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ORIGINAL ARTICLE

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Alveolar bone loss in adults as assessed on panoramic radiographs. (II) Multilevel models

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Abstract The aim of this study was to delineate factors influencing the severity of bone loss in randomly selected orthopantomograms of adult patients seeking treatment by the dental service of the German Armed Forces. A total of 240 panoramic exposures was available for analysis, 60 in each of the age groups <30, 30–39, 40–49, and ≥50. For each tooth, distances between the coronal landmark (CL) cemento-enamel junction or margin of restoration, and alveolar crest (AC), and bone level (BL) were measured with a calliper to the nearest 0.1 mm. Multilevel models revealed that bone levels decreased by 0.05 mm each year of life, on average. Bone loss was more pronounced in the maxilla, especially at molars. Infrabony lesions were strongly associated with deficient restorations and periapical lesions. Periapical pathology was also associated with radiographic evidence for furcation involvement. In this predominantly male population, periodontal bone loss gradually increased with age, but prevalence of infrabony defects was very low. Multilevel modelling indicated strong associations between infrabony defects and insufficient restorations and periapical pathology.

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Introduction

Periodontitis, a chronic inflammation of the supportive apparatus of the tooth, is characterized by progressive loss of, in particular, alveolar bone. Bone loss as assessed on radiographs usually has an even pattern, i.e. appears at equal levels on mesial and distal aspects of neighbouring teeth. Infrabony lesions have been described as angular or vertical bone loss. They seem to increase the risk of progression of the disease if appropriate treatment is not given [31]. Treatment of critical size (say, 4 mm or more [25]) infrabony lesions usually involves regenerative techniques [6]. In a companion paper [28] infrequent occurrence of infrabony pockets of that size, as seen on randomly sampled panoramic radiographs of the radiological archive of a greater dental unit at the German Armed Forces, was demonstrated. These data were in accordance with other studies [33] suggesting a limited relevance of regenerative treatments in nonspecialized dental practice.

Whether infrabony lesions develop depends mainly on the thickness of the alveolar bone [36]. However, angular bone loss has also been associated with occlusal trauma [12, 30], infected root canal systems [19], or defective or otherwise insufficient restorations [5]. In an elderly Finnish population [35], the number of infrabony defects was positively associated with the number of overhanging proximal restorations.

For analysis of subject and tooth-related factors with a possible influence on bone loss, hierarchical, or multilevel, modelling has particularly important potential [3]. The aim of the current study was to determine the distribution of bone loss within the oral cavity as assessed on panoramic radiographs of patients in different age classes sampled at the radiological archive of a greater dental unit at the German Armed Forces, and to analyze the effects of age, restorations, and periapical status by applying multilevel modelling [13].

Material and methods

The origin and analysis of 240 orthopantomograms from dentate patients of the German Armed Forces' Medical Centre in Bonn, Germany, has been described in detail in the companion paper [28]. Briefly, 60 radiographs in each of four age classes (under 30 years of age, 30–39, 40–49, and 50 years and older) were considered. Radiographs with sufficient contrast and brightness were checked by one investigator (UM) for the presence of measurable distances between teeth's cemento-enamel junction or, if missing, another suitable landmark, and the alveolar bone crest and bottom of the defect. They were selected if respective measurements could be made on more than 80% of the teeth. All films had been exposed to an X-ray source (Heliomat, Siemens, Bensheim, Germany) and automatically developed under controlled conditions (Periomat, Dürr Dental, Bietigheim-Bissingen, Germany). Enlargement factors of radiographs were calculated in two dimensions by exposing steel balls with a diameter of 5 mm in custom-made acrylic splints. Vertical enlargement varied between 14 and 16% in regions of the anterior teeth, 16 and 20% in the premolar regions, and 22 and 28% in the molar regions.

Radiographs were inspected in a darkened room on a viewing box (Maier, Garmisch-Partenkirchen, Germany). On every erupted tooth the following landmarks were identified at mesial and distal surfaces:

1. The coronal landmark (CL) was the interproximal projection of the cemento-enamel junction or, if destroyed after restorative therapy, the apical termination of a restoration or crown margin.
2. The bone level (BL) was the most coronal interproximal projection of a periodontal ligament space having a constant width. If a periodontal ligament space was not visible, the observer had to choose a point where the alveolar crest (AC) crossed the root surface [4].
3. If no infrabony lesion was visible on the radiograph, BL was identical to AC. Otherwise, AC was measured as follows. The perpendicular from the most coronal part of the interproximal alveolar bone was raised to the root axis. The intersection between this perpendicular and the root surface was the second apical landmark, AC.

Measurements of the distances between CL and BL, and between AC and BL were made with a calliper to the nearest 0.1 mm. If one or more of these landmarks could not be determined, the tooth was excluded from the study. Whenever caries had destroyed the cemento-enamel junction, the respective tooth was also excluded.

Possible furcation involvement of multirooted teeth was graded as 0 (no furcation involvement), 1 (probable furcation involvement), or 2 (definite furcation involvement). Translucencies in the furcation area and, at proximal sites of maxillary teeth, specific diagnostic characteristics such as the furcation arrow [15] were considered. The condition of the apical periodontium was graded as follows: 0 (no root canal filling, no apical widening of the periodontal ligament space), 1 (any root canal filling, no apical widening of the periodontal ligament space), 2 (apical osteolysis up to 3 mm diameter), 3 (apical osteolysis of more than 3 mm diameter), 4 (apical resection).

Finally, interproximal restorations were assessed: 0 (no or acceptable restoration), 1 (restoration imperfection less than 0.5 mm), 2 (overt imperfection of restoration margin, 0.5 mm or more). Reliability of bone level measurements was determined in 12 orthopantomograms which were independently examined by three observers. The results have been reported in the companion paper [28].

Statistical analysis

Primary variables of this study were *bone loss* and depth of *infrabony defect*. On bitewing radiographs the normal distance between the cemento–enamel junction and AC was approximately 1.9 mm with 95% confidence [16]. Therefore, bone loss was only assumed if the distance between CL and BL exceeded 2 mm. The hierarchical structure of the data was considered by applying multilevel modelling [11]. Variance components models without explanatory variables were constructed first, to assess variability at each of three levels, site, tooth, and patient. Subsequently, three-level random intercept models including patient, tooth, and site level explanatory variables were built, which may be written as:

$$y_{ijk} \sim N(XB, \Omega)$$

$$y_{ijk} = \beta_{0ijk} + \sum_m \beta_m x_{mk} + \sum_n \gamma_n z_{njk} + \sum_p \delta_p t_{pijk} + v_k + u_{jk} + e_{ijk}.$$

The distributional assumption is given in the first line. The response variable (bone level parameters), y_{ijk}, has a mean specified by the fixed part XB and a random part consisting of a set of random variables described by the covariance matrix Ω. x, z, and t are patient-, tooth-, and site-level variables, and subscripts k, j, and i refer to patient, tooth, and site, respectively. The random variables distributions are specified as:

$$v_j \sim N\left(0, \sigma_v^2\right), u_{jk} \sim N\left(0, \sigma_u^2\right), e_{jk} \sim N\left(0, \sigma_e^2\right).$$

Subsequently, by using information obtained in random intercept models, coefficients for restoration overhangs and periapical pathology were allowed to vary at the patient level. Because frequency distribution of infrabony defects was severely skewed and bimodal with peaks at 0, and between 2 and 3 mm, defect categories (in mm steps) were modelled assuming Poisson distribution [26]. Binary response models were performed for furcation involvement (0, 1). For further information, see Rasbash et al. [34]. Multilevel modelling was performed using software *MLwiN* 1.10 (Centre for Multilevel Modelling, Institute for Education, University of London).

Results

Radiographs of mainly male (98%) patients, 19 to 62 years of age (mean±standard deviation 38.8±11.9 years), were examined. Mean ages of patients in different age groups were 22.4±2.3, 34.7±2.6, 44.7±2.9, and 53.5±3.0 years. The total number of teeth was 6,490, and bone levels could be assessed for 6,309 (97%).

To obtain information about factors possibly influencing bone loss and infrabony defects, multilevel models were constructed which consider the hierarchical structure of the data. Three-level (patient, tooth, site), variance components models (Table 1) revealed means (±standard error) of bone loss and infrabony component of 0.783±0.072 and 0.094±0.012 mm, respectively. In both models considerable variation at all levels was ascertained. For example, 62% of total variance occurred at the patient level. Respective figures at the tooth and site levels were 27% and 12%. In contrast, for infrabony component of bone loss most variation occurred at the site (63%) and tooth (29%) levels.

In subsequent multilevel models jaw, tooth-type, and site were set up as categorical variables. In addition, age (year), restoration (categorical, 0–2), and periapical condition (categorical, 0–4) were entered as explanatory variables. The models are presented in Table 2. In general, bone levels decreased, on average, by 0.05 mm for each year of life. Infrabony defects were also positively associated with age. Bone loss and infrabony component were more pronounced in the maxilla and at molars. Proximal bone loss was associated with the presence of imperfect restoration margins (3.8% less than 0.5 mm, and 1.5% of teeth more than 0.5 mm). Infrabony lesions were associated with restorations with highly unacceptable restoration margins. Whereas 12% teeth presented with radiographic signs of a nonvital pulp, bone loss and, in particular, its infrabony component were strongly associated with periapical lesions with a diameter of more than 3 mm (0.28% of teeth). Thus, if present, this condition increased the infrabony component by more than 0.4 mm compared with a (probably) vital tooth without periapical pathology. When considering the reduction in 2×log likelihood (618.48 and 243.70, respectively) both models were significantly improved by including explanatory variables (16 degrees of freedom, $P<0.001$).

Frequency distribution of infrabony defects was severely skewed to the left (at 96.9% of sites no infrabony component was observed) and bimodal (second peak between 2 and 3 mm). Therefore, Poisson multilevel models were fit for infrabony component categories (0–8, mm-steps). If coefficients of restoration overhangs and periapical pathology (apical periodontitis or resection) were allowed to vary at the higher level, the random part of the model (left part of Table 3) indicated considerable patient variation for both site covariates. Furthermore, there was a negative covariance between intercept (infrabony defect category) and slopes of both overhangs (−0.517±0.252) and periapical pathology (−1.259±0.426) suggesting lower likelihood of both conditions in cases of deeper infrabony defects. Moreover, a positive covariance (2.159±0.669) was observed between overhangs and periapical pathology.

Probable (145) or definitive furcation involvement (100) was diagnosed in 245 of 2,185 molars and maxillary premolars (11%). A binary response, multilevel (patient, site) model (right part of Table 3) revealed, apart from asso-

Table 1 Three-level variance components models for bone loss and infrabony component

	Estimates (se)	
	Bone loss	Infrabony component
Mean (intercept)	0.783 (0.072)	0.094 (0.012)
Variances		
Subject (level 3—$\sigma_{0v}{}^2$)	1.216 (0.113)	0.027 (0.003)
Tooth (level 2—$\sigma_{0u}{}^2$)	0.530 (0.012)	0.101 (0.004)
Site (level 1—$\sigma_{0e}{}^2$)	0.230 (0.004)	0.219 (0.004)
Total variance	1.976	0.347
−2×log likelihood	28,120.730	20,337.950

Table 2 Three-level (patient, tooth, site) random intercept models for bone loss and infrabony component

	Estimates (se)	
	Bone loss	Infrabony component
Fixed effects (covariates)		
Intercept	−1.158 (0.211)	−0.166 (0.041)
Age (year)	0.051 (0.005)	0.006 (0.001)
Jaw[a]		
Mandible	−0.256 (0.020)	−0.037 (0.012)
Tooth type[b]		
Lateral incisor	0.043 (0.036)	0.027 (0.021)
Canine	−0.048 (0.037)	0.035 (0.022)
First premolar	−0.078 (0.039)	0.034 (0.023)
Second premolar	−0.004 (0.038)	0.037 (0.022)
First molar	0.240 (0.039)	0.102 (0.023)
Second molar	0.394 (0.038)	0.162 (0.022)
Third molar	0.251 (0.046)	0.065 (0.027)
Site[c]		
Distal	0.001 (0.009)	−0.055 (0.009)
Restoration margin imperfection		
Up to 0.5 mm	0.143 (0.035)	0.017 (0.028)
More than 0.5 mm	0.277 (0.056)	0.178 (0.044)
Periapex		
Root canal treatment/ no pathology	0.054 (0.055)	0.060 (0.048)
Apical osteolysis≤3 mm	0.033 (0.067)	0.068 (0.058)
Apical osteolysis>3 mm	0.291 (0.108)	0.427 (0.093)
Apical resection	−0.135 (0.121)	−0.121 (0.102)
Random effects variances		
Subject (level 3—$\sigma_{0v}{}^2$)	0.873 (0.082)	0.021 (0.003)
Tooth (level 2—$\sigma_{0u}{}^2$)	0.483 (0.011)	0.097 (0.004)
Site (level 1—$\sigma_{0e}{}^2$)	0.229 (0.004)	0.218 (0.004)
Total variance	1.585	0.336
−2×log likelihood	27,502.250	20,094.250

[a]Reference: maxilla
[b]Reference: central incisor
[c]Reference: mesial

Table 3 Infrabony component category (0–8, mm steps) and furcation involvement (0,1) fitted by Poisson, two-level (patient, site) random slope model (link function log) and binomial, two-level random slope (link function logit) model, respectively

	Estimates (se)	
	Infrabony category	Furcation involvement
Fixed effects (covariates)		
Intercept	−5.393 (0.251)	−6.485 (0.409)
Age class (1–4)	0.539 (0.088)	1.094 (0.139)
Bone-loss category (0–10)	0.665 (0.012)	0.202 (0.054)
Infrabony category (0–8)		0.260 (0.060)
Severe overhang (>0.5 mm)	1.159 (0.199)	−0.145 (0.359)
Periapical pathology	0.607 (0.329)	2.390 (0.368)
Random effects variances		
Subject (level 2)		
$\sigma_{0v}{}^2$ Intercept	1.279 (0.169)	1.925 (0.337)
$\sigma_{3v}{}^2$ Overhang	1.367 (0.455)	
$\sigma_{4v}{}^2$ Periapical pathology	4.489 (1.303)	1.234 (1.474)
$\sigma_{02v}{}^2$ Intercept/ overhang	−0.517 (0.252)	
$\sigma_{03v}{}^2$ Intercept/ periapical pathology	−1.259 (0.426)	−0.807 (0.717)
$\sigma_{23v}{}^2$ Overhang/ periapical pathology	2.159 (0.669)	
Site (level 1—$\sigma_{0e}{}^2$)	1.000 (0.000)	1.000 (0.000)

ciations with age class and bone level covariates, a strong association with any kind of periapical pathology. For example, the odds of observing furcation involvement in multi-rooted teeth were increased 11-fold (95% confidence interval 5.3–22.5) if any apical periodontitis/resection was present (73 of 141 cases with root canal fillings). Again, a negative covariance with the intercept (furcation involvement) was noticed (−0.807) which was not significant because of considerable data reduction (only multi-rooted teeth were considered). Restorations were not associated with furcation involvement.

Discussion

In the companion paper [28] the distribution of bone loss and infrabony lesions was described on 240 panoramic radiographs of predominantly male patients seeking general dental care. It was demonstrated that bone loss virtually did not occur before age 30. Average bone level gradually decreased in each decade up to 50 years and older, when it reached about 1.8 mm. The assumed overall slow regression of bone levels is in accordance with several cross-sectional and longitudinal studies on alveolar bone loss [1, 7, 17, 32, 33]. Regarding the depth of infrabony components of bone loss a similar trend was observed [28]. Mean values of patients' averages, and bivariate quantile plots illustrating the frequency distributions of bone level measurements, demonstrated that infrabony defects were more prevalent and deeper at mesial than at distal sites. This observation was also in accordance with other studies [33, 37]. Quantile plots of frequency distributions showed decisive differences in bone level between the youngest (<30 years of age) and second youngest age group (30–39 years). Bone loss became more widespread with age. Rather deep infrabony defects of 4 mm or more were generally rare and occurred in a small percentage of sites only after age 40 years.

A major objective of the first part of this study [28] was to gain information on the prevalence of infrabony lesions suitable for regenerative periodontal treatment. Indications for periodontal regeneration are, however, not only limited by the morphology of osseous defects. Patient characteristics such as systemic disease, smoking, or oral hygiene, all involved in the pathogenesis of periodontal disease itself [29], may be relative contraindications for regenerative surgery. Even correct margins of restorations may affect periodontal health if placed subgingivally [23], and particularly imperfections have been shown to substantially alter the subgingival ecosystem [24]. Together with other plaque-retaining factors they clearly increase the risk of alveolar bone loss [5]. Infrabony defects in combination with furcation involvement may prevent the desired regeneration, especially in maxillary premolars and molars [37]. There are also reports of the relationship between reduced marginal bone loss and endodontic infections [19, 20]. Multilevel modelling as an analytical tool for hierarchical dental data has recently attracted substantial interest [10]. In the current study, three-level (patient, tooth, site) random intercept models were constructed, primarily to determine the effect of age on bone level, bone loss patterns in the oral cavity, and the effects of local factors like restorations and periapical condition acting simultaneously in a given oral cavity. The models confirmed the age-dependent decrease of bone levels, and that bone loss and infrabony defects were more pronounced in the maxilla and at molars. Infrabony defects were actually deeper at mesial sites. An imperfect interproximal restoration affected the bone level, in particular if it was larger than 0.5 mm, a situation which was strongly associated with infrabony defects. That overhanging restorations are associated with decreased bone levels and attachment loss has been reported by numerous authors [9, 14, 21]. In the current study restorations with moderately imperfect margins (up to 0.5 mm) led to 0.14 mm more bone loss, on average than sites without restorations or acceptable margins. The high prevalence of insufficient restorations (29%) and their strong relationship with infrabony defects is of special concern. Infrabony defects were, on average, 0.18 mm deeper if a severe overhang (>0.5 mm) was present, whereas overall bone level was reduced by 0.28 mm. The data are in accordance with both unilevel and multilevel analyses of data acquired in a longitudinal study over six years [2, 3], in which plaque-retentive factors were significantly associated with developing or ongoing bone loss.

That both infrabony defects and furcation involvement seemed to be associated with periapical pathology is of special interest. Some evidence has been presented that persistent endodontic infection is associated with periodontitis in general and angular defects in particular [19, 20]. In a longitudinal study in periodontitis-prone patients [22] endodontically infected teeth lost significantly more alveolar bone than teeth with no signs of periapical pathology. The authors speculated that the infected root canal may act as a reservoir for bacteria, which contribute to both periapical and marginal inflammation in the periodontal connective tissue. In addition, these authors also presented evidence for a higher risk of furcation involvement in endodontically treated mandibular molars [18]. Moreover, bone loss seems to be more pronounced in teeth with metal posts [8], and these authors list potential causes for bone loss and mention faulty preparation technique of the root canal including high temperature and persisting root canal infection.

If, in the current study, coefficients of restoration overhangs and periapical pathology (apical periodontitis or resection) were allowed to vary at the patient level, the random part of the model indicated a negative covariance between infrabony defect category and slopes of both overhangs and periapical pathology, suggesting lower likelihood of both conditions for deeper infrabony defects. In fact, on a patient level, depth of infrabony defects (i.e., severity of plaque-induced periodontal disease) was negatively correlated with apical periodontitis. Thus, occurrence of either condition seems to be independent of different patient categories. The potential to model the covariance structure of complex data is one of the advantages of multilevel modelling over marginal models, for example generalized estimating equation models, which usually treat the existence of any random parameters as nuisance [13]. In-depth analysis may also explain, at least in part, the seemingly controversial result of a study on the impact of endodontic conditions on marginal bone loss in rather young patients with no or minor signs of periodontal disease [27]. In that study, teeth with radiographic signs of root canal treatment and/or endodontic infection had significantly reduced marginal bone support compared to contralateral vital teeth. The difference was not significant at the patient level, however, i.e., after summarizing observations among patients to fulfil necessary assumptions for the authors' statistical analysis.

This study used orthopantomograms for measurement of bone levels and identification of infrabony defects in a predominantly male population. In particular deep infrabony defects of 4 mm or more with a potential for superior healing after guided tissue regeneration were found in not more than 16% of the patients. These lesions were virtually confined to individuals 40 years and older. Multilevel modelling demonstrated that infrabony defects were associated with overhanging restorations and periapical pathology. Periapical pathology was also associated with furcation involvement. These factors may further limit indications for periodontal regenerative measures.

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