



COMORBIDITIES

Periodontal disease and influence of periodontal treatment on disease activity in patients with rheumatoid arthritis and spondyloarthritis

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Abstract

The aim of this study was to assess the prevalence of periodontal disease and the effect of periodontal treatment in patients with rheumatoid arthritis (RA) and spondyloarthritis (SpA). Forty-four RA patients, thirty SpA patients and thirty-nine healthy volunteers were recruited to the study. Periodontal examination included the approximal plaque index (API), bleeding on probing (BoP), probing depth (PD) and number of teeth. Samples from the deepest periodontal pockets were taken for the detection of *Porphyromonas gingivalis* DNA with the use of the polymerase chain reaction. All subjects with periodontitis, who completed the study, received periodontal treatment consisting of scaling/root planing and oral hygiene instructions. Disease activity scores, clinical and laboratory parameters were assessed before and 4–6 weeks after periodontal treatment. No significant difference in the prevalence of periodontal disease and the presence of *P. gingivalis* DNA were found in RA and SpA patients compared to healthy controls. Significantly higher API (80% vs 63%; $p=0.01$) and a lower number of teeth (20 vs 25, $p=0.001$) were found in RA patients. BoP was significantly elevated in SpA patients (51% vs 33%, $p=0.02$). Disease activity measured by the DAS28(CRP) was significantly reduced in RA patients after periodontal treatment ($p=0.002$). Clinical and biochemical parameters were not improved in SpA patients. Nonsurgical periodontal treatment had an impact on the decrease in RA activity. Periodontal examination is necessary in patients with RA to detect and treat periodontitis at an early stage.

Keywords Rheumatoid arthritis · Spondyloarthritis · Periodontitis · *Porphyromonas gingivalis* · Periodontal treatment

Introduction

Periodontal disease is highly prevalent in the global population. It was estimated that in 2010 severe periodontitis affected 10.8% or 743 million people worldwide [1]. Periodontal disease, initiated by oral bacteria accumulated in dental plaque, is characterized by destructive inflammation of teeth-supporting tissues. Although the inflammatory process is local, it has been shown that periodontitis can influence systemic health. Various studies demonstrated that periodontal disease was associated with cardiovascular disease, diabetes and adverse pregnancy outcomes [2, 3].

Rheumatoid arthritis (RA) is an autoimmune disease characterized by symmetric polyarthritis. The inflammatory process typically affects small joints of hands and feet. If untreated, it may result in structural damage of the joints involved and lead to the loss of their function and the patient's significant disability. Recent studies have shown that periodontal disease could be linked to rheumatic diseases, in particular to RA [4, 5]. Periodontitis and RA share

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similar risk factors, in particular cigarette smoking [6, 7]. Proinflammatory cytokines, including tumor necrosis factor (TNF)- α , drive bone destruction in both diseases [8]. Moreover, the specific immune response to citrullinated proteins represents a key feature in the pathophysiology of RA. For this reason, *Porphyromonas gingivalis*, the major pathogen associated with periodontitis, is of special interest. *P. gingivalis* is the only known Prokaryote that produces the enzyme peptidylarginine deiminase (PAD) able to citrullinate its own and the host's proteins [9, 10]. Unlike the human enzyme, bacterial PAD deiminates both free arginine and C-terminal arginine residues [9]. It has been hypothesized that different mechanism of citrullination could lead to the breaking of immune tolerance and contribute to the development of immune response to endogenous citrullinated proteins in susceptible individuals through the generation of neoepitopes [11].

Spondyloarthritis (SpA) is a heterogeneous group of chronic, inflammatory diseases, including ankylosing spondylitis (AS), psoriatic arthritis (PsA), arthritis associated with inflammatory bowel disease and other conditions. Distinct disorders from the SpA family share similar clinical manifestations, such as inflammation of axial joints, in particular sacroiliitis, asymmetric oligoarthritis, dactylitis and enthesitis. It has been suggested that, in addition to genetic predisposition, the microbiome may play a role in the pathogenesis of SpA [12]. Recently, some researchers have also demonstrated that periodontal disease was more prevalent in patients with AS, PsA and psoriasis [13, 14].

Considering these reports suggesting an association between rheumatic diseases, in particular RA, and periodontal disease, we investigated the prevalence of periodontal disease and the presence of *P. gingivalis* DNA in the samples from periodontal pockets in Polish patients with RA and SpA. Furthermore, we assessed the impact of periodontal treatment on the activity of RA and SpA.

Materials and methods

Study population

The study was designed as both case–control and intervention study. Forty-four RA patients, thirty SpA patients, including twenty-six AS patients and four PsA patients with spinal involvement, and thirty-nine healthy volunteers were enrolled in this study. All participants in RA and SpA groups met the EULAR/ACR 2010 or the ASAS 2009/2011 criteria, respectively, and were recruited from patients hospitalized between 2011 and 2016 in the Department of Rheumatology and Internal Medicine, Wrocław Medical University. Healthy controls selected from hospital staff or their relatives were divided into two groups matched to patients in

terms of age and sex. Exclusion criteria included: (1) number of present teeth < 6; (2) periodontal treatment within the previous 3 months; (3) chronic infections (HIV infection, hepatitis B or C); (4) chronic disorder requiring chronic or intermittent use of antibiotics; (5) advanced kidney or liver insufficiency; (6) unbalanced diabetes; (7) pregnancy or breast feeding.

The study was conducted according to the principles of the Declaration of Helsinki and was approved by the Bioethics Committee of Wrocław Medical University (no. 818/2012). Written informed consent was obtained from all patients and healthy controls prior to the inclusion into the study.

Periodontal examination and periodontal treatment

For all study participants, clinical periodontal examination was performed by the same periodontologist with a wide clinical experience in the Department of Oral Pathology, Wrocław Medical University. The following clinical periodontal parameters were evaluated: (1) approximal plaque index (API) [15]; (2) bleeding on probing index (BoP) [16]; (3) probing depth (PD); (4) number of teeth present. The presence of dental plaque, bleeding on probing and probing depth were assessed at four sites per tooth: mesial, distal, buccal and lingual using a manual periodontal WHO probe. The periodontal status was assessed according to the simplified periodontal disease classification of Offenbacher, where five clinical conditions are described: healthy periodontium (PD \leq 3 mm, BoP < 10%), gingivitis (PD \leq 3 mm, BoP > 10%) and periodontitis—P1 (PD \geq 4 mm, BoP < 10%), P2 (PD \geq 4 mm, 10% < BoP < 50%), P3 (PD \geq 4 mm, BoP \geq 50%) [17].

All patients with diagnosed periodontitis received non-surgical periodontal treatment. During the first visit, supragingival and subgingival calculus were removed with ultrasonic scalers, and oral hygiene instructions with recommendations to use chlorhexidine toothpaste, mouthwash and/or tooth gel were given. In the case of presence of PD \geq 4 mm, root planing was performed using subgingival scalers and hand curettes under local anesthesia on the next visit. The treatment procedures were conducted over the course of 1–4 visits, depending on the extent of periodontal lesions.

In all study participants, swabs from the deepest periodontal pockets or interdental spaces, depending on periodontal status, were taken for detection of *P. gingivalis* DNA.

Detection of *Porphyromonas gingivalis* DNA

Genetic analyses were performed in the Laboratory of Molecular Biology Research, Department of Oral Pathology, Wrocław Medical University. Genomic DNA from clinical

samples was obtained using the modified CTAB method [18, 19]. Some changes were made in the DNA isolation process to adapt the method to laboratory conditions and the equipment available. Each microbrush with material taken from periodontal pockets or interdental spaces was stored in a freezer at -20°C . Each brush was placed in a 1.5 ml Eppendorf tube. 100 μl of sterile water was added and the content was mixed in a vortex apparatus. After 3 min, the brushes were removed from the tubes and 70 μl of 10% SDS (sodium dodecyl sulfate) and 50 μl of 1 mg/ml proteinase K (SIGMA Aldrich, St. Louis, Missouri, USA) were added, and the tubes were incubated at 65°C . Then, 100 μl of 5 M NaCl and 100 μl CTAB/NaCl (0.274 M CTAB (Hexadecyl trimethylammonium bromide, 0.877 M NaCl, Sigma Aldrich) were added to each tube, and they were once again incubated at 65°C . 750 μl of chloroform (Chloroform: Isoamyl Alcohol Mixture 24: 1, Fluka Analytical) was added to each tube and mixed in a vortex apparatus for 10 s. The mixture in the tubes was centrifuged in a MiniSpin[®] centrifuge (Eppendorf) for 5 min at 12,000 rpm. Then, the supernatant was transferred and 0.6 volume of isopropanol was added (2-propanol, 99% SIGMA Aldrich). After 30-min incubation of the material at -20°C to precipitate the DNA, the material was centrifuged for 30 min at 12,000 rpm, the supernatant from the DNA pellet was drained and the DNA was dried at room temperature. Finally, 100 μl of water (Sigma Aldrich) was added to each test tube. Samples were stored at -20°C .

The polymerase chain reaction (PCR) was described in detail in the publication by Radwan-Oczko et al. [20]. The mixture obtained from the PCR was subjected to electrophoresis. The presence of a DNA band at the level of 405 base pairs was considered a positive result of the reaction.

Clinical and biochemical assessment of RA and SpA activity

In RA and SpA patients, clinical and biochemical activity of the disease was evaluated in the Department and Clinic of Rheumatology and Internal Medicine, Wroclaw Medical University, at a baseline and 4–6 weeks after the completion of periodontal therapy. Clinical activity was evaluated based on the history and physical examination including the number of tender and swollen joints. Biochemical activity was assessed by laboratory markers, such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). The tests were performed in a certified laboratory at the University Hospital using commercially available test kits. In addition, TNF- α , matrix metalloproteinase (MMP)-3 and MMP-9 levels were also determined before and after periodontal treatment. Blood samples received from the subjects were centrifuged at 3500 RPM and isolated serum was stored in a freezer at -25°C until immunological testing.

The serum levels of TNF- α , MMP-3 and MMP-9 were determined using commercial ELISA kits (Human TNF- α Immunoassay Quantikine ELISA, R&D Systems, Minneapolis, USA, Human MMP-3 Coated ELISA Kit, Thermo Fisher Scientific, Waltham, Massachusetts, USA, Human MMP-9 Coated ELISA Kit, Thermo Fisher Scientific, Waltham, Massachusetts, USA, respectively) according to the manufacturer's instructions.

Furthermore, to evaluate the improvement in disease activity after the completion of periodontal treatment, the Disease Activity Score (DAS28), the Simplified Disease Activity Index (SDAI) and the Clinical Disease Activity Index (CDAI) were used in RA patients, while the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and the Ankylosing Spondylitis Disease Activity Score (ASDAS) were used in SpA patients. Improvement in physical function was assessed with the Health Assessment Questionnaire (HAQ) in RA patients and with the Bath Ankylosing Spondylitis Functional Index (BASFI) in SpA patients.

Statistical analysis

The results were presented as median with the minimum and maximum values for continuous variables and as numbers or percentages for categorical variables. Wilcoxon's signed-rank test was applied to compare samples before and after periodontal treatment. To compare parameters between RA and SpA patients and both control groups, Mann–Whitney test was performed for continuous variables, and Chi squared test was performed for categorical variables. The correlation between periodontal and rheumatic parameters was analyzed by Pearson or Spearman correlation coefficients, as appropriate. Two-sided p values less than 0.05 were considered statistically significant. All data were analyzed using STASTICA 12 PL software.

Results

Demographic and medical history data of RA and SpA patients are presented in Table 1. Gender ratios and the body mass index (BMI) were similar in all study groups. There was a significant difference in the number of current smokers. The characteristics of the disease and current antirheumatic treatments are given in Table 1. The vast majority of patients in the RA group were seropositive. In both study groups, patients suffered from long-standing disease.

Prevalence of periodontal disease and periodontal parameters

Of all the patients, periodontitis was diagnosed in 33 of 44 (75%) RA patients, 9 (20%) had gingivitis, and only 2 (5%)

Table 1 Background and disease characteristics in groups of patients and controls

Characteristics	RA (<i>n</i> = 44)	Controls for RA (<i>n</i> = 29)	<i>p</i> value	SpA (<i>n</i> = 30)	Controls for SpA (<i>n</i> = 25)	<i>p</i> value
Age: median (min–max), years	58 (28–80)	50 (29–69)	0.04	43 (27–61)	45 (28–69)	0.76
Sex: ratio female/male	33/11	19/10	0.38	4/26	5/20	0.51
BMI: median (min–max), kg/m ²	25 (19–36)	26 (19–36)	0.23	26 (19–41)	25 (20–36)	0.96
Current smoking (%)	12 (27)	1 (3)	0.009	8 (27)	1 (4)	0.02
Former smoking (%)	25 (57)	7 (24)	0.006	15 (50)	7 (28)	0.1
Disease duration: median (min–max), years	13 ± 9	–	–	12 ± 8	–	–
Bony erosions present (%)	24 (55)	–	–	–	–	–
RF-positive (%)	38 (88)	–	–	–	–	–
Anti-CCP-positive (%)	41 (95)	–	–	–	–	–
Current treatment with DMARDs (%)	36 (82)	–	–	8 (27)	–	–
Current treatment with biologic agents (%)	12 (27)	–	–	16 (53)	–	–
Current treatment with glucocorticoids (%)	26 (59)	–	–	5 (17)	–	–

RA rheumatoid arthritis, SpA spondyloarthritis, BMI Body Mass Index, RF rheumatoid factor, anti-CCP anticyclic citrullinated peptide antibodies, DMARDs disease-modifying antirheumatic drugs

had healthy periodontium. In turn, 20 of 30 (67%) SpA patients had periodontitis, 8 (27%) had gingivitis, and 2 (6%) had healthy periodontium. No difference was observed in the prevalence of periodontal disease in RA and SpA patients compared to the corresponding control groups ($p = 0.15$; $p = 0.88$). Table 2 shows periodontal parameters in patients with RA and healthy subjects. RA patients had poor oral hygiene—the mean API value was significantly higher in RA patients than in the controls (80% vs 63%). Patients with RA had a lower number of teeth, as well (20 vs 25). A significant correlation was found between the percentage of periodontal pockets ≥ 4 mm deep and disease duration in the RA group (Fig. 1). RA patients with longstanding disease had less periodontal pockets ≥ 4 mm deep. Table 2 shows periodontal parameters in patients with SpA and controls. Bleeding on probing, as a measure of gingival inflammation, was significantly increased in patients with SpA compared to the control subjects (51% vs 33%).

Prevalence of *Porphyromonas gingivalis* DNA

P. gingivalis DNA was detected in samples from periodontal pockets in 13 of 32 (41%) patients with RA and 6 of 21 (29%) patients with SpA. Positive results for *P. gingivalis* DNA were received in 7 of 16 (44%) subjects in the control group for RA and 4 of 12 (33%) subjects in the control group for SpA. There was no significant difference between the groups of patients and corresponding control groups. The detection of *P. gingivalis* DNA in the samples from periodontal pockets did not correlate with the presence of rheumatic disease, but were related to periodontitis. Negative results for *P. gingivalis* DNA were received in all the subjects with gingivitis or healthy periodontium ($p = 0.012$, Fig. 2).

Table 2 Periodontal parameters and self-reported oral habits in groups of patients and controls

Characteristics	RA (<i>n</i> = 44)	Controls for RA (<i>n</i> = 29)	<i>p</i> value	SpA (<i>n</i> = 30)	Controls for SpA (<i>n</i> = 25)	<i>p</i> value
API: median (min–max), %	91 (20–100)	66 (12–100)	0.005	73 (7–100)	80 (14–100)	0.82
BoP: median (min–max), %	35 (5–100)	28 (0–92)	0.10	51 (0–100)	28 (0–92)	0.03
Percentage of periodontal pockets ≥ 4 mm deep: median (min–max), %	9 (0–85)	3 (0–59)	0.14	8 (0–59)	6 (0–59)	0.46
Number of teeth: median (min–max)	20 (9–32)	26 (16–32)	0.002	27 (9–32)	27 (16–32)	0.34
Number of visits to the dentist: median (min–max), per year	1 (0–4)	1 (0–12)	0.07	1 (0–4)	1 (0–4)	0.44
Teeth brushing: median (min–max), per day	2 (1–3)	2 (0–3)	0.10	2 (0–3)	2 (0–3)	0.72

RA rheumatoid arthritis, SpA spondyloarthritis, API approximal plaque index, BoP bleeding on probing

Fig. 1 Correlation between percentage of periodontal pockets ≥ 4 mm deep and disease duration in RA group

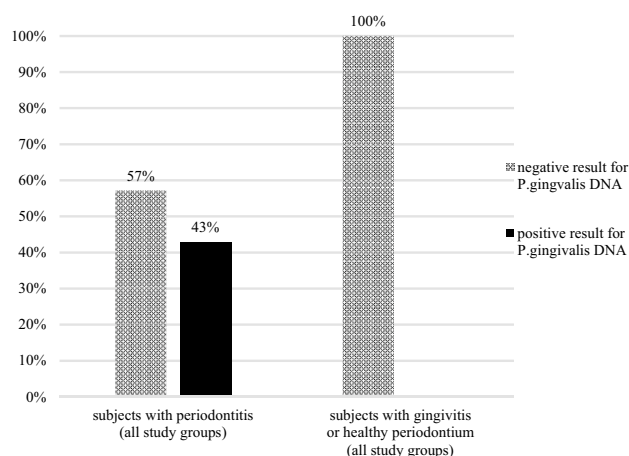
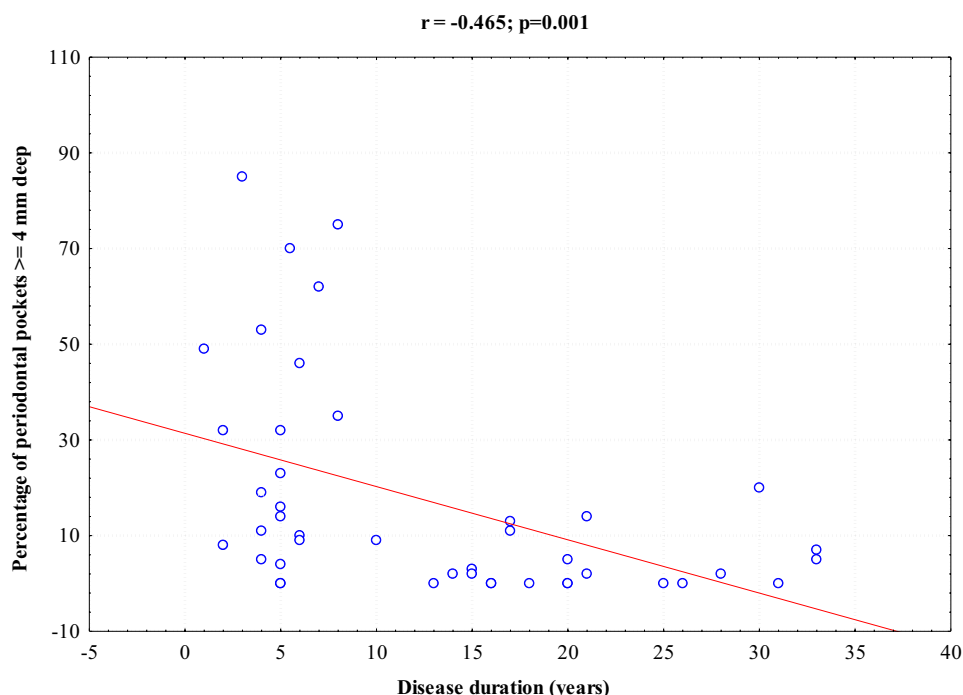


Fig. 2 Prevalence of *Porphyromonas gingivalis* DNA in study groups with respect to their periodontal status

Periodontal treatment

Finally, 22 of 44 patients with RA and 12 of 30 patients with SpA completed periodontal treatment and were included for further evaluation. All other patients diagnosed with periodontitis refused to complete periodontal treatment or participate in a follow-up visit for personal reasons or due to other medical conditions. Table 3 and 4 present rheumatological evaluation and inflammatory markers before and 4 to 6 weeks after periodontal treatment in patients with RA and SpA. After the completion of periodontal treatment, the disease activity measured by the DAS28(CRP), SDAI and

CDAI was significantly reduced in RA patients ($p = 0.002$; $p = 0.004$; $p = 0.004$, respectively). Clinical parameters and patients' functional capacity measured with the HAQ were significantly improved, as well (Table 3). No significant decrease in inflammatory markers, TNF- α , MMP-3 and MMP-9 levels at 4–6 weeks following periodontal treatment was found (Table 3). Disease activity indices, clinical and laboratory parameters did not show any significant improvement after periodontal treatment in SpA patients (Table 4).

Discussion

Recently, some studies have demonstrated that the prevalence of periodontitis was higher in individuals with RA, although the vast majority of them included small numbers of patients. The published data may be difficult to interpret due to different methods of periodontal examination and different definitions of periodontitis. In the present study, we did not find a significantly higher prevalence of periodontal disease in RA and SpA patients compared to their corresponding control groups, although the small sample size and confounding factors such as smoking status, age and gender should be noted. Likewise, some other researchers reported similar prevalence of periodontitis in RA patients and the controls [21, 22]. Furthermore, periodontal status could be influenced by medications commonly used in rheumatic diseases. Mayer et al. demonstrated that anti-TNF- α therapy resulted in a significant reduction in periodontal inflammation determined by BoP and PD [23]. In our study,

Table 3 Disease activity scores, clinical and laboratory parameters before and after periodontal treatment in RA patients

Characteristics	Before treatment (<i>n</i> = 22)	After treatment (<i>n</i> = 22)	<i>p</i> value
Number of tender joints	4 (0–21)	2 (0–11)	0.04
Number of swollen joints	2.5 (0–15)	1 (0–7)	0.01
VAS (mm)	42.5 (10–90)	40 (0–80)	0.01
Morning stiffness (min)	30 (5–150)	20 (0–120)	0.24
DAS28 (ESR)	4.32 (1.89–7.3)	3.84 (2.03–5.65)	0.04
DAS28 (CRP)	3.26 (1.31–5.66)	2.76 (1.1–4.28)	0.002
SDAI	16.36 (4–53.27)	13 (1–29)	0.001
CDAI	15 (3–50)	12 (0–28)	0.002
HAQ	1.5 (0.25–2.75)	1.5 (0–2.5)	0.01
ESR (mm)	17 (1–68)	22 (2–61)	0.79
CRP (mg/dl)	3.53 (0.14–29.33)	3.64 (0.08–12.36)	0.31
TNF- α (pg/ml)	8.33 (0.1–320.05)	1.16 (0.23–41.78)	0.31
MMP-3 (pg/ml)	14.94 (2.87–443.69)	17.24 (3.88–325.93)	0.77
MMP-9 (pg/ml)	142.22 (54.59–1334.26)	147.96 (59.93–714.68)	0.71

VAS visual analogue scale, DAS Disease Activity Score, SDAI Simplified Disease Activity Index, CDAI Clinical Disease Activity Index, HAQ Health Assessment Questionnaire, ESR erythrocyte sedimentation rate, CRP C-reactive protein, TNF- α tumor necrosis factor- α , MMP matrix metalloproteinase

Values are presented as median with minimum and maximum

Table 4 Disease activity scores, clinical and laboratory parameters before and after periodontal treatment in SpA patients

Characteristics	Before treatment (<i>n</i> = 12)	After treatment (<i>n</i> = 12)	<i>p</i> value
Schober's test (cm)	1.7 (0–5)	0.8 (0.2–4)	0.17
Ott's test (cm)	0.8 (0–4.5)	0.5 (0.4–2.7)	0.8
Finger-to-floor distance (cm)	28 (3–49)	39 (0–44)	0.64
Occiput-to-wall distance (cm)	6 (0–25)	7 (0–20)	0.67
Chest expansion (cm)	3 (1.5–8)	3 (1–4.5)	0.16
VAS (mm)	35 (0–98)	27.5 (0–60)	0.58
Morning stiffness (min)	47.5 (0–240)	45 (10–120)	1
BASDAI	3.6 (0.1–9)	4.4 (1–6.1)	0.62
ASDAS (ESR)	2.16 (0.51–5.11)	2.24 (1.04–4.01)	0.86
ASDAS (CRP)	2.49 (0.55–5.11)	2.62 (0.47–3.95)	0.88
BASFI	3.3 (0–9.4)	3.2 (1.8–7.9)	0.28
ESR (mm)	11 (2–64)	20.5 (2–101)	0.06
CRP (mg/dl)	3.57 (0.61–34.24)	9.86 (0.62–31.87)	0.18
TNF- α (pg/ml)	13.93 (0.85–985.35)	0.89 (0.1–1031.92)	0.31
MMP-3 (pg/ml)	8.62 (2.46–37.73)	9.74 (5.24–36.8)	0.69
MMP-9 (pg/ml)	156.33 (34.52–1405.56)	215.1 (122.44–1224.38)	0.27

Values are presented as median with minimum and maximum

VAS visual analogue scale, BASDAI Bath Ankylosing Spondylitis Disease Activity Index, ASDAS Ankylosing Spondylitis Disease Activity Score, BASFI Bath Ankylosing Spondylitis Functional Index, ESR erythrocyte sedimentation rate, CRP C-reactive protein, TNF- α tumor necrosis factor- α , MMP matrix metalloproteinase

almost one-third of patients with RA and more than half of patients with SpA were taking biologic agents during the project. In RA patients, the percentage of probing pockets ≥ 4 mm deep was inversely correlated with the duration of the disease. Less severe periodontal lesions in patients with long-standing disease might be explained by the beneficial effects of long-term treatment with antirheumatic drugs,

including nonsteroidal anti-inflammatory drugs (NSAIDs) and biologic agents. On the other hand, corticosteroids used in RA can increase the risk of infection due to the suppression of the immune system [24]. As steroid therapy induces a decrease in intestinal calcium absorption, it can lead to bone demineralization [25]. Beeraka et al. evaluated oral health, including periodontal condition, in patients receiving

corticosteroids for at least 3 months [26]. They found that patients on steroids exhibited significantly deeper PD and higher levels of clinical attachment loss (CAL) of the periodontal ligament. In our study, the vast majority of patients with RA received corticosteroids as a long-term regiment or during flares which could affect periodontal parameters.

In the present study, RA patients had a significantly higher API compared to the controls. Poor oral hygiene in RA patients might be partially attributable to difficulties in teeth brushing caused by a disability. The vast majority of patients in the RA group suffered from long-standing disease and more than a half of them had bone erosions in hands confirmed by an X-ray. That could result in joint deformities and loss of joint function. In addition, smoking could lead to plaque accumulation [27]. A significantly higher number of patients in the RA group smoked, which could negatively influence oral hygiene. Patients with RA had a lower number of teeth, as well. It has to be noted that tooth loss is often a consequence of local inflammatory processes in periodontal tissues and is strongly correlated with periodontitis [28]. In addition, more than half of patients in the RA group were treated with biologic agents during the study or in the past. Biologics are known to increase the risk of bacterial infections. Before starting biological therapies, some patients with advanced periodontal disease or progressive dental caries might need a tooth extraction as a prophylaxis of odontogenic infections.

In the present study, BoP, as a measure of gingival inflammation, was significantly increased in patients with SpA compared to the control subjects, although the prevalence of periodontal disease, including gingivitis, was similar in both groups. As mentioned before, some researchers have recently suggested a possible impact of drugs used in rheumatic diseases on periodontal parameters. Pers et al. found that RA patients with periodontitis treated with infliximab had decreased CAL, which could be associated with bone loss inhibition as a consequence of TNF- α blocking [29]. On the other hand, gingival inflammation measured by the modified gingival index (MGI) and papillary bleeding index (PBI) was increased after infliximab treatment. In contrast, Fabri et al. did not confirm any significant difference in gingival inflammation in patients treated with TNF- α inhibitors [30]. In the present study, more than half of patients were receiving anti-TNF therapy. In addition, NSAIDs, which should be the first-line treatment of AS, could have some beneficial effects on the periodontal status. In the SpA group, all patients had been receiving NSAIDs in the past on a regular basis, and the vast majority of them were treated with these drugs during the project, which could have influenced the periodontal parameters.

We found no significant difference in the prevalence of *P. gingivalis* DNA in the samples from periodontal pockets in RA patients compared to the controls. These findings are

consistent with other studies published so far [31, 32]. De Smitt et al. observed no difference in *P. gingivalis* presence between RA patients and the controls, based on the culture of subgingival plaque samples, although they confirmed elevated antibody titers against this periopathogen in RA patients [32]. Using nested-PCR for the detection of *P. gingivalis* DNA from subgingival plaque samples, Mikuls et al. also found that subgingival colonization by *P. gingivalis* was not different between RA patients and the controls [31]. In our study, positive results for *P. gingivalis* DNA did not correlate with the presence or severity of RA (data not shown), but as expected, they were related to periodontitis. It may be hypothesized that *P. gingivalis* plays a role in RA development only in susceptible individuals with periodontal disease and other risk factors.

Considering some recent studies that have reported a higher prevalence of periodontitis in patients with AS or psoriatic arthritis, we also evaluated the presence of *P. gingivalis* in SpA patients. To our knowledge no previous study addressed this question. No significant difference was found in the prevalence of *P. gingivalis* DNA in the samples from periodontal pockets in SpA patients compared to the controls. Using 16S rRNA gene sequencing to examine oral plaque bacterial communities, Bisanz et al. did not identify specific bacteria profiles associated with SpA [33]. On the other hand, Rinaudo-Gaujous et al. observed elevated antibody titers against *P. gingivalis* in SpA patients [34].

Current reports demonstrating the association between periodontal disease and RA have raised the question if periodontal treatment might have some beneficial effects on the disease activity in RA. In our study, the RA patients receiving periodontal treatment showed a significant decrease in disease activity measured by the DAS28(CRP) and DAS28(ESR). An improvement in the SDAI, CDAI and functional capacity measured by the HAQ were found, as well. These results are consistent with previous studies suggesting the beneficial effects of periodontal therapy in RA [35–37]. Certain researchers reported significant reduction in ESR and CRP levels in RA patients receiving periodontal treatment [37]. Periodontal disease is a local inflammation that can not only lead to the destruction of dental supporting tissues, but can also be associated with systemic inflammatory host responses [38]. D'Aiuto et al. demonstrated a reduction in CRP and IL-6 levels after periodontal treatment [39]. Considering these results, it has been hypothesized that periodontal treatment can have a beneficial influence on RA activity by decreasing inflammatory markers [37]. In our study, no significant decrease was found in the inflammatory markers, TNF- α , MMP-3 and MMP-9 levels after periodontal treatment in the RA group. However, we observed an improvement in the VAS score, the number of swollen and tender joints, which could influence the decrease in disease activity measured by the DAS28.

Possible interferences due to the changes in medication for RA could be a limitation of this study. During the project, 8 patients with RA required a modification of their long-term treatment because of acute flares, which could have influenced the clinical parameters and disease activity. However, when we compared RA patients on stable doses of antirheumatic drugs with RA patients who needed a change in their routine medication, we did not find a significant difference in the decrease in the DAS28 and other parameters (data not shown). This can be in favor of the hypothesis that periodontal treatment might have beneficial effects on RA activity. A small number of patients is another weakness of this study. Moreover, not all recruited patients required periodontal treatment, considering their periodontal status. Finally, 11 RA patients with periodontitis did not complete periodontal treatment for various reasons and were not included in further evaluation.

Few recent studies have reported a higher prevalence of periodontitis in patients with ankylosing spondylitis and psoriatic arthritis [13, 14]. Therefore, we evaluated a possible impact of periodontal treatment on the disease activity in SpA. In our study, SpA patients receiving periodontal treatment did not show a significant decrease in disease activity measured by the BASDAI and ASDAS. There was no significant reduction in inflammatory markers, TNF- α , MMP-3 and MMP-9 levels after periodontal treatment, either. It has to be noticed that during the project, 2 patients with SpA interrupted their biological treatment which could lead to the exacerbation of their symptoms and an increase in inflammatory markers. The small sample size and modification of antirheumatic treatment should be taken into account while interpreting the data.

Conclusions

Periodontal treatment seems to have beneficial effects on the activity of RA. Although we did not find any significant difference in the prevalence of periodontal disease in patients with RA and SpA, the small sample size, various confounding factors including smoking, and the potential effect of antirheumatic drugs on the periodontal status should be considered. Further large-scale clinical and interventional studies adjusted for risk factors and accounting for antirheumatic treatment are needed to clarify the association between rheumatic diseases, particularly RA, and periodontal disease.

Compliance with ethical standards

Ethical standards The study was conducted according to the principles of the Declaration of Helsinki. It was approved by the Bioethics Com-

mittee of Wrocław Medical University, approval no. 818/2012 (date: 23.11.2012).

Informed consent Informed consent was obtained from all individual participants included in the study.

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