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Prevalence of Peri-implant Diseases: Analyses of Associated Factors

ABSTRACT

Aim: Identify the relationship between specific factors (age, sex, smoking, time of prosthesis in function, implant location, and width of peri-implant keratinized mucosa) and peri-implant diseases in patients from the Center of Research and Continuing Education in Implant Dentistry (CEPID) at the Federal University of Santa Catarina (UFSC), Brazil.

Materials and Methods: A cross-sectional study was conducted in 193 patients that had received 725 external-hexed cylindrical implants supporting functional prosthesis for at least 1 year (range from 1-9 years). Clinical examination included probing depths, bleeding on probing and/or suppuration. Radiographic exam was conducted to measure peri-implant bone levels.

Results: There was no statistically significance in the association between prevalence of peri-implant diseases and age, sex, time with prostheses in function and implant location variables independently. There was a statistically significant association between the independent variables of smoking and the width of keratinized peri-implant mucosa less than 2 mm, and the presence of peri-implant diseases. When all the categories were evaluated together in relation with the peri-implant diseases, the prostheses in function for 5 years and more had association with presence of both, peri-implant mucositis an peri-implantitis. Peri-implantitis prevalence was higher for males with the prostheses in use for 5 years or more. Peri-implant mucositis was more associated with the participants over 57 years of age, with systemic disease and with the prostheses in function for more than 5 years.

Conclusions: Smoking habits and the width of peri-implant keratinized mucosa as independent variables were associated with the prevalence of peri-implant diseases.

CLINICAL RELEVANCE

Scientific rationale for study: The literature is controversial in regards to the risk variables and the individuals that present a higher risk to develop peri-implant diseases. In addition, few studies have been carried out with the intent to identify the possible variables that may influence the occurrence of peri-implant diseases. Principal findings: An association of the prevalence of peri-implant diseases and the variables age, sex, time with prostheses in function and implant location, was not found. However, the presence of peri-implant diseases was found to be associated with smoking habits and the quantity of peri-implant keratinized mucosa. Practical implications: The results of the present study suggest possible factors that may play a role in the prevalence of peri-implant diseases.

1. INTRODUCTION

Biological complication of dental implants; such as, peri-implant mucositis and peri-implantitis have been described; however, peri-implant disease prevalence data are inconsistent.[1-4] Our previous study showed that peri-implant mucositis has a prevalence of 23% and peri-implantitis of 8% in a total of 200 randomly selected patients from the same clinical institution.[5] The presence of risk variables needs to be clarified in order to distinguish health from the disease process that affects peri-implant tissues.[6] The literature is controversial in regards to the risk variables and the individuals that present a higher risk of developing peri-implant diseases. In addition, few studies have been carried out with the intent to identify possible variables that may influence the occurrence of peri-implant diseases.[7-9]

The precise effects of local or systemic factors on the longevity of dental implant, when related to its platform engagement and prosthetic scheme are still unknown. Therefore, the present study was carried out with the intent to identify local and systemic factors that may regulate the host response and favor the loss of osseointegration.[10-15] The low success rate of dental implants is not related to sex or age; although systemic conditions associated with the increase in age may require modification in the treatment plan.[16] Therefore, the presence of chronic diseases and the long-term use of medications should be considered when evaluating dental implant longevity,[12,17] due to the fact that the longer the implant is in function, the lower the success rate.[11] In addition, poor oral hygiene, smoking[13,18-20] and diabetes[21] have already been identified as risk factors for the development of peri-implant diseases.

This study aims to identify the association between various patient variables, such as: age; sex; smoking; time of implant supported prosthesis in function; implant location; and, quantity of peri-implant keratinized mucosa, with presence of peri-implant diseases in patients from the Center of Studies of Continuing Education in Implant Dentistry (CEPID) of the Federal University of Santa Catarina (UFSC).

2. MATERIALS AND METHODS

The ethics committee of the UFSC approved the present study and an informed consent was obtained from each participating individual.

Sample selection

193 patients from the CEPID-UFSC database were randomly selected. This group of patients presented with a total amount of 725 external-hexed cylindrical implants which supported prosthesis placed for the minimum of 1 year and the maximum of 9 years, from the period from 2001 through 2010. From a total of 131 (67.9%) of patients presenting healthy dental implants, 46 (23.8%) of the patients presented at least 1 implant with peri-implant mucositis and 8.3 (8.3%) of the patients with at least 1 implant with peri-implantitis.[5]

Surgical protocol

All the implants were placed with the platform leveled at the alveolar crest. The crest or the edentulous ridge was leveled with a round carbide bur when the implant was planned to be placed at a lower level then the existing bony ridge. The surgical protocol employed by the CEPID-UFSC clinic, which includes leveling the bony ridge to allow a straight butt-joint between the implant and the surrounding one, resulted in a predictable bone loss of less than 2mm after 1 year in service.[22]

Data collection

After the prostheses were removed, the following data was collected:

- Bone level: A bone loss of 2mm or more was considered peri-implantitis, when associated with presence of probing depth (PD) > 4 mm and bleeding/suppuration upon probing.
- BOP index; The presence or absence was registered after the introduction of 1 mm of the periodontal probe (PCV12PT Hu-Friedy Inc., Chicago, IL) into the gingival sulcus with a gingival "sweep" movement.[23] Data was analyzed after removal of the periodontal probe and 30 seconds elapsed.
- PD; the PD measurements were collected on the mesial-buccal, mid-buccal, distal-buccal, mesial-lingual, mid-lingual and distal-lingual of each tooth. The deepest site closest to the indicated anatomical sites was the registered probing depth. Each examiner was calibrated for a gentle probing pressure of 0.25 N.
- Width of peri-implant Keratinized Mucosa (WKM); the measurement of the WKM was collected from the buccal aspect from the site that presented the lowest value. The groups were divided into 2; ≤ 2 mm, and > 2 mm.

Radiographic analysis

Bone level was measured around the dental implants using the parallel cone technique in order to obtain radiographic images (Kodak Insight film, Carestream, INC., New York, EUA) for analyses. The radiographs were digitalized by image analysis program (Digimizer® versão 3.7.0, Medical Software Brolkstraat, Belgium). The distances from the implant platform to the first radiographic evidence of bone contact on the mesial (MBL); and, on the distal (DBL) aspects of each implant were registered. The measurements were made at baseline (T0) by only one calibrated examiner, different from the clinical examiner; and, repeated after 7 days (T7). The mean bone loss value obtained from both measurements (T0 and T7) was used as the final measurement for each site. For the final measurement for each implant, a mean bone loss value was established by summing the mesial and distal mean values and dividing it by sum by 2.

Group analysis and division

The following criterion was used as the definition for the clinical and radiographic analyses. Peri-implant mucositis was considered when the probing depth was of ≤ 4mm with presence of BOP around an implant presenting < 2 mm of bone loss. Data was compiled according to each implant and 4 sites (mesial, distal, mid-buccal and palatal/lingual). Peri-implantitis was defined when PD was 4mm or more, associated with BOP and/or suppuration, and bone loss ≥ 2mm. Bone loss was evaluated from the data compiled from 2 sites (mesial and distal) only, due to the inability to evaluate the mid-buccal and lingual/palatal implant sites in an x-ray.

Local and systemic factors were studied in order to verify a possible relationship with peri-implant diseases, such as: age; sex; smoking; time of implant supported prosthesis in function; implant location; and, quantity of peri-implant WKM. Additional information related to systemic health was gathered in the groups: hormonal replacement, chemotherapy, menopause, thyroid alterations, Diabetes Mellitus, alcohol use and cardiac problems. For statistical analyzes, they were divided into two groups: 1) healthy; and 2) non-healthy.

The healthy (without BOP) dental implants were divided into 2 groups in order to further allow discussion of the basic aim of this study, knowing that peri-implant bone loss of ≥ 2mm, even in the absence of BOP, could suggest history of peri-implant diseases.

Statistical analyses

All the data were compiled and compared between groups. The inter-examiner reproducibility of the MBL and DBL measurements was tested with the intra-class correction coefficient (ICC).

The data collected was inserted in an excel sheet designed for this study. Next, the data was exported to the software SPSS 18.0, where it was analyzed. The Chi-Square or Fisher's Exact tests were used to evaluate the association between the dependent variables (Peri-implant mucositis, peri-implantitis and WKT) with the significance being the value of $p < 0.05$. The prevalence ratios (PR) and its respective confidence intervals (95%) were estimated by means of Poisson's regression log-linear model with an estimator.

3. RESULTS

The sample size was composed of 193 patients that summed a total amount of 725 dental implants. The patient age ranged from 14 to 85 years, with an average of 52.67 (IC95% 52,12 – 54,21) years. Gender was distributed 32.6% as 67.4% females. Sample details and socio-demographic data are presented in Table 1. Table 2 presents the distribution of sex and peri-implant disease prevalence category.

Table 1. Description of participants according to sex, age and scholarity.

Variables	Sample (n=193)	Implants placed (n=725)
	n (%)	n (%)
Sex		
Male	67 (34,7)	266 (36,7)
Female	126 (65,2)	459 (63,3)
Age (years)		
Up to 48 years	95 (49.2)	258 (35.6)
49-57 years	50 (25.9)	247 (34.1)
Over 57 years	48 (24.8)	220 (30.3)
Scholarity		
Up to 8th grade	33 (17,1)	118 (16,3)
Up to 12th grade	84 (43,5)	330 (45.5)
College	76 (40.4)	277 (38.2)
TOTAL	193 (100,0)	725 (100,0)

Table 2. Distribution of the participants according to sex and peri-implant disease category prevalence

Groups	Sex		Total
	Male	Female	
Healthy	46	85	131
Peri-implant mucositis	13	32	45
Peri-implantitis.	4	12	16
Total	63	129	192

Regarding the time the implant supported prostheses were in function, 137 patients (480 implants) had the prostheses for up to 5 years, and 55 patients (245 implants) for more than 5 years. The mean time interval with the prostheses in function was of 4.02 years (standard deviation of 1.67 years). The results associating the peri-implant disease prevalence categories are presented in Table 3.

Table 3. Distribution of participants according with the peri-implant disease prevalence categories and the time of prostheses was in function

Groups	Time of prostheses in function		Total
	Up to 5 years	More than 5 years	
Healthy	98	33	131
Peri-implant mucositis	32	13	45
Peri-implantitis	7	9	16
Total	137	38	192

In the analyzes of the association of the independent variables with the outcome of peri-implant mucositis and peri-implantitis; age, general health and time the prostheses in function were the variables that presented association with peri-implant mucositis. Sex and time the prostheses were in function were associated with peri-implantitis *(Table 4)*.

Table 5. Distribution of the participants according with sex and smoking

		Sex		
		Male	Female	Total
Smoking	Yes	33	30	63
	No	30	99	129

The distribution of participants, according to sex and smoking, is presented in Table 5. Table 6 presents the distribution of the participants, according with the smoking and the prevalence category of peri-implant diseases. There was an association between the prevalence of smoking and the peri-implant diseases, where the value of P was 0.027.

Table 7. Distribution of the dental implant health statuses according with the quantity of WKM

Groups*	Quantity of WKM		Total
	≤2mm	≥2mm	
Healthy implants	334	156	490
Peri-implant mucositis	101	65	166
Peri-implantitis	51	17	68
Total	486	238	724

Of the 724 dental implants, 248 were placed in anterior sites and 476 in posterior sites. Table 8 presents the distribution of the implants according to the location and presence of peri-implant diseases.

Table 8. Distribution of the dental implant health statuses according with the location

Groups*	Location		Total
	Anterior	Posterior	
Healthy implants	161	328	489
Peri-implant mucositis	63	103	166
Peri-implantitis	24	44	68
TOTAL	248	475	723

The variables that presented statistically significant associations were submited to Poisson regression analysis with robust estimation. The prevalence of peri-implant mucositis in the older participants was 35% (1-0,65*100) higher than for

Table 6. Distribution of the participants according with smoking status and the prevalence category of peri-implant diseases

Factors		Groups			
		Healthy patients;	Patients with peri-implant mucositis	patients with peri-implantitis	Total
smoking	Yes	44	12	07	63
	No	87	33	33	129

* 1) Healthy patients; 2) Patients with peri-implant mucositis; 3) patients with peri-implantitis.

Table 4. Distribution of the association values between the independent variables with peri-implant mucositis and peri-implantitis

	Absence of peri-impalnt mucositis		Presence of peri-implant mucositis		p	Absence of peri-implantitis		Presence of peri-implantitis		p
	n	%	n	%		n	%	n	%	
Sex					0.279					0.004*
Male	211	79.3	55	20.7		252	94.7	14	5.3	
Female	348	75.8	111	24.2		405	88.2	54	11.8	
Age					0.002*					0.384
up to 48 years	181	70.2	77	29.8		239	92.6	19	7.4	
49 to 57 years	194	78.5	53	21.5		221	89.5	26	10.5	
More than 57 years	184	83.6	36	23.5		197	89.5	23	10.5	
Scholarity					0.659					0.537
Up to 8th grade	88	74.6	30	25.4		107	90.7	11	9.3	
Up to 12th grade	259	78.5	71	21.5		303	91.8	27	8.2	
College	212	76.5	65	23.5		247	89.2	30	10.8	
Smoking					0.845					0.893
Yes	227	77.5	66	22.5		265	90.4	28	9.6	
No	332	76.9	100	23.1		392	90.7	40	9.3	
General Health					0.005*					0.747
Non-healthy	281	81.7	63	18.3		313	91.0	31	9.0	
Healthy	278	73.0	103	27.0		344	90.3	37	9.7	
Implant site					>0.001*					0.249
Anterior	170	68.5	78	31.5		229	92.3	19	7.7	
Posterior	389	81.7	87	18.3		427	89.7	49	10.3	
Prostheses in use					0.014*					0.003*
> 5 years	357	74.4	123	25.6		446	92.9	34	7.1	
≤ 5 years	202	82.4	43	17.6		211	86.1	34	13.9	

* Significance level α<0.05

the younger participants. The prevalence of peri-implant mucositis in the posterior implants was 41% higher than for the anterior implants. The prevalence of peri-implant mucositis in prostheses in use for 5 years or more was 29% higher than for the ones in function for less than 5 years.

The chance of this population presente peri-implantitis is almost twice (1.97) as high for prostheses that have been more than 5 years in function compared to less that this time *(Table 10)*.

Table 9. Association of the prevalence of peri-implant mucositis with the prevalence of the independent variables

	RC (IC95%)	p
Age		
Up to 48 years	1	
49 to 57 years	0.81 (0.58 – 1.11)	0.199
More than 57 years	0.65 (0.44 – 0.96	0.032*
Scholarity		
Up to 8th grade	1	
Up to 12th grade	0.82 (0.55 – 1.22)	0.341
College	0.99 (0.66 – 1.47)	0.970
Smoking		
No	1	
Yes	1.17 (0.88 – 1.55)	0.278
General Health		
Health	1	
non-healthy	0.79 (0.58 – 10.7)	0.138
Implant site		
Anterior	1	
Posterior	0.59 (0.45 – 0.77)	>0.001*
prostheses in function		
> 5 years	1	
≤ 5 years	0.71 (0.50 – 0.99)	0.045*

Table 10. Association of the prevalence of peri-implantitis with the prevalence of the independent variables

	RC (IC 95%)	p
Implant site		
Anterior	1	
Posterior	1.38 (0.84 – 2.25)	0.199
Prostheses in function		
> 5 years	1	
≤ 5 years	1.97 (1.26 – 3.08)	0.003*

4. DISCUSSION

In the present study, 760 dental implants were evaluated in 200 patients. Sixty-nine percent of the patients presented healthy implants, 23% presented at least 1 implant with peri-implant mucositis, and 8% of the participants presented at least 1 implant with peri-implantitis.

Of all the factors analyzed, sex alone did not show association with the prevalence variables, concurring with Ferreira and coworkers (2006).[6] However, sex and time the prostheses was in function, together, were associated with the prevalence of peri-implantitis. Smoking habits showed association with higher rates of peri-implant diseases; as already described in a meta-analysis conducted by Strietzel and coworkers (2007),[24] and recently by Souza and coworkers (2012).[25]

The association of the peri-implant WKM with the peri-implant tissue health is controversial. In the present study, a narrow peri-implant WKM (< 2mm) in the "healthy with bone loss" and the "Peri-implantitis groups; and the association of the peri-implant band of WKM of > 2mm with the "healthy groups without bone loss" and "Mucositis" indicate that a higher amount of WKM may favor the maintenance of peri-implant health, concurring with Costa and coworkers (2012).[26] These results are contrary to Block and coworkers (1996).[27] Other studies were not able to correlate the presence of peri-implant WKM with peri-implant health.[28-30] Roos-Jansåker and coworkers (2006b)[9] showed that the presence of peri-implant WKM was associated with peri-implant mucositis, and that this association could be related to the fact that the recession, and consequent less peri-implant pocket formation, can be more common in areas without WKM.

In regards to the "implant location", the results of the present study showed to be contrary to the ones presented by Serino & Turri (2011)[31] and similar to the results presented by Fransson and coworkers (2009),[2] where they suggested that

peri-implantitis occurred in regions of the oral cavity without a specific association. Studies[2,13,32] have shown a significant statistical difference only in regards to the anterior region of the mandible. A possible cause of the conflicting results could be found in Fransson and coworkers (2009)[2] study. This study justifies the importance of establishing a numerical equivalence of the implants placed in the anterior and posterior regions. In the present study, 248 implant were placed in the anterior region, and 475 were placed in the posterior region of the oral cavity.

Aiming to optimize the success rate of dental implants, studies seek to identify factors that could be associated with peri-implant bone loss.[10-16] Conflicting results are evident in the literature when comparing studies that analyze factors associated with the prevalence of peri-implant diseases. It is not understood if there is an association between the location and presence of the peri-implant WKM with peri-implant health. There is a clear need for further studies to clarify these questions. It is necessary to evaluate other factors that may play a role as to a more direct association with the development of peri-implant diseases. Some examples are: the correct position of the dental implant, the correct seating of the prosthetic abutment, the type of prostheses that allow ideal oral hygiene, the use of angled abutments, and the presence of residual excess cement in cement-retained implant prostheses. In spite of the scientific strive in elucidate the problems related to the maintenance of peri-implant health, important questions still haven't reached consensus, and have generated different perspectives in the literature. As examples, the different hypotheses (concepts) of peri-implantitis are stated; in addition to various causes for peri-implant bone loss. These are factors that have been debated over many years and still haven't reached a common denominator. These questions play an important role in the decision of how to isolate the factors associated with peri-implant diseases in order to reach a scientific conclusive answer. The results of the present study suggest that there are possible factors that may play a role in the peri-implant diseases. Further longitudinal studies are needed in order to clarify the potential variables involved in dental implant loss due to peri-implant diseases.

5. CONCLUSION

Considering the factors studied, smoking habits and quantity of peri-implant WKM ≤ 2mm showed to have an association with peri-implant diseases when evaluated alone. When all the categories were evaluated together in relation to the peri-implant diseases, the prostheses in function for 5 years and more had association with presence of both, peri-implant mucositis an peri-implantitis. Peri-implantitis prevalence was higher for males with the prostheses in use for 5 years or more. Peri-implant mucositis was more associated with the participants over 57 years of age, with systemic disease and with the prostheses in function for more than 5 years.

REFERENCES

1. Berglundh, T., L. Persson, and B. Klinge, 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*, 2002;**29** Suppl 3: p. 197-212; discussion 232-3.
2. Fransson, C., *et al.*, Prevalence of subjects with progressive bone loss at implants. *Clin Oral Implants Res*, 2005;**16**(4): p. 440-6.
3. Pjetursson, B.E., *et al.*, A systematic review of the survival and complication rates of fixed partial dentures (FPDs) after an observation period of at least 5 years. *Clin Oral Implants Res*, 2004;**15**(6): p. 625-42.
4. Roos-Jansaker, A.M., *et al.*, Nine- to fourteen-year follow-up of implant treatment. Part I: implant loss and associations to various factors. *J Clin Periodontol*, 2006;**33**(4): p. 283-9.
5. Buttendorf, A.R.F., C. F.; Oliveira de Souza, J. G.; Dalagl, H.; Bianchini, M, A., Prevalence of Peri-implant Disease - Part 1. *Dentistry* 2014;**4**(6): p. 1-4.
6. Ferreira, S.D., *et al.*, Prevalence and risk variables for peri-implant disease in Brazilian subjects. *J Clin Periodontol*, 2006;**33**(12): p. 929-35.
7. Bragger, U., *et al.*, Associations between clinical parameters assessed around implants and teeth. *Clin Oral Implants Res*, 1997;**8**(5): p. 412-21.
8. Karoussis, I.K., *et al.*, Effect of implant design on survival and success rates of titanium oral implants: a 10-year prospective cohort study of the ITI Dental Implant System. *Clin Oral Implants Res*, 2004;**15**(1): p. 8-17.
9. Roos-Jansaker, A.M., *et al.*, Nine- to fourteen-year follow-up of implant treatment. Part II: presence of peri-implant lesions. *J Clin Periodontol*, 2006;**33**(4): p. 290-5.
10. Alsaadi, G., *et al.*, Impact of local and systemic factors on the incidence of failures up to abutment connection with modified surface oral implants. *J Clin Periodontol*, 2008;**35**(1): p. 51-7.
11. Artzi, Z., G. Carmeli, and A. Kozlovsky, A distinguishable observation between survival and success rate outcome of hydroxyapatite-coated implants in 5-10 years in function. *Clin Oral Implants Res*, 2006;**17**(1): p. 85-93.
12. Bornstein, M.M., N. Cionca, and A. Mombelli, Systemic conditions and treatments as risks for implant therapy. *Int J Oral Maxillofac Implants*, 2009;**24** Suppl: p. 12-27.
13. Lindquist, L.W., G.E. Carlsson, and T. Jemt, A prospective 15-year follow-up study of mandibular fixed prostheses supported by osseointegrated implants. Clinical results and marginal bone loss. *Clin Oral Implants Res*, 1996;**7**(4): p. 329-36.
14. Mombelli, A. and N. Cionca, Systemic diseases affecting osseointegration therapy. *Clin Oral Implants Res*, 2006;**17** Suppl 2: p. 97-103.
15. Moy, P.K., *et al.*, Dental implant failure rates and associated risk factors. *Int J Oral Maxillofac Implants*, 2005;**20**(4): p. 569-77.
16. Sugerman, P.B. and M.T. Barber, Patient selection for endosseous dental implants: oral and systemic considerations. *Int J Oral Maxillofac Implants*, 2002;**17**(2): p. 191-201.

17. Cionca, N., *et al*., Amoxicillin and metronidazole as an adjunct to full-mouth scaling and root planing of chronic periodontitis. *J Periodontol*, 2009;**80**(3): p. 364-71.
18. Haas, R., *et al*., The relationship of smoking on peri-implant tissue: a retrospective study. *The Journal of Prosthetic Dentistry*, 1996;**76**(6): p. 592-6.
19. Esposito, M., *et al*., Biological factors contributing to failures of osseointegrated oral implants. (II). Etiopathogenesis. *Eur J Oral Sci*, 1998;**106**(3): p. 721-64.
20. Baelum, V. and B. Ellegaard, Implant survival in periodontally compromised patients. *J Periodontol*, 2004;**75**(10): p. 1404-12.
21. Fiorellini, J.P., *et al*., The effect of insulin therapy on osseointegration in a diabetic rat model. *Clin Oral Implants Res*, 1999;**10**(5): p. 362-8.
22. Albrektsson, T., *et al*., Osseointegrated titanium implants. Requirements for ensuring a long-lasting, direct bone-to-implant anchorage in man. *Acta Orthop Scand*, 1981;**52**(2): p. 155-70.
23. Ainamo, J. and I. Bay, Problems and proposals for recording gingivitis and plaque. *Int Dent J*, 1975;**25**(4): p. 229-35.
24. Strietzel, F.P., *et al*., Smoking interferes with the prognosis of dental implant treatment: a systematic review and meta-analysis. *J Clin Periodontol*, 2007;**34**(6): p. 523-44.
25. de Souza, J.G., M.A. Bianchini, and C.F. Ferreira, Relationship between smoking and bleeding on probing. *J Oral Implantol*, 2012;**38**(5): p. 581-6.
26. Costa, F.O., *et al*., Peri-implant disease in subjects with and without preventive maintenance: a 5-year follow-up. *J Clin Periodontol*, 2012;**39**(2): p. 173-81.
27. Block, M.S., *et al*., Hydroxyapatite-coated cylindrical implants in the posterior mandible: 10-year observations. *Int J Oral Maxillofac Implants*, 1996;**11**(5): p. 626-33.
28. Wennstrom, J.L., F. Bengazi, and U. Lekholm, The influence of the masticatory mucosa on the peri-implant soft tissue condition. *Clin Oral Implants Res*, 1994;**5**(1): p. 1-8.
29. Bengazi, F., J.L. Wennstrom, and U. Lekholm, Recession of the soft tissue margin at oral implants. A 2-year longitudinal prospective study. *Clin Oral Implants Res*, 1996;**7**(4): p. 303-10.
30. Zitzmann, N.U., *et al*., Experimental peri-implant mucositis in man. *J Clin Periodontol*, 2001;**28**(6): p. 517-23.
31. Serino, G. and A. Turri, Extent and location of bone loss at dental implants in patients with peri-implantitis. *J Biomech*, 2011;**44**(2): p. 267-71.
32. Ekelund, J.A., *et al*., Implant treatment in the edentulous mandible: a prospective study on Branemark system implants over more than 20 years. *Int J Prosthodont*, 2003;**16**(6): p. 602-8.