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Condition of the Oral Cavity in Patients After Heart Transplantation: A Preliminary Report

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Background: The constant impairment of the immune system caused by lifelong use of immunosuppressive drugs in patients after heart transplantation has a significant impact on oral cavity health. The aim of this study was to analyze the health of the oral cavity in patients after heart transplantation, with particular regard to occurring pathogens.

Material/Methods: The study included 25 patients after heart transplantation. The research scheme was divided into 2 parts. The first part consisted of a survey on general health and oral hygiene habits. The second part of the examination consisted of an analysis of the health of the oral cavity: the mucosa, periodontium, and hard dental tissues. Particular attention was paid to PET (test for the presence of pathogens causing periodontitis/periimplantitis) and CAT (diagnostic test for the presence of *Candida* in the oral cavity), which are real-time PCR tests used to detect pathogens causing periodontitis and microorganisms present in oral candidiasis.

Results: The conducted research and in-depth analysis of the results showed that the oral health condition in patients after heart transplantation is not satisfactory, regardless of the time that has elapsed since the surgery, sex, age, hygiene habits, or the type of immunosuppression used. The oral cavity of patients after heart transplantation is colonized with *Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis*, *Treponema denticola,* and *Candida albicans*.

Conclusions: The cooperation of the dentist with the attending physician at each stage of the treatment should play an unquestionable role.

Keywords: Heart Transplantation • Microbiota

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Background

The recommended method of treatment in end-stage heart failure patients without absolute contraindications is heart transplantation. This procedure is the treatment of last resort in patients who are refractory to medical or device therapy. After the transplantation, the recipient has to take lifelong immunosuppressive drugs enabling graft protection from host alloimmunity. These drugs have a number of significant adverse effects, including susceptibility to oncogenic and infectious factors. Permanent impairment of the immune system also influences the health of the oral cavity. The microbiome of the gastrointestinal tract and the oral cavity may play a significant role in modulation of the recipient's inflammatory processes. Particularly noteworthy in this context is the assessment of the health of hard tooth tissues, oral mucosa, and periodontium [1-4]]. Currently, periodontitis is classified as a "complex" disease, characterized by the interaction of genes with environmental factors. Risk factors for periodontitis include genetic polymorphism, obesity, smoking, general diseases, sex, age, and race. In turn, bacteria linked to poor oral health (eg, *Treponema denticola and Porphyromonas gingivalis*) are associated with heart failure severity and accompanying processes [5]. The microbiota differs among particular subtypes of solid organ recipient (heart transplant recipients, liver transplant recipients) and varies with the time elapsed since transplantation. Studies of this phenomenon are ongoing [6].

The key to achieving the balance of the condition of the oral cavity and therapeutic success is to combine the maintenance of proper oral hygiene by the patient with professional dental care [7-9].

The aim of this study was to evaluate the condition of the oral cavity in patients after heart transplantation and to assess pathogens colonizing their dental pockets. We divided the whole group of patients in 2 subgroups according to time elapsed since transplantation. We hypothesized that long-term exposition to immunosuppressive drugs significantly affects the oral microbiota. We assessed the long-term oral flora changes in patients after transplantation, and whether the duration of taking immunosuppressive drugs affects the oral microbiome. According to ISHLT [10], the mean survival of patients after heart transplantation is 12.5 years. Patients after 10 years may have beneficial factors improving survival. The role of the microbiome in graft rejection and systemic inflammation is still being discussed. We assessed whether there were significant differences between these 2 groups.

We used PET (test for the presence of pathogens causing periodontitis/periimplantitis) and CAT (diagnostic test for the presence of *Candida* in the oral cavity) (MIP Pharma) molecular and biological tests, based on the PCR (polymerase chain reaction) technique, which is a good complement to clinical trials. Their use allows for an individual approach to the patient and the possibility of implementing appropriate therapy.

Material and Methods

We enrolled consecutive heart transplant recipients who attended the outpatient clinic in our regional transplant center between September 2019 and August 2020. We examined 25 heart transplant recipients, including 18 men and 7 women, aged 18 to 69 years, divided into 2 groups:
Group 1: 13 patients up to 10 years after heart transplantation.
Group 2: 12 patients over 10 years after heart transplantation.

The study assessed health of the oral cavity, including the mucosa, periodontal tissues, and hard dental tissues, in people after heart transplantation. The study included a questionnaire in which patients were asked about gender, age, height, and weight, course of dental treatment (frequency of visits, reasons for visiting the dentist), bleeding gums during brushing, mouth and tongue burning, and reduced sense of taste. They were also asked about the type of toothbrush they use, dental floss, mouthwash, other hygiene utensils, the number of meals a day, and the consumption of food or sweetened fluids after brushing their teeth in the evening. Hard tooth tissues were assessed in both groups. The DMF indicator was used for this purpose. It provides information on the number of decayed teeth in a given population or in 1 person with permanent dentition. It is the ratio of the sum of teeth affected by caries (D – decayed teeth), teeth removed due to caries (M – missing teeth), and teeth filled (F – filled teeth) to the number of all examined teeth. This is the average DMF number for a given person. This study was conducted with the use of basic diagnostic tools used in dentistry.

In addition, oral hygiene was assessed using the following indicators:

Approximate Plaque Index API according to Lange [11], which is based on registering the presence of plaque in the interdental spaces. The examination is performed on half of the dentition on the lingual side and on half of the dentition on the vestibular side. Quadrants 1 and 3 are examined from the lingual side, while quadrants 2 and 4 are assessed from the vestibular side of the mouth. During the examination, we assessed the presence of plaque – (+) or the absence of plaque – (-).

$$\text{API} = \frac{\text{sum of interdental spaces with plaque}}{\text{sum of all assessed interdental spaces}} \times 100\%$$

API values:

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100-70% – poor hygiene
70-40% – average hygiene; improvement needed
39-25% – hygiene quite good
<25% – optimal hygiene

– Oral hygiene index OHI according to Green and Vermillion [12]. It is used to control the effectiveness of hygiene procedures. It is the sum of the plaque index and the tartar index. The most common indicator is limited to 6 teeth. We examined the cheek surfaces in teeth 16 and 26 and the lingual surfaces were examined on teeth 36 and 46, while in teeth 11 and 31 we examined labial surfaces. The values obtained for the examined teeth (surfaces) were summed and divided by the number of all examined teeth. The numerical values of the sediment and limescale indicators can range from 0 to 3, and the total value of the hygiene index is from 0 to 6. The evaluation criteria are as follows:
0 – no plaque or calculus;
1 – plaque or supragingival calculus covering up to 1/3 of the tooth surface;
2 – plaque or supragingival calculus covering more than 1/3 and less than 2/3 of the tooth surface or individual strands of the subgingival calculus;
3 – plaque or supragingival calculus covering more than 2/3 of the tooth surface or a thick band of subgingival calculus around the tooth neck.

In the periodontium, the depth of the pockets and the degree of loss of connective tissue attachment were assessed. Using these values, we can determine the morbidity and advancement of periodontal diseases. Hence, for a healthy periodontium, these values should not exceed 3 mm for the depth of the pocket (in relation to the gingival fissure), and there should be no loss of connective tissue attachment. Exceeding these values proves the occurrence of periodontitis.

In relation to periodontal tissues, the degree of tooth mobility as analyzed using the Hall mobility scale was also considered. It is another indicator where values may demonstrate periodontitis and its advancement, which is a static measurement of tooth mobility. The examination is carried out using the handle of a mirror or a probe and a finger. The evaluation criteria are as follows:
0 – minimal or no mobility of the tooth in the labio-lingual direction (physiological mobility);
1 – tooth mobility in the lingual, labio-buccal direction with a range not exceeding 1 mm;
2 – the mobility of the tooth in the dental arch in the labio-lingual direction is greater than 1mm, but not exceeding 2 mm;
3 – tooth mobility in the horizontal (labio-lingual) and/or vertical directions disrupting articulation.

The periodontal treatment needs were also assessed with the use of the CPITN (community periodontal index for treatment needs) index according to Ainamo et al [13]. The examination is performed using a WHO 621 periodontal probe. Its results are recorded in 6 dentition sextants excluding the third molars. Only the highest code in the sextant is taken into account. Testing in each sextant is only possible if there are at least 2 teeth that do not require extraction. The symptoms coded by the indicator are as follows:
0 – no supragingival calculus and "iatrogenic recesses" (prone to plaque retention), the depth of the pockets does not exceed 3 mm; no bleeding after careful probing of the pocket;
1 – no supragingival calculus and "iatrogenic recesses", the depth of the pockets does not exceed 3 mm; bleeding occurs in at least 1 area after carefully probing the pocket;
2 – the current supragingival calculus and "iatrogenic recesses", the depth of the pockets does not exceed 3 mm;
3 – the depth of the pockets is 3.5 to 5.5 mm;
4 – there is at least 1 pocket exceeding 5.5 mm.

Interpretation of the CPITN index:
TN0 – code 0 was present in all sextants. It proves healthy periodontium;
TN1 – in at least 1 sextant there was code 1 and in no other sextant this value was greater. Patients should be helped to improve their oral hygiene;
TN2 – at least in 1 sextant there was code 2 or 3 and no code 4. With such values, attention should be paid to improving oral hygiene, removal of dental calculus, and "iatrogenic recesses";
TN3 – at least in 1 sextant there was a code 4. In this situation, comprehensive periodontal treatment should be performed.

Additional tests included tests for the presence of pathogens causing periodontitis (PET) and diagnostic tests for the presence of *Candida* (CAT), which received special attention in the project. (**Table 1**).

Anaerobic gram-negative bacilli are grouped into specific complexes: dark green, red, orange, yellow, and dark purple complexes. The presence of bacteria in periodontal pockets assigned to a given complex is connected with the depth of the pockets. Bacteria of the yellow and dark purple complex are classified as symbionts in the healthy periodontium. The orange complex contains pathogens that can be found in pockets 4 to 6 mm deep. In pockets exceeding 6 mm in depth, we can find dark green (*Aggregatibacter actinomycetemcomitans*) and red (*Porphyromonas gingivalis*, *Treponema denticola*, *Tannerella forsythia*) complex pathogens, considered the most virulent in relation to periodontal tissues [14]. The infectious agents present in the oral cavity are also yeasts of the genus *Candida*. The main representative of this genus is the yeast *Candida albicans* [7].

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Table 1. Diagnostic tests for the presence of pathogens causing periodontitis (PET) and diagnostic tests for the presence of Candida (CAT) (data from the manufacturer of the tests).

PET	CAT
In vitro diagnostic test for the determination of pathogens associated with the formation and development of periodontitis/periimplantitis	An in vitro diagnostic test for the determination of pathogens that cause oral fungal infection
Is a quantitative and qualitative test for the presence of periopathogens in gingival pockets	Is a quantitative and qualitative test for the presence of pathogens in gingival pockets
Uses the Real-Time PCR method, which ensures high sensitivity and specificity	Uses the Real-Time PCR method, which ensures high sensitivity and specificity
In the project, the test used was the "standard" version, where pathogens (*Aggregatibacter actinomycetencomitans*, *Porphyromonas gingivalis* and *Treponema denticola* were identified) and the total number of bacteria was determined	In the project, the test used was the "standard" version, where pathogens *Candida albicans*, *C. glabrata*, *C. krusei*, *C. tropicalis*, *C. parapsilosis/metapsilosis/orthopsilosis* are identified and the total number of pathogens is determined
The determination of pathogens in the gingival pockets was possible by taking a proper sample of the bacterial plaque	Determination of pathogens was possible by taking the correct sample by rubbing the places presumably infected with yeast using points
Using tweezers, a sterile paper point was placed in the gingival pocket. It was introduced to its bottom and left for about 10-20 seconds, then the point was placed in a transport tube. Transport tubes in the diagnostic kit were sent to the analytical laboratory of MIP Pharma GmbH, the test result along with the individual treatment recommendation were received by mail and e-mail	The samples for testing were taken with points from places presumably infected with yeast, and the points was placed in a transport tube. The transport tubes in the diagnostic kit were sent to the analytical laboratory of MIP Pharma GmbH, the test result together with the individual treatment recommendation were received by mail and e-mail

Inclusion Criteria

We included consecutive adult patients after heart transplantation, who regularly attended an outpatient clinic in a regional transplant center. The participants signed written informed consent for participation in the study. The study was performed in accordance with the Declaration of Helsinki. The Bioethics Committee of the Medical University of Silesia approved the study (decision No. KNW/0022/KB1/35/I/19).

Exclusion criteria

The project did not involve patients who did not consent to participate in the study, patients who did not show willingness to cooperate in the study, incapacitated people, soldiers, prisoners, persons with business or private ties with the person conducting the examination, or persons undergoing orthodontic treatment. Toothless patients, patients with active gingival bleeding, patients with insufficient number of teeth to assess oral hygiene indicators and to conduct PET and CAT tests were also excluded from the study.

Statistical Methods

We presented categorical variables as counts and percentages. Continuous variables are expressed as means and standard deviations for normally distributed data or median with lower and upper quartiles. To verify the normal distribution of data, we used the Shapiro-Wilk test. The chi-square test was utilized to compare categorical variables, and the *t* test or the Mann-Whitney U test was used to compare continuous variables. A *P* value <0.05 was considered statistically significant.

Results

Mean age of the 13 patients (3 women) up to 10 years after transplantation was 45.8±16.2 (Group 1.). The mean age of 12 patients (4 women) over 10 years after transplantation was 55.8±15.0 years (Group 2). The mean time from transplantation in Group 1 was 7.2±2.2 and in Group 2 it was 14.0±3.8 years. In Group 1, 11 (92.3%) patients received tacrolimus and 1 (7.7%) received cyclosporine A as a basic regimen. In Group 2, 8 (58.3%) patients received tacrolimus and 5 (41.7%) received cyclosporine. None of the investigated patients received steroids, anticonvulsants, dihydropyridine calcium channel blockers, verapamil, or diltiazem. Clinical characteristics of the 2 groups are presented in **Table 2**.

Statistical analysis of hygiene habits shows that the groups were comparable. No significance difference between groups was noted in use of dental floss or mouthwash (*P*>0.05). In

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Table 2. Clinical characteristics of the 2 analyzed groups.

Clinical parameter	Group No.1 (≤10 years after HTx), 13 pts., N (%)	Group No.2 (>10 years after HTx), 12 pts., N (%)
Diabetes	6 (46.2%)	7 (58.3%)
Impaired glucose tolerance	5 (38.5%)	2 (16.7%)
Hypertension	6 (46.2%)	12 (100%)
Chronic kidney disease (eGFR<30 ml/min/1.73 m^2)	0 (%)	4 (33.3%)
Dyslipidemia	7 (53.8%)	7 (58.3%)
Obesity	1 (7.7%)	1 (8.3)
Chronic obstructive pulmonary disease	0 (0%)	1 (8.3%)

HTx – heart transplantation.

Table 3. Data on hygiene habits.

Oral hygiene habits	Group No. 1	Group No.2
Dental floss and rinse (P>0.05)	30.8%	25%
Oral hygiene started as teenager (P>0.05)	58.3%	92.3%
Oral hygiene started in the age of 20 years (P>0.05)	25%	7.7%
Oral hygiene started in the age of 30 years (P>0.05)	16.7%	7.7%
Toothbrushing time (P>0.05)	2.6 minutes	2.8 minutes
Toothbrushing frequency (P>0.05)	1.8 time a day	1.9 time a day
Toothbrush replacement frequency (P>0.05)	3.2 months	3.5 months

Group 1, only 30.8% of respondents used dental floss and mouthwash, while in Group 2 it was 25%. Groups 1 and 2 started performing oral hygiene at a similar age: 58.3% vs 92.3% as a teenager, 25% vs 7.7% by age 20 years, and 16.7% vs 7.7% by age 30 years, but the differences between groups were not statistically significant (*P*>0.05). Toothbrushing time, toothbrushing frequency, and toothbrush replacement frequency also proves homogeneity and similarity between groups, with no statistically significant difference (*P*>0.05). The average time of brushing teeth in Group 1 was 2.6 minutes, while in Group 2 it was 2.8 minutes. In Group 1, the patients brushed their teeth 1.8 times a day on average, and 1.9 times a day in group No. 2. Regarding the frequency of toothbrush replacement, patients in Group 1 replaced toothbrushes on average every 3.2 months, while those in Group 2 replaced brushes every 3.5 months on average. Data on hygiene habits are presented in **Table 3**.

No statistically significant (*P*>0.05) difference was observed in the mean DMF values in groups 1 and 2. The mean DMF index in Group 1 was 16.1, while in Group 2 it was 18.1.

In the case of the remaining indices, API and OHI the differences between Group 1 and Group 2 were not statistically significant (0.7 vs 0.6, 1.6 vs 1.4; *P*> 0.05), for CPTIN: 46.2% TN1, 53.8% TN2 vs 16.7% TN1 and 83.3% TN2; *P*>0.05, which indicates the similarity and homogeneity of both groups.

The degree of mobility of the teeth was not significantly different between groups (*P*>0.05). In Group 1, 76.9% of the respondents had a degree of mobility of 0, and 23.1% had a degree of 1, while in Group 2 it was 66.7% vs 33.3%. Oral health indicators assessment is summarized in **Table 4**.

All patients taking Cyclosporin A developed hyperplastic gingivitis (1 in Group 1 and 5 in Group 2). Pathologic pockets (defined as periodontal fissure >3 mm in depth) were present despite the type of basic immunosuppressive regimen. However, in patients taking tacrolimus, it was present in 6 (50.0%) patients in Group 1 vs 5 (71.4%) in Group 2, but it was present in all patients taking cyclosporine A in both groups. These data are summarized in **Table 5**.

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Table 4. Oral health indicators assessment.

Oral hygiene index	Group No. 1	Group No. 2
DMF (P>0.05)	16.1	18.1
API (P>0.05)	0.7	0.6
OHI (P>0.05)	1.6	1.4
CPTIN – TN1 (P>0.05)	46.2%	16.7
CPTIN – TN2 (P>0.05)	53.8%	83.3%
Degree of mobility of the teeth – I° (P>0.05)	76.9%	66.7%
Degree of mobility of the teeth – II° (P>0.05)	23.1%	33.3%

Table 5. The prevalence of hyperplastic gingivitis and pathological pockets in the analyzed groups depending on the type of immunosuppression.

Symptoms in patients taking	Cyclosporin A		Tacrolimus	
	Group No. 1	Group No. 2	Group No. 1	Group No. 2
Hyperplastic gingivitis	1 (100%)	5 (100%)	–	–
Pathologic pockets	1 (100%)	5 (100%)	6 (50%)	5 (71.4%)

Table 6. The percentage distribution of the bacteria and *Candida albicans* detected in the analyzed groups.

Bacterial pathogenes	Group No. 1	Group No. 2
Treponema denticola	61.5%	75.0%
Porphyromonas gingivalis	–	41.6%
Aggregatibacter actinomycetencomitans	–	16.7%
Candida albicans	76.9%	58.3%

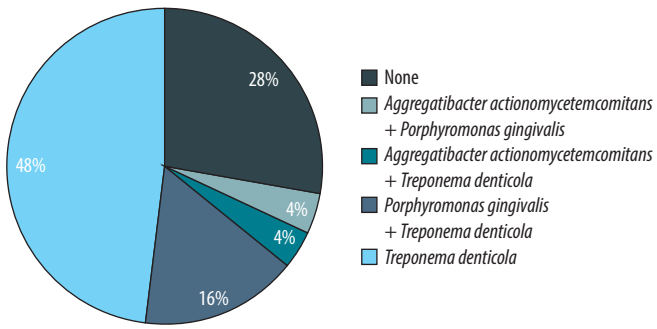

Figure 1. Summarized occurrence of the bacterial pathogens observed in dental pockets in all patients.

The presence of bacterial and fungal infections in both analyzed groups is presented in **Table 6**.

In Group 1, all the bacterial infections coexisted with fungal infection. In 6 patients, 2 bacterial pathogens coexisted: in 4 cases *Treponema denticola* and *Porphyromonas gingivalis*, in 1 case *Treponema denticola* and *Aggregatibacter actinomycetemcomitans,* and in 1 case *Aggregatibacter actinomycetemcomitans* with *Porphyromonas gingivalis*. *Candida albicans* in 5 patients coexisted with *Treponema denticola (*in 2 *patients Treponema denticola* and *Porphyromonas gingivalis)*. In 1 patient *Porphyromonas gingivalis* and *Aggregatibacter actinomycetemcomitans* coexisted, and in 1 patient *Candida albicans* occurred without bacterial infection. **Figure 1** summarizes the occurrence of bacterial pathogens.

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Table 7. Depth of gingival pockets according to pathogen in patients with negative and positive PET results.

Depth of gingival pockets according to pathogen	Negative PET result	Positive PET result
Aggregatibacter actinomycetencomitans (P>0.05)	3.9 mm	4.5 mm
Porphyromonas gingivalis (P=0.04)	3.8 mm	4.5 mm
Treponema denticola (P<0.001)	4.2 mm	3.25 mm

The analysis of the depth of the gingival pockets – 3.9 (0.8) mm in Group 1 vs 3.9 (0.8) mm in Group 2 – and the correlating loss of connective tissue attachment indicated no statistically significant differences (*P*>0.05). The minimum pocket depth in both groups was 3 mm. The deepest pocket depth was 6 mm in Group 1 and 5 mm in Group 2.

The values of gingival pockets were also statistically analyzed in patients with negative and positive PET results in relation to all detected pathogens (*Aggregatibacter actinomycetemcomitans, Porphyromonas gingivalis* and *Treponema denticola*). These data are presented in **Table 7**.

Subjects with more than 1 bacterial pathogen versus the remaining group showed only a trend towards deeper pockets – 4.3 (0.6) mm vs other patients 3.7 (0.6) (*P*>0.5).

Discussion

The conducted research and an in-depth analysis of the results showed that the oral health of patients after heart transplantation is not satisfactory, regardless of the time elapsed since the surgery, sex, age, hygiene habits, or the type of immunosuppression used. This applies to both the condition of the tooth's hard tissues and the periodontium. Particular attention should be paid to the need for people taking immunosuppressive drugs to be especially careful in oral hygiene, considering the possibility of odontogenic (inflammatory) foci affecting the transplanted organ and the entire body. Similar observations concerning hygiene negligence were shown by numerous authors [15-19]. Particular attention should be paid to the fact that patients with impaired immune system are extremely exposed to superinfections, such as around the mouth, with various types of pathogens. This is associated with a decrease in cellular and humoral immunity, thus increasing the risk of fungal, bacterial, or viral infections, mainly oral candidiasis and periodontitis [16,20]. Thus, in 96% of the surveyed people, regardless of the type of immunosuppression, fungal infection of the oral cavity with the pathogen *Candida albicans* was found. Particular attention was drawn to this by Siahi-Benlarbi et al [19], who in their studies found 100% of superinfection with *Candida albicans* in the study group, which were children after heart transplant. Similar observations were made in the work of Dongari-Bagtzoglou et al [21]. To date, there have been no studies devoted to exact identification of pathogens causing periodontitis among patients after heart transplantation, but much is known about this disease [15-18,22-27]. Kurzeja et al [15] drew attention to the particular susceptibility to proliferative gingivitis, mainly in young people. McGaw et al [28] proveda directly proportional relationship between the depth of the gingival pockets and the dose of an immunosuppressive drug. In our study, 84% of all patients had at least 1 pathogen responsible for periodontal disease, regardless of the type of immunosuppressive therapy. The dental pockets' microbiota slightly differed between patients up to and over 10 years after transplantation. The most common was *Treponema denticola*, accounting for 61% of all bacteria present. In the group up to the 10 years after transplant, it was the only bacterial pathogen diagnosed in the pockets. We also found that the presence of *Porphyromonas gingivalis* and *Treponema denticola* was associated with aggravated local periodontitis. Low-intensity local inflammation can aggravate the chronic proinflammatory state, which in turn may have an immunomodulatory effect. In the study of Bohn et al [5], the 2 pathogens present in the oral cavity were associated with generalized inflammation, endotoxemia, and heart failure severity in heart failure patients. As shown by other authors, the microbiota of organ transplant recipients may enhance rejection by producing metabolites that activate humoral and cell-mediated alloreactivity [29]. On the other hand, some microorganisms may enhance graft tolerance [30]. Further investigations of the role of these pathogens in chronic inflammation and graft rejection may be valuable.

Our results clearly showed the presence of pathogens causing periodontitis and oral candidiasis in the oral cavity of patients after heart transplantation. We showed a connection between presence of particular pathogens in dental pockets and the advancement of gingival tissue destruction.

This is why proper dental care for patients after organ transplantation is so important. It should be noted that in the case of patients with pathogens causing inflammation in the oral cavity, proper dental care and implementation of appropriate treatment can completely eliminate them.

Study Limitations

A significant limitation of the study is its small sample size. Due to this fact some correlations did not reach statistical

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significance. In more numerous groups we could have performed age- and sex-matched analyses. It would be also interesting to investigate the whole gastrointestinal tract microbiota in relation to graft tolerance.

Conclusions

The obtained results show that oral hygiene and the condition of hard tooth tissues and periodontium in patients after heart transplantation is not satisfactory. More than once, the respondents noted full involvement in the underlying disease, without a sufficient focus on the health of the oral cavity. Impairment of the immune system caused by the continued intake of immunosuppressants increases the likelihood of oral fungal, bacterial, or viral infections. The detected pathogens in patients after heart transplantation were *Candida albicans, Aggregatibacter actinomycetemcomitans, Porphyromonas gingivalis,* and *Treponema denticola.* Cyclosporin A therapy, which causes proliferative gingivitis, further aggravates this problem in periodontal tissues.

Proper preparation of the patient's oral cavity before starting immunosuppressive therapy and appropriate dental care after heart transplantation will reduce the incidence of complications and minimize the risk of their generalization. The cooperation of the dentist with the attending physician at each stage of treatment should play an important role.

Declaration of Figures' Authenticity

All figures submitted have been created by the authors, who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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