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ORIGINAL ARTICLE

Relationship between periodontitis and rheumatoid arthritis in Vietnamese patients

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ABSTRACT

Objective: This study aimed to survey periodontal status of Vietnamese patients with rheumatoid arthritis (RA) and investigates the association between periodontitis and RA in these patients.

Materials and methods: We conducted a cross-sectional descriptive study on 150 RA patients and another 150 patients with osteoarthritis (OA). RA was evaluated using the DAS28 disease activity score based on C-reactive protein levels (DAS28-CRP), disease activity classification, and serum levels of RA biomarkers. Periodontal status was determined using periodontal indices.

Results: The proportion of periodontitis cases in the RA group was significantly higher than the OA group (67 and 28%, respectively). The rate of severe periodontitis observed in the RA group was also significantly higher than that in the OA group (22.7 and 8%, respectively). RA patients with periodontitis had higher DAS28-CRP scores, disease activity levels, ACPA positivity and higher serum levels of CRP and ACPAs. Periodontitis is associated with an increased risk for RA (odds ratio [OR]: 5.14, 95% confidence interval [CI]: 3.14 – 8.41) and with higher disease activity classification (OR: 2.7, 95% CI: 1.14 – 6.42).

Conclusions: Vietnamese RA patients often presented with a more serious periodontal condition than OA patients. We observed an association between periodontal disease (PD) status and clinic symptoms and biochemical/immunological characteristics of RA.

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Introduction

Periodontitis and rheumatoid arthritis (RA) are two chronic inflammatory conditions with active and inactive periods. These conditions are characterized by systemic inflammatory responses, in periodontal tissues and joints, respectively, that are associated with hard and soft tissue destruction [1,2]. Other similarities between the two diseases include pathophysiological progression, immune regulation, heredity, inflammatory cell infiltration, as well as involvement of enzymes and cytokines in immune response [3]. Periodontitis is caused by an infection of specific bacteria types in the dental biofilm and characterized by chronic inflammation leading to structural damage of connective tissue and bone [4]. It is the most common cause of tooth loss, adversely affecting the quality of life in adults [5,6]. Although there are many studies suggesting an association between RA and periodontitis [7], evidence for this is limited in South East Asian countries. A recent study reported that the incidence of periodontitis in patients with RA in Indonesia and Thailand was 71 [8] and 99% [9], respectively. Periodontal disease (PD) does not only affect teeth but also one's general health status. Reports have shown increased rates of diabetes mellitus [10], atherosclerosis [11], myocardial infarction [12], stroke [13] and RA [14] in patients with periodontitis [3].

Porphyromonas gingivalis (Pg), which can cause RA, is also found in patients with periodontitis. Its disease-causing mechanism involves the release of peptidyl arginine deiminase (PAD), citrullinating excess arginine at the start of the peptide chain, creating anti-citrullinated protein autoantibodies (ACPAs) and leading to RA [15–17]. As a typical autoimmune disease, RA expresses chronic progression of symptoms at the joints and throughout the body. Its manifestations vary and can impact many organs, including the bones and connective tissues. RA occurs in all populations at a precedence rate of 0.5 – 1% in adults. In Vietnam, 0.5% of the population has RA. Further, 20% of all arthritic patients are diagnosed with RA, and the disease is hereditary in some cases [18].

De Pablo et al. studied 4461 people over 60 years of age and found that increasing incidences of periodontitis and RA among those with total tooth loss [19]. Recently, studies conducted in untreated RA patients have shown that the

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Supplemental data for this article can be accessed here.

incidence of periodontitis in these patients was 4.28 times higher than that in treated patients [20,21]. However, the relationship between PD and RA in Vietnamese patients remains unclear. This study aimed to survey periodontal status of Vietnamese patients with RA and investigates the association between periodontitis and RA in these patients. We investigated RA and PD indices as well as related socioeconomic status and health conditions of RA patients.

Materials and methods

Sample collection

One hundred and fifty Vietnamese adults with RA, aged 27–84 years, were recruited at the Department of Rheumatology, Cho Ray Hospital, Ho Chi Minh City between October 2012 and August 2013 (RA group). The control group included 150 patients diagnosed with osteoarthritis (OA group). Study procedures were clearly explained to all participants and all of them provided written informed consent.

The sample size was calculated using the following formula for analytical and experimental study: $n = \frac{\{Z_{(1-\alpha/2)}\sqrt{2\bar{P}(1-\bar{P})} + Z_{(1-\beta)}\sqrt{P_1(1-P_1)+P_2(1-P_2)}\}^2}{(P_1-P_2)^2}$. In a pilot study, we found that rate of periodontitis was 40% in RA patients and 25% in OA patients. Using $\alpha = 5\%$, power of 80%, we got $n = 120$ patients for each group. To avoid sampling error, the sample size was increased by 20% to obtain 150 patients for each group. The two groups were matched for age and gender. There were 354 patients who met the sampling criteria and agreed to participate in the study; 54 patients were excluded due to insufficient test results and/or age and gender unmatching. The final sample consisted of 150 patients with RA and 150 patients without RA.

RA was diagnosed using the ACR/EULAR 2010 guideline (American College of Rheumatology/European League Against Rheumatism) [22]. Periodontal condition was determined by a periodontist following the criteria of the Centre for Disease Control and Prevention as well as the American Academy of Periodontology (CDC and AAP) [23]. RA patients with other polyarthritis conditions such as polymyalgia, gout, pseudogout, spinal stiffness, Sjögren's syndrome, diabetes mellitus, malignant diseases, and patients with fewer than 4 teeth (regardless of the third molars) were excluded.

Periodontal disease assessments

Case definitions proposed for population-based surveillance of periodontitis are summarized in Table 1 [24,25]. The research facilities included a mirror, a William probe, a frontal light, visual analogue scale (VAS) pain scales and questionnaires for RA patients (Supplementary document S1). The periodontal examination investigator is a dentist who examined and determined periodontal indicators for all study participants. The arthritis investigator is a specialized medical doctor who determined DAS28-CRP. The secretary was a sixth-year dental student who interviewed and recorded data. Team members were trained by experts before the study, and the calibration for measurements achieved consistency from 80 to 90.4% (Supplementary document S2). The variables collected from interviews included age, sex, address, education level, occupation, smoking status and duration of RA. The periodontal indices were plaque index (PII) (according to Silness and Loe [26]), gingival index (GI) (according to Loe and Silness [27]), %BOP (percentage of sites with bleeding on probing), probing pocket depth (PPD) and clinical attachment loss (CAL). Measurement was performed at six positions in all teeth.

RA clinical assessments

RA disease activity was assessed based on C-reactive protein (DAS28-CRP), which in particular takes into account tender joint count (TJC28, 0–28), swollen joint count (SJC28, 0–28), C-reactive protein level (CRP, mg/L), and patient global health self-assessment of his/her condition *via* VAS [28]. The 28 tender or swollen joint scores target the shoulders, elbows, wrists, metacarpophalangeal joints, proximal interphalangeal joints and the knees. The following equation was used to compute the score: DAS28-CRP = 0.56*sqrt(TJC28) + 0.28*sqrt(SJC28) + 0.36*ln(CRP + 1) + 0.014*GH + 0.96. The DAS28-CRP was then calculated based on the aforementioned factors. Patients were then categorized into four disease condition groups as follows: remission (DAS28-CRP $<$ 2.3), low ($2.3 \leq$ DAS28-CRP $<$ 2.7), moderate ($2.7 \leq$ DAS28-CRP $<$ 4.1) and high disease activity ($4.1 \leq$ DAS28-CRP).

Measurements of serum rheumatoid factor, ACPAs, ESR and CRP levels

Serum concentrations of rheumatoid factor (RF) and CRP were determined using a latex particle-enhanced method [29–31]. RF serum levels were categorized as follows: RF positive $>$ 12 IU/mL and RF negative $<$ 12 IU/mL. Normal level of serum CRP was defined as $<$ 6 mg/L. Serum levels of ACPAs were determined using enzyme-linked immunosorbent assay (ELISA) according to the instructions of the manufacturer [32]. Serum ACPAs was considered negative when $<$ 25 IU/mL and positive when $\geq$ 25 IU/mL. ESR (Erythrocyte sedimentation rate) was measured by flow through the capillary tube [33]. Normal ESR serum was defined as 5–10 mm/h.

Medical ethics

The Ethics Committee of the University of Medicine and Pharmacy at Ho Chi Minh City approved the study protocol (No.1781/DHYD-HD). Signed informed consent was obtained from all participants before enrolment.

Statistical analyses

Stata software version 15 (StataCorp LLC, College Station, TX) was used for data analysis. Mean and standard deviation were presented in case of normal distribution; median and quadratic distribution were included otherwise. Differences

Table 1. Case definitions proposed for population-based surveillance of periodontitis.

Case	Definition†
No periodontitis	No evidence of mild, moderate or severe periodontitis
Mild periodontitis	≥2 interproximal sites with AL ≥3 mm and ≥2 interproximal sites with PD ≥4 mm (not on the same tooth) or one site with PD ≥5 mm
Moderate periodontitis	≥2 interproximal sites with AL ≥4 mm (not on the same tooth) or ≥2 interproximal sites with PD ≥5 mm (not on the same tooth)
Severe periodontitis	≥2 interproximal sites with AL ≥6 mm (not on the same tooth) and ≥1 interproximal site with PD ≥5 mm

These definitions are now commonly referred to as the CDC–AAP case definitions for surveillance of periodontitis [24,25].
†Third molars excluded; total periodontitis is defined as the sum of mild, moderate and severe disease.

between the two groups were assessed by t-test for two independent samples. Mann–Whitney U-test was used for median and quartile range. Differences in quantitative parameter values among the groups were assessed by Kruskal–Wallis test for intergroup comparison. Chi-square or Fisher tests were used for rate comparison. The odds ratios (OR) and 95% confidence intervals (CI) were also reported. Statistical significance was defined as $p < .05$.

Results

Characteristics of research samples

Of the 150 RA patients, aged between 27 and 84 years, 82% were female. The percentage of patients living in Ho Chi Minh City was very low (10%); most of them came from other provinces (Table 2). In the RA group, the proportion of postmenopausal women was 45.5%. The median duration of illness was 3 years (range: 1.5 – 8 years). More than half of the patients (56.7%) used corticosteroid for RA. There were no significant differences in age, sex and occupation in the two groups with and without RA.

Next, we focussed on the RA group and investigated the details of these patients. The group of patients who did not finish primary school accounted for the highest proportion (29.3%), and nearly 60% of these patients only completed primary school or lower. Those who did not attend school accounted for 8.7%. Most patients did not know about PD and their effects. The rate of patients who did not have oral check-up was very high, up to 79.3%; 92% of the participants did not know about the relationship between PD and other systemic diseases. The rate of smoking in RA male patients was 62.9%, whereas only 11.3% of the female patients smoked (Table 3).

Comparison of periodontal status between RA and OA groups

There were similarities in periodontal indicators and number of teeth remaining between the two groups (Table 4). The periodontitis rate in the RA group was 67% higher than that in the OA group ($p < .001$, Figure 1(A)). Among patients with both RA and PD, most had moderate (44%) or severe periodontitis (22.7%) ($p < .001$, Figure 1(B)).

Relationship among periodontal status, clinical characteristics and immunohistochemical features of RA patients

All clinical parameters of RA, such as pain sensation and disease activity DAS28-CP, were higher in the PD group compared to the non-PD group ($p < .05$, Table 5). There was an association between PD and RA with an OR of 5.14 (95% CI: 3.14 – 8.41, Figure 1(A)). The increase in RA activity was also associated with periodontal diagnosis (OR: 2.7, 95% CI: 1.14 – 6.42, Figure 1(C)). Additionally, there was a positive correlation among CRP levels, ACPAs levels, ACPAs categories and severity of periodontitis ($p < .05$, Table 6). Finally, there was a weak correlation between the level of periodontal status and serum ACPAs (Spearman's $r = 0.32$, $p < .001$).

Discussion

Our study was the first to investigate the relationship between periodontitis and RA in Vietnamese patients. We chose OA patients as the control group as described in previous studies [34,35]. Participants in both groups were similar in age, sex and condition. OA participants were also seen for their disease, thus ruling out the possibility of other systemic diseases, which might be undetected in otherwise healthy controls. In this study, PDs were more prevalent and exacerbated in the RA group than that in the control group (67 *vs.* 28%). This is similar to findings from Susanto et al. (Indonesia) (71%) [8], but lower than the results from studies by Khantisopon et al. (Thailand) (99.9%) or Okada et al. (Japan) (86.9%) [9,36]. The observed difference might be due to the use of various classification systems for PD, which is a challenge in clinical studies of PD. Interestingly, our results were similar to those found in Korean patients with a prevalence of periodontitis in RA patients being 63.6 *vs.* 34.1% in

Table 2. Characteristics of RA ($n = 150$) and OA ($n = 150$) groups in the study.

Parameters	RA group $N = 150$ (%)	OA group $N = 150$ (%)	*P*
Gender			
Male	27 (18)	24 (16)	.645*
Female	123 (82)	126 (84)	
Age (year)	51.7 (10.4)	52.9 (11.5)	.356†
Group of age (year)			
≤40	22 (14.7)	21 (14)	.121*
41–≤50	48 (32)	41 (27.3)	
51–≤60	56 (37.3)	47 (31.3)	
>60	24 (16)	41 (27.3)	
Residence ($n = 276$)			
HCM city	17 (11.3)	9 (7.1)	.235*
Others	133 (88.7)	117 (92.9)	

There was no significant difference between two groups. *p* Values were calculated by Chi-square test* and t test†, with a *p* value of < .05 being statistically significant.

Table 3. Detailed characteristics of RA patients ($n = 150$) based on the response to questionnaire about socioeconomic status and health conditions (Supplementary document S1).

Information	Number	%
Menopause ($n = 121$)		
Not yet	66	54.5
Yes	55	45.5
Education		
Do not go to school	13	8.7
Not yet completed elementary school	44	29.3
Completed elementary school	32	21.3
Completed secondary school	36	24.0
Completed high school	18	12.0
Undergraduate/postgraduate	7	4.7
Occupation		
Farmer	52	34.7
Manual labour	28	18.7
Intellectual labour	56	37.3
Housewife, retired	14	9.3
Monthly income ($n = 145$)		
<39 EUR (1 mil VND)	44	30.3
39–<117 EUR (1–3 mil VND)	48	33.1
117–<195 EUR (3–5 mil VND	31	21.4
≥195 EUR (5 mil VND)	22	15.2
RA duration (year) median, range	3	1.5–8
Corticosteroids usage		
Yes	85	56.7
No	65	43.3
Smoking (all male) ($n = 27$)		
Yes	17	62.9
No	10	37.1
Knowledge about periodontitis		
Yes	28	18.7
No	122	81.3
Knowledge about the relationship between RA and periodontitis		
Yes	12	8
No	138	92
Routine dental check-up		
Yes	31	20.7
No	119	79.3

Table 4. Periodontal condition in RA and OA groups.

Parameters	RA group $N = 150$	OA group $N = 150$	P	OR (95% CI)
Plaque index (median [range])	1.8 (1.1 – 2)	1.2 (0.8 – 1.6)	<.001§	2.26 (1.58 – 3.22)
Gingival index (median [range])	1.1 (0.8 – 1.2)	1 (0.5 – 1.1)	.009§	1.64 (1.01 – 2.75)
%Bleeding on probing of sites (%, median [range])	0.1 (0 – 0.2)	0.1 (0 – 0.2)	.962§	1.50 (0.38 – 5.90)
PPD (mm, median [range])	1.1 (0.8 – 1.5)	1.1 (0.8 – 1.6)	.813§	0.95 (0.61 – 1.49)
CAL (mm, median [range])	1.7 (1.3 – 2.5)	1.7 (1.2 – 2.3)	.180§	1.13 (0.92 – 1.38)
CAL level				
<3 mm	128 (85.3%)	131 (87.3%)	.850*	1
3–5 mm	17 (11.3%)	14 (9.3%)		1.24 (0.59 – 2.63)
>5 mm	5 (3.3%)	5 (3.3%)		1.02 (0.29 – 3.62)
Number of remaining teeth (median [range])	21.8 (15 – 25)	23 (17 – 26)	.070§	0.97 (0.94 – 1.01)
Number of lost teeth (median [range])	6.3 (3 – 13)	5 (2 – 11)	.070§	1.03 (0.99 – 1.06)

The periodontal indices were PII: plaque index; GI: gingival index; %BOP: percentage of sites with bleeding on probing; PPD: probing pocket depth; CAL: clinical attachment loss. All measurements were performed at six positions for each tooth.
p Values were calculated by Chi-square test* and Mann–Whitney U test§, with a p value of $< .05$ being statistically significant.

controls [37]. Our findings of periodontal status in the RA group were comparable to those of Heredia et al.'s study in American Latinos [38]. Also, Bello-Gualtero et al. found that individuals at risk for RA and those with early RA showed higher periodontal indices than the controls, which was similar to our observation [39].

In this study, we used the periodontal classification by the 2012 CDC and AAP standards, which are widely used in community research [23]. Most of the RA patients had low incomes (63%) and only completed primary education or lower (>98%). They also had little awareness of oral diseases. Further, most patients did not know about PD and its impacts (81.3%) and first heard about PD in the study. The rate of patients who did not have oral examination was also very high, up to 79.3%. This was higher than the statistic for the general Vietnamese population, in which 62% did not have routine dental check-ups, according to the 2019 Vietnamese national oral health survey [40]. Further, 92% did not know about the relationship between PD and systemic diseases, which indicates the lack of knowledge about periodontitis, in addition to low income and education level. Therefore, it is necessary to improve oral hygienic education in RA patients. In comparison to other countries in the area, Vietnamese RA patients shared similar characteristics on sex,

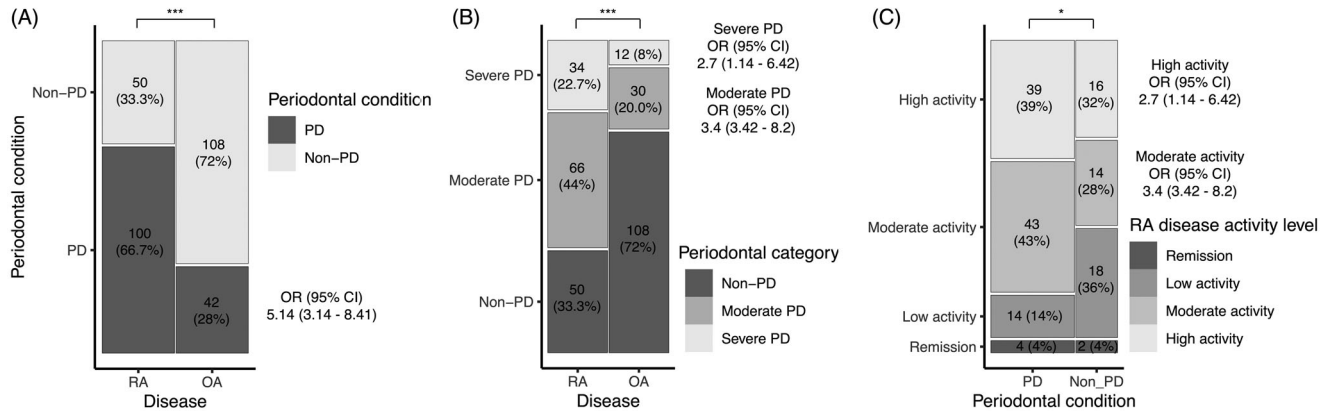

Figure 1. Comparison of disease status between patient groups. A: Periodontal condition in RA and OA patients (Chi-square $^{***}p < .001$). B: Three periodontal categories in RA and OA patients (Chi-square $^{***}p < .001$). C: RA disease activity levels in PD and non-PD groups within the RA cohort (Fisher test, $^{*}p < .05$).

Table 5. Clinical features of RA in patients with or without PD.

Parameters	PD group $N = 100$	Non-PD group $N = 50$	p
VAS (mm, median [range])	50 (30 – 70)	40 (20 – 50)	.003§
TJC28 (median [range])	5 (3 – 20)	3 (2 – 5)	.007§
SJC28 (median [range])	5 (3 – 13)	3 (1 – 9)	.028§
DAS28-CRP (median [range])	4.7 (3.5 – 6.3)	3.9 (3 – 5.5)	.008§

RA disease activity was assessed using C-reactive protein (DAS28-CRP), which in particular takes into account tender joint count (TJC28), swollen joint count (SJC28) and patient's general assessment of his/her condition.
p Values were calculated by Mann–Whitney U test§, with a p value of $< .05$ being statistically significant.

were recorded low because most patients only presented with localized periodontitis (i.e. less than 30% of examined sites had periodontal pocket and bleeding), and the examination result was the average of all teeth, with six positions per tooth. Therefore, we defined the mild and moderate periodontitis depending on the number of positions involved so that the qualitative results would be meaningful [14]. The case definition is presented in Table 1.

Among the patients with PD, the majority had moderate and severe periodontitis. The DAS28-CRP disease activity was

Table 6. Characteristics of immunocompromised RA including C-reactive protein levels (CRP), serum concentrations of rheumatoid factor (RF), erythrocyte sedimentation rate (ESR) and anti-citrullinated protein autoantibodies (ACPAs).

	Level of periodontal status				
Parameters	Severe PD $N = 34$	Moderate PD $N = 66$	Non- PD $N = 50$	p	Spearman's r
CRP (mg/L, median [range])	18.6 (4.2 – 65)	12 (3.5 – 30.4)	11.2 (5.1 – 30.5)	.02§	
RF (IU/mL, median [range]) ($n = 145$) RF category	34.1 (8 – 198)	24.3 (8 – 136.6)	8.4 (8 – 80.5)	.137§	
Positive	20 (26%)	38 (49.4%)	19 (24.7%)	.104*	
Negative	13 (19.1%)	27 (39.7%)	28 (41.2%)		
ESR (mm/h, median [range])	49 (15 – 74)	48 (27 – 76)	43 (20 – 72.5)	.444§	
Serum ACPAs (IU/mL, median [range])	484 (48 – 953)	103.5 (10 – 568)	17 (5 – 173)	<.001§	.32 ($p < .001$)
ACPAs category					
Positive	26 (28.6%)	42 (46.2%)	23 (25.3%)	.016*	
Negative	8 (13.6%)	24 (40.7%)	27 (45.8%)		
ACPAs level					
<25 IU/mL	8 (13.6%)	24 (40.7%)	27 (45.8%)	.033¢	
25–1000 IU/mL	18 (25.7%)	32 (45.7%)	20 (28.6%)		
>1000 IU/mL	8 (38.1%)	10 (47.6%)	3 (14.3%)		

p Values were calculated by Chi-square test*, Kruskal–Wallis test§ and Fisher test¢, with a p value of $< .05$ being statistically significant.

age and educational level with Thai patients, but they are older than Indonesian and Chinese patients [8,9,41].

The smoking rate in Vietnamese RA patients enrolled in this study was lower than Thai RA patients by 50% (11 *vs.* 22%) but still higher than Indonesian and Korean (about 6–7%) [8,9,42]. Moreover, periodontal status was worse than that of the other countries' reports, including remaining teeth, PPD, %BOP. In this study, Vietnamese RA patients on average only had 22 remaining teeth, which were much lower than findings from other countries (Thai and Indonesian RA patients: 26 teeth, Korean patients: 25 teeth). It could be explained by the worse periodontal status described above. We observed low PPD index and %BOP in our study. At the time of examination, quantitative indicators

significantly higher in the RA patients with PD, compared to RA patients without PD. In our study, PD odds in RA patients was 5.14 (95% CI: 3.14 – 8.41). Additionally, among RA patients, the odds of high RA activity in PD patients was 2.7 (95% CI: 1.14 – 6.42). This finding confirms the association and synergetic effect of both RA and PD, similar to the results of Okada et al. and Dissick et al. [36,43]. As for the immune-histochemical characteristics, worse periodontal status in RA patients was associated with higher levels of CRP and ACPAs. Self-antibody ACPAs were related to the incidence and the severity of PD in RA patients. Our results were similar to those reported by Dissick et al. [43]. The incidence of PD in RA patients with ACPA-positivity was higher than that of patients with negative ACPAs, consistent with

the results by Demmer et al. [44]. However, we did not find other correlations between PD and RA indices, as described by Kim et al. [42]. There was a positive correlation among CRP levels, ACPAs levels, ACPAs categories and severity of periodontitis. In addition, there was a weak correlation between periodontal status and serum ACPAs. However, in Romero-Sanchez's study [45], bleeding on probing was associated with elevated CPR levels ($p = .05$), and ESR was associated with more severe PD ($p = .044$). This difference would be explained by the diversity of disease severity and biological features of subjects included in these studies.

Conclusions

In this study, periodontitis rate in the RA group was 2.5 times higher than that in the OA group. Severe and moderate periodontitis were common in the RA group. Periodontal status was proportional to RA disease activity DAS28-CRP, RF positivity, and ACPAs positivity. RA patients with periodontitis also showed more severe complications than those without. There is a positive relationship between the severity of RA and periodontal categories in Vietnamese patients. Therefore, interdisciplinary management for both diseases is necessary to ensure a comprehensive treatment.

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Disclosure statement

The authors declare that they have no competing interests.

Informed consent

Signed informed consents were obtained from all participants before inclusion.

Author contributions

Study conception and design: V.B.N, T.T.N, N.C-N.H, T.A.L, H.T.H; acquisition of data: V.B.N, T.T.N; analysis and interpretation of data: V.B.N, N.C-N.H, T.A.L, H.T.H; drafting of manuscript: V.B.N, T.T.N, N.C-N.H; critical revision: V.B.N, T.T.N, N.C-N.H, T.A.L, H.T.H.

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Availability of data and materials

The datasets used and/or analysed in this study are available upon reasonable request to the corresponding author.

References

[1] Bingham CO, 3rd, Moni M. Periodontal disease and rheumatoid arthritis: the evidence accumulates for complex pathobiologic interactions. Curr Opin Rheumatol. 2013;25(3):345–353. May
[2] Detert J, Pischon N, Burmester GR, et al. The association between rheumatoid arthritis and periodontal disease. Arthritis Res Ther. 2010;12(5):218.
[3] Genco RJ, Williams RC. Periodontal disease and overall health: a clinician's guide. Yardley (PA): Professional Audience Communications Inc.; 2010.
[4] Lovegrove JM. Dental plaque revisited: bacteria associated with periodontal disease. J N Z Soc Periodontol. 2004;(87):7–21.
[5] Ong G. Periodontal disease and tooth loss. Int Dent J. 1998; 48(S3):233–238.
[6] Ferreira MC, Dias-Pereira AC, Branco-de-Almeida LS, et al. Impact of periodontal disease on quality of life: a systematic review. J Periodont Res. 2017;52(4):651–665.
[7] Araujo VM, Melo IM, Lima V. Relationship between periodontitis and rheumatoid arthritis: review of the literature. Med Inflamm. 2015;2015:1–15.
[8] Susanto H, Nesse W, Kertia N, et al. Prevalence and severity of periodontitis in Indonesian patients with rheumatoid arthritis. J Periodontol. 2013;84(8):1067–1074.
[9] Khantisopon N, Louthrenoo W, Kasitanon N, et al. Periodontal disease in Thai patients with rheumatoid arthritis. Int J Rheum Dis. 2014;17(5):n/a–8.
[10] Preshaw PM, Alba AL, Herrera D, et al. Periodontitis and diabetes: a two-way relationship. Diabetologia. 2012;55(1):21–31.
[11] Beukers NG, van der Heijden GJ, van Wijk AJ, et al. Periodontitis is an independent risk indicator for atherosclerotic cardiovascular diseases among 60 174 participants in a large dental school in the Netherlands. J Epidemiol Community Health. 2017;71(1): 37–42.
[12] Xu S, Song M, Xiong Y, et al. The association between periodontal disease and the risk of myocardial infarction: a pooled analysis of observational studies. BMC Cardiovasc Disord. 2017;17(1):50.
[13] Lafon A, Pereira B, Dufour T, et al. Periodontal disease and stroke: a meta-analysis of cohort studies. Eur J Neurol. 2014;21(9): 1155–1161, e66-7.
[14] Rodriguez-Lozano B, Gonzalez-Febles J, Garnier-Rodriguez JL, et al. Association between severity of periodontitis and clinical activity in rheumatoid arthritis patients: a case-control study. Arthritis Res Ther. 2019;21(1):27.
[15] Hajishengallis G. Periodontitis: from microbial immune subversion to systemic inflammation. Nat Rev Immunol. 2015;15(1):30–44.
[16] Rosenstein ED, Greenwald RA, Kushner LJ, et al. Hypothesis: the humoral immune response to oral bacteria provides a stimulus for the development of rheumatoid arthritis. Inflammation. 2004; 28(6):311–318.
[17] Scher JU, Abramson SB. Periodontal disease, porphyromonas gingivalis, and rheumatoid arthritis: what triggers autoimmunity and clinical disease? Arthritis Res Ther. 2013;15(5):122.
[18] Minh Hoa TT, Darmawan J, Chen SL, et al. Prevalence of the rheumatic diseases in urban Vietnam: a WHO-ILAR COPCORD study. J Rheumatol. 2003;30(10):2252–2256.
[19] de Pablo P, Dietrich T, McAlindon TE. Association of periodontal disease and tooth loss with rheumatoid arthritis in the US population. J Rheumatol. 2008;35(1):70–76.
[20] Payne JB, Golub LM, Thiele GM, et al. The link between periodontitis and rheumatoid arthritis: a periodontist's perspective. Curr Oral Health Rep. 2015;2(1):20–29.
[21] Potikuri D, Dannana KC, Kanchinadam S, et al. Periodontal disease is significantly higher in non-smoking treatment-naive rheumatoid arthritis patients: results from a case-control study. Ann Rheum Dis. 2012;71(9):1541–1544.
[22] Kay J, Upchurch KS. ACR/EULAR 2010 rheumatoid arthritis classification criteria. Rheumatology. 2012;51(6):vi5–9.

[23] Eke PI, Page RC, Wei L, et al. Update of the case definitions for population-based surveillance of periodontitis. J Periodontol. 2012;83(12):1449–1454.
[24] Page RC, Eke PI. Case definitions for use in population-based surveillance of periodontitis. J Periodontol. 2007;78(7s):1387–1399.
[25] Machtet EE, Christersson LA, Grossi SG, et al. Clinical criteria for the definition of "established periodontitis". J Periodontol. 1992; 63(3):206–214.
[26] Silness J, Loe H. Periodontal disease in pregnancy. Ii. Correlation between oral hygiene and periodontal condtion. Acta Odontol Scand. 1964;22(1):121–135.
[27] Loe H, Silness J. Periodontal disease in pregnancy. I. Prevalence and severity. Acta Odontol Scand. 1963;21(6):533–551.
[28] Prevoo ML, van 'T Hof MA, Kuper HH, et al. Modified disease activity scores that include twenty-eight-joint counts. Development and validation in a prospective longitudinal study of patients with rheumatoid arthritis. Arthritis Rheum. 1995;38(1): 44–48. Jan(
[29] Price CP, Trull AK, Berry D, et al. Development and validation of a particle-enhanced turbidimetric immunoassay for C-reactive protein. J Immunol Methods. 1987; 99((2):205–211.
[30] Winkles JW, Lunec J, Gray L. Automated enhanced latex agglutination assay for rheumatoid factors in serum. Clin Chem. 1989; 35(2):303–307.
[31] Ingegnoli F, Castelli R, Gualtierotti R. Rheumatoid factors: clinical applications. Dis Markers. 2013;35((6):727–734.
[32] Bugatti S, Manzo A, Montecucco C, et al. The clinical value of autoantibodies in rheumatoid arthritis. Front Med (Lausanne). 2018;5:339.
[33] Litao MK, Kamat D. Erythrocyte sedimentation rate and C-reactive protein: how best to use them in clinical practice. Pediatr Ann. 2014;43(10):417–420.
[34] Gonzalez SM, Payne JB, Yu F, et al. Alveolar bone loss is associated with circulating anti-citrullinated protein antibody (ACPA) in patients with rheumatoid arthritis. J Periodontol. 2015;86(2): 222–231.
[35] Mikuls TR, Payne JB, Yu F, et al. Periodontitis and *Porphyromonas gingivalis* in patients with rheumatoid arthritis. Arthritis Rheumatol. 2014;66((5):1090–1100.
[36] Okada M, Kobayashi T, Ito S, et al. Antibody responses to periodontopathic bacteria in relation to rheumatoid arthritis in Japanese adults. J Periodontol. 2011;82(10):1433–1441.
[37] Choi IA, Kim JH, Kim YM, et al. Periodontitis is associated with rheumatoid arthritis: a study with longstanding rheumatoid arthritis patients in Korea. Korean J Intern Med. 2016;31(5):977–986.
[38] Heredia PA, Lafaurie GI, Bautista-Molano W, et al. Predictive factors related to the progression of periodontal disease in patients with early rheumatoid arthritis: a cohort study. BMC Oral Health. 2019;19(1):240.
[39] Bello-Gualtero JM, Lafaurie GI, Hoyos LX, et al. Periodontal disease in individuals with a genetic risk of developing arthritis and early rheumatoid arthritis: a cross-sectional study. J Periodontol. 2016;87(4):346–356.
[40] Trinh DH, Nguyen THM, Tran CB. Vietnamese national oral health survey. Hanoi. 2019;101.
[41] Zhao X, Liu Z, Shu D, et al. Association of periodontitis with rheumatoid arthritis and the effect of non-surgical periodontal treatment on disease activity in patients with rheumatoid arthritis. Med Sci Monit. 2018;24:5802–5810.
[42] Kim JH, Choi IA, Lee JY, et al. Periodontal pathogens and the association between periodontitis and rheumatoid arthritis in Korean adults. J Periodontal Implant Sci. 2018;48(6):347–359.
[43] Dissick A, Redman RS, Jones M, et al. Association of periodontitis with rheumatoid arthritis: a pilot study. J Periodontol. 2010;81(2): 223–230.
[44] Demmer RT, Molitor JA, Jacobs DR, Jr, et al. Periodontal disease, tooth loss and incident rheumatoid arthritis: results from the First National Health and Nutrition Examination Survey and its epidemiological follow-up study. J Clin Periodontol. 2011;38(11): 998–1006.
[45] Romero-Sanchez C, Rodriguez C, Santos-Moreno P, et al. Is the treatment with biological or non-biological DMARDS a modifier of periodontal condition in patients with rheumatoid arthritis? Curr Rheumatol Rev. 2017;13((2):139–151.