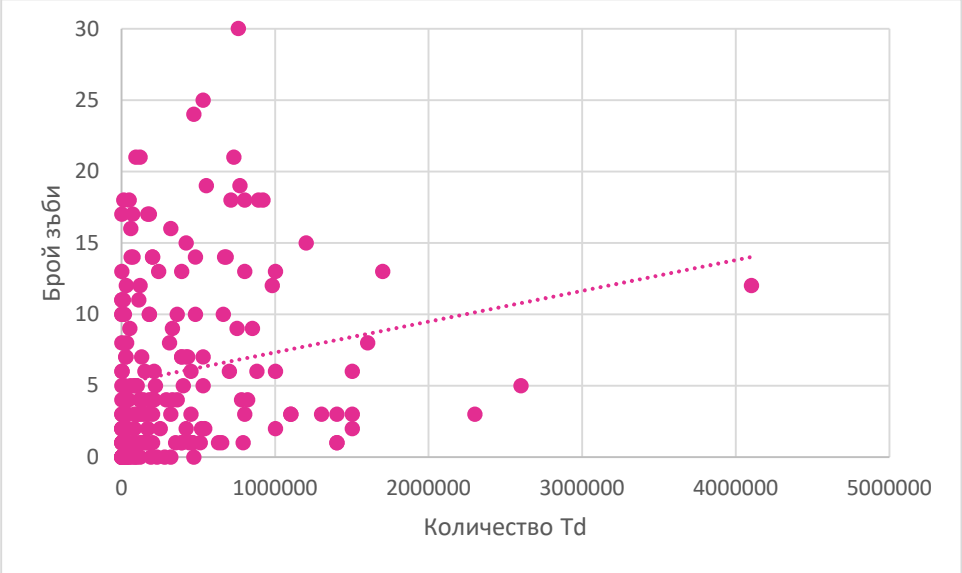

Fig. 29 – Correlation between the number of teeth with deep periodontitis and the amount and Td in subgingival plaque.

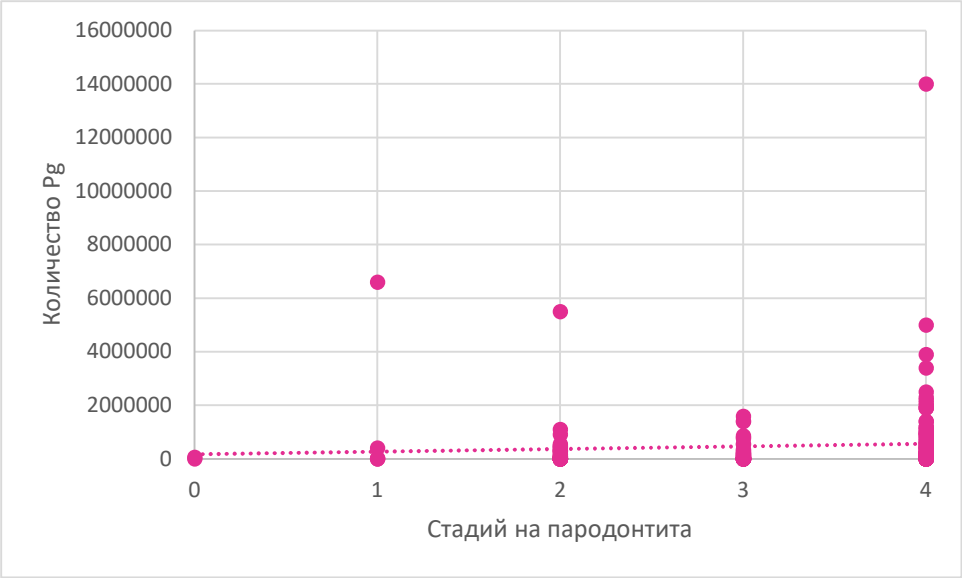

Fig. 30 – Correlation between the severity of periodontitis and the amount of Pg in subgingival plaque.

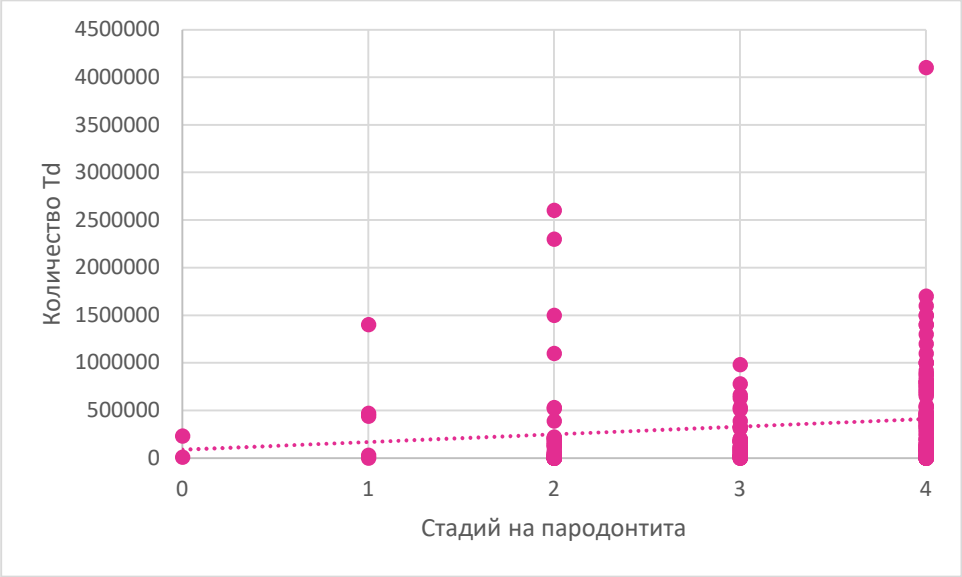

Fig. 31 – Correlation between the severity of periodontitis and the amount of Td in subgingival plaque.

The results of the comparative analysis of the mean values of clinical attachment loss (CAL) depending on the number of isolated periodontal pathogens showed a statistically significant difference between the groups ($p < 0.05$), indicating that the species diversity of the pathogens has a significant impact on the degree of periodontal damage. Greater attachment loss was

observed with an increase in the number of isolated periodontal pathogens, which is clearly visualized in Fig. 32.

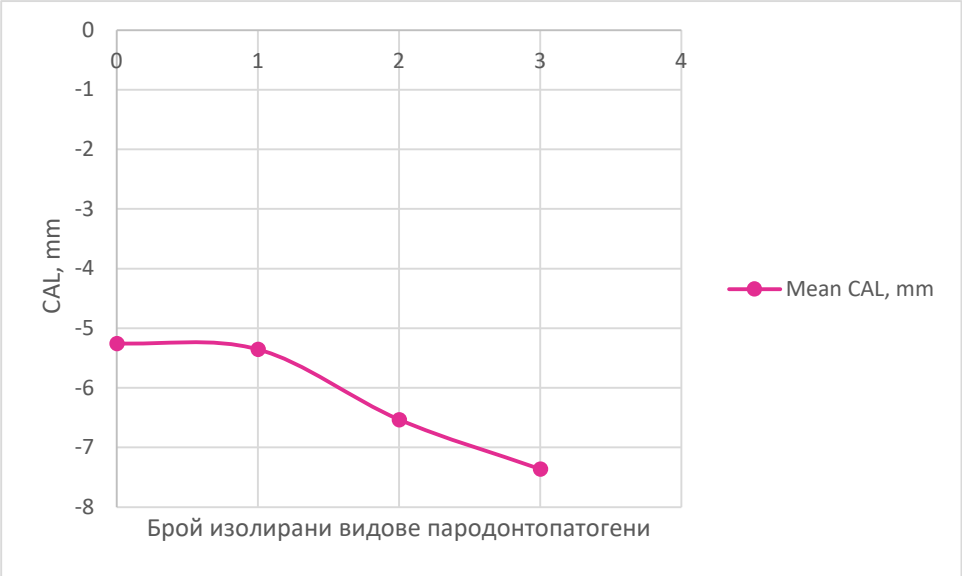

Fig. 32 – Decrease in the average CAL value depending on the number of isolated periodontal pathogens.

2.3. Results and analysis of the results of task 3

Within the framework of the implementation of task 3, a targeted analysis of the frequency and distribution of coronary pathology among the studied patients was conducted, with a focus on stenotic and thrombotic changes in the coronary arteries. Additionally, possible relationships between the microbiological profile of the subgingival flora, clinical periodontal status and the severity of coronary disease were investigated, in order to identify potential biological mechanisms linking chronic periodontal inflammation with atherosclerotic processes in the cardiovascular system.

The study of the coronary arteries gave the following results presented in tables 18 – 21.

Indicator	Yes	No
Thrombosis	35	164
Slow flow	7	192
Diffuse coronary artery disease	26	173
Atonic changes	14	185
Stenosis	152	47

Table 18 – Presence of coronary pathology.

Indicator	Patients	Missing	Median	Min.	Max.	Q1	Q3
LM max %	199	0	0	0	100	0.00	0.0
LAD max %	199	0	20	0	100	0.00	80.0
RCx max %	197	2	0	0	100	0.00	50.0
RCA max %	199	0	20	0	100	0.00	70.0
SSI	199	0	5.00	0.00	61.0	0.00	16.0

Table 19 – Results of the study for arterial stenosis of individual branches of the coronary arteries and severity of SSI.

Indicator	Severe periodontitis	Patients	Missing	Median	Min.	Max.	Q1	Q3
LM max %	**Yes**	149	0	0	0	100	0.00	0.0
	No	50	0	0.00	0	60	0.00	0.0
LAD max %	**Yes**	149	0	40	0	100	0.00	80.0
	No	50	0	20.00	0	100	0.00	57.5
RCx max %	**Yes**	147	2	20	0	100	0.00	50.0
	No	50	0	0.00	0	100	0.00	20.0
RCA max %	**Yes**	149	0	20	0	100	0.00	75.0
	No	50	0	0.00	0	100	0.00	35.0
SSI	**Yes**	149	0	7.00	0.00	61.0	0.00	18.05
	No	50	0	0.00	0.00	32.0	0.00	10.08

Table 20 – Presence of stenosis of the branches of the coronary arteries and severity of SSI depending on the presence of severe periodontitis (stage III and IV).

Indicator	Stage of periodontitis	Patients	Missing	Median	Min.	Max.	Q1	Q3
LM max %	0	2	0	0.00	0	0	0.00	0.00
	1	5	0	0	0	0	0.00	0.00
	2	43	0	0	0	60	0.00	0.00
	3	41	0	0	0	60	0.00	0.00
	4	108	0	0.00	0	100	0.00	0.00
LAD max %	0	2	0	10.00	0	20	5.00	15.00
	1	5	0	20	0	40	0.00	30.00
	2	43	0	20	0	100	0.00	65.00
	3	41	0	20	0	100	0.00	80.00
	4	108	0	40.00	0	100	0.00	80.00
RCx max %	0	2	0	50.00	20	80	35.00	65.00
	1	5	0	0	0	20	0.00	20.00
	2	43	0	0	0	100	0.00	30.00
	3	40	1	0.00	0	100	0.00	42.50
	4	107	1	20	0	100	0.00	55.00
RCA max %	0	2	0	47.50	20	75	33.75	61.25
	1	5	0	0	0	20	0.00	20.00
	2	43	0	0	0	100	0.00	45.00
	3	41	0	0	0	100	0.00	70.00
	4	108	0	20.00	0	100	0.00	75.00
SSI	0	2	0	6.00	5.00	7.00	5.50	6.50
	1	5	0	0.00	0.00	0.00	0.00	0.00
	2	43	0	1.00	0.00	32.00	0.00	13.00
	3	41	0	0.00	0.00	53.50	0.00	19.00
	4	108	0	7.50	0.00	61.00	0.00	18.13

Table 21 – Presence of stenosis of the branches of the coronary arteries and severity of SSI depending on the stage of periodontitis.

The results of the study of the correlation between indicators of periodontal disease and indicators of coronary artery damage are presented in Table 22.

Indicator	BoP, %		Number of teeth with BoP & PPD > 5 mm		Mean PPD, mm		Mean CAL, mm		Periodontitis (stage)	
	Spearman's rho	p-value	Spearman's rho	p-value	Spearman's rho	p-value	Spearman's rho	p-value	Spearman's rho	p-value
LM max %	0.100	0.158	0.180*	0.011	0.011	0.877	-0.116	0.103	0.147*	0.038
LAD max %	-0.062	0.386	0.037	0.601	-0.011	0.873	-0.177	0.013	0.167*	0.018
RCx max %	-0.085	0.235	0.038	0.599	0.017	0.807	-0.113	0.113	0.116	0.104
RCA max %	0.042	0.553	0.094	0.187	0.092	0.194	-0.201**	0.004	0.166*	0.019
SSI	-0.098	0.167	0.073	0.303	0.062	0.383	-0.199**	0.005	0.166*	0.019

Table 22 – Study of the correlation between periodontal disease indicators and the presence of coronary obstruction.

The results of the analysis of the correlation between the amount of microorganisms and the severity of CAD are presented in Table 23.

Indicator	Aggregatibacter actinomycetemcomitans		Porphyromonas gingivalis		Treponema denticola		Total microbial count	
	Spearman's rho	p-value	Spearman's rho	p-value	Spearman's rho	p-value	Spearman's rho	p-value
LM max %	0.138	0.052	-0.020	0.774	0.108	0.129	0.035	0.620
LAD max %	0.081	0.256	0.065	0.363	-0.021	0.764	0.069	0.336
RCx max %	-0.008	0.906	-0.039	0.583	-0.050	0.489	-0.062	0.390
RCA max %	0.098	0.166	0.009	0.903	0.066	0.356	-0.073	0.304
SSI	0.098	0.168	0.036	0.612	-0.006	0.935	-0.074	0.300

Table 23 – Results of the study of the correlation between the amount of microorganisms and the severity of coronary artery stenosis.

Table 24 presents the results of the analysis of the association between the severity of periodontal disease and the presence of coronary artery stenosis.

Periodontitis (stage)		Presence of stenosis		Total	χ^2	df	p
		No	Yes				
0	Number	0	2	2	14.4	4	0.006
	%	0.0 %	1.3 %	1.0 %			
1	Number	2	2	4			
	%	4.3 %	1.3 %	2.0 %			
2	Number	12	32	44			
	%	25.5 %	21.1 %	22.1 %			
3	Number	17	24	41			
	%	36.2 %	15.8 %	20.6 %			
4	Number	16	92	108			
	%	34.0 %	60.5 %	54.3 %			
Total	Number	47	152	199			
	%	100.0 %	100.0 %	100.0 %			

Table 24 – Study of the association between the presence of coronary artery stenosis and the severity of periodontitis.

We examined whether the presence of severe periodontitis was associated with the presence of coronary thrombosis and diffuse coronary artery disease among patients. The results are presented in Table 25 and Table 26.

Severe periodontitis	Thrombosis		Total	χ^2	df	p
	No	Yes				
Yes	122	27	149	0.116	1	0.733
No	42	8	50			
Total	164	35	199			

Table 25 – Results of the study of the association between the presence of severe periodontitis and the presence of coronary artery thrombosis.

Severe periodontitis	Diffuse CAD		Total	χ^2	df	p
	No	Yes				
Yes	127	22	149	1.51	1	0.219
No	46	4	50			
Total	173	26	199			

Table 26 – Results of the study of the association between the presence of severe periodontitis and diffuse disease.

Table 27 presents the results of the study of the correlation between the severity of coronary obstruction measured by SSI and the levels of CRP and TnI.

Table 28 presents the results of the study of the correlation between CRP and indicators of periodontal inflammation.

Indicator	Troponin I		CRP	
	Spearman's rho	p-value	Spearman's rho	p-value
SSI	0.527***	<.001	0.341***	<.001

Table 27 – Results of a study of the correlation between SSI and the biochemical indicators CRP and TnI.

Indicator	Aa		Pg		Td		Total microbial count	
	Spearman's rho	p-value	Spearman's rho	p-value	Spearman's rho	p-value	Spearman's rho	p-value
CRP	-0.022	0.760	0.167*	0.020	0.051	0.482	-0.043	0.552

Table 28 – Results of the study of the correlation between the level of CRP and the amount of microorganisms in subgingival plaque.

Indicator	PI, %		BoP, %		Mean CAL, mm		Mean PPD, mm		Number of teeth with BoP & PPD > 5mm		Stage of periodontitis	
	Spearman's rho	p-value	Spearman's rho	p-value	Spearman's rho	p-value	Spearman's rho	p-value	Spearman's rho	p-value	Spearman's rho	p-value
CRP, mg/L	0.053	0.465	-0.015	0.832	-0.109	0.129	-0.059	0.416	-0.013	0.862	0.109	0.129

Table 29 – Results of the study of the correlation between CRP level and periodontitis indicators.

As expected, the most common form of coronary pathology identified in the study population was stenosis, followed by thrombosis. Other forms of coronary damage were significantly less common (Figure 33).

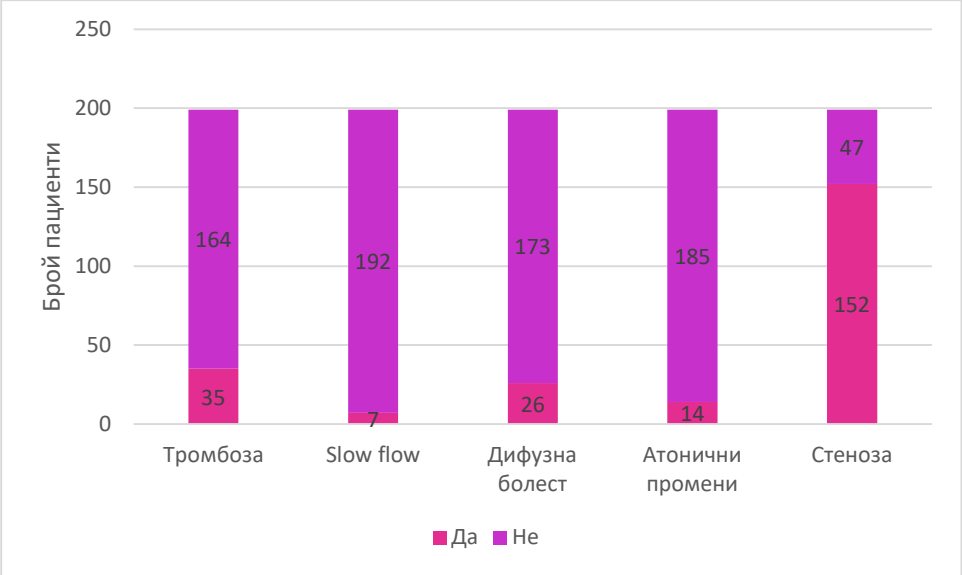

Fig. 33 – Types of coronary pathology among the sample.

Of the 199 patients, 152 (76.4%) had stenosis of at least one of the coronary branches, which strongly suggests coronary atherosclerosis. In the remaining 47 patients, no stenosis was detected, but in view of the existing phenomenon of positive vascular remodeling, the presence of AS cannot be categorically excluded, despite the absence of stenotic lesions on imaging.

We performed a correlation analysis between periodontal clinical indicators – mean clinical attachment loss (CAL), degree of periodontitis – and the severity of stenosis of the different coronary branches, as well as the total SYNATX score I, which is used to objectively assess the anatomical complexity and prevalence of coronary disease.

We found a weak but statistically significant positive correlation between:

• The severity of stenosis of the anterior descending artery (LAD) and the right coronary artery (RCA) with the mean CAL (Figure 34 and 35);

• Severity of left main (LM), LAD and RCA stenosis with stage of periodontitis (Figure 36 – 38);

• SYNATX score I with CAL and stage of periodontal disease (Figure 39 and 40).

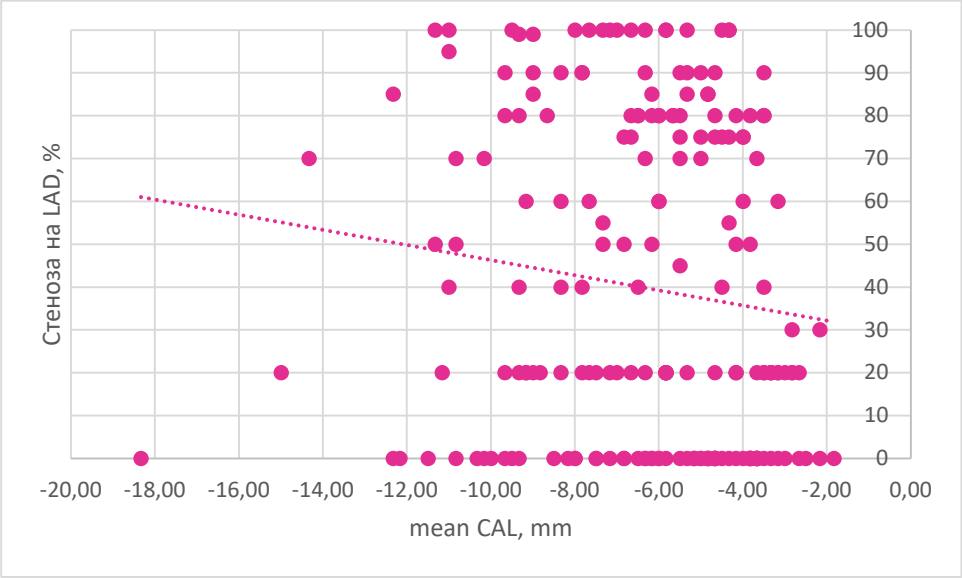

Fig. 34 – Correlation between the mean CAL value and the degree of LAD stenosis.

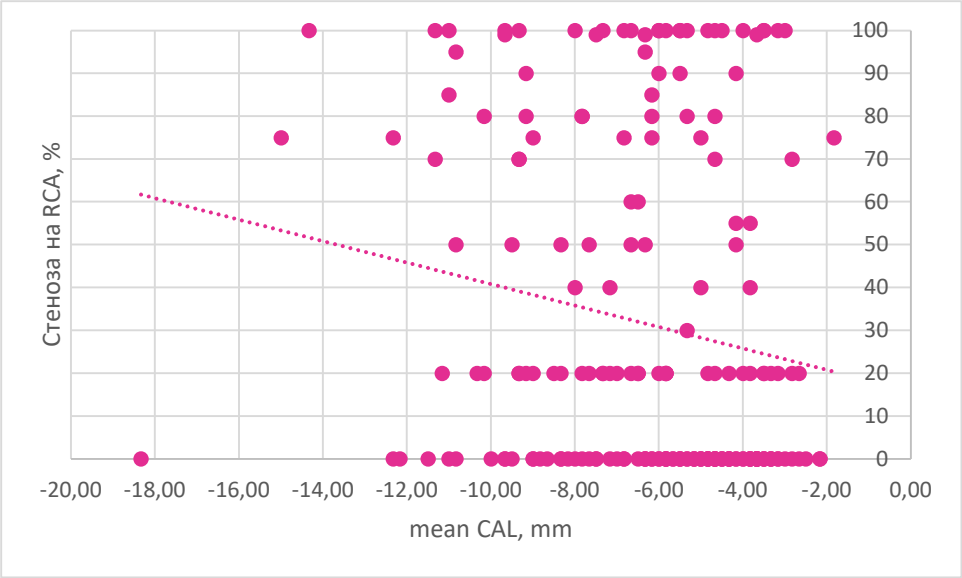

Fig. 35 – Correlation between the mean CAL value and the degree of RCA stenosis.

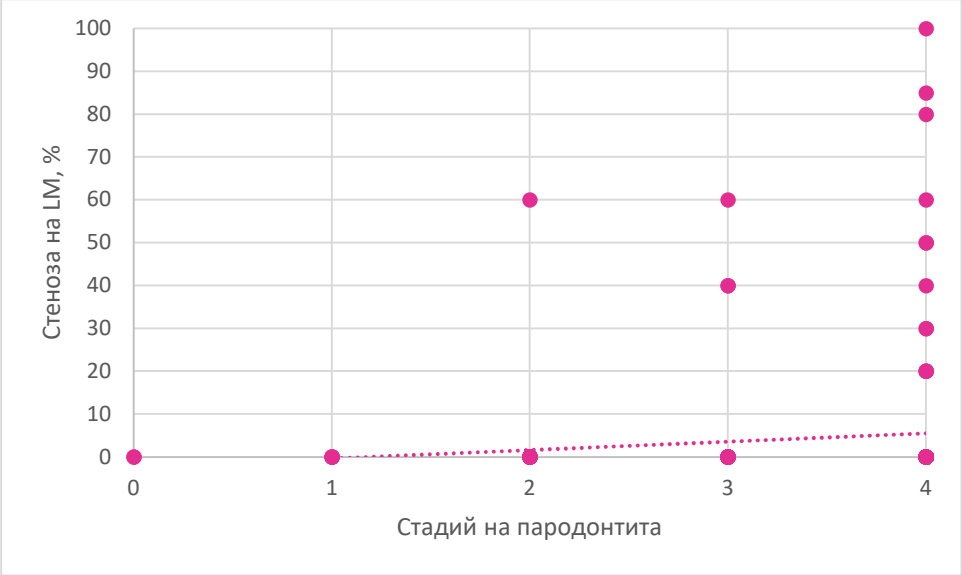

Fig. 36 – Correlation between the degree of LM stenosis and the stage of periodontitis.

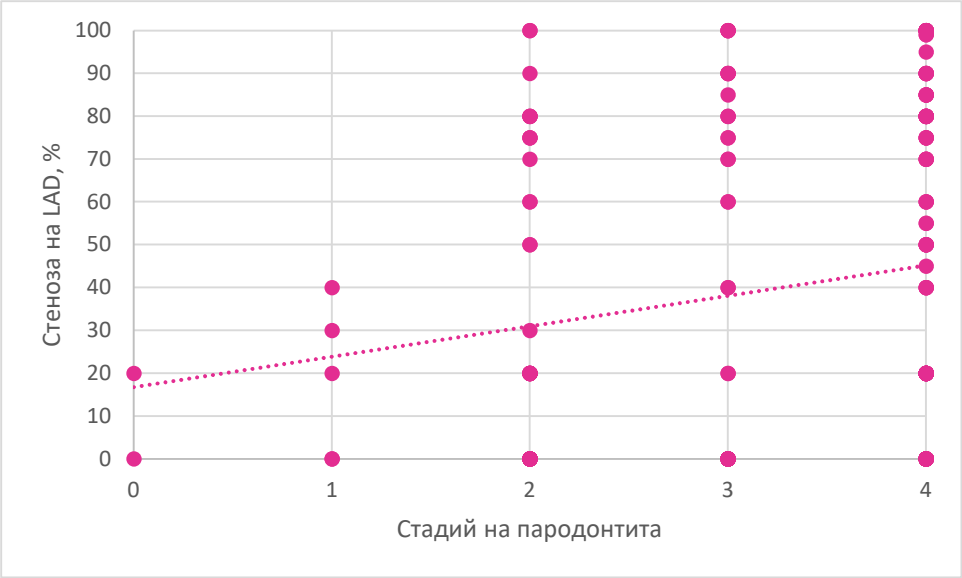

Fig. 37 – Correlation between the degree of LAD stenosis and the stage of periodontitis.

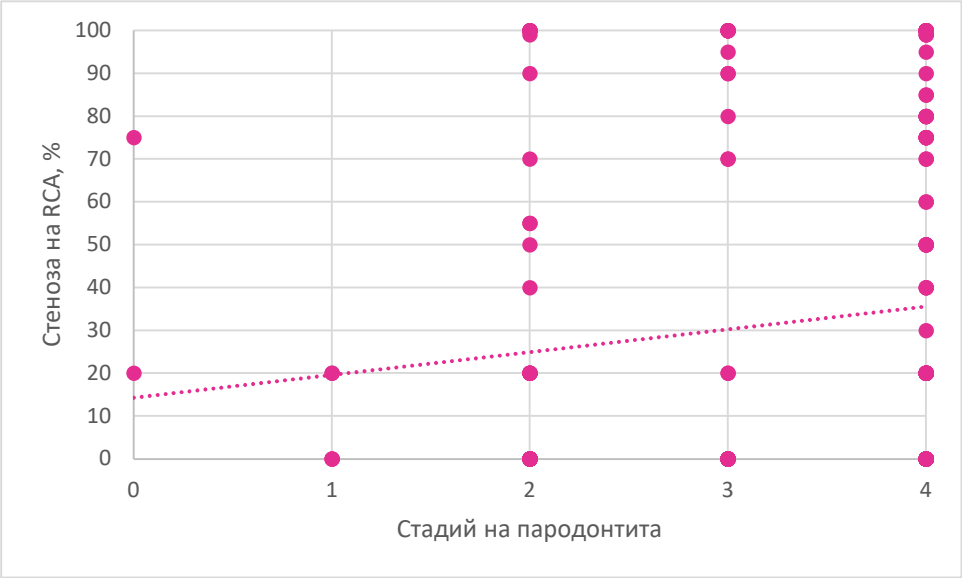

Fig. 38 – Correlation between the degree of RCA stenosis and the stage of periodontitis.

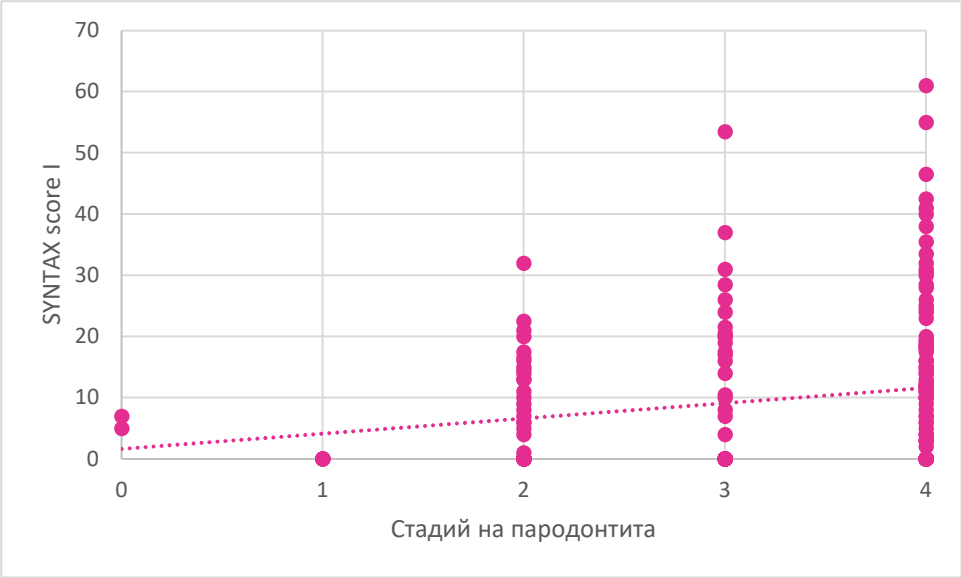

Fig. 39 – Correlation between SYNTAX score I and the stage of periodontitis.

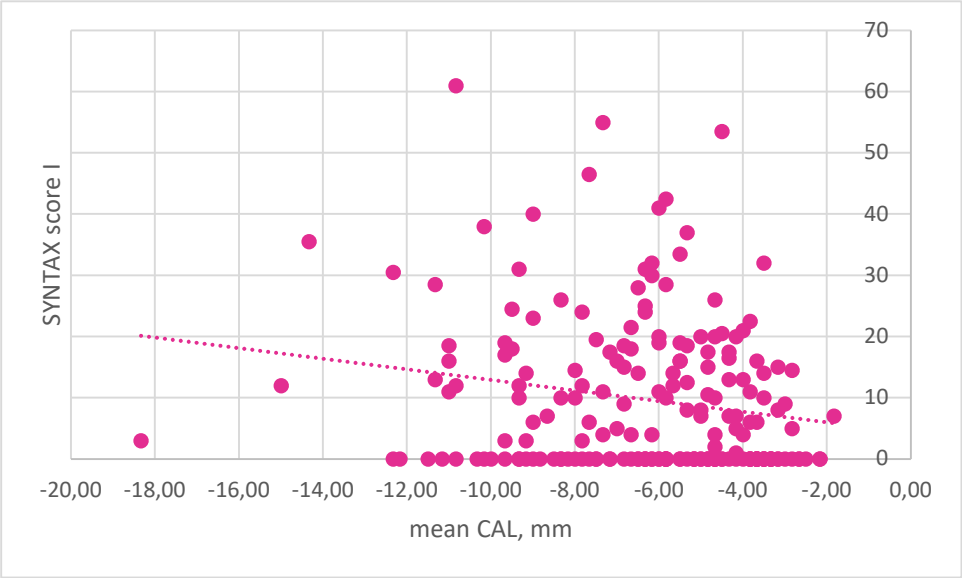

Fig. 40 – Correlation between SYNTAX score I and the average CAL value.

The study of the association between periodontal disease and the presence of stenosis showed that a more severe stage of periodontitis was associated with a higher incidence of coronary stenosis/atherosclerosis among patients (Fig. 41).

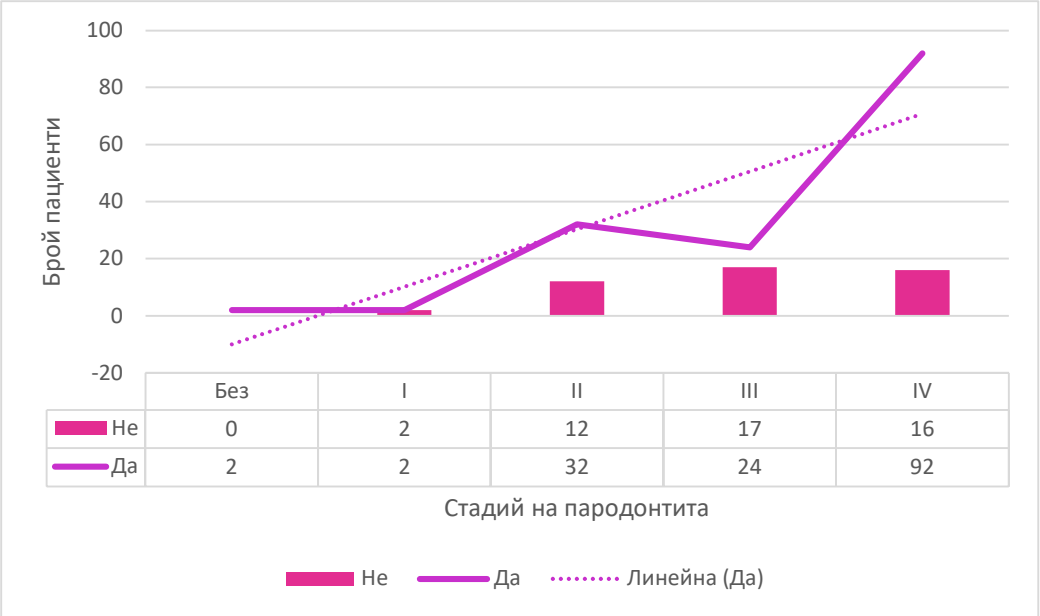

Fig. 41 – Increase in cases of coronary artery stenosis with increasing severity of periodontitis.

No association was found between the presence of severe periodontitis and the presence of thrombosis ($x2 = 0.116$, $p = 0.733$) or diffuse coronary artery disease ($x2 = 1.51$, $p = 0.219$) among the studied patients.

An additional focus of the analysis was on inflammatory markers and their possible relationship with microbiological and clinical parameters. We found a significant positive correlation between SYNATX score I and troponin I and C-reactive protein (CRP) levels in the blood (Fig. 42 and 43). Of particular interest is the observation that the amount of P. gingivalis correlated with CRP levels ($\rho = 0.167$, $p = 0.020$), although such a relationship was not found for the other bacterial species studied, nor with the total amount of microorganisms in the subgingival plaque (Fig. 44). There was also a lack of correlation between CRP levels and the severity of periodontal disease overall (Table 29), suggesting that P. gingivalis may induce a systemic inflammatory response regardless of the clinical severity of local periodontal damage.

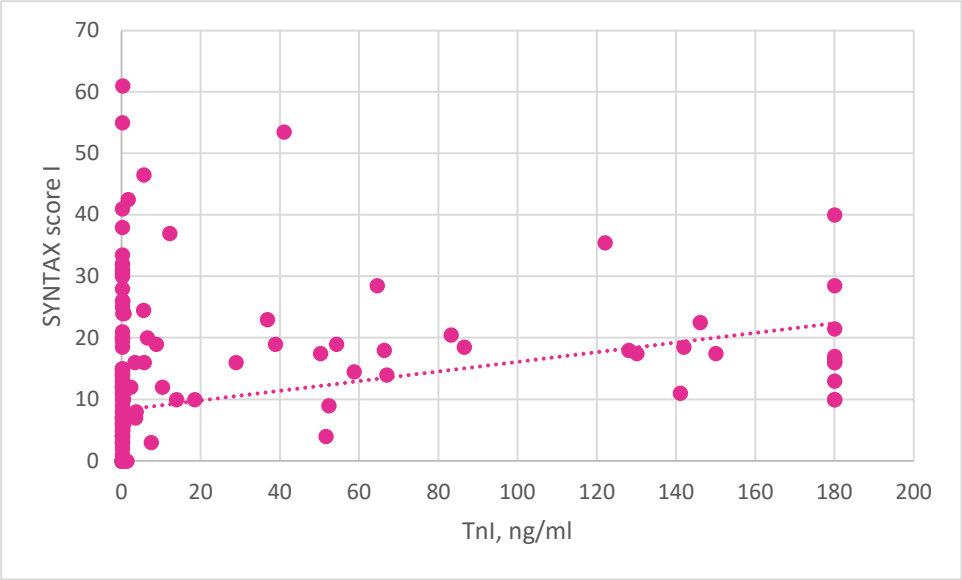

Fig. 42 – Correlation between troponin I level and SYNTAX score I.

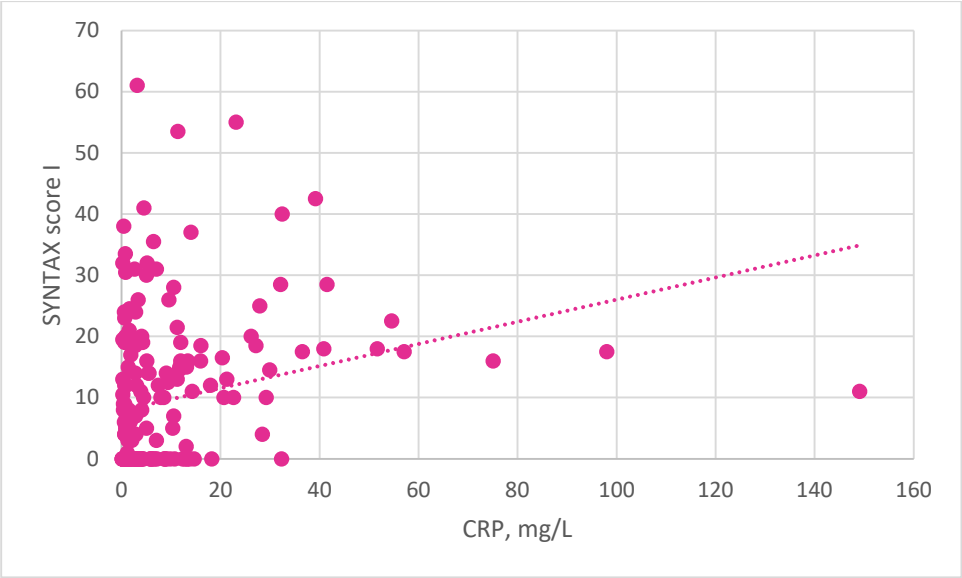

Fig. 43 – Correlation between CRP level and SYNTAX score I.

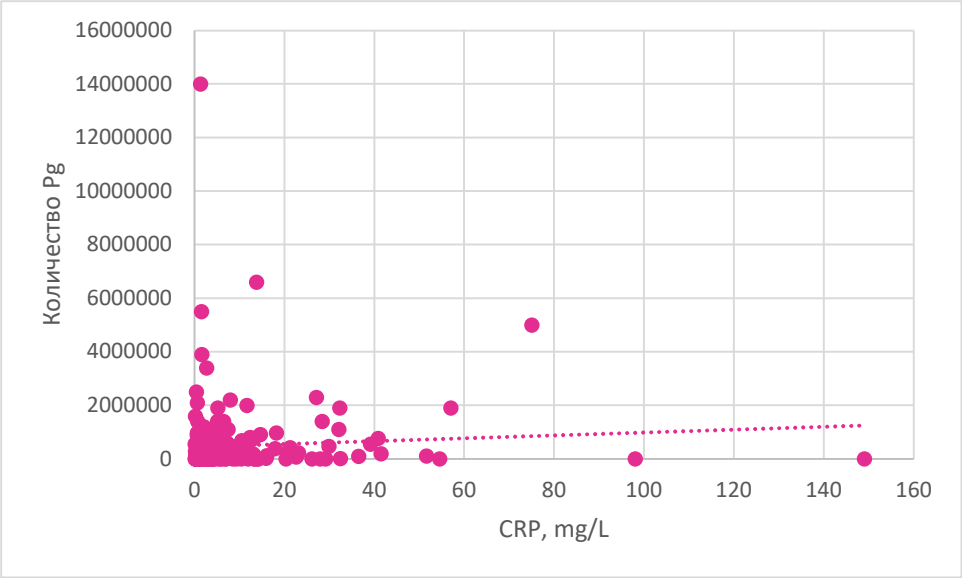

Fig. 44 – Correlation between CRP level and P. gingivalis.

3. DISCUSSION

3.1. Discussion of the results of task 1

The aim of this cross-sectional study was to investigate the possible association between the severity of periodontal infection and the presence of coronary artery disease (CAD), by analyzing various risk factors, clinical indicators and biochemical parameters among hospitalized patients with cardiovascular pathology.

We found that approximately two-thirds of the patients were male. This observation is consistent with data from epidemiological studies that show a higher incidence of cardiovascular disease (CVD) among men and identify male gender as an independent risk factor for the development of atherosclerosis (AC) and its associated clinical manifestations as reported in a number of publications: Falk et al., 2006 [97], Law et al., 2004 [190], McKeown et al., 2004 [232].

A trend towards overweight and obesity was found in both sexes. Overweight, especially in the context of central (abdominal) obesity, is a recognized component of the metabolic syndrome and is associated with chronic inflammation, insulin resistance and increased cardiovascular risk.

As expected, 90% of the studied patients had concomitant arterial hypertension. In addition, 49% of them were active smokers and 24% suffered from diabetes mellitus. This emphasizes the multifactorial nature of vascular pathology and the importance of the combined effect of classical risk factors for CVD, such as arterial hypertension, smoking and diabetes. According to the available scientific evidence, each of these factors individually, and even more so their combination, contributes to endothelial dysfunction, accelerated atherogenesis and a worse prognosis (Falk et al., 2006 [97], Law et al., 2004 [190]).

Analysis of the lipid profile showed that dyslipidemia was not a leading risk factor for CVD among the studied cohort. This supports the modern concept of an inflammatory etiology of atherosclerotic changes, as reported by Libby & Theroux 2005 [195], and Libby, 2002 [197].

The results presented so far show that despite the importance of dyslipidemia as a modifiable risk factor, it is not the only or mandatory prerequisite for the development of atherosclerotic changes. Among the studied population, the leading risk factors are male gender, overweight and arterial hypertension.

Regarding periodontal status, only two out of all 199 participants did not show clinical evidence of periodontitis. Impressive is the fact that 149 patients (74.9%) had advanced periodontitis – stages III and IV according to the EFP classification. This percentage is significantly higher than the data reported in the international epidemiological reports of the EFP 390. The lack of systematized national data on the incidence of periodontal diseases in Bulgaria limits the possibility of direct comparison, but the available information allows with high probability to assume that the prevalence of periodontitis in the country is higher than the average global levels.

The clinical assessment of PI (according to O'Leary) and bleeding index on probing (according to Ainamo & Bay) is presented in Fig. 16. With a reference value for PI < 10%, the results clearly demonstrate that almost all patients have poor control over oral hygiene. Despite the possible influence of the hospital environment on hygiene habits, the comparison with the BoP results supports the thesis of chronic neglect of oral hygiene practices.

The study of clinical attachment (Clinical Attachment Loss – CAL) found apical migration of the periodontal attachment of varying severity, with the premolars being the most severely affected. This finding can be explained by the smaller root surface of the premolars, their anatomical position in the dental arch, as well as the functional overload in cases of missing molars, which contributes to bone destruction in periodontal diseases.

The study of periodontal indicators in these 199 patients shows a tendency for poor awareness regarding the importance of oral hygiene and the prevention of periodontal diseases. At the same time, the widespread prevalence of periodontitis among the studied patients, especially in advanced stages, supports the concept of its importance as an independent risk factor for the development of CVD, as summarized by Sanz et al., 2020 [301]. It is worth noting that among the studied patients, the prevalence of periodontitis outpaces that of the risk factors for CVD approved by the European Society of Cardiology [308], such as male gender, obesity, arterial hypertension, diabetes mellitus. On the other hand, the presence of periodontitis is associated with some of these diseases and conditions and this relationship is supported by numerous studies. A bidirectional relationship between the presence of periodontitis and diabetes mellitus has been demonstrated (Bui et al., 2019 [46]), and chronic infection in periodontitis may lead to poorer blood sugar control and increased insulin requirements (Nishimura et al., 2003 [253], Preshaw et al., 2012 [282]). There is evidence that periodontal infection may contribute to the development of arterial hypertension, demonstrated by Viafara-García et al., 2019 [354], and numerous epidemiological studies support the association between periodontitis and obesity:

Ekuni et al. 2008 [87], Genco et al., 2005 [115], Haffajee & Socransky, 2009 [133], Linden et al., 2007 [201], Manco et al., 2009 [221].

The totality of these data indicates that periodontal infection probably has a complex effect on a systemic level in the body, causing pathophysiological changes at different levels and in different organs and systems, which emphasizes the need for enhanced primary and secondary prevention of periodontal diseases with a view not only to oral, but also to systemic health.

3.2. Discussion of the results of task 2

Within the second direction of our study, a microbiological analysis was performed to determine the frequency and co-presence of major periodontal pathogens in the subgingival plaque of patients with different degrees of periodontal disease. Particular attention was paid to the three key microorganisms – Treponema denticola (Td), Porphyromonas gingivalis (Pg) and Aggregatibacter actinomycetemcomitans (Aa), which are part of the well-described microbial complexes associated with advanced periodontal destruction (Socransky et. al, 1998 [322]).

The results of the PET test showed that the most frequently isolated periodontal pathogen was T. denticola, followed by P. gingivalis and A. actinomycetemcomitans (Fig. 19). This distribution corresponds to the hierarchy of dominance of representatives of the so-called "red complex", which is closely associated with clinically manifested and advanced form of periodontitis, described in the literature (Bale et al., 2017 [24], Hajishengallis et al., 2012 [136], Haubek & Johansson, 2014 [148], Sokransky & Haffajee, 2006 [323]).

The results of the correlation analysis between the amounts of P. gingivalis and T. denticola in subgingival plaque are consistent with published data (Dashper et al. [67], Grenier [129], Kigure et al. [178], Nilius et al. [252], Socransky et al. [322], Yoneda et al. [383]), according to which these microorganisms are often found together in patients with periodontitis, and interact in the formation of mature biofilms and immune modulation of the host.

We found a positive correlation between the BoP value and the amount of T. denticola, as well as with the total amount of microorganisms. Interestingly, the correlation with the total amount of microorganisms is stronger than with the amount of T. denticola alone. This suggests that the intensity of the local inflammatory response – measured by BoP – is more related to the quantitative burden of the biofilm than to the isolated presence of a specific pathogen. Such a relationship supports the idea that the total microbial mass may prevail over species specificity as a factor in the induction of inflammation in periodontal tissue, as summarized by Socransky & Haffajee, 2006 [323].

Our positive correlation between the mean probing depth and the amount of P. gingivalis and T. denticola confirms their contribution to the progression of periodontal destruction and the pathogenesis of deeper pockets characterized by chronic bacterial invasion and impaired epithelial barrier response (Cekici et al., 2014 [52]).

We found that higher abundance of the studied periodontal pathogens (A. actinomycetemcomitans, P. gingivalis and T. denticola) in subgingival plaque was associated with lower mean values of clinical attachment level. This relationship implies that higher abundance of these pathogens is associated with greater attachment loss, which is a clinical marker of advanced periodontal destruction. No such correlation was found for total microbial abundance, highlighting that in the case of structural-tissue loss, the stage of periodontal progression is more closely related to the presence of specific, highly virulent species than to the total microbial mass (Socransky & Haffajee, 2006 [323]).

We found that the abundance of T. denticola and P. gingivalis in subgingival plaque correlated positively with the number of teeth affected by deep periodontal pockets (PPD > 5 mm) as well as with the overall severity of the disease. This observation is consistent with the data that red complex microorganisms are identified predominantly in advanced periodontal lesions and have a leading role in disease progression (Yang HW et al., 2004 [375]).

These results confirm the etiological significance of Aggregatibacter actinomycetemcomitans (Aa), Porphyromonas gingivalis (Pg) and Treponema denticola (Td) as major microorganisms involved in the pathogenesis of periodontitis (Bale et al., 2017 [24], Hajishengallis et al., 2012 [136], Haubek & Johansson, 2014 [148], Socransky & Haffajee, 2006 [323]). Additionally, the established relationship between increased species diversity of isolated pathogens and greater clinical attachment loss is consistent with previously published data by Chen et al., 2017 [57], which demonstrated a more unfavorable periodontal status in patients with a richer microbiome in the subgingival plaque.

3.3. Discussion of the results of task 3

The aim of the third part of the study was to determine whether there is a relationship between the severity of periodontal damage and the nature of coronary pathology, in particular - the degree of stenosis of the main arterial branches, SYNATX score I, as well as some biomarkers of inflammation and myocardial damage.

In accordance with expectations, the most common form of established coronary pathology in the studied population was stenosis, followed by thrombosis in frequency. Other forms of coronary damage were found significantly less frequently. This distribution reflects the typical clinical profile of patients with chronic ischemic heart disease, confirming that stenotic changes associated with the accumulation of atheromatous plaque are a leading mechanism in the pathogenesis of the disease, as reported in earlier publications (Grech, 2004 [125], Tuzcu et al., 2001 [343]).

Our results from the study of the correlation between SSI and CAL are in line with data published by Joshi et al., 2022 [169], which also reported a relationship between periodontal and coronary lesions. In contrast, in the present study, no correlation was found between SYNATX score I and the presence or amount of specific periodontal pathogens, nor between the total microbial load and the severity of coronary pathology.

Sharma et al., 2019 [317] investigated the relationship between oral inflammatory load and SSI in patients with CAD, and found no correlation. We also found no correlation between the presence and severity of local periodontal inflammation and SSI.

We found that a more severe stage of periodontal disease was associated with a more frequent presence of coronary stenosis, and this association was statistically significant ($p < 0.01$). This confirms the results of previous studies that found a similar association between periodontitis and obstructive coronary artery disease: Accarini & de Godoy, 2006 [7], Alaoui-El-Azher et al., 2010 [11], Lee et al., 2019 [191], Yang J et al., 2013 [376], and highlights the possibility of a common inflammatory pathway between the two conditions.

We found a significant positive correlation between SYNATX score I and troponin I levels. Such a relationship was also reported by Akkuş et al., 2018 [10]. This correlation is somewhat expected, considering that TnI is a cardioprotein that is released upon cardiomyocyte damage and its high levels correspond to myocardial necrosis/infarction.

The levels of C-reactive protein (CRP) in the blood of the studied patients also correlated positively with the SSI value. A number of other authors have also reached this conclusion: Akboga et al., 2023 [9,] Akkuş et al., 2018 [10], Ozdemir, 2020 [269], Xing et al., 2019 [371]. These data support the concept of AS and in particular CAD as a result of systemic inflammation in the body.

Of particular interest is the observation that the amount of P. gingivalis in subgingival plaque correlates with CRP levels, although such a relationship was not found for the other bacterial species studied, nor with the total amount of microorganisms in subgingival plaque. Similar results were reported by Noack et al., 2001 [254]. Mikuls et al., 2009 [240] reported a correlation between the titer of antibodies against P. gingivalis and CRP levels.

There was also no correlation between CRP levels and the severity of periodontal disease in general, suggesting that P. gingivalis may induce a systemic inflammatory response regardless of the clinical severity of local periodontal damage. In contrast, Davison et al., 2021 [69] reported a correlation between periodontitis indicators (PI, BoP, PPD ≥ 5 mm, CAL, PPD), but they studied a significantly smaller cohort of patients (n = 42).

The results of our study highlight the importance of P. gingivalis not only as a local pathogen, but also as a potential mediator in the pathway between chronic periodontal inflammation and systemic diseases such as atherosclerosis and myocardial infarction and are more in support of the hypothesis of indirect (probably immune) mechanisms linking oral and systemic pathology than direct bacterial invasion, although we cannot exclude the latter categorically. Further experimental and clinical work is needed to confirm the causal relationships and to clarify the potential pathophysiological mechanisms.

In addition to the above, these results raise the question of whether the detection of P. gingivalis in periodontally healthy individuals also leads to systemic effects in the inflammatory response.

In the final part of the analysis, possible associations between periodontal status and two specific forms of coronary pathology – thrombosis and diffuse coronary artery disease, which also arise from atherosclerotic processes – were examined (See Results, Tables 25 and 26). The results obtained did not show a statistically significant relationship between these conditions and severe periodontitis. However, this lack of established relationship does not completely exclude the possibility of a relationship – especially in the context of different subtypes of periodontal and coronary disease. In this context, it would be appropriate to conduct

qualitatively new case-control studies that would provide higher analytical power when examining such complex interactions.

IV. CONCLUSION

The present study provides new and significant evidence in support of the hypothesis of a relationship between the severity of periodontal infection and coronary artery disease (CAD). The data from the analysis showed that severe periodontitis (stage III and IV) was highly prevalent among patients with CAD, found in 74.9% of the subjects included in the study. This highlights the potential epidemiological and clinical importance of periodontal status in patients with cardiovascular pathology.

A statistically significant correlation was found between the degree of coronary stenosis and periodontal clinical indicators, including clinical attachment loss (CAL) and the severity of periodontitis. These data support the concept of a potential biological link between chronic periodontal inflammation and atherosclerotic changes in the vascular wall. However, no association was found between the presence of specific periodontal pathogens – T. denticola, P. gingivalis, A. actinomycetemcomitans – and the degree of coronary stenosis, which draws attention to the possibility that other factors (e.g. immune, systemic or genetic) may mediate the interaction between oral infection and vascular pathology.

On the other hand, the analysis revealed a significant positive correlation between the values of SYNTAX Score I (SSI) – an objective marker of the anatomical severity of CAD – and the levels of troponin I and C-reactive protein (CRP), which correspond to established biomarkers of myocardial damage and systemic inflammation. Of particular interest is the observation that the amount of P. gingivalis showed a statistically significant positive correlation with CRP levels, while such a correlation was not observed with the other bacterial species studied, nor with the indicators of periodontal disease or the severity of periodontal status in general. This suggests that P. gingivalis may induce a systemic inflammatory response regardless of the clinical severity of local periodontal damage, thus acting as a possible inflammatory trigger in the pathogenesis of atherosclerosis.

This finding is of particular importance, as it indicates that the role of P. gingivalis is not limited to local periodontal inflammation, but may extend to a systemic level, with the possibility of involvement in endothelial dysfunction, induction of autoimmune processes or dysregulation of the innate immune response.

In summary, the results of the present study emphasize the need for an integrated clinical approach to patients with cardiovascular diseases, in which the deteriorated periodontal status is considered a significant risk factor. Timely diagnosis, prevention and control of periodontal

infections may have direct clinical significance for the progression and complications of coronary disease, especially in patients with a high SYNTAX Score I. These data support the paradigm for the so-called "oral-systemic connection" and lay the foundation for future multidisciplinary studies and clinical guidelines aimed at better integrated risk management in cardiovascular and periodontal diseases.

V. CONCLUSIONS

1. Arterial hypertension (in 90% of patients), obesity (80%) and male gender (66%) are confirmed as leading classical risk factors for CVD.

2. Dyslipidemia does not stand out as a leading risk factor among this population, which supports the inflammatory hypothesis for the genesis of AS.

3. The prevalence of periodontitis in the studied group exceeds (in 99% of patients) that of the classical risk factors for CVD, which requires a reassessment of the role of periodontal infection in the pathogenesis of CVD.

4. Data from the study of the gingival and plaque index among patients indicate poor control of supragingival plaque and chronic neglect of oral hygiene practices.

5. Severe periodontitis (stage III–IV) is widespread among patients with coronary artery disease (CAD) – found in 74.9% of the studied population, which confirms a high concomitant frequency of both pathologies.

6. There is a statistically significant, although weak correlation between the degree of coronary stenosis and periodontal clinical indicators – most notably clinical attachment loss (CAL) and severity of periodontitis, especially with respect to LAD and RCA stenosis.

7. SYNTAX Score I – as an integral indicator of the severity of coronary disease – correlates positively with the severity of periodontitis and with the value of CAL, which suggests a relationship between complicated atherosclerotic pathology and advanced periodontal disease.

8. The most frequently isolated periodontal pathogens are T. denticola and P. gingivalis, which are often found together, with a positive correlation between them and indicators of local inflammation (BoP, PPD).

9. The mean CAL value increases with the number of isolated periodontal pathogens, indicating that greater microbial diversity is associated with more severe periodontal destruction.

10. The amount of P. gingivalis shows a statistically significant positive correlation with CRP levels in the blood, suggesting a possible role of this pathogen as a mediator of systemic inflammation, regardless of local periodontal severity.

11. No correlation was found between the amount of periodontal pathogens and SYNTAX Score I, which points to indirect and probably immune-mediated mechanisms of interaction between the microbiome and atherosclerosis.

12. No relationship has been established between severe periodontitis and the presence of thrombosis or diffuse coronary artery disease, which does not exclude, but does not categorically confirm, the hypothesis of the involvement of periodontal infection in these specific forms of vascular pathology.

VI. CONTRIBUTIONS

Original contributions:

1. For the first time, the association between periodontitis and diffuse coronary artery disease was studied, as a separate form of atherosclerotic vascular involvement, which contributes to expanding the concept of the diversity of cardiovascular manifestations potentially associated with periodontal infection.

2. A working model for multidisciplinary research was developed, which can be applied in future studies on the relationship between systemic and oral diseases.

Confirmatory contributions:

1. A statistically significant correlation was found between the amount of P. gingivalis and CRP levels, demonstrating a possible role of this pathogen in the induction of systemic inflammation.

2. It was found that the more severe stage of periodontitis is associated with a higher frequency of coronary artery stenosis, which supports the concept of periodontitis as a contributing factor in the pathogenesis of atherosclerosis.

3. A statistically significant correlation was found between the clinical attachment loss (CAL) and SYNTAX Score I, confirming the relationship between the severity of periodontal damage and the complexity of coronary pathology.

4. A lack of correlation was found between the amount of periodontal pathogens and the degree of coronary stenosis, which supports the thesis that systemic inflammation may be mediated by indirect mechanisms, and not only by the quantitative presence of specific microorganisms.

5. No correlation was found between SYNTAX Score I and the total microbial load in the subgingival plaque in patients with coronary artery disease.

6. It has been shown that patients with a higher number of isolated periodontal pathogenic species show a greater loss of clinical attachment, which confirms data on the negative role of microbial diversity in the progression of periodontal destruction.

7. A statistically significant positive correlation between the amounts of P. gingivalis and T. denticola in the subgingival flora was confirmed, consistent with the known microbiological synergism between the two pathogens within the red complex.

8. The potential for including periodontal status in the assessment of cardiovascular risk was identified, which offers a new approach for early diagnosis and prevention of CAD.

9. The dissertation argues for the need for integrated cardio-dental care, in which dentists and cardiologists jointly assess patients with increased inflammatory and vascular risk.

Appendix No. 1

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ПРИ МУ – ВАРНА
Заседание на 25.11.2021 г.

Предвид обявената извънредна епидемична обстановка в страната, свързана с разпространението на COVID-19 и предвид нарастващия брой на заболелите, и на основание чл. 8, ал. 7 от Правилника за работа на Комисията по етика на научните изследвания в МУ – Варна, заседанието на Комисията се проведе чрез платформата Webex Cisco. В 14.30 ч. започна заседанието, на което дистанционно участваха редовните членове, а именно:

Председател: Проф. Бистра Галунска, д.фарм.

Редовни членове:

1. Проф. д-р Албена Керековска, д.м.
2. Проф. д-р Йото Йотов, д.м.
3. Проф. д-р Мария Цанева, д.м.
4. проф. д.б.н. Диана Иванова
5. Проф. д-р Радосвета Андреева-Борисова, д.м.н.
6. Доц. д-р Десислава Ванкова, д.м.
7. Д-р Александър Златаров, д.м.
8. Иванка Кондова – юрист

На заседанието, по уважителни причини, не взеха участие: Проф. д-р Методи Абаджиев, д.м.н. Доц. Веселина Славова, д.ф.

Заседанието на Комисията по Етика на научните изследвания (КЕНИМУВ) при МУ-Варна има кворум и протече по предварително обявения дневен ред. То беше ръководено от проф. Бистра Галунска, д.фарм. Протоколът води Мирослава Николова от отдел „Административен" на Научноизследователския институт към МУ-Варна.

Заседанието на Комисията има кворум и се проведе по предварително обявения **дневен ред**:

1. Разглеждане, изготвяне и приемане на становище на Комисията относно начална оценка на етичните аспекти на научни изследвания:

.....

1.3. „Имат ли отношение пародонталните инфекции върху прогресията на коронарната патология" с гл. изследовател д-р Росица Христова - Първа катедра по вътрешни болести, МУ – Варна

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Заседанието на Комисията по Етика на научните изследвания (КЕНИМУВ) при МУ-Варна има кворум и протече по предварително обявения дневен ред. То беше открито и ръководено от проф. Бистра Галунска, д.фарм. Протоколът води Мирослава Николова от отдел „Административен" на Научноизследователския институт към МУ-Варна.

.....

По **т. 1.3.** от дневния ред проф. д-р Йото Йотов, д.м. представи акценти от доклада си относно заявено научно изследване на тема: „Имат ли отношение пародонталните инфекции върху прогресията на коронарната патология" с гл. изследовател д-р Росица Христова - Първа катедра по вътрешни болести, МУ – Варна.

Комисията изслуша доклада на рецензента, който представя обобщена информация за научното изследване и оценка на етичните аспекти.

Взимайки предвид доклада на рецензента и след проведено обсъждане от членовете на Комисията единодушно се препоръчва проучването да бъде изцяло с ретроспективен характер т.е. да се работи само с данни от медицинската документация.

На базата на приложените документи, доклада на рецензента за оценка на етичните аспекти, Комисията гласува както следва:

Гласували: 9

Одобрили: 9 Против: няма Въздържали се: няма

РЕШЕНИЕ: Комисията по етика на научните изследвания при МУ - Варна одобрява провеждането на научното изследване: „Имат ли отношение пародонталните инфекции върху прогресията на коронарната патология“ с гл. изследовател д-р Росица Христова Христова - Първа катедра по вътрешни болести, МУ – Варна.

Във връзка с изискването за извършване на текущ надзор на хода на проучването /съгласно Наредба № 31 за определяне на правилата за добра клинична практика., чл. 203, ал. 5 от Закона за здравето и Правилника на КЕНИ (2012 г.)/

Главният изследовател се задължава:

- Да уведоми писмено Комисията по етика на научните изследвания при МУ-Варна за **стартирането** на научното изследване;
- Да представи на Комисията **писмен доклад** за **прогреса** на проучването - в срок до 1 година от неговото начало, включващ данни относно броя участващи в изследването до момента лица, броя прекратени участия и причините за тях, отчитани ползи и рискове за участниците, направени промени в одобреното изследване и друга важна нова информация, както и очаквана продължителност на проучването;
- Да представи на Комисията **писмен окончателен доклад** при приключване на научното изследване;
- Да информира писмено Комисията при планиране от изследователския екип на **промени** в методите, плана, процедурите или постановката на вече одобреното проучване;
- Местната Комисия по етика на научните изследвания е създадена и работи съгласно правилата на Добрата клинична практика и съобразно изискванията на национални и международни документи в областта на етиката на научните изследвания и научните публикации. Комисията спазва законите и наредбите, действащи на територията на Република България.

.....

Поради изчерпване на дневния ред, заседанието бе закрито от проф. Бистра Галунска, д.фарм.

ПРЕДСЕДАТЕЛ КЕНИМУВ:
_____/п/_____ (проф. Б. Галунска, д.ф.)

СЕКРЕТАР КЕНИМУВ:
_____/п/_____ (М. Николова)

Вярно с оригинала,
(М. Николова)

Appendix No. 2

Изследване за наличие на пародонтоални патогени

Благодарим Ви за участието в това изследване! С него Вие допринасяте за развитието на науката, както в България, така и извън границите на страната.

В тази листовка ще намерите информация какво представлява изследването и какви са ползите от него.

Какво е пародонтит? Пародонтитът е заболяване, увреждащо пародонта (тъканите, които задържат зъба на мястото му). Локалните усложнения при прогресията на това заболяване при липса на лечение, включват кървене от венците, неприятен дъх от устата, повишена подвижност (разклащане) на зъбите и в крайна сметка тяхната загуба. Системните усложнения на нелекувания пародонтит са свързани с повишен риск от сърдечно-съдови заболявания, деменция, затруднен контрол на нивата на кръвна захар при диабет и др.

Пародонтитът е инфекция – причинява се от бактерии. Пародонтитът е **най-разпространеното заболяване** сред възрастното население.

Какво са пародонталните патогени? Пародонталните патогени са няколко вида бактерии, които са свързани с възникването и развитието на пародонтит. От устната кухина пародонталните патогени и техните продукти могат да навляза в кръвообращението и да се разпространят в тялото, причинявайки някои от изброените по-горе усложнения.

Какво представлява изследването? Изследването, което ще Ви бъде направено включва регистриране на **пародонтален статус** и вземане на **проба за изследване наличието на пародонтални патогени.**

Пародонталният статус включва измерване на няколко параметъра около всеки наличен в устата зъб, за да се оцени състоянието на тъканите на пародонта. **Изследването е неинвазивно**. Възможно е усещане за дискомфорт в участъци, които са възпалени.

След като пародонталният статус е регистриран, ще ви бъде взета проба за PET-test от 5 участъка в устата, чрез поставяне за 20 секунди на хартиен щифт в мястото. Целта на изследването е да докаже наличието на пародонтални патогени, както и да определи тяхното количество.

Какво значение има това за мен? Наличието на пародонтит и пародонтални патогени означава заболяване на зъбодържащия апарат и изисква лечение, тъй като нелекувано състоянието води до загуба на зъби. Тъй като сте пациент преминал коронарна ангиография, доказването на наличието на пародонтит и пародонтални патогени при Вас, може да помогне за установяване на връзка между двете състояния и подобряване на лечението и профилактиката и на двете заболявания.

Appendix No. 3

ИНФОРМИРАНО СЪГЛАСИЕ

Аз, долуподписаният

……,

давам съгласието си резултатите от проведените изследвания по време на хоспитализация във Втора клиника по кардиология-инвазивна, УМБАЛ „Света Марина“ да бъдат използвани за изследователски цели по проект „Коронарна патология и заболявания на пародонта“.

Изследовател:

…… …

/подпис и имена/

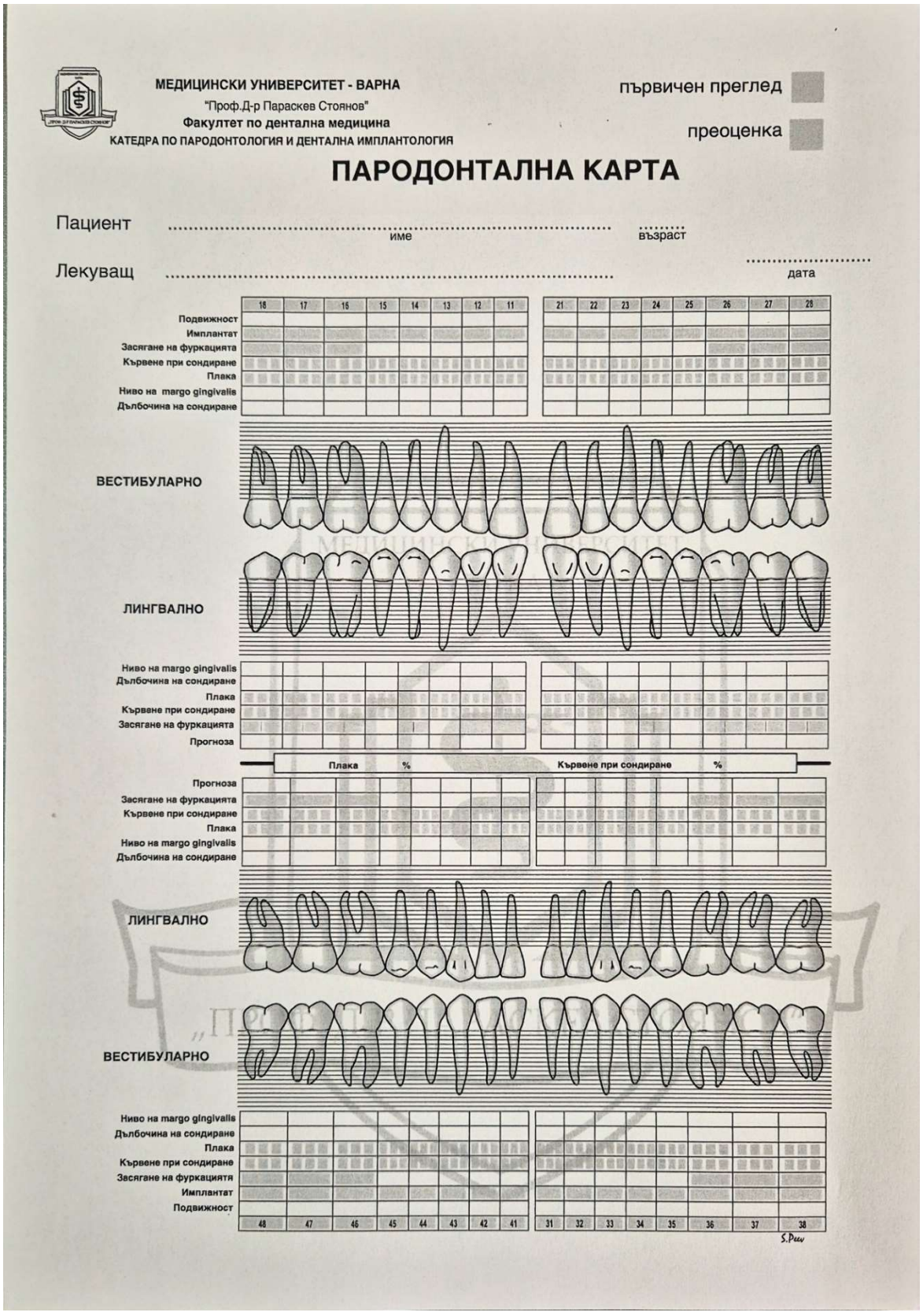
Подпис на пациент:

……..

Дата:

гр. Варна

Appendix No. 4



МЕДИЦИНСКИ УНИВЕРСИТЕТ - ВАРНА
"Проф.Д-р Параскев Стоянов"
Факултет по дентална медицина
КАТЕДРА ПО ПАРОДОНТОЛОГИЯ И ДЕНТАЛНА ИМПЛАНТОЛОГИЯ

първичен преглед
преоценка

ПАРОДОНТАЛНА КАРТА

Пациент ..... име ..... възраст

Лекуващ ..... дата

18 17 16 15 14 13 12 11 | 21 22 23 24 25 26 27 28

Подвижност
Имплантат
Засягане на фуркацията
Кървене при сондиране
Плака
Ниво на margo gingivalis
Дълбочина на сондиране

ВЕСТИБУЛАРНО

ЛИНГВАЛНО

Ниво на margo gingivalis
Дълбочина на сондиране
Плака
Кървене при сондиране
Засягане на фуркацията
Прогноза

Плака % Кървене при сондиране %

Прогноза
Засягане на фуркацията
Кървене при сондиране
Плака
Ниво на margo gingivalis
Дълбочина на сондиране

ЛИНГВАЛНО

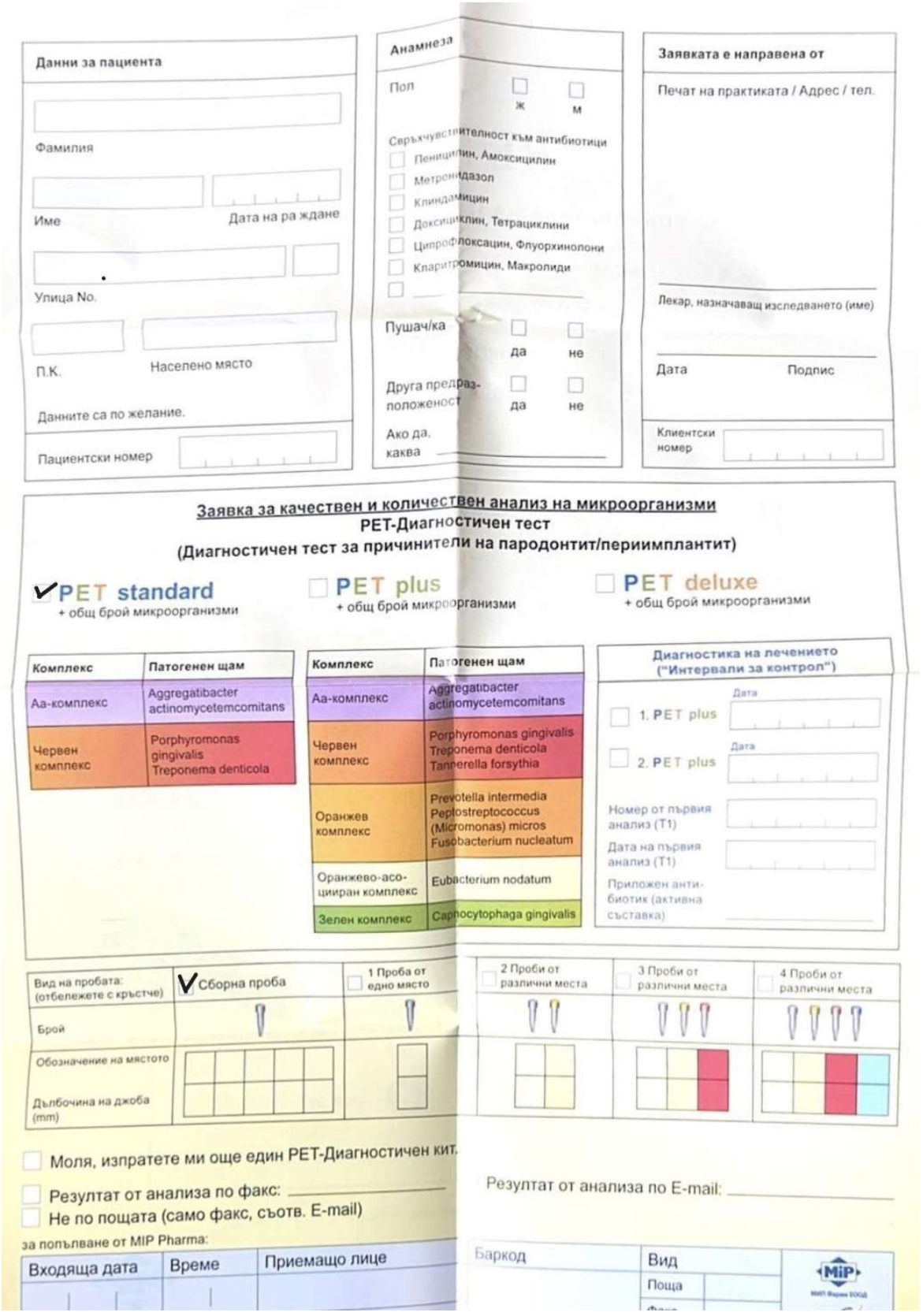
ВЕСТИБУЛАРНО

Ниво на margo gingivalis
Дълбочина на сондиране
Плака
Кървене при сондиране
Засягане на фуркациятя
Имплантат
Подвижност

48 47 46 45 44 43 42 41 | 31 32 33 34 35 36 37 38

S.Pesh

Appendix No. 5



Данни за пациента

Фамилия

Име

Дата на ра ждане

Улица No.

П.К.

Населено място

Данните са по желание.

Пациентски номер

Анамнеза

Пол ☐ ж ☐ м

Свръхчувствителност към антибиотици

- ☐ Пеницилин, Амоксицилин
- ☐ Метронидазол
- ☐ Клиндамицин
- ☐ Доксициклин, Тетрациклини
- ☐ Ципрофлоксацин, Флуорхинолони
- ☐ Кларитромицин, Макролиди
- ☐ ____

Пушач/ка ☐ да ☐ не

Друга предраз-положеност ☐ да ☐ не

Ако да, каква ____

Заявката е направена от

Печат на практиката / Адрес / тел.

Лекар, назначаващ изследването (име)

Дата Подпис

Клиентски номер

Заявка за качествен и количествен анализ на микроорганизми

PET-Диагностичен тест

(Диагностичен тест за причинители на пародонтит/периимплантит)

☑ PET standard
+ общ брой микроорганизми

☐ PET plus
+ общ брой микроорганизми

☐ PET deluxe
+ общ брой микроорганизми

Комплекс	Патогенен щам
Аа-комплекс	Aggregatibacter actinomycetemcomitans
Червен комплекс	Porphyromonas gingivalis Treponema denticola

Комплекс	Патогенен щам
Аа-комплекс	Aggregatibacter actinomycetemcomitans
Червен комплекс	Porphyromonas gingivalis Treponema denticola Tannerella forsythia
Оранжев комплекс	Prevotella intermedia Peptostreptococcus (Micromonas) micros Fusobacterium nucleatum
Оранжево-асо-цииран комплекс	Eubacterium nodatum
Зелен комплекс	Capnocytophaga gingivalis

Диагностика на лечението ("Интервали за контрол")

☐ 1. PET plus Дата

☐ 2. PET plus Дата

Номер от първия анализ (T1)

Дата на първия анализ (T1)

Приложен анти-биотик (активна съставка)

Вид на пробата: (отбележете с кръстче)	☑ Сборна проба	☐ 1 Проба от едно място	☐ 2 Проби от различни места	☐ 3 Проби от различни места	☐ 4 Проби от различни места
Брой					
Обозначение на мястото					
Дълбочина на джоба (mm)					

☐ Моля, изпратете ми още един PET-Диагностичен кит.

☐ Резултат от анализа по факс: ____

☐ Не по пощата (само факс, съотв. E-mail)

Резултат от анализа по E-mail: ____

за попълване от MIP Pharma:

Входяща дата	Време	Приемащо лице

Баркод	Вид
	Поща

DISSERTATION RELATED PUBLICATIONS

1. Nyagolova A, Slavova V, Angelova R, et al. (December 08, 2024) Periodontitis in Patients Undergoing Coronary Angiography: A Cross-Sectional Study. Cureus 16(12): e75320. doi:10.7759/cureus.75320

2. Slavova, V., Peev, S., Nyagolova, A., & Tsoneva, Z. (2025). Peri-implantitis. Scripta Scientifica Medicinae Dentalis, 11(1). doi:http://dx.doi.org/10.14748/ssmd.v11i1.10139

3. Slavova V, Nyagolova A (June 11, 2025) Comparative Severity of Coronary Artery Disease in Patients With Peri-Implantitis Versus Periodontitis: A Prospective Observational Study. Cureus 17(6): e85794. doi:10.7759/cureus.85794