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Peri-implantitis and late implant failures in postmenopausal women: a cross-sectional study

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Abstract

Aim: Systemic bone loss is a major cause of fractures in postmenopausal women and may also affect the jawbone; however, its consequences on the success of dental implants remain poorly understood.

Materials and Methods: In this cross-sectional study, the relation between self-reported osteoporosis and the success rate of dental implants in an adult female population was evaluated. The primary outcome parameters were the occurrence of peri-implantitis and late implant failures. Women with unknown bone status were excluded from the study. The potential confounders age, recipient site, smoking, periodontal disease and time of loading were recorded.

Results: Data from 203 women with a mean age of 63 ± 9 years and 967 dental implants were investigated. The patients were classified according to their medical history into one of three groups: osteoporosis (47 women), osteopenia (16 women) and healthy controls (140 women). Patients with unknown bone status ($n = 26$) were excluded. The multi-level statistical analysis showed no association between peri-implantitis [odds ratio (OR) 2.1; $p = 0.6$] or implant failure [hazards ratio (HR) 2.5; $p = 0.2$] and systemic bone loss.

Conclusions: No relation was found between osteoporosis and peri-implantitis in an adult female population.

Key words: dental implant; late implant failure; osteoporosis; peri-implant disease; peri-implantitis

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Postmenopausal osteoporosis is a metabolic disease in which a negative balanced bone turnover causes a steady decline in bone volume and quality (Riggs & Parfitt 2005). More bone is removed by the bone-resorbing osteoclasts than is replaced by the bone-forming osteoblasts (Riggs & Parfitt 2005). As a consequence of the compromised integrity of the skeleton, the risk of vertebra and hip fractures increases in approximately one-third of the elderly female population. Being a systemic disease, osteoporotic changes also occur in the jawbone. Preclinical studies in rodents (Tanaka et al. 2002, Rawlinson et al. 2009) and in larger animals (Johnson et al. 2002, Dvorak et al. 2008, 2009) revealed the negative impact of ovariectomy, which models the postmenopausal hypogonadism, on the structural integrity of the jawbone (Adami et al. 2009). Considering that the jawbone provides the anchor of natural teeth and dental implants, postmenopausal women are considered at risk for tooth loss and implant loss.

Clinical attempts to find an association of osteoporosis with tooth loss and implant loss have produced inconsistent results. Osteoporosis has been associated with increased tooth loss (Payne et al. 1999, Inagaki et al. 2005) and periodontitis (Brennan et al. 2007, Gomes-Filho et al. 2007), but these results have not been reliably confirmed by other studies (Famili et al. 2005, Phipps et al. 2007). However, natural teeth are not necessarily representative for dental implants. The periodontium and the peri-implant tissues are different and might thus respond differently to the biologic changes that occur in the osteoporotic patients. Osteoporosis was associated with implant loss up to abutment connection in some studies (Alsaadi et al. 2007), but not in studies focusing on late implant loss (Alsaadi et al. 2008a). Catabolic bone remodelling has been suggested as a risk factor for early implant failure due to poor local bone quality and quantity (Alsaadi et al. 2007). A tendency

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towards higher implant failures was found in patients with radical hysterectomy (Alsaadi et al. 2008b) but not in patients with osteoporosis using implants with modified surfaces.

Peri-implantitis is characterized by inflammatory lesions in peri-implant tissues of an infectious nature and associated with loss of supporting bone and consequently of the dental implant (Berglundh et al. 2011, Mombelli & Decaillet 2011). The imbalanced bone status in oestrogen deficiency may also have a relationship with oral infectious disease possibly by providing a more susceptible environment for bacteria (Brennan-Calanan et al. 2008). Certain periodontal pathogens decreased in oestrogen-deficient women using hormone replacement therapy (Tarkkila et al. 2010). Observations support a substantial impact of oestrogen in the regulation of immune function. Oestrogen receptors have been identified on monocytes, T and B lymphocytes and oestrogen deficiency results in a marked increase in pro-inflammatory cytokines (Clowes et al. 2005). Demonstration of a relationship between osteoporosis and periodontitis is complex because both are multifactorial diseases and both share common mechanisms. Thus, a biological plausibility exists, suggesting that at least part of the periodontal destruction is influenced by systemic bone loss (Martinez-Maestre et al. 2010). Osteoporosis is a disease with impaired bone remodelling but not bone regeneration in the axial skeleton, which does not seem to be true for the jaw (Shibli et al. 2008). So far, only one preliminary study focused on peri-implantitis and its association with osteoporosis (Maximo et al. 2008).

This low level of evidence inspired us to perform a cross-sectional study in an adult female population of our centre. We hypothesized that late implant loss and the occurrence of peri-implantitis are associated with osteoporosis or osteopenia, according to the definition of the WHO (Adami et al. 2009). This study contributes to the knowledge on age-related changes in elderly females in the field of implantology. The demand for dental implants in elderly women is rising and thus more information on the potential complications/treatment failures is needed.

Material and Methods

Data collection

We obtained and analysed data from female patients over 45 years of age presenting at the Department of Oral Surgery (Medical University Vienna) for an annual dental implant recall between June 2009 and July 2010. Patients who were lost to follow-up after implant insertion were invited to a recall appointment. A total of 203 women with 967 dental implants, with a minimum of one dental implant being in situ for at least 1 year after prosthetic loading, were originally enrolled in this study. The two-stage surgical protocol was followed for all surgeries and thus fulfils a high degree of homogeneity.

Patients were asked about a recent T-score, fragility fracture and osteoporosis medication or referred to a DEXA measurement. Patients not being aware of their bone status, due to the lack of a bone mineral density (BMD) assessment, were excluded from the study. No general examination was made at the Department of Oral Surgery. Patients in doubt were referred to their general practitioner or family doctor. The patient group entering statistical analysis consisted of 177 women with 828 dental implants. The study protocol was approved by the ethical review board of the Medical University Vienna (EK Nr. 108/2009).

Procedures

Using direct interview data, the general health and the behavioural history of the patients were recorded. The following aspects were assessed based on a printed questionnaire: osteoporosis/osteopenia according to the WHO criteria, incidence of fragility fracture, smoking habits, thyroid disorder, diabetes, medication and a history of periodontitis. Patients who underwent a BMD assessment by DEXA were aware of their bone status, and yet the precise T-scores were frequently unknown. In addition, two independent examiners performed clinical and radiographic examination. Clinical examination included ''bleeding on probing'' or suppuration and pocket probing depth at four aspects per implant: mesial, buccal, distal and lingual/palatal sight of each implant. Radiographic examination included panoramic tomography and, if necessary, intra-oral radiography to evaluate peri-implant bone loss. If needed, computer tomography was performed to detect bone changes. Patients with positive bleeding on probing and/or suppuration, probing depth over 5 mm and radiographic bone loss were diagnosed as having peri-implantitis (Heitz-Mayfield 2008, Lindhe & Meyle 2008). Radiographic bone loss was assessed according to the baseline radiographs after implant insertion, if available. Implants being lost or removed after abutment connection due to peri-implantitis were categorized as late implant loss. Early implant loss up to abutment connection was not considered in this study. The patients' age, implant position (upper/lower jaw; anterior/posterior region), previous bone augmentation, the surface of the implants (turned/moderately rough/rough) and the date of insertion were also recorded. Based on the surface roughness, implants have been categorized as smooth ($S_a < 0.5\ \mu m$), moderately rough (S_a: 1.1–2.0) and rough ($S_a > 2\ \mu m$) (Lang & Berglundh 2011).

Statistical analysis

The statistical association between bone disease and peri-implantitis and bone disease and implant loss was evaluated on a patient basis ($n = 177$) by cross-tabulation and the Fisher exact test. The association between several risk factors and peri-implantitis was also evaluated on an implant basis ($n = 828$) and tested using logistic regression. Between-patient effects due to the occurrence of several implants within one patient were accounted for by a mixed modelling approach (Zuur et al. 2009), allowing a random intercept for each patient. The effect of risk factors on implant loss was evaluated by a cox proportional hazards model (Andersen & Gill 1982), with each patient defining a cluster. For both analyses, each risk indicator was evaluated with a univariate approach, and also within a multiple regression to control for confounding effects. The magnitude of the effect of an explanatory variable was estimated by an odds ratio (OR) or a risk ratio (RR) with a 95% confidence interval (CI). A p-value smaller than 0.05 was considered significant. R version 2.9.2 (R Foundation for Statistical Computing, Vienna, Austria) was used for statistical computations. The package ''glmmML'' was used for estimating parameters of the mixed-effects logistic regression. The package ''survival'' was used for estimating the parameters of the cox proportional hazards model, with the option ''cluster = patient'' to account for multiple implants within each patient (variance estimation based on grouped jacknife). For the Fisher exact test, the function fisher.test was applied.

Results

Clinical characteristic

Among the original 203 patients, a total of 177 women with 828 implants from different manufacturers were aware of their bone status: 26% had osteoporosis, 9% had osteopenia and 65% had no bone density changes. Each of these patients received a mean number of 5 ± 3 of implants (min.1-max.19), with a mean follow-up time of 6.0 ± 4 years (min.1-max.24 years). Approximately half of the dental implants (52.2%) were placed in the upper jaw and 47.8% were located in the lower jaw. In the anterior jaw (pre-maxilla, interforaminal region), 57.4% of dental implants were inserted. In the posterior maxilla and mandible, 42.6% dental implants were placed. We had 19.9% dental implants with a turned surface and 74.9% dental implants with a moderately rough surface, mostly anodized (TiUnite®), and 5.2% implants with a rough surface topography. Peri-implantitis was recorded in 13.3% of the implants and 23.7% of patients (Table 1). While 13.6% of the patients experienced a late implant loss, 8.3% of the implants were lost after abutment connection. This corresponds to a survival rate of 91.7% (Table 2). If we consider the prevalence of 23.7% peri-implantitis and 13.6% implant loss in this population and a prevalence of around 30% osteoporotic patients, a sample size of 200 patients with osteoporosis and 200 healthy controls would be necessary to achieve a power of 0.8 for future studies.

Table 1. Cross-table indicating the prevalence (%) of peri-implant lesions evidenced by bone loss in addition to pocket depths and bleeding/suppuration on a patient basis ($n = 177$) measured at the mesial, distal, buccal and lingual sites per implant *versus* the self-reported systemic bone status

Bone status	Peri-implantitis		Row total
	yes	no	
Healthy	27	88	115
	23.5%	76.5%	65%
Osteopenia	4	12	16
	25%	75%	9%
Osteoporosis	11	35	46
	23.9%	76.1%	26%
Column Total	42	135	177
	23.7%	76.3%	

Fisher's exact test for count data, two-sided $p = 0.96$.

Table 2. Cross-table indicating the prevalence (%) of late implant loss, after abutment connection on a patient basis ($n = 177$) *versus* the self-reported systemic bone status

Bone status	Implant loss		Row total
	yes	no	
Healthy	15	100	115
	13%	87%	65%
Osteopenia	3	13	16
	18.75%	81.25%	9%
Osteoporosis	6	40	46
	13%	87%	26%
Column Total	24	153	177
	13.6%	86.4%	

Fisher's exact test for count data two-sided $p = 0.74$.

Evaluation of associations

According to the mixed modelling approach, the analysis suggests no association between bone status and implant loss (HR 1.04; CI 0.09–11.73 for osteopenia $p = 0.98$ and HR 2.49; CI 0.57–10.91 $p = 0.22$ for osteoporosis). Similarly, the analysis indicated no relation between bone status and peri-implantitis (OR 0.5; CI 0.007–37.43; $p = 0.75$ for osteopenia and OR 2.07; CI 0.14–30.03; $p = 0.59$ for osteoporosis). In the multivariate analysis, no significant association could be found for the occurrence of peri-implantitis and the known risk indicators from different studies such as smoking, history of periodontitis, plaque and diabetes ($p > 0.05$; Table 3). Yet, patients with a history of periodontitis showed a significantly lower hazard ratio (HR) compared with patients without (HR 0.21; CI 0.05–0.98; $p = 0.05$). A tendency towards a lower risk of peri-implantitis could be found for bone augmentation preceding implant insertion (OR 0.2; CI 0.04–1.07; $p = 0.05$). The implant surface and location in the jaw were taken into account. Although there was an association between peri-implantitis and rough surface topography compared with turned implant surfaces, significance was not reached (OR 23.59; CI 0.86–647.89; $p = 0.06$). Moderately rough surface topography did show a significantly lower association compared with turned surfaces ($p = 0.001$), and yet in multivariate analysis, no significance could be reached (OR 0.34; CI 0.04–2.7; $p = 0.3$). Nevertheless, late implant loss was strongly associated with moderately rough implant surfaces (HR 3.61; CI 0.93–14.02; $p = 0.06$) compared with implants with a turned surface (Table 4). According to statistical analysis, the location in the jaw does not have a significant influence on peri-implantitis. The interforaminal region seems to be the less affected region (OR 0.51; CI 0.073–3.6; $p = 0.5$ for the lower jaw and OR 2.7; CI 0.94–7.77; $p = 0.066$ for lateral teeth). Implant length and diameter were assessed but not evaluated in statistical analysis. Other parameters like immediate implant placement or the amount of attached gingiva were not evaluated.

Discussion

Osteoporosis is considered a potential risk factor for tooth loss and periodontal disease; however, there is no general consensus for this association in the literature (Dervis 2005, Buencamino et al. 2009, Martinez-Maestre et al. 2010). Similarly, the existence of a relationship between osteoporosis and late implant loss due to peri-implantitis is a matter of debate (Holahan et al. 2008, Bornstein et al. 2009, Tsolaki et al. 2009). The role of osteoporosis in diseases of the stomatognathic system remains controversial. Many studies have focused on periodontal disease and its possible association with osteoporosis (Martinez-Maestre et al. 2010). The majority suggests a relationship between the two diseases. Periodontitis and peri-implantitis are not fundamentally different, and yet there is a difference in host reaction (Heitz-Mayfield & Lang 2010, Berglundh et al. 2011), and more rapid progression of peri-implant lesions could be observed. Peri-implant diseases are infectious in nature (Lang & Berglundh 2011) and bone loss during disease progression is mediated by inflammatory reactions as in periodontitis. Nevertheless, peri-implantitis exhibits signs of acute inflammation, a ''self-limiting'' process by a protective connective tissue as in periodontal lesions does not occur and neutrophils as well as macrophages occur in a larger proportion than in periodontitis. Recent findings indicate a site-specific, bacterial-driven immune reaction rather than a patient-associated systemic condition (Renvert et al. 2011). In most cases, the composition of the flora is similar to the flora encountered in periodontitis but occasionally peri-implant lesions may be linked to a different microbiota, pathogens that are important in extra-oral infections (Mombelli & Decaillet

Table 3. Analysis of potential risk indicators for the outcome event peri-implantitis

Risk indicator Peri-implantitis	Univariate analysis			Multivariate analysis		
	OR	CI	*p*-value	OR	CI	*p*-value
Age	0.95	0.87–1.05	0.34	0.99	0.87–1.13	0.93
Lower jaw	1.06	0.39–2.91	0.91	0.51	0.07–3.60	0.50
Lateral jaw	1.42	0.71–2.85	0.32	2.70	0.94–7.77	0.07
Smoking	4.14	0.62–27.78	0.14	4.17	0.43–40.65	0.22
Osteopenia	1.12	0.04–28.73	0.94	0.50	0.01–37.43	0.75
Osteoporosis	1.10	0.13–9.21	0.93	2.07	0.14–30.03	0.59
Diabetes	2.21	0.14–35.61	0.58	2.81	0.13–59.33	0.51
Plaque	0.57	0.12–2.72	0.48	0.46	0.06–3.61	0.46
Thyroid disease	0.99	0.15–6.59	0.99	2.13	0.2–22.93	0.53
Augmentation	0.70	0.29–1.68	0.43	0.2	0.04–1.01	0.05*
Periodontitis	0.76	0.14–4.07	0.75	0.57	0.06–5.86	0.64
Years in situ	1.07	0.94–1.22	0.28	0.83	0.64–1.07	0.16
Implant surface (S_a: 1.1–2.0 μm)	0.13	0.03–0.45	0.001**	0.34	0.04–2.70	0.30
Implant surface (S_a: >2.0 μm)	3.63	0.3–43.92	0.31	23.59	0.86–647.89	0.06

*A p-value <0.05 was considered significant.
**$p<0.01$ highly significant.
OR, odds ratio; CI, confidence interval.

Table 4. Survival analysis of risk indicators for the outcome event implant loss

Risk indicator Implant loss	Univariate analysis			Multivariate analysis		
	HR	CI	*p*-value	HR	CI	*p*-value
Age	0.97	0.93–1.02	0.20	0.98	0.92–1.03	0.43
Lower jaw	0.51	0.23–1.13	0.1	0.41	0.1–1.74	0.23
Lateral jaw	1.61	0.98–2.65	0.06	1.27	0.57–2.81	0.57
Smoking	2.14	0.85–5.39	0.10	2.36	0.7–7.98	0.17
Osteopenia	0.93	0.21–4.18	0.93	1.04	0.09–11.73	0.98
Osteoporosis	1.28	0.41–4.05	0.67	2.49	0.57–10.91	0.22
Diabetes	1.44	0.61–3.38	0.41	3.77	0.79–18.06	0.1
Plaque	1.65	0.53–5.10	0.38	1.49	0.4–5.51	0.55
Thyroid disease	1.41	0.54–3.71	0.48	2.40	0.52–11.09	0.26
Augmentation	1.20	0.45–3.23	0.71	0.59	0.17–2.04	0.40
Periodontitis	0.67	0.26–1.76	0.42	0.21	0.05–0.98	0.05*
Years in situ	1.07	0.94–1.22	0.28	0.83	0.64–1.07	0.16
Implant surface (S_a: 1.1–2.0 μm)	1.89	0.55–6.58	0.31	3.61	0.93–14.02	0.06
Implant surface (S_a: >2.0 μm)	0.58	0.1–3.56	0.56	1.55	0.13–18.0	0.73

*A p-value <0.05 was considered significant.
HR, hazard ratio; CI, confidence interval.

2011). Not uniquely, the capacity to express bone-stimulating factors, but also the cell capacity to react to these factors, may alter with increasing age and hormonal changes (Augat et al. 2005). It is generally recognized that osteoporosis and ageing are associated with a spontaneous increase in pro-inflammatory cytokines, whereas levels of bone-forming factors are decreased in osteoporotic patients (Marco et al. 2005). Osteoimmunologic research indicates a strong influence of steroid hormones on host reaction (Gruber 2011). The lack of sexual hormones has a direct effect on immune function and promotes uncoupling of bone remodelling towards a catabolic state. The impact of oestrogen deficiency on the periodontal disease has been postulated, but the influence in peri-implant disease remains unknown. It also accounts true for vitamin D, which is reduced in postmenopausal women, and represents an important regulator on immune function and bone homeostasis. The imbalance in peri-implantitis and periodontitis takes places at a local level (Lerner 2006a, b), which could be enhanced by a systemic catabolic state like in osteoporosis. Therefore, the question remains open as to whether osteoporosis influences peri-implant disease and its clinical endpoint late implant loss.

This cross-sectional study used a combined approach of personal interviews to gather information on bone status and clinical examination to discriminate between peri-implantitis and implants without any diagnostic findings. The results reported herein demonstrate that in an adult female population, the occurrences of peri-implantitis and implant loss were not associated with self-reported bone status, e.g. osteoporosis, osteopenia and healthy control. In agreement with the findings of the present study, osteoporosis was no risk factor for implant loss after abutment connection, but during the early phase of osseointegration in other retrospective studies (Alsaadi et al. 2007, Alsaadi et al. 2008a, b). Reviews and other studies based on this topic concluded that osteoporosis is not a contraindication for implant placement (Holahan et al. 2008, Bornstein et al. 2009, Tsolaki et al. 2009). In accordance with our findings, peri-implantitis was not associated with osteoporosis (Maximo et al. 2008). Surprisingly, the rate of peri-implantitis in our population is somewhat lower compared with a recent consensus report (Lindhe & Meyle 2008). This is likely because women have a lower prevalence of peri-implantitis (Koldsland et al. 2011) and implant loss than men, which might explain the discrepancy (Ferreira et al. 2006, Roos-Jansaker et al. 2006, Montes et al. 2007). Together, these epidemiologic findings play a role in the individualized patient education and treatment planning. Furthermore, the prevalence in a specific population is necessary for future studies in order to enable precise sample size calculations.

The present study also assessed different parameters possibly being associated with peri-implantitis. Having a history of smoking, plaque at the implant site and implant time in function were not associated with peri-implantitis in the present study, which is congruent with recent studies (Koldsland et al. 2011). The small number of participants might have influenced the results. Interestingly, a history of periodontitis (OR 0.83) could not be identified as a risk indicator in this analysis, although patients with a history of periodontitis are being treated at the Department of Periodontology before implant insertion and are part of a stringent recall.

The choice of implant design seems to play a key role in primary stability (Dos Santos et al. 2009), survival rate in poor bone quality (Khang et al. 2001), anatomic location and tobacco abuse (Balshe et al. 2008, 2009). Increased implant surface design influences not only early implant survival (Alsaadi et al. 2008b, Bratu et al. 2009) but also

late implant prognosis. The quality of the titanium surface is of decisive importance for both osseointegration and re-osseointegration (Persson et al. 2001). Experimental studies on peri-implantitis (Berglundh et al. 2007) describe a higher progression in rough surface implants, probably due to bacterial colonization, which correlates with surface roughness (Quirynen & Bollen 1995). Nevertheless, recent results are not in accordance with these findings as the thickness of the 3-day-old biofilm was not influenced by surface roughness alone, as shown by the high values for biofilm thickness formed on machined titanium (Al-Ahmad et al. 2010). Also, in the present study, an association between peri-implantitis and rough implant surface design was observed (OR 23.59, $p = 0.06$) and late implant loss with moderately roughened implants (HR 3.61, $p = 0.06$) compared with turned implant surfaces. Yet, the distribution in surface types was uneven (74.9% moderately roughened implants) and therefore the findings have to be interpreted with care.

According to the present results, bone augmentation techniques as a local factor showed less peri-implantitis (OR 0.2, $p = 0.05$) and a tendency towards a higher survival rate (HR 0.58, $p = 0.4$). Implants replacing teeth in atrophic jaws often have long abutments, creating pseudo pockets, which may be a reason for the protective effect of bone augmentation techniques. On the other hand, in most augmentative procedures, deproteinized bovine bone (Bio Oss®, Geistlich, Wolhusen, Switzerland) is used in combination with autologous bone grafts (Esposito et al. 2008). Recent studies report not only a very slow resorption of deproteinized bovine bone in vivo but also the downregulation of pro-inflammatory cytokine activity, especially TNF-α in vitro (Amerio et al. 2010).

On the other hand, maxillary molars are rather affected by peri-implant lesions in the present study, which is congruent with recent studies (Koldsland et al. 2011). According to the study of Fransson et al. (2009), the upper lateral region is the second most frequent region affected by peri-implantitis. Nevertheless, in their study, authors found the lower anterior region to be the most affected position for peri-implantitis.

The main limitation of this study is that the ascertainment of bone status was by patient report, which may introduce a bias, as the original data of bone density measurements were not included in the study. According to the IOF (International Osteoporosis Foundation), 30% of the postmenopausal women have osteoporosis, which is in accordance with our epidemiologic data. In addition, osteoporotic patients are often subjected to pharmacologic therapies that may have an impact on the peri-implant tissue, similar to reports on periodontal disease (Rocha et al. 2004). Pharmacologic therapies were not considered in the present study. Moreover, the present study was underpowered; only 46 patients with osteoporosis (11 with peri-implantitis and six with implant loss) could be enrolled. If we consider the prevalence of peri-implantitis and implant loss in this population and a prevalence of around one-third osteoporotic patients, a sample size of four hundred patients would be necessary to achieve reliable data in future studies.

Conclusion

Respecting the limitations of this cross-sectional study, the data suggest that postmenopausal osteoporosis is not a risk factor for implant loss and peri-implantitis. The present cross-sectional study can be considered ''preliminary'' and provides the basis for the design of larger studies in the future.

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Clinical Relevance

Scientific rationale for the study: Based on the current scientific evidence, it is unknown whether peri-implantitis and osteoporosis are associated. Prevalence data regarding peri-implant disease are controversial. Little is known about patient-related risk factors that may affect peri-implant tissues, especially when considering systemic catabolic bone diseases.

Principal findings: The analysis suggests no association between bone status and implant loss. Similarly, the analysis revealed no association between bone status and peri-implantitis.

Practical implications: Postmenopausal osteoporosis seems not to be a risk factor for implant loss and peri-implantitis.