

Using Periodontal Staging and Grading System as a Prognostic Factor for Future Tooth Loss: A Long-Term Retrospective Study.

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ABSTRACT:

Background: A new classification of periodontal diseases aimed to identify periodontal disease based on a multidimensional staging and grading system has been recently proposed. However, up to date, its prognostic predictive capability has not been investigated. The aim of this study was to assess if parameters included in the new classification were predictive of tooth loss after a long-term follow-up (> 10 years) in patients with periodontitis.

Methods: Patients presented with periodontitis at the University of Michigan between January 1996 and January 2004 were screened and categorized according to the new classification of periodontitis. Number/Reasons of teeth loss in patients who underwent at least one session/year of maintenance during the entire follow-up period were extracted and utilized to analyze the prognostic capabilities of variables (Staging, Grading and Extent) included in the new classification.

Results: A total number of 292 patients with a mean follow-up of 289.7 ± 79.6 months were included. 31 (10.6%) patients were classified as Stage 1, 85 (29.1%) as Stage 2, 146 (50%) as Stage 3, and 30 (10.3%) as Stage 4. For grading, 34 (11.7%) were classified as Grade A, 193 (66.1%) as Grade B, and 65 (22.2%) as Grade C. Results of multilevel Cox regression analyses revealed a statistically significant association between stage (HR:3.73 between stage 4 and Stage 1) and grade (HR: 4.83 between grade C and grade A) at baseline and periodontal related tooth loss, while no differences were detected for the extent of periodontitis.

Conclusion: This study provides the initial evidence regarding the predictive ability of the new classification of periodontitis. Patients in either Stage 4 or Grade C showed a significantly higher periodontal-related tooth loss.

INTRODUCTION:

Periodontitis is one of the most common chronic diseases and is considered to be one of the leading causes of adult tooth loss (TL) ¹. Depending on the population, 14-74% of young adults and up to 96% of older adults were likely to be affected by this disease ². The risk of progression of periodontitis has been associated with smoking ³⁻⁵, diabetes ⁶, age ^{7,8}, and the presence and duration of periodontal maintenance (PM) ^{9,10}. During the last half century, multiple studies have documented the long-term effectiveness of active periodontal therapy, and PM in preventing TL in periodontitis patients ¹¹⁻¹⁴. Although an overall high tooth survival rate was reported following periodontal therapy, there was a discrepancy in the number of teeth lost among such studies. This discrepancy can be attributed to the differences in the failure rate reporting methodology, as well as the differences in the main study design. For instance, the majority of studies included the overall TL without specifying the cause of failure (e.g., tooth fracture, related pathology, caries, endodontic problems, and even strategic extractions). In such cases, it is safe to suggest that some of the extracted teeth were periodontally stable. An additional factor that might have played a significant role in the TL discrepancy among the studies is the inclusion of third molars into the overall TL. Extraction of the third molars might have been due to prophylactic means or other reasons such as partial eruption. If so, this would account for approximately 16% of the total TL ^{15,16}.

A new classification of periodontal diseases aimed to identify periodontal disease based on a multidimensional staging and grading system has been proposed ¹⁷. Staging is dependent upon the severity and complexity of disease, whereas Grading is intended to assess the likelihood of the disease progressing at a greater rate than normally expected or responding less predictably to therapy ¹⁷.

To the best of our knowledge, there are currently no published clinical studies that evaluate the reliability of staging and grading as a prognostic factor of future TL. Hence, the aim of this study was to assess the long-term (>10 years) tooth loss after non-surgical and, if indicated, surgical periodontal therapy in a cohort of patients with periodontitis (categorized by the staging and grading system) in a university setting.

MATERIALS AND METHODS:

This study was conducted in accordance with the Helsinki Declaration of 1975, as revised in 2013. The protocol of the present study was approved by the University of Michigan, School of Dentistry, Institutional Review Board for Human Studies (HUM00157260). This retrospective study involved all of the periodontal patients screened and treated in the time period between January 1966 and January 2004 at the University of Michigan School of Dentistry, Ann Arbor, MI, USA. It was conducted by obtaining anonymized data; hence, there was no need for informed consent.

Inclusion criteria:

- Patients meeting the case definition of periodontitis ¹⁷
- Patients treated for periodontal disease (at least a session of scaling and root planing [SRP]/diseased area) and maintained for ≥ 10 years at the University of Michigan School of Dentistry.
- Patients with a complete periodontal chart and full mouth radiographic series at baseline (T0) and at the last documented visit (T1).
- Patients with complete history of diabetes and self-reported smoking history at baseline.
- Patients receiving at least one PM/year throughout the entire follow-up period.
- Patients whose teeth have been extracted at the University of Michigan School of Dentistry.

Exclusion criteria:

- Patients treated or maintained in centers outside the University of Michigan School of Dentistry.
- Patients with inaccessible files due to bad debt, destroyed record, or deceased.
- Smokers not reporting the number of cigarette/days or diabetic patients that do not report Hemoglobin A1c (HbA1c) test results for diabetes.
- Patients not undergoing PM for >12 months during the studied period.

Data collection and patient classification

The physical and digital records of the patients that met the predetermined eligibility criteria were screened and evaluated by three examiners (MQ, AR, MS). General information of the patient (e.g., age and gender), patient periodontal status, number of PM/year and relevant medical history (history of smoking and diabetes) were collected. Patient charts were searched for TL by comparing the number of teeth at T0 and T1. Whenever a tooth was found missing, the date and cause of extraction were registered. Furthermore, third molars were not included in the analysis. At the time of staging and grading patients, when it was not possible to determine the cause for TL (TL before T0), loss due to periodontitis was assumed. Percentage of radiographic bone loss (BL, in %) was primarily measured from peri-apical radiographs¹⁸. Probing pocket depths and clinical attachment levels were evaluated at six sites per tooth. Information about masticatory dysfunction, drifting, flaring, bite collapse, and plaque accumulation (not consistently available) were collected in patient records. Before staging and grading were determined, the patient must have met the case definition for periodontitis as defined by the 2018 World Workshop¹⁷. Subsequently, each patient received a baseline diagnosis (Stage: 1, 2, 3, or 4; Grade A, B, or C and Extent Localized, Generalized) by the same investigator (MS), after being calibrated by one of the chief authors of the classification (HG)¹⁷. Although the layered format of the new classification was adhered to, newer algorithms with decision trees were used to help clarify certain aspects of the classification¹⁹.

Statistical analysis

Statistical analysis was performed using a dedicated software application*. Comparison among demographic measurements was performed with the use of the chi-square test and the Kruskal-Wallis test after assessment of the absence of normal distribution. In addition, post-hoc comparison for continuous variables was performed by means of the Tukey test. Correlations among the analyzed variables (e.g., stage, grade, extent, gender, age) were assessed by calculating the Pearson coefficient. Statistical significance was analyzed via the Chi-squared test. For survival analysis, both tooth-level and patient-level measurements were extracted. In particular, the number and identifier of tooth presence/absence at baseline were extracted for each patient. In addition, to calculate periodontal-related and other-cause-related loss, the time of loss at baseline, and reason of loss (periodontal- and/or non-periodontal-related, or absence of TL) were extracted for each tooth in each patient in the study. Absolute tooth survival at 10, 20 and 30-years follow-up was calculated for both periodontal-related and all-causes TL. Univariate analyses were evaluated at the tooth level using the logrank test plotting Kaplan-Meier survival curves. In addition, multilevel Cox Regression frailty models were used in order to assess the association among predictive variables (stage, grade, extent, gender, age, and average number of maintenances per year) and TL while taking into account for the clustering of teeth within patients²⁰

RESULTS

- Characteristics of patient cohort

A total number of 292 patients (140 males and 152 females) with a follow-up of 289.7 ± 79.6 (mean \pm standard deviation) months (range 120 to 570) were included in this retrospective analysis. At baseline, patients had a mean age of 47.3 ± 12.1 years (range 17 to 76) with a total of 7414 teeth

* SPSS 24 (IBM, Chicago, USA), and STATA 15.0 (StataCorporation, College Station, TX: StataCorp LP).

(3704 maxillary and 3710 mandibular). The total number of maxillary teeth in each patient was on average 12.64 ± 1.8 , while mandibular teeth were 12.81 ± 1.58 . Furthermore, 4920 teeth were single-rooted teeth (16.92 ± 2.06 at patient-level), while 2494 were multi-rooted teeth (8.34 ± 2.20 at patient-level). All of the included patients underwent an average of 2.2 ± 0.68 maintenance sessions per year (range 1.01 to 6.20) during the follow-up period.

- Categorization of patients according to the 2018 classification

According to the 2018 classification, in regard to the entire cohort of 292 patients: 31/292 (10.6%) were classified as Stage 1, 85/292 (29.1%) as Stage 2, 146/292 (50.0%) as Stage 3, and 30/292 (10.3%) as Stage 4. As shown on Table 1, baseline results revealed that patients in Stage 1 had a lower average age, and a higher number of multi-rooted teeth when compared to the patients in Stages 2, 3 and 4. As expected, patients in Stage 4 had the lowest number of both total, maxillary and mandibular teeth at baseline. As for grading: 34/292 (11.7%) were classified as Grade A, 193/292 (66.1%) as Grade B, and 65/292 (22.2%) in Grade C. Differences were detected for the baseline measurements among the three groups analyzed (Grade A, B and C) regarding the age of the included patients. In addition, periodontal disease was classified as localized in 211/292 (72.3%) and generalized in 80/292 (27.4%) of the patients, while only one patient showed a molar/incisor pattern. No differences were detected according to the extent of periodontitis except for the presence of a longer average follow-up in the cohort for patients with a generalized disease. Comparison of each treatment groups according to the studied variables was provided in the supplementary Table 1 in online *Journal of Periodontology*.

- Analysis of tooth survival according to the 2018 classification

Tooth-level univariate analysis of tooth survival revealed a significant association between stage and grade at baseline, and either periodontal-related tooth loss or overall tooth loss. On the contrary, no

differences were detected for the extent of periodontitis (Figure 1). Absolute analysis of tooth loss from baseline to the defined time points (10, 20- and 30-years follow-up) was completed (Table 2). Overall, increased tooth loss was related to a higher stage and grade but not to the extent of the disease. Similar results were found when the absolute analysis of tooth loss for 0-10, 10-20, 20-30 years of follow-up was performed (Table 3). The influence of variables defined in the 2018 classification for tooth survival was analyzed using a multilevel cox regression frailty models. Such models calculated and adjusted the number of tooth loss for potential interacting covariates, while taking into consideration the clustering of teeth within patients. The multivariate analysis revealed that Stage 4 and Grade C patients had a higher risk of periodontal-related tooth losses (Table 4). No differences were detected for the extent of periodontitis. In addition, the age of patients at baseline appeared to have a significant correlation with the number of periodontal-related tooth loss during follow-up ($p < 0.01$). In regard to the overall TL, patients in Stage 2 and 3 lost fewer teeth than patients initially seen in Stage 1. Grading was an independent predictor of the overall tooth loss. This was observed by the patients in Grade B that lost more teeth than patients classified as Grade A, and lost fewer teeth than patients in Grade C.

DISCUSSION

Personalized medicine, as currently envisioned, seeks to help clinicians select disease prevention and treatment strategies that will most likely help patients by taking into account individual variability in genes, environmental factors, and lifestyle. The new periodontal classification was intended to be a step toward the introduction of personalized medicine for treatment of periodontitis. Based on disease severity, complexity, the evidence of past disease progression, and presence of risk factors, stage and grade of a patient indicate the difficulty of treating and maintaining the patient long-term based on patient-level classifications that will guide the selection of treatment best suited for the case. In addition, the need for complex rehabilitation (interdisciplinary treatment) can also be assessed.

To support clinical decision-making, it is necessary to rely on scientific evidence derived from long-term data based on compliant patients. That is the reason why in the present report, only patients receiving regular PM during the entire follow-up period were included. This might have influenced the outcome of the results, decreasing the number of patients classified as Stage 1 and 4. Indeed, it is possible that patients in Stage 1 (not presenting an advanced periodontal disease) did not feel the necessity for a long-term regular maintenance. Similarly, Stage 4 patients might have been less compliant due to a previous history of extensive tooth loss, and a need for a crucial economic outlay (often not available) to pay for more comprehensive and multidisciplinary rehabilitations. In the present paper, the majority of the patients were staged as 3. This correlates with what was noted in a recent publication where the majority of the patients treated, and followed long-term in a university setting were also classified as Stage 3²¹, and the new classification had a reflection on TL occurring during the observation period of the selected patients. In the present article, this trend was present when the overall TL was evaluated, but it was more evident when only teeth lost due to periodontal disease were included. The new classification emphasizes that identifying TL due to periodontal disease is of prime importance and TL due to other causes may not be directly relevant to classification of periodontal disease²².

The present study confirms that the dose-dependence relationship between smoking/diabetes and grade introduced in the new classification is predictive of future tooth loss since the multilevel Cox regression showed a hazard ratio for periodontal tooth loss of 4.83 for Grade C patients compared with Grade A patients. The deleterious effect of cigarette smoking on the periodontium, and its dose-dependent effect, was previously reported in a large NHANES study (12,329 adults), where people smoking >30 cigarettes per day presented an odds ratio (OR) of 19.8 to develop periodontitis²³. Furthermore, it has been extensively studied that cigarette smoking is the source of more than 4,000 reported toxins, like carbon monoxide, oxidizing radicals, carcinogens (e.g. nitrosamine), and nicotine²⁴. Similarly, the biological implications of uncontrolled diabetes has been shown to impair osseous healing and bone turnover, and to affect the wound healing and alter the function of neutrophils, monocytes, and macrophages²⁵. As reported for Pima Indians with Type 2 diabetes had an increased

risk of destructive periodontitis with an OR of 2.81 when measured by clinical attachment loss and an OR of 3.43 when bone loss was used to measure the disease ²⁶.

The present paper is not exempt from limitations. Firstly, the grade was decided at baseline, but it is possible that a patient during the follow-up has stopped/started smoking, therefore decreasing or increasing the degree of risk. The same argument applies to diabetes. Moreover, as shown on Table 3, the predictive value of Stage and Grade was lost after 20 years of follow-up. Such findings suggest focusing on the need to "re-stage" the patients after a long follow-up considering the teeth lost in order to figure out whether the predictive value of the new classification could be recovered. Also, we did not calculate the influence of smoking or diabetes status changes after baseline. This is due to the fact that if we decide to look into this aspect, it will require a total different statistical model that might mislead readers. Finally, all patients included in the study were treated by different clinicians. This can lead to heterogeneity in the choice to extract or maintain one or more teeth.

CONCLUSION

Results of this long-term, retrospective, single-center cohort study suggests that the new periodontal disease classification has prognostic capability for tooth loss in patients who regularly seek periodontal care. Patients in Stage 4 and/or Grade C showed a significantly higher number of periodontal-related tooth loss. Such findings indicate the need to further explore the study of a personalized approach for the treatment of such categorized patients.

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Figure Legend:

Figure 1: Tooth-level univariate analysis of tooth survival; a) Effect of stage on the survival rate; b) Effect of grade on the survival rate; c) Effect of the extent on the survival rate

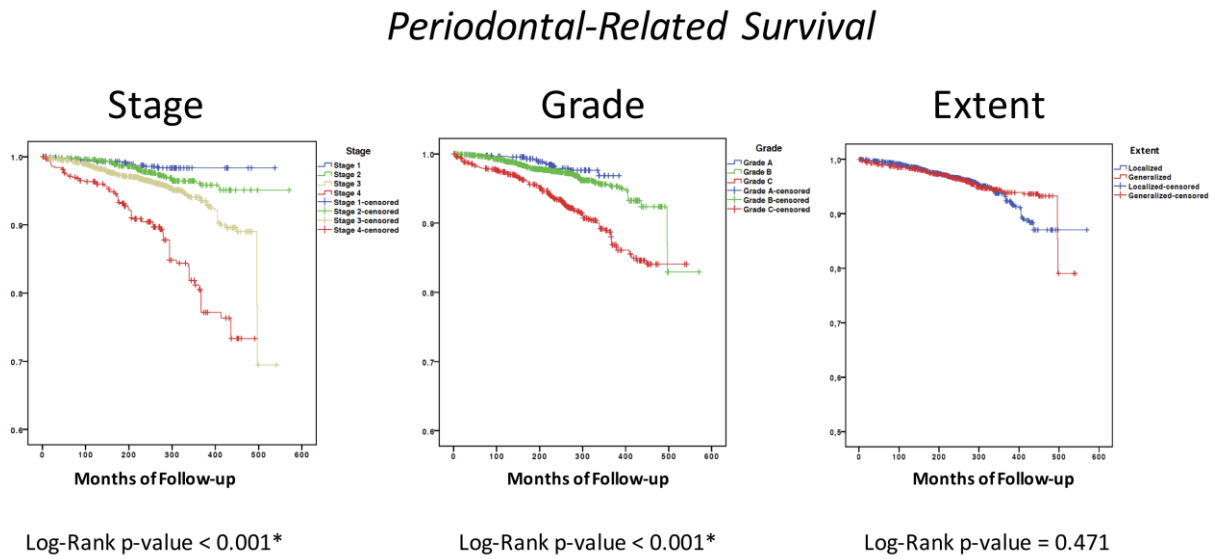


Table 1. Profile of the treatment groups according to variables at the patient and tooth level.

	Stage				p-Value	Grade			P-Value	Extension			p-Value	Total
	1	2	3	4		A	B	C		Loc	Gen	Inc-mol pattern		
Number of Subjects	31	85	146	30	///	34	193	65		211	80	1	///	292
Follow-up (months)	288.7 ±	285.1 ±	292.2 ±	292.4 ±	0.64	262.4 ±	286.1 ±	315.7 ±	0.10	280.2 5±	315.26 ±	248	0.007 [†]	///
	84.08	83.89	74.89	86.17		61.83	76.5	91.4		72.23	92.86			
Number of males	10	45	72	13	0.234	13	90	37	0.172	98	41	1	0.444	140
Number of females	21	40	74	17		21	103	28		113	39	0		152
Age (years)	41.19 ±	48.04 ±	47.57 ±	50.05 ±	0.026*	56.29 ±	47.22 ±	43.06 ±	0.000 [†]	47.9 ±	45.9±	N/A	0.429	///
	13.00	12.13	11.30	13.13		12.47	11.37	11.65		12.18	11.81			
Number of maxillary teeth	13.29 ±	13.00 ±	12.76 ±	10.40 ±	0.000 [†]	12.64 ±	12.71 ±	12.45 ±	0.743	12.57 ±	12.84 ±	N/A	0.434	3704
	0.97	1.78	1.42	2.48		1.78	1.79	1.88		1.92	1.47			
Number of mandibular teeth	13.48 ±	13.12 ±	12.96 ±	10.70 ±	0.000 [†]	12.88 ±	12.90 ±	12.76 ±	0.495	12.80 ±	12.89 ±	N/A	0.446	3710
	0.85	1.27	1.43	1.95		1.56	1.53	1.72		1.55	1.65			
Number of single-rooted teeth	17.45 ±	17.26 ±	17.13 ±	15.53 ±	0.000 [†]	17.00 ±	17.15 ±	16.72 ±	0.215	17.03 ±	17.03 ±	N/A	0.873	4920
	0.99	1.38	1.37	2.05		1.68	1.41	1.67		1.56	1.38			
Number of multi-rooted teeth	9.29 ±	8.82 ±	8.58 ±	8.40 ±	0.000 [†]	8.42 ±	8.46 ±	8.18 ±	0.926	8.31 ±	8.63 ±	N/A	0.233	2494
	1.24	1.72	1.80	2.64		2.21	2.02	2.30		2.19	1.85			
Number of maintenance sessions per year	2.08 ±	2.17 ±	2.29 ±	2.07 ±	0.840	2.21 ±	2.19 ±	2.28 ±	0.780	2.23 ±	2.15 ±	N/A	0.480	///
	0.53	0.67	0.73	0.54		0.68	0.66	0.74		0.71	0.58			
Number of teeth for patient at	26.77 ±	26.13 ±	25.71 ±	21.20 ±	0.000 [†]	25.50 ±	25.61 ±	25.08 ±	0.585	25.40 ±	25.70 ±	23	0.385	7414

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baseline	1.67	2.63	2.70	3.59	3.10	2.96	3.18	3.07	2.90
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Number of teeth at baseline	831	2221	3730	632	867	4937	1610	5334	2057	23	7414
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Note. Gen (Generalized), Loc (Localized), Inc-mol (Incisor-molar), * $p < 0.05$, † $p < 0.01$, ‡ $p < 0.001$,

Table 2: Distribution of teeth floss or both periodontal-related and overall- reasons. For such analysis, an absolute survival (loss) rate at 10, 20- and 30-years' follow-up was taken into consideration

	Periodontal-Related Teeth Loss			Overall Teeth Loss			
	<i>Baseline to 10 years' follow-up</i>	<i>Baseline to 20 years' follow-up</i>	<i>Baseline to 30 years' follow-up</i>	<i>Baseline to 10 years' follow-up</i>	<i>Baseline to 20 years' follow-up</i>	<i>Baseline to 30 years' follow-up</i>	
Stage	1	0.10 ± 0.39	0.24 ± 0.52	0.25 ± 0.50	0.26 ± 0.68	0.67 ± 1.15	1.33 ± 1.53
	2	0.07 ± 0.26	0.47 ± 0.91	1.00 ± 1.69	0.20 ± 0.56	0.87 ± 1.41	2.67 ± 2.97
	3	0.17 ± 0.39	0.48 ± 0.85	1.17 ± 1.53	0.35 ± 0.57	1.30 ± 1.29	2.78 ± 2.73
	4	1.43 ± 1.62	3.43 ± 3.46	4.43 ± 4.43	1.43 ± 1.62	4.43 ± 4.04	6.57 ± 4.89
	<i>p-value</i>	0.000 [†]	0.000 [†]	0.087	0.000 [†]	0.004 [†]	0.210
Grade	A	0.09 ± 0.38	0.50 ± 0.72	0.80 ± 0.84	0.38 ± 0.70	1.42 ± 1.35	2.00 ± 1.41
	B	0.27 ± 0.69	1.54 ± 1.09	0.93 ± 1.93	0.62 ± 1.23	1.56 ± 2.14	2.50 ± 2.81
	C	0.91 ± 1.73	1.65 ± 2.21	2.65 ± 2.96	1.34 ± 1.94	2.67 ± 2.82	4.41 ± 4.06
	<i>p-value</i>	0.000 [†]	0.000 [†]	0.042*	0.000 [†]	0.011	0.301
Extent	<i>Loc</i>	0.07 ± 0.27	0.44 ± 0.89	1.04 ± 1.58	0.23 ± 0.51	1.12 ± 1.43	2.85 ± 3.07
	<i>Gen</i>	0.59 ± 1.10	1.36 ± 2.42	2.05 ± 3.14	0.68 ± 1.13	2.11 ± 1.85	3.64 ± 3.72
	<i>Inc-Mol</i>	N/A	N/A	N/A	N/A	N/A	N/A
	<i>p-value</i>	0.582	0.876	0.380	0.298	0.491	0.753

Note. Gen (Generalized), Loc (Localized), Inc-mol (Incisor-molar), * $p < 0.05$, [†] $p < 0.01$, [‡] $p < 0.001$.

Table 3: Distribution of teeth floss or both periodontal-related and overall- reasons. For such analysis, the absolute survival (loss) rate between each interval of 10 years' follow-up was taken into consideration

	Periodontal-Related Teeth Loss			Overall Teeth Loss			
	Baseline to 10 years' follow-up	From 10 to 20 years' follow-up	From 20 to 30 years' follow-up	Baseline to 10 years' follow-up	From 10 to 20 years' follow-up	From 20 to 30 years' follow-up	
Stage	1	0.10 ± 0.39	0.16 ± 0.37	0.42 ± 0.67	0.26 ± 0.68	0.68 ± 0.85	0.67 ± 0.58
	2	0.07 ± 0.26	0.45 ± 1.17	0.74 ± 1.26	0.20 ± 0.56	1.22 ± 1.98	1.80 ± 1.86
	3	0.17 ± 0.39	0.35 ± 0.69	0.72 ± 0.89	0.35 ± 0.57	1.02 ± 1.48	1.48 ± 2.11
	4	1.43 ± 1.62	1.42 ± 1.98	0.70 ± 1.57	1.43 ± 1.62	2.04 ± 2.39	2.14 ± 2.41
	<i>p</i> -value	0.000 [‡]	0.000 [‡]	0.720	0.000 [‡]	0.065	0.490
Grade	A	0.09 ± 0.38	0.42 ± 0.65	0.72 ± 1.27	0.38 ± 0.70	1.00 ± 0.83	1.50 ± 0.71
	B	0.27 ± 0.69	0.32 ± 0.84	0.57 ± 1.00	0.62 ± 1.23	1.03 ± 1.67	1.33 ± 1.97
	C	0.91 ± 1.73	0.88 ± 1.52	0.94 ± 1.09	1.34 ± 1.94	1.51 ± 2.04	2.12 ± 2.06
	<i>p</i> -value	0.000 [‡]	0.000 [‡]	0.331	0.000 [‡]	0.104	0.279
Extent	<i>Loc</i>	0.07 ± 0.27	0.45 ± 1.03	0.64 ± 1.03	0.23 ± 0.51	1.15 ± 1.71	1.73 ± 2.20
	<i>Gen</i>	0.59 ± 1.10	0.50 ± 1.11	0.74 ± 1.16	0.68 ± 1.13	1.14 ± 1.73	1.50 ± 1.77
	<i>Inc-Mol</i>	N/A	N/A	N/A	N/A	N/A	N/A
	<i>p</i> -value	0.582	0.944	0.772	0.298	0.911	0.731

Note. *Gen* (Generalized), *Loc* (Localized), *Inc-mol* (Incisor-molar), **p* < 0.05, [†]*p* < 0.01, [‡]*p* < 0.001.
N/A: Not available

Table 4. Results from stepwise multilevel Cox regression analyses. Data of all variables were recorded at T1

Variables	Periodontal-Related Survival			Overall Survival		
	HR	95%(CI)	<i>p</i> -value	HR	95%(CI)	<i>p</i>
Stage	1 (ref)	1.00	-	1.00		
-	2	0.89 (0.32-2.52)	0.832	0.38 (0.20-0.73)		
0.004*	3	1.51 (0.54-4.16)	0.429	0.52 (0.26-0.98)		
0.043*	4	3.73 (1.27-10.93)	0.016*	0.84 (0.40-1.52)		
0.654						
Grade	A (ref)	1.00	-	1.00		
-	B	1.82 (0.77-4.30)	0.172	2.87 (1.60-5.17)		
0.00*	C	4.83 (1.84-12.67)	0.001*	4.45 (2.25-8.80)		
0.00*						
Ext.	Local	1.00	-	1.00		
-	Gen	0.73 (0.45-1.18)	0.207	0.95 (0.66-1.37)		
0.768						

Sex	Female	1.00	-	1.00
	Male	0.84 (0.56-1.27)	0.418	0.74 (0.54-1.01)
Age		1.03 (1.02-1.06)	0.001*	1.04 (1.01-1.46)
N° maintenances		1.14 (0.86–1.43)	0.684	1.17 (0.88–1.49)

HR: Hazard ratio

Ext: Extent

Local: Localized

Gen: Generalized

*: $p < 0.05$