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Prevalence and risk factors for peri-implant diseases in Japanese adult dental patients

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Abstract: We investigated the prevalences and risk factors for peri-implant diseases in Japanese adult dental patients attending a follow-up visit at dental hospitals or clinics as part of their maintenance program. This cross-sectional multicenter study enrolled patients with dental implants who attended regular check-ups as part of a periodontal maintenance program during the period from October 2012 through September 2013. Patients with implants with at least 3 years of loading time were included in the study. The condition of peri-implant tissue was examined and classi¿ed into the following categories: healthy, peri-implant mucositis, and peri-implantitis. Patients were also evaluated for implant risk factors. A total of 267 patients (110 men, 157 women; mean age: 62.5 ± 10.7 years) were analyzed. The prevalence of patient-based peri-implant mucositis was 33.3% (n = 89), and the prevalence of peri-implantitis was 9.7% (n = 26). Poor oral hygiene and a history of periodontitis were strong risk factors for peri-implant disease. The present prevalences were lower than those previously reported. The quality of periodontal therapy before and after implant installation and patient compliance and motivation, as indicated by plaque control level, appear to be important in maintaining peri-implant tissue health.

Keywords: multicenter study; peri-implant mucositis; peri-implantitis; prevalence.

Introduction

Peri-implant diseases are classi¿ed into two categories: peri-implant mucositis and peri-implantitis (1). Peri-implant mucositis is a reversible inÀammatory reaction in the mucosa surrounding a functional dental implant. Peri-implantitis is an inÀammatory reaction associated with functional deterioration of supporting bones around a dental implant. These are the most frequent long-term complications of dental implants (1-5). However, the absence of widely accepted diagnostic criteria for these pathologies complicates the interpretation of published values for prevalence (1,6,7). The Consensus of the Seventh European Workshop on Periodontology indicates that the key parameter for diagnosis of peri-implant

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mucositis is bleeding on gentle probing (<0.25 N). Moreover, peri-implantitis was de¿ned as a change in the level of the crestal bone in conjunction with bleeding on probing, with or without concomitant deepening of peri-implant pockets (1). A number of studies have reported fairly high prevalences for peri-implant mucositis and peri-implantitis (5,8-12). Some evidence suggests that poor oral hygiene (9), history of periodontitis (13,14), smoking (15), lack of keratinized mucosa (16), and implant surface topography (17) are associated with peri-implant mucositis and peri-implantitis. Furthermore, periodontally compromised patients who did not completely adhere to supportive periodontal therapy had a higher implant failure rate (18,19).

Several studies have noted similarities in the pathogenesis of periodontitis and peri-implantitis (20-22). Speci¿cally, periodontal pathogens can translocate from periodontally involved teeth to peri-implant sulci in partially dentate patients (23,24). These ¿ndings highlight the importance of periodontal treatment of residual dentition before placement of osseointegrated dental implants (14,25). However, a recent hypothesis holds that the core microbiota in peri-implantitis and periodontitis exhibits intraindividual variation (26,27).

To better understand the prevalence of peri-implant diseases and the risk factors associated with these diseases in Japanese adults, we investigated the prevalence and risk factors for peri-implant diseases in Japanese adult dental patients who received periodontal treatment by periodontal specialists before placement of dental implants. All were enrolled in a periodontal maintenance program that included routine follow-up visits at dental hospitals or private dental clinics af¿liated with the Japanese Society of Periodontology (JSP).

Materials and Methods

Sample

This cross-sectional study enrolled patients who were included in a periodontal maintenance program by periodontal specialists (with follow-up visits every 1-12 months) in dental hospitals or private dental clinics af¿liated with the JSP. The study was approved by the Ethics Committee of the JSP (JSP2012001). All patients with dental implants, more than 3 years of follow-up after loading, and consecutive attendance at periodontal maintenance appointments between October 2012 and September 2013 were enrolled. They were assigned to the study cohort from an implant registry in a random order based on the scheduling of their last routine consultation. Written informed consent was obtained from each patient after all procedures had been explained in detail. A total of 267 patients (one implant and one natural tooth per patient were included) were interviewed to update their medical and dental histories, according to the protocols of this study, and were categorized by age, sex, smoking habit, implant manufacturer, surface topography, use of a one- or two-stage surgical approach, presence of a screw- or cement-retained implant restoration, and history of periodontal disease (as determined by a review of periodontal charts before and after implant treatment). Periodontal treatment before placement of the dental implant and the standardized periodontal maintenance check-ups were performed by periodontal specialists. These check-ups included a complete periodontal examination comprising determination of probing pocket depth (PPD) (the deepest values for implant and natural teeth in the same oral cavity were registered), modi¿ed plaque index (mPlI) and modi¿ed sulcus bleeding index (mSBI) for implants (20), plaque index (PlI) (28) and gingival index (GI) (29) for natural teeth, bleeding on probing (BOP), suppuration, tooth/implant mobility, and width of buccal keratinized mucosa, as well as an X-ray (intraoral or panoramic radiographs) examination. A diagnosis of peri-implant mucositis was de¿ned as bleeding on gentle probing (<0.25 N), and peri-implantitis was de¿ned as changes in the level of the crestal bone in conjunction with BOP (1). Gingivitis was de¿ned as the presence of clinical signs of inÀammation con¿ned to the gingiva and associated with teeth showing no attachment loss. Chronic periodontitis (CP) is associated with accumulation of plaque and calculus, has a slow to moderate rate of disease progression, and is characterized as slight, moderate, or severe (slight: 1-2 mm of clinical attachment loss; moderate: 3-4 mm of clinical attachment loss; severe: ≥5 mm of clinical attachment loss). Aggressive periodontitis differs from the chronic form primarily in the rapid rate of disease progression seen in otherwise healthy individuals, the absence of large accumulations of plaque and calculus, and the presence of a family history of aggressive disease suggestive of a genetic trait (30).

Quanti¿cation of periodontal bacteria from subgingival plaque samples

Subgingival plaque samples were collected from two sites (the deepest PPD sites for implant and natural teeth in the same oral cavity). Before sampling, supragingival plaque was removed with sterile cotton pellets. Sterile paper points were then inserted into the sample site, retained for 10 seconds (three times), and then immediately sent to a medical laboratory (BML Corporation, Tokyo, Japan) for bacterial analysis. Aggregatibacter

actinomycetemcomitans (A. a.), Prevotella intermedia (P. i.), Porphyromonas gingivalis (P. g.), and total bacteria were quanti¿ed using the modi¿ed Invader PLUS assay, as described previously (31,32).

Measurement of IgG titers against periodontal bacteria

Serum was extracted from a 50-μL sample of whole capillary blood obtained from the middle ¿ngertip, and device-treated serum was obtained according to procedures prescribed by Leisure, Inc. (Tokyo, Japan). IgG titers against A. actinomycetemcomitans, P. intermedia, Eikenella corrodens (E. c.), and P. gingivalis were determined using an enzyme-linked immunosorbent assay. The details of the measurement method are described in detail elsewhere (33).

Statistical analysis

Differences among the three groups (healthy peri-implant tissue, peri-implant mucositis, and peri-implantitis) were analyzed by one-way ANOVA with the post-hoc Turkey-Kramer test. The chi-square test for independence con¿rmed by Fisher's exact probability test was used to determine whether a history of chronic periodontitis was associated with healthy peri-implant tissue or peri-implant mucositis. The associations of implant design and prosthesis type with peri-implant diseases were analyzed by the Kruskal-Wallis test or the Mann-Whitney U test (34).

Results

The age, sex, smoking habit, PPD, BOP, suppuration, and mobility distributions for the participants are shown in Table 1. A total of 267 patients (mean ± SD age, 62.5 ± 10.7 years) were included in the analysis. The group aged 60 to 69 years was the largest age group (114; 42.7%); 22 smokers were included in this study. Eight smokers exhibited peri-implant mucositis, but there was no peri-implantitis in these smokers. The average numbers of residual teeth and dental implants per participant were 20.9 ± 5.9 teeth and 3.8 ± 3.2 pieces. Average PPD (deepest value for implant and natural teeth in the same oral cavity) was 3.4 ± 1.6 mm for implants and 4.0 ± 2.0 mm for natural teeth. BOP was detected in 43.1% of implants and in 50.2% of natural teeth. Suppuration was detected in 6% of implants and in 4.5% of natural teeth. Twenty-nine (11%) natural teeth exhibited tooth mobility; there was no mobility (0%) in implants (Table 1). The most common interval between follow-up visits was 3 months (139; 52.1%), followed by intervals of 6 months (36; 13.5%), 2 months (25; 9.4%), 1 month (20; 7.5%), and 4 months (19; 7.1%). Causal factors for tooth extraction were periodontitis (122; 46%), tooth fracture (61; 22.8%), caries (43; 16.1%), apical periodontitis (5; 1.9%), external injury (5; 1.9%), birth defect (3; 1.1%), re-implantation (2; 0.7%), tooth perforation (1; 0.4%), and unknown reasons (25; 9.4%) (Table 2A). Two (0.8%) patients had one-piece implants, 82 (30.7%) had soft-tissue level (two-piece) implants, and 183 (68.5%) had bone-level (two-piece) implants. Ninety-nine (37%) had screw-retained implant prostheses, and 168 (63%) had cement-retained implant prostheses. The prevalences of healthy peri-implant tissue, peri-implant mucositis, and peri-implantitis were 152 (57%), 89 (33.3%), and 26 (9.7%), respectively (Table 2A). Associations of implant design (soft-tissue level or bone level) and prosthesis type (screw- or cement-retained) with peri-implant diseases were analyzed with a nonparametric test (Table 2B). Implant design and prosthesis type were not signi¿cantly associated with peri-implant diseases.

Figure 1 shows the sites and numbers of dental implants in the maxilla and mandible. The total numbers of dental implants in the maxilla and mandible were 420 and 566 pieces, respectively. The upper and lower ¿rst molars were the most frequent sites for dental implants. Figure 2 shows the implant systems used, in the order of their

Table 1 Characteristics and of subjects and clinical ¿ndings for participants

Age, years	62.5 ± 10.7
20~29	5 (2%)
30~39	5 (2%)
40~49	19 (7%)
50~59	58 (22%)
60~69	114 (42%)
70~79	56 (21%)
80~89	19 (4%)
Males	110 (41%)
Females	157 (59%)
Smoker	22 (8%)
Nonsmoker	245 (92%)
Implant number	3.8 ± 3.2
Residual teeth number	20.9 ± 5.9
PPD (mm)	(Imp) 3.4 ± 1.6
	(Teeth) 4.0 ± 2.0
BOP	(Imp) 115 (43.1%)
	(Teeth) 134 (50.2%)
Suppuration	(Imp) 16 (6.0%)
	(Teeth) 12 (4.5%)
Mobility	(Imp) 0 (0%)
	(Teeth) 29 (11%)

n = 267, Mean ± SD, PPD: probing pocket depth, BOP: bleeding on probing

Table 2A Associations of causal factors of tooth extraction, implant design, and prosthesis type with prevalence of peri-implant diseases

Causal factors of tooth extraction	
Periodontitis	122 (46.0%)
Fracture tooth	61 (22.8%)
Caries	43 (16.1%)
Apical periodontitis	5 (1.9%)
External injury	5 (1.9%)
Birth defect	3 (1.1%)
Re-implantation	2 (0.7%)
Perforated tooth	1 (0.4%)
Unknown	25 (9.4%)
Implant design	
One-piece	2 (0.8%)
Soft-tissue level (two-piece)	82 (30.7%)
Bone level (two-piece)	183 (68.5%)
Type of prosthesis	
Screw-retained	99 (37.0%)
Cement-retained	168 (63.0%)
Peri-implant diseases	
Healthy peri-implant tissue	152 (57.0%)
Peri-implant mucositis	89 (33.3%)
Peri-implantitis	26 (9.7%)

n = 267

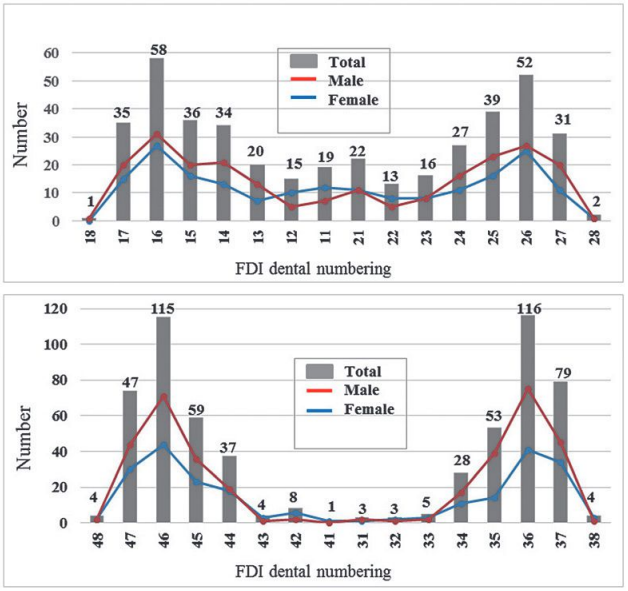

Fig. 1 Sites and numbers of dental implants. Upper: maxilla. Lower: mandible. There were 420 dental implants in the maxilla and 566 in the mandible. The upper and lower ¿rst molars were the most frequent sites of dental implants.

Table 2B Associations of peri-implant diseases with implant design and prosthesis type

	One-piece (2)	Soft-tissue level (82) two-piece	Bone-level (183) two-piece	Screw-retained (99)	Cement-retained (168)
Healthy peri-implant tissue	2 (100%)	47 (57.3%)	103 (56.3%)	54 (54.5%)	98 (58.3%)
Peri-implant mucositis	0 (0%)	26 (31.7%)	63 (34.4%)	36 (36.4%)	53 (31.6%)
Peri-implantitis	0 (0%)	9 (11.0%)	17 (9.3%)	9 (9.1%)	17 (10.1%)

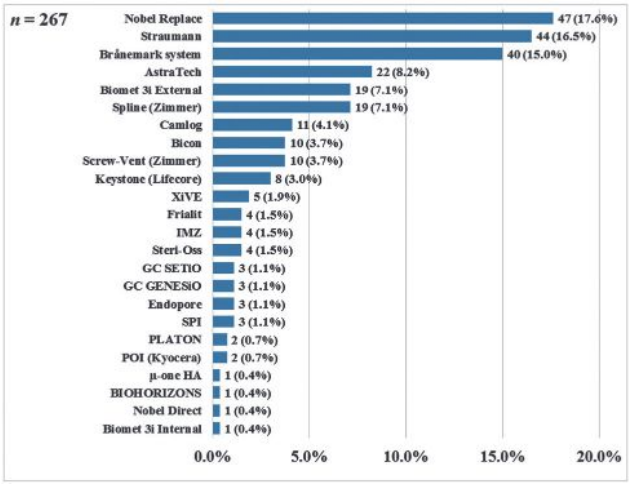

Fig. 2 Implant systems used.

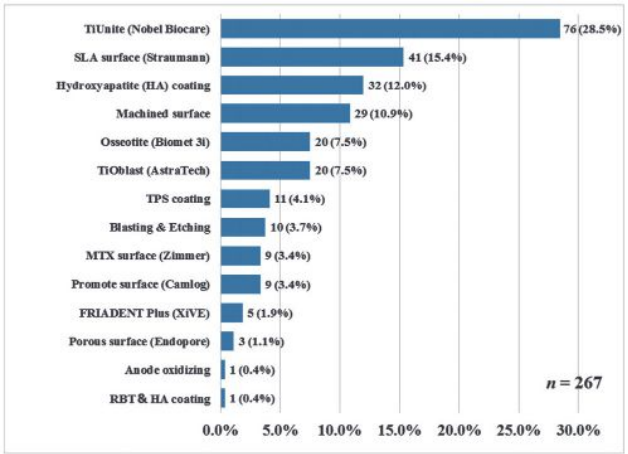

Fig. 3 Surface textures of implant bodies.

frequency of use. The three most frequently used dental implants were the Nobel Replace (47; 17.6%), Straumann (44; 16.5%), and Brånemark systems (40; 15.0%). Figure 3 shows the surface textures of the implant bodies. The three most frequently used implant surfaces were TiUnite (76; 28.5%), SLA surface (41; 15.4%), and hydroxyapatite (32; 12%). Bone graft substitutes were used for 77 patients (29%) during dental implant surgery, and the details are shown in Table 3. The two most frequently used bone graft substitutes were autologous bone (33;

Table 3 Bone graft substitutes

Autologous bone	33 (43%)
β-TCP	30 (39%)
FDBA	5 (6.5%)
DFDBA	2 (2.6%)
Bio-Oss	2 (2.6%)
Periosteum	1 (1.3%)
Boneject	1 (1.3%)
β-TCP+Hydroxyapatite	1 (1.3%)
GEM 21S	1 (1.3%)
Hydroxyapatite	1 (1.3%)

n = 77, FDBA: Freeze-dried bone allograft; DFDBA: Demineralized freeze-dried bone allograft; Bio-Oss: Geistlich, Wolhusen, Switzerland; Boneject: KOKEN Co., Ltd, Tokyo, Japan; GEM21: Osteohealth, NY, USA.

Table 4 Functional duration of implants

Mean functional duration, months	76.6 ± 46.1
>260	1 (0.4%)
240~259	2 (0.8%)
220~239	2 (0.8%)
200~219	3 (1.1%)
180~199	3 (1.1%)
160~179	8 (3.0%)
140~159	7 (2.6%)
120~139	14 (5.2%)
100~119	24 (9.0%)
80~99	25 (9.4%)
60~79	54 (20.2%)
40~59	77 (28.8%)
36~39	47 (17.6%)

n = 267, Mean ± SD.

Table 5 Patient comorbidities

Disease (149 per 267 participants)	No.
Hypertension	57
Hyperlipidemia	22
Cardiovascular disorders	15
Diabetes mellitus	11
Stomach disease	8
Thyroid dysfunction	6
Gout	5
Liver ailment	4
Asthma	4
Rheumatoid arthritis	4
Glaucoma	4
Kidney disease	3
Osteoporosis	3
Cataract	2
Stroke	1

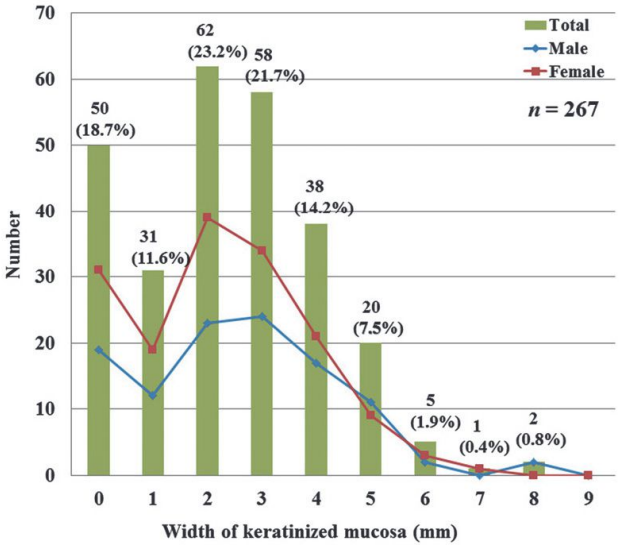

Fig. 4 Width of keratinized mucosa around implants. The width of keratinized mucosa (mm) at the buccal center of implants is represented by the bars. Blue line: men; red line: women.

43%) and β-tricalcium phosphate (30; 39%). Duration of implant function is shown in Table 4. Mean duration of function was 76.6 ± 46.1 months. In total, 149 patients (56%, Table 5) reported comorbidities, and 37 had more than one comorbidity. The most frequent pre-existing medical condition was hypertension (n = 57). Twenty-two patients had hyperlipidemia, 15 had cardiovascular disorders, and 11 had diabetes mellitus.

The width of keratinized mucosa at the buccal center of the implant is shown in Fig. 4. Men and women did not differ in the width of keratinized mucosa. The width was 2 mm in 62 (23.2%) patients, 3 mm in 58 (21.7%), 0 mm in 50 (18.7%), 4 mm in 38 (14.2%), and 1 mm in 31 (11.6%). There was no association between peri-implant diseases and the width of keratinized mucosa.

Table 6A shows the results of bacterial analyses of plaque samples from the deepest PPD sites of implants and natural teeth. The bacterial count of A. actinomycetemcomitans was undetectable in 261 (97.8%) and 262 (98.1%) samples from implants and natural teeth, respectively. P. intermedia was undetectable in 220 (82.4%) and 210 (78.7%) samples from implants and natural teeth, respectively, and P. gingivalis could not be detected in 188 (70.4%) and 183 (68.5%) samples of implants and natural teeth, respectively. We divided the 267 participants into three groups (healthy peri-implant tissue, peri-implant mucositis, and peri-implantitis), to investigate mean subgingival bacterial counts in the

Table 6A Comparison of subgingival bacterial counts in the pockets

Bacterial counts (Log_{10})		0	≥0.01	≥1	≥2	≥3	≥4	≥5	≥6
Total bacteria	Implant	0	0	0	0	67	137	58	5
	Natural teeth	0	0	0	0	72	102	84	9
A. actinomycetemcomitans	Implant	261	0	3	1	2	0	0	0
	Natural teeth	262	0	0	1	4	0	0	0
P. intermedia	Implant	220	0	29	11	6	1	0	0
	Natural teeth	210	0	22	19	15	1	0	0
P. gingivalis	Implant	188	0	17	31	23	7	1	0
	Natural teeth	183	0	7	23	36	17	1	0

n = 267

Table 6B Mean subgingival bacterial counts in the pockets of implant and natural teeth

Implant sites (Log_{10})	Total bacteria		A. a.	P. i.		P. g.	
Healthy peri-implant tissue	4.43 ± 0.67	**	0.03 ± 0.28	0.25 ± 0.67	**	0.56 ± 1.11	**
Peri-implant mucositis	4.41 ± 0.67	**	0.09 ± 0.50	0.33 ± 0.77	*	0.83 ± 1.39	**
Peri-implantitis	4.93 ± 0.82		0.05± 0.25	0.80 ± 1.32		2.17 ± 1.77	
Natural teeth sites (Log_{10})	**Total bacteria**		**A. a.**	**P. i.**		**P. g.**	
Healthy peri-implant tissue	4.51 ± 0.72		0.02 ± 0.25	0.41 ± 0.91		0.75 ± 1.41	
Peri-implant mucositis	4.55 ± 0.77		0.13 ± 0.61	0.67 ± 1.21		1.22 ± 1.63	**
Peri-implantitis	4.84 ± 0.86		0.00 ± 0.00	0.36 ± 0.90		1.87 ± 1.93	

Mean ± SD, *P < 0.05, **P < 0.01

Table 7A IgG titers against periodontal bacteria

IgG titer	≤−1.0	≥−1.0	≥−0.5	≥0	≥0.5	≥1.0	≥1.5	≥2.0	≥2.5	≥3.0	≥3.5	≥4
A. actinomycetemcomitans	0	43	151	39	10	5	2	0	2	1	0	1
P. intermedia	0	84	128	29	7	2	1	1	0	1	1	0
E. corrodens	3	70	144	22	9	1	3	2	0	0	0	0
P. gingivalis	13	21	33	44	40	36	36	19	5	3	1	3

n = 254

Table 7B Mean IgG titers against periodontal bacteria, by group

IgG titer	A. a.	P. i.	E. c.	P. g.
Healthy peri-implant tissue	−0.18 ± 0.53	−0.33 ± 0.49	−0.31 ± 0.44	3.58 ± 6.92
Peri-implant mucositis	−0.17 ± 0.75	−0.29 ± 0.43	−0.35 ± 0.38	5.53 ± 11.58
Peri-implantitis	−0.22 ± 0.49	−0.21 ± 0.97	−0.27 ± 0.72	6.87 ± 11.12

Mean ± SD

deepest PPD sites of implants and natural teeth in the same oral cavity. Mean bacterial counts of total bacteria, A. a., and P. i. in the deepest PPD sites of natural teeth, and mean bacterial counts of A. a. at the implant site, were very similar among the three groups. The mean bacterial counts of total bacteria, P. i., and P. g. at the implant sites of the peri-implantitis group were signi¿cantly higher than those for the healthy peri-implant tissue and peri-implant mucositis groups. The mean bacterial count of P. g. at natural teeth sites of the peri-implantitis group was signi¿cantly higher than in the healthy peri-implant tissue group (Table 6B). Table 7A shows the results of IgG titers against periodontal bacteria (A. a., P. i., E. c., and P. g.). The IgG titer against P. gingivalis was highest among these periodontal bacteria. We then divided the participants into three groups (healthy peri-implant tissue, peri-implant mucositis, and peri-implantitis), to examine mean IgG titers. The mean IgG titers against A. a., P. i., and E. c. were very low and quite similar. The mean IgG titer of P. g. was highest in the peri-implantitis group;

Table 8 Association between peri-implant diseases and clinical parameters of implants

	mPlI	mSBI	PPD
Healthy peri-implant tissue	0.3 ± 0.6	0.0 ± 0.0	2.7 ± 1.2
	**	**	**
Peri-implant mucositis	1.0 ± 0.7 **	1.3 ± 0.5 **	3.9 ± 1.1 **
	**	**	**
Peri-implantitis	0.9 ± 0.9	1.7 ± 0.9	5.6 ± 2.0

Mean ± SD, **P < 0.01

Table 9A Association between history of peridontal diseases and peri-implant diseases

History of peridontal diseases before implant treatment	Healthy peri-implant tissue	Peri-implant mucositis	Peri-implantitis
Healthy	2 (100%)	0	0
Gingivitis	2 (25%)	6 (75%)	0
Slight CP	52 (71.2%)	13 (17.8%)	8 (11.0%)
Moderate CP	66 (56.9%)	40 (34.5%)	10 (8.6%)
Severe CP	30 (45.5%)	29 (43.9%)	7 (10.6%)
Aggressive periodontitis	0	1 (50%)	1 (50%)

Table 9B Occurrence of peri-implant diseases in the slight, moderate and severe CP patients

History of chronic periodontitis	Peri-implant diseases			Signi¿cance (P-value)		
	Healthy peri-implant tissue	Peri-implant mucositis (PM)	Peri-implantitis (PI)	Healthy vs PM	Healthy vs PI	PM vs PI
Slight CP	52	13	8	8.33E-11	1.35E-13	0.238
Moderate CP	66	40	10	0.00061	4.74E-14	1.67E-06
Severe CP	30	29	7	0.861	8.31E-06	1.71E-05

however, the difference was not signi¿cant (Table 7B). Table 8 shows data on the associations of peri-implant diseases with clinical parameters (mPlI, mSBI, and PPD). The scores for clinical parameters were signi¿cantly higher in the peri-implant mucositis and peri-implantitis groups than in the healthy peri-implant tissue group. The mSBI scores and PPD were signi¿cantly higher in the peri-implantitis group than in the peri-implant mucositis group.

Analysis of the association between history of periodontal diseases and peri-implant diseases is shown in Table 9A. Periodontal condition before implant treatment was classi¿ed into six groups (healthy, gingivitis, slight CP, moderate CP, severe CP, and aggressive periodontitis). Among patients with slight CP, moderate CP, or severe CP before implant treatment, 71.2%, 56.9%, and 45.5%, respectively, had healthy peri-implant tissue; 17.8%, 34.5%, and 43.9% had peri-implant mucositis; and 11%, 8.6%, and 10.6% had peri-implantitis. The chi-square test for independence was used to test the null hypothesis that history of periodontitis before implant treatment and the extent of peri-implant disease were independent. The results indicated that slight CP was signi¿cantly associated with healthy peri-implant tissue and that moderate and severe CP were signi¿cantly associated with healthy peri-implant tissue and peri-implant mucositis (Table 9B).

Discussion

We investigated a sample of patients who had been treated for periodontitis in dental hospitals or private dental clinics before implant placement. They had received one or more implants, were followed for more than 3 years after loading, and were consecutively examined at periodontal maintenance appointments. The prevalences of peri-implant mucositis and peri-implantitis were 33.3% and 9.7%, respectively. Estimating the frequency of peri-implant disease is dif¿cult and depends greatly on assessment procedures. Variability in the prevalence of peri-implant disease might be attributable to differences between studies in the clinical parameters used to assess and de¿ne the disease. In the present study, we used the diagnostic criteria suggested in the Consensus of the Seventh European Workshop on Periodontology. Peri-implant mucositis was de¿ned as bleeding on gentle probing, and peri-implantitis was de¿ned as changes in the level of the crestal bone in conjunction with BOP.

Previous studies reported varying prevalence and inci-

dence rates for peri-implant disease, perhaps because of variation in the duration of prosthesis use (1,35). Studies of the incidence of peri-implant disease suggest that the follow-up period for an implant system should be at least 5 years (8,35). In the present study, the average functional duration was 76.6 months (6.38 years); thus, we believe that the present results are valid.

Different types of implant systems were used in this study, and variability in surface characteristics could have inÀuenced the prevalence of peri-implant diseases (17,36). However, no clinical differences were seen between the systems, as the vast majority of ¿xtures used a TiUnite (28.5%), SLA surface (15.4%), or hydroxyapatite coating (12.0%).

Zupnik et al. reported that implant failure was strongly associated with diabetes (37), whereas another report found no association (38). In this study, diabetes was not associated with the development of peri-implant diseases, perhaps because only a small number of patients with diabetes were enrolled.

Smoking was identi¿ed as a strong risk factor for peri-implant diseases (6,15,35,38-41). As compared with nonsmokers, smokers have a 31-fold chance of having peri-implantitis (39). However, a previous study (40) reported peri-implantitis rates of 23.53% for smokers and 16.51% for nonsmokers, but the difference was not signi¿cant. Twenty-two smokers, 52 former smokers, and 193 nonsmokers were included in the present study. Among the 22 smokers, eight (36.4%) had peri-implant mucositis, but none had peri-implantitis (0%). Among the 52 former smokers, 17 (32.7%) had peri-implant mucositis, and four had peri-implantitis (8%). Among the 193 nonsmokers, 64 (33.2%) had peri-implant mucositis, and 22 had peri-implantitis (11.4%). These results suggest that smoking is not associated with development of peri-implant diseases.

It remains unclear whether a zone of keratinized mucosa is required to maintain the health of peri-implant tissue. Several reviews noted insuf¿cient evidence for the need for keratinized mucosa around implants to maintain peri-implant tissue health (16,35,42,43). In the present study, the width of keratinized mucosa was not associated with development of peri-implant diseases.

The effects of implant overload on bone and implant loss in clinically well-integrated implants have not been comprehensively studied. In animal experiments, overload mimicked by supra-occlusal contacts in the presence of inÀammation signi¿cantly increased plaque-induced bone resorption (44). With respect to implant prosthodontics, the risk for peri-implantitis was 3.6 times higher for cemented restorations, 2.4 times higher when wear facets were present on the prosthetic crown, and 16.1 times higher for full-mouth rehabilitations (45). In the present study, prosthesis type (screw- or cement-retained) was not signi¿cantly associated with peri-implant diseases (Table 2B).

P. intermedia counts were signi¿cantly higher at implant sites in the peri-implantitis group, and P. gingivalis counts were higher in the implant and natural-teeth sites in the peri-implantitis groups (Table 6B). Therefore, P. intermedia and P. gingivalis might be associated with development of peri-implantitis. However, several recent studies reported that the microbial composition of bio¿lm was more complex in peri-implant disease than in periodontal disease. The prevalence of periodontopathic bacteria is not high in peri-implantitis (26,27,46,47). Future studies may help to clarify these ¿ndings.

IgG titers were signi¿cantly higher in periodontitis patients than in healthy controls, especially among those with sites of PPD greater than 4 mm (33). The mean IgG titer against P. gingivalis was highest in the peri-implantitis group; however, the differences were not statistically signi¿cant (Table 7B).

Previous studies suggest that oral hygiene conditions are an important variable associated with peri-implant health (9,48,49). In this study, high index scores for mPlI were signi¿cantly associated with development of peri-implant mucositis and peri-implantitis. In addition, high index scores for mSBI and deeper PPD were signi¿cantly associated with development of peri-implant mucositis and peri-implantitis (Table 8). These results suggest that a high plaque score increases the risk of developing peri-implant diseases. Thus, patient compliance, including plaque control and supportive therapy, may be important in peri-implant diseases.

Several studies reported that individuals with histories of periodontal disease appear to have a higher risk of peri-implant diseases (13,14,50). In the present study, we divided patients with CP into three groups (slight, moderate, and severe CP). The presence of slight CP before implant treatment was signi¿cantly associated with healthy peri-implant tissue, and the presence of moderate or severe CP was signi¿cantly associated with healthy peri-implant tissue and peri-implant mucositis (Table 9A, B).

In conclusion, the patient-based prevalences of peri-implant mucositis and peri-implantitis were 33.3% and 9.7%, respectively. These values are lower than those reported previously. The present results suggest that poor oral hygiene and a history of periodontitis are strong risk factors for peri-implant diseases. Patient compliance with elements such as periodontal therapy before and

after implant placement, plaque control, and supportive therapy may be crucial in maintaining the health of peri-implant tissue.

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ConÀict of interest

The authors have no conÀicts of interest to declare.

References

1. Lang NP, Berglundh T (2011) Periimplant diseases: where are we now?--consensus of the seventh European workshop on periodontology. J Clin Periodontol 38, Suppl 11, 178-181.
2. Lindhe J, Berglundh T, Ericsson I, Liljenberg B, Marinello C (1992) Experimental breakdown of peri-implant and periodontal tissues. A study in the beagle dog. Clin Oral Implants Res 3, 9-16.
3. Pontoriero R, Tonelli MP, Carnevale G, Mombelli A, Nyman SR, Lang NP (1994) Experimentally induced peri-implant mucositis. A clinical study in humans. Clin Oral Implants Res 5, 254-259.
4. Esposito M, Hirsch JM, Lekholm U, Thomsen P (1998) Biological factors contributing to failures of osseointegrated oral implants. (II). Etiopathogenesis. Eur J Oral Sci 106, 721-764.
5. Zitzmann NU, Berglundh T (2008) De¿nition and prevalence of peri-implant diseases. J Clin Periodontol 35, 8 Suppl, 286-291.
6. Lindhe J, Meyle J (2008) Peri-implant diseases: consensus report of the sixth European workshop on periodontology. J Clin Periodontol 35, 8 Suppl, 282-285.
7. Lachmann S, Stehberger A, Axmann D, Weber H (2013) The peri-implant health in patients attending an annual recall program. A clinical and microbiological study in 74 patients from the Tübingen Implant Registry. Clin Oral Implants Res 24, 1300-1309.
8. Berglundh T, Persson L, Klinge B (2002) A systematic review of the incidence of biological and technical complications in implant dentistry reported in prospective longitudinal studies of at least 5 years. J Clin Periodontol 29, Suppl 3, 197-212.
9. Ferreira SD, Silva GL, Cortelli JR, Costa JE, Costa FO (2006) Prevalence and risk variables for peri-implant disease in Brazilian subjects. J Clin Periodontol 33, 929-935.
10. Roos-Jansåker AM, Renvert H, Lindahl C, Renvert S (2006) Nine- to fourteen-year follow-up of implant treatment. Part III: factors associated with peri-implant lesions. J Clin Periodontol 33, 296-301.
11. Koldsland OC, Scheie AA, Aass AM (2010) Prevalence of peri-implantitis related to severity of the disease with different degrees of bone loss. J Periodontol 81, 231-238.
12. Mir-Mari J, Mir-Or¿la P, Figueiredo R, Valmaseda-Castellón E, Gay-Escoda C (2012) Prevalence of peri-implant diseases. A cross-sectional study based on a private practice environment. J Clin Periodontol 39, 490-494.
13. Roccuzzo M, Bonino F, Aglietta M, Dalmasso P (2012) Ten-year results of a three arms prospective cohort study on implants in periodontally compromised patients. Part 2: clinical results. Clin Oral Implants Res 23, 389-395.
14. Pjetursson BE, Helbling C, Weber HP, Matuliene G, Salvi GE, Brägger U et al. (2012) Peri-implantitis susceptibility as it relates to periodontal therapy and supportive care. Clin Oral Implants Res 23, 888-894.
15. Strietzel FP, Reichart PA, Kale A, Kulkarni M, Wegner B, Küchler I (2007) Smoking interferes with the prognosis of dental implant treatment: a systematic review and meta-analysis. J Clin Periodontol 34, 523-544.
16. Lin GH, Chan HL, Wang HL (2013) The signi¿cance of keratinized mucosa on implant health: a systematic review. J Periodontol 84, 1755-1767.
17. Teughels W, Van Assche N, Sliepen I, Quirynen M (2006) Effect of material characteristics and/or surface topography on bio¿lm development. Clin Oral Implants Res 17, Suppl 2, 68-81.
18. Roccuzzo M, De Angelis N, Bonino L, Aglietta M (2010) Ten-year results of a three-arm prospective cohort study on implants in periodontally compromised patients. Part 1: implant loss and radiographic bone loss. Clin Oral Implants Res 21, 490-496.
19. Costa FO, Takenaka-Martinez S, Cota LO, Ferreira SD, Silva GL, Costa JE (2012) Peri-implant disease in subjects with and without preventive maintenance: a 5-year follow-up. J Clin Periodontol 39, 173-181.
20. Mombelli A, Van Oosten MAC, Schürch E, Lang NP (1987) The microbiota associated with successful or failing osseointegrated titanium implants. Oral Microbiol Immunol 2, 145-151.
21. Renvert S, Lindahl C, Renvert H, Persson GR (2008) Clinical and microbiological analysis of subjects treated with Brånemark or AstraTech implants: a 7-year follow-up study. Clin Oral Implants Res 19, 342-347.
22. Shibli JA, Melo L, Ferrari DS, Figueiredo LC, Faveri M, Feres M (2008) Composition of supra- and subgingival bio¿lm of subjects with healthy and diseased implants. Clin Oral Implants Res 19, 975-982.
23. Botero JE, González AM, Mercado RA, Olave G, Contreras A (2005) Subgingival microbiota in peri-implant mucosa lesions and adjacent teeth in partially edentulous patients. J Periodontol 76, 1490-1495.
24. Quirynen M, Vogels R, Peeters W, van Steenberghe D, Naert I, Haffajee A (2006) Dynamics of initial subgingival colonization of 'pristine' peri-implantpockets. Clin Oral Implants Res 17, 25-37.

25. Cho-Yan Lee J, Mattheos N, Nixon KC, Ivanovski S (2012) Residual periodontal pockets are a risk indicator for peri-implantitis in patients treated for periodontitis. Clin Oral Implants Res 23, 325-333.
26. Koyanagi T, Sakamoto M, Takeuchi Y, Maruyama N, Ohkuma M, Izumi Y (2013) Comprehensive microbiological ¿ndings in peri-implantitis and periodontitis. J Clin Periodontol 40, 218-226.
27. Maruyama N, Maruyama F, Takeuchi Y, Aikawa C, Izumi Y, Nakagawa I (2014) Intraindividual variation in core microbiota in peri-implantitis and periodontitis. Sci Rep 4, 6602.
28. Silness J, Löe H (1964) Periodontal disease in pregnancy. II. Correlation between oral hygiene and periodontal condition. Acta Odontol Scand 22, 121-135.
29. Löe H, Silness J (1963) Periodontal disease in pregnancy. I. Prevalence and severity. Acta Odontol Scand 21, 533-551.
30. Armitage GC (1999) Development of a classi¿cation system for periodontal diseases and conditions. Ann Periodontol 4, 1-6.
31. Tadokoro K, Yamaguchi T, Kawamura K, Shimizu H, Egashira T, Minabe M et al. (2010) Rapid quanti¿cation of periodontitis-related bacteria using a novel modi¿cation of Invader PLUS technologies. Microbiol Res 165, 43-49.
32. Morozumi T, Kubota T, Abe D, Shimizu T, Komatsu Y, Yoshie H (2010) Effects of irrigation with an antiseptic and oral administration of azithromycin on bacteremia caused by scaling and root planing. J Periodontol 81, 1555-1563.
33. Kudo C, Naruishi K, Maeda H, Abiko Y, Hino T, Iwata M et al. (2012) Assessment of the plasma/serum IgG test to screen for periodontitis. J Dent Res 91, 1190-1195.
34. Kanda Y (2013) Investigation of the freely available easy-to-use software 'EZR' for medical statistics. Bone Marrow Transplant 48, 452-458.
35. Heitz-May¿eld LJ (2008) Peri-implant diseases: diagnosis and risk indicators. J Clin Periodontol 35, 8 Suppl, 292-304.
36. Renvert S, Polyzois I, Claffey N (2011) How do implant surface characteristics inÀuence peri-implant disease? J Clin Periodontol 38, Suppl 11, 214-222.
37. Zupnik J, Kim SW, Ravens D, Karimbux N, Guze K (2011) Factors associated with dental implant survival: a 4-year retrospective analysis. J Periodontol 82, 1390-1395.
38. Anner R, Grossmann Y, Anner Y, Levin L (2010) Smoking, diabetes mellitus, periodontitis, and supportive periodontal treatment as factors associated with dental implant survival: a long-term retrospective evaluation of patients followed for up to 10 years. Implant Dent 19, 57-60.
39. Rinke S, Ohl S, Ziebolz D, Lange K, Eickholz P (2011) Prevalence of periimplant disease in partially edentulous patients: a practice-based cross-sectional study. Clin Oral Implants Res 22, 826-833.
40. Simonis P, Dufour T, Tenenbaum H (2010) Long-term implant survival and success: a 10-16-year follow-up of non-submerged dental implants. Clin Oral Implants Res 21, 772-777.
41. Atieh MA, Alsabeeha NHM, Faggion Jr CM, Duncan WJ (2013) The frequency of peri-implant diseases: a systematic review and meta-analysis. J Periodontol 84, 1586-1598.
42. Wennström JL, Derks J (2012) Is there a need for keratinized mucosa around implants to maintain health and tissue stability? Clin Oral Implants Res 23, Suppl 6, 136-146.
43. Brito C, Tenenbaum HC, Wong BK, Schmitt C, Nogueira-Filho G (2014) Is keratinized mucosa indispensable to maintain peri-implant health? A systematic review of the literature. J Biomed Mater Res B Appl Biomater 102, 643-650.
44. Naert I, Duyck J, Vandamme K (2012) Occlusal overload and bone/implant loss. Clin Oral Implants Res 23, Suppl 6, 95-107.
45. Dalago HR, Schuldt Filho G, Rodrigues MA, Renvert S, Bianchini MA (2016) Risk indicators for peri-implantitis. A cross-sectional study with 916 implants. Clin Oral Implants Res doi: 10.1111/clr.12772.
46. Kumar PS, Mason MR, Brooker MR, O'Brien K (2012) Pyrosequencing reveals unique microbial signatures associated with healthy and failing dental implants. J Clin Periodontol 39, 425-433.
47. Dabdoub SM, Tsigarida AA, Kumar PS (2013) Patient-speci¿c analysis of periodontal and peri-implant microbiomes. J Dent Res 92, 12 Suppl, 168S-175S.
48. Zitzmann NU, Berglundh T, Marinello CP, Lindhe J (2001) Experimental peri-implant mucositis in man. J Clin Periodontol 28, 517-523.
49. Mombelli A, Décaillet F (2011) The characteristics of bio¿lms in peri-implant disease. J Clin Periodontol 38, Suppl 11, 203-213.
50. De Boever AL, Quirynen M, Coucke W, Theuniers G, De Boever JA (2009) Clinical and radiographic study of implant treatment outcome in periodontally susceptible and non-susceptible patients: a prospective long-term study. Clin Oral Implants Res 20, 1341-1350.