Statistical analyses

Data were analyzed in 304 (164 men, 140 women) subjects examined as dentate in 2002 and in whom the levels of serum albumin were evaluated. Statistical analyses were performed as follows.

Initially, the number of periodontal disease events was considered as a dependent continuous variable and the unit of analysis was the subject. Gender (male, female), smoking habit (current smoker, ex-smoker, never smoked), BMI (<20, ≥20), the highest CAL (<6mm, ≥6mm), the number of teeth present (1-9, 10-19, 20-32) and serum values of nutritional and biochemical parameters were selected as independent variables. Student's *t*-test and analysis of variance (ANOVA) was employed to compare the differences. In addition, we defined a serum albumin concentration ≤4.0g/dl as low, according to a previous report (Phillips et al. 1989) and compared the number of periodontal disease events between subjects with serum albumin concentrations ≤4.0g/dl and >4.0g/dl at baseline using Student's *t*-test.

Furthermore, multiple linear regression analysis was used to estimate the effect on periodontal disease events for the serum albumin level while controlling for confounding factors. The number of periodontal disease events was used as the dependent variable, while variables that showed significant relationships with the number of periodontal disease events at p

<0.05 in initial analyses were selected as independent variables.

We also compared the number of periodontal disease events between subjects in whom the mean serum albumin concentrations over 4 years were ≤4.0g/dl and >4.0g/dl. Data were available in 284 (153 men, 131 women) subjects examined as dentate in 2002 and in whom the levels of serum albumin were evaluated.

All calculations and statistical analyses were performed using the STATA ™ software package (Stata Corp. Texas, USA).

Results

Overall, 296 subjects dropped out during the study. Serum albumin concentrations at baseline were 4.3± 0.2 g/dl for study subjects and 4.3± 0.3 g/dl for the group who dropped out during the study. There was no significant difference between the groups (p=0.12; Student's t-test).

The serum albumin level of the participants was 3.4 to 5.0 g/dl with a mean of 4.3± 0.2 g/dl (not shown in the table). It was found that male subjects and current smokers had a significantly high number of periodontal disease events (p<0.0001, p=0.0004), respectively. Subjects with 20-32 teeth also showed a high number of periodontal disease events compared with subjects who had 1-9 or 10-19 teeth (p<0.0001). Moreover, subjects who had teeth with CAL ≥6mm showed a high number of

periodontal disease events (p<0.0001). There were no significant differences between BMI, IgG, total protein and calcium, and periodontal disease events (Table 1).

In addition, subjects with lower serum albumin concentrations (≤4.0g/dl) at baseline had a significantly higher number of periodontal disease events compared with subjects with higher serum albumin concentrations (>4.0g/dl) at baseline (10.4±6.7 vs. 7.9±5.2, respectively; p=0.007, Student's t-test) (Fig. 1). Furthermore, subjects with lower mean serum albumin concentrations (≤4.0g/dl) over 4 years had a significantly higher number of periodontal disease events compared with subjects with higher mean serum albumin concentrations during the 4 years (>4.0g/dl) (9.8±6.1 vs. 7.9±5.1, respectively; p=0.025, Student's t-test) (Fig. 2).

According to the results of final multiple regression models, serum albumin concentrations at baseline had a significant effect on the number of periodontal disease events (standardized correlation coefficient= -0.10; p=0.032), which was independent of other covariates (Table 2).

Discussion

There was no significant difference in serum albumin concentration between the subjects who were targeted in this study and those who dropped out; therefore, we thought that the subjects in this study were

representative of the community.

To our knowledge, this is the first longitudinal study to demonstrate an association between periodontal diseases and serum albumin levels in the elderly. In this longitudinal investigation, a significant association was found between the numbers of periodontal disease events over 4 years and serum albumin levels at baseline in elderly subjects after controlling for confounding factors by multiple linear regression analysis. The standardized regression coefficient of serum albumin levels at baseline was -0.10 (p=0.032). We observed an inverse independent relationship between the serum albumin concentration and periodontal disease.

This relationship might be explained by the possible influence of nutritional aspects (Ogawa et al. 2006). Indeed, several reports have indicated a relation between the nutritional condition and serum albumin (Magagnotti et al. 2000; Giordano et al. 2001), although some studies have observed an association between nutritional aspects and periodontal disease (Nishida et al. 2000; Amarasena et al. 2005). An unfavorable nutritional status, which indicated lower serum albumin levels, is responsible for periodontal disease progression.

The serum albumin value might be a good marker for a subject's general health condition. Many conditions, such as malnutrition, inflammatory disorders, liver disease and renal disease reduce serum

albumin levels (Herrmann et al. 1992; Rigaud et al. 2000; Walrand et al. 2000). In these cases, subjects with low serum albumin concentration are likely to have decreased immunocompetence with an increased risk of infection (Goubran et al. 1996). Measurement of the serum albumin level is a common clinical practice and an important aspect of the general condition of elderly people (Corti et al. 1994).

The relationship between malnutrition and reduced resistance to infection has been suggested by several epidemiologic studies. In malnutrition, most host defense mechanisms are suppressed, especially in reduced cell-mediated immunity. One feasible reason is the reduction in mature fully differentiated T lymphocytes (Nezu et al. 1994). Moreover, malnutrition promotes salivary gland hypofunction, impaired immunity, and an early shift in the oral microbial ecology toward a preponderance of anaerobic organisms. Immune suppression impacts negatively on the natural history of inflammatory periodontal diseases (Enwonwu et al. 2001).

Furthermore, serum albumin can act as an antioxidant in scavenging free radicals (Halliwell et al. 1990). A low albumin level, therefore, might modulate initial cellular damage and help trigger or enhance the irreversible degenerative processes that are the pathological basis of most inflammatory, ischemic, and proliferative diseases (Corti et al. 1994).

Therefore, in terms of the association between serum albumin concentration and periodontal disease, a decreased serum albumin level might directly influence periodontal disease progression.

In this study, serum albumin concentrations ≤4.0g/dl were defined as low, according to Phillips's report (Phillips et al. 1989). In this report, they demonstrated a marked increase in mortality with decreasing serum albumin concentrations that persisted even after adjusting for age, social class, town of residence, cigarette smoking, serum total cholesterol, serum total calcium and systolic blood pressure. Individuals with <4.0 g/dl albumin had a crude all-cause mortality rate six times that of men with a serum albumin of 4.8 g/dl or more.

In conclusion, the findings of the present study suggest that serum albumin concentration is a significant risk predictor of periodontal disease progression. Furthermore, low serum albumin concentration may impair the periodontal condition.

Acknowledgements

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Table 1. Relationship between subject characteristics, dental status, blood pressure, serum blood parameters for nutritional and biochemical values, serum disease markers and periodonatal disease events

	Non-Smokers (N=165)				Smokers (N=139)			
	No. of subjects	Periodontal disease events[†]			No. of subjects	Periodontal disease events[†]		
		Mean	SD	*p*-value		Mean	SD	*p*-value
Serum Albumin (g/dl)								
>4	145	6.66	4.80	0.0024	119	9.39	5.22	NS*
≤4	20	10.45	7.33		20	10.35	6.30	
Gender								
Male	35	9.03	5.72	0.0155	129	9.74	5.51	NS*
Female	130	6.60	5.07		10	6.90	1.79	
BMI[‡]								
<20	37	7.27	5.78	NS*	33	10.61	4.92	NS*
≥20	128	7.07	5.17		106	9.20	5.49	
No. of teeth present								
1-9	29	2.62	2.43	<0.0001	16	4.19	2.07	<0.0001
10-19	36	5.75	3.37		44	8.23	3.26	
20-32	100	8.91	5.56		79	11.34	5.86	
Highest CAL[§] (mm)								
<6	79	5.57	4.67	0.0003	29	7.17	6.18	0.0074
≥6	86	8.53	5.46		110	10.15	4.99	
High blood pressure								
≤140	115	7.15	4.95	NS*	80	9.76	5.24	NS*
>140	50	7.04	6.05		59	9.22	5.58	
Low blood pressure								
≤90	160	7.11	5.33	NS*	128	9.51	5.38	NS*
>90	5	7.20	4.32		11	9.82	5.56	
GOT								
≤40	162	7.14	5.32	NS*	136	9.59	5.38	NS*
>40	3	6.00	3.61		3	7.00	5.29	
GPT								
≤35	158	7.15	5.33	NS*	133	9.51	5.31	NS*
>35	7	6.29	4.54		6	10.00	7.32	
γ-GTP								
<60	163	7.17	5.30	NS*	127	9.57	5.39	NS*
≥60	2	3.00	1.41		12	9.17	5.39	
IgG (mg/dl)								
<1000	3	12.33	8.08	NS*	9	10.67	4.00	NS*
1000-1900	144	6.94	5.24		121	9.45	5.48	
>1900	18	7.61	5.17		9	9.44	5.46	
Total protein (g/dl)								
<6.5	2	8.00	4.24	NS*	5	8.60	5.18	NS*
≥6.5	163	7.10	5.31		134	9.57	5.40	
Calcium (mEg/l)								
<6.5	55	7.82	5.54	NS*	67	9.63	5.91	NS*
≥6.5	110	6.76	5.16		72	9.44	4.86	

[†]Number of teeth with periodontal disease progression during 4 years.

[‡]Body mass index.

[§]Clinical attachment level.

*Not significant.

Fig. 1.

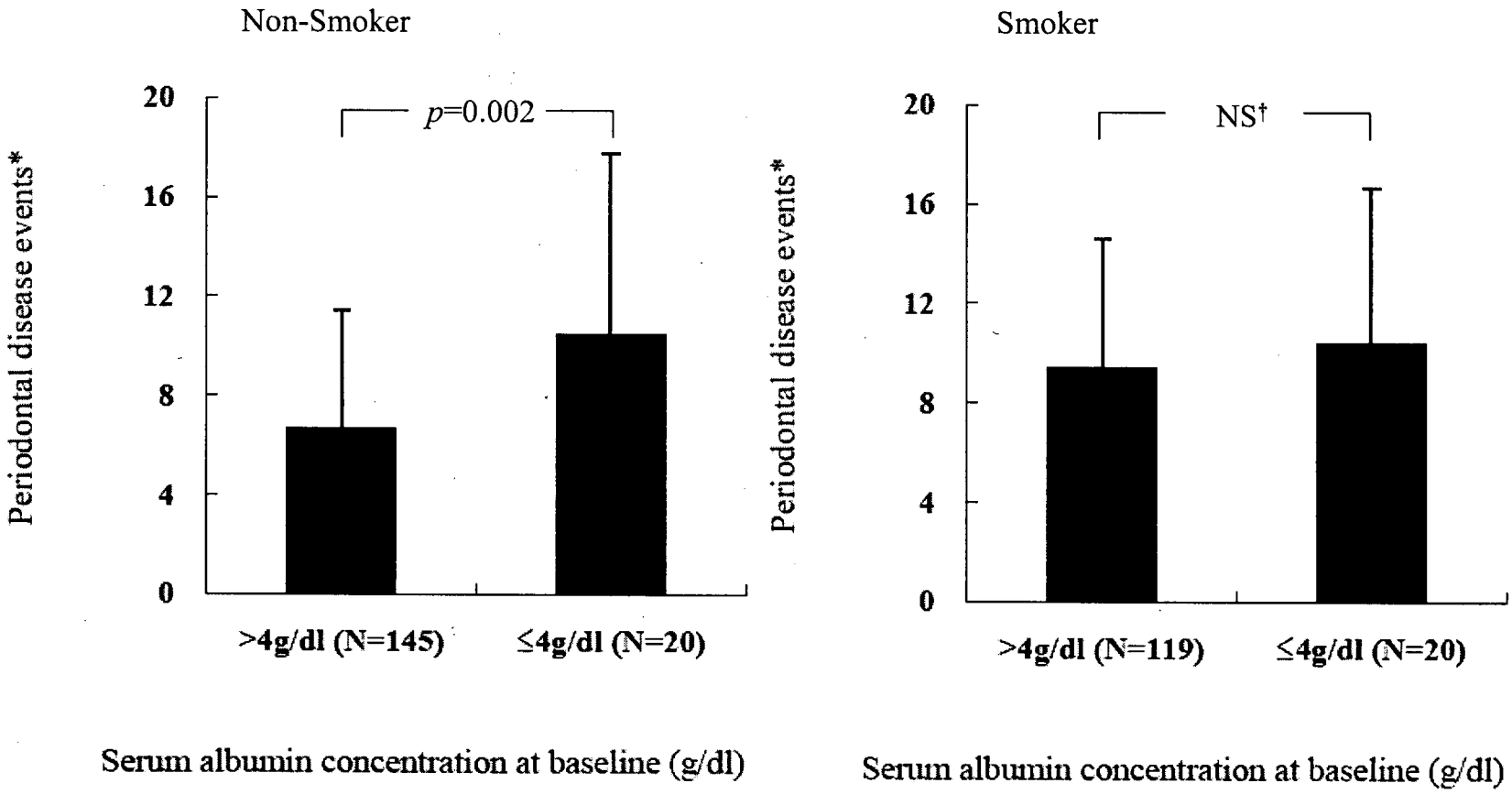
Non-Smoker
Periodontal disease events*
20
16
12
8
4
0
p=0.002
>4g/dl (N=145)
≤4g/dl (N=20)
Serum albumin concentration at baseline (g/dl)
Smoker
Periodontal disease events*
20
16
12
8
4
0
NS†
>4g/dl (N=119)
≤4g/dl (N=20)
Serum albumin concentration at baseline (g/dl)

Fig. 1. Relationship between periodontal disease events and serum albumin concentration at baseline, stratified by smoking status.

* Number of teeth with periodontal disease progression during 4 years. †Not significant

Fig. 2.

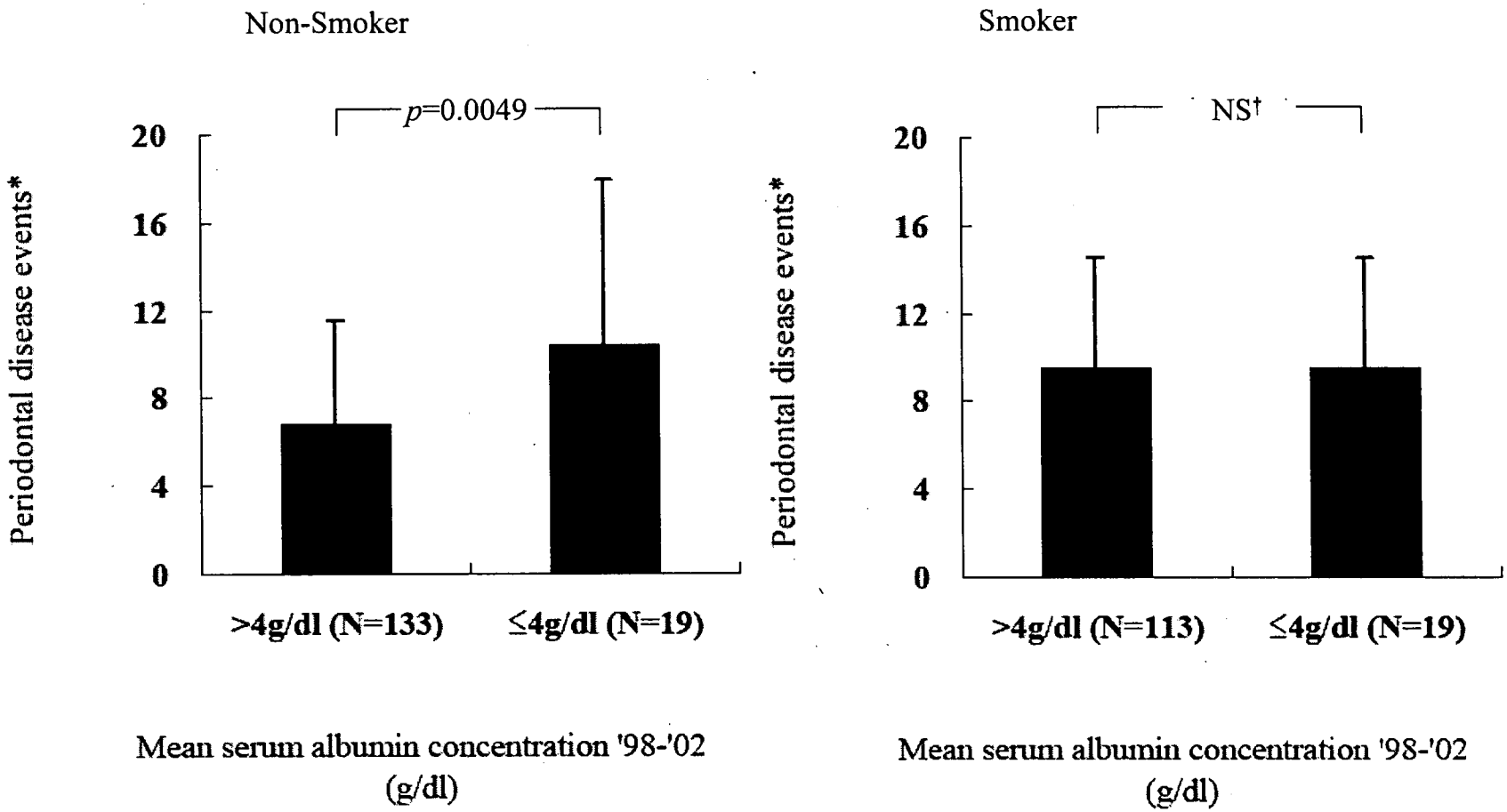
Non-Smoker
p=0.0049
Periodontal disease events*
20
16
12
8
4
0
>4g/dl (N=133)
≤4g/dl (N=19)
Mean serum albumin concentration '98-'02 (g/dl)
Smoker
NS†
Periodontal disease events*
20
16
12
8
4
0
>4g/dl (N=113)
≤4g/dl (N=19)
Mean serum albumin concentration '98-'02 (g/dl)

Fig. 2. Relationship between periodontal disease events and the mean serum albumin concentration during 4 years, stratified by smoking status.
* Number of teeth with periodontal disease progression during 4 years. †Not signigicant

Table 2. Multiple linear regression and associated p values

Non-Smokers						
	Dependent variable					
	Periodontal disease events[†]					
Independent variables	coefficient	standard error	p-value	95% CI[‡]		Std. Coef[§]
Serum albumin (g/dl)	-3.54	1.46	0.017	-6.42	-0.65	-0.16
Gender	0.77	0.88	0.385	-0.97	2.50	0.06
No. of teeth present	0.28	0.04	<0.001	0.19	0.36	0.43
Highest CAL[¶]	0.60	0.17	0.001	0.26	0.93	0.23
Constant	13.31	6.64	0.047	0.21	26.42	
						R^2=0.3005, p<0.001

Smokers						
	Dependent variable					
	Periodontal disease events[†]					
Independent variables	coefficient	standard error	p-value	95% CI[‡]		Std. Coef[§]
Serum albumin (g/dl)	-1.08	1.63	0.51	-4.31	2.15	-0.05
Gender	0.91	1.57	0.563	-2.20	4.02	0.04
No. of teeth present	0.34	0.06	<0.001	0.23	0.45	0.47
Highest CAL[¶]	0.71	0.19	<0.001	0.34	1.08	0.29
Constant	1.19	7.48	0.874	-13.60	15.98	
[†]Number of teeth with periodontal disease progression during 4 years.						R^2=0.2538, p<0.001

[‡]Confidence interval.

[§]Standardized coefficients.

[¶]Clinical attachment level.

Table 1. Relationship between subject characteristics, dental status, blood pressure, serum blood parameters for nutritional and biochemical values, serum disease markers and periodonatal disease events

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≥6.5	110	6.76	5.16		72	9.44	4.86	

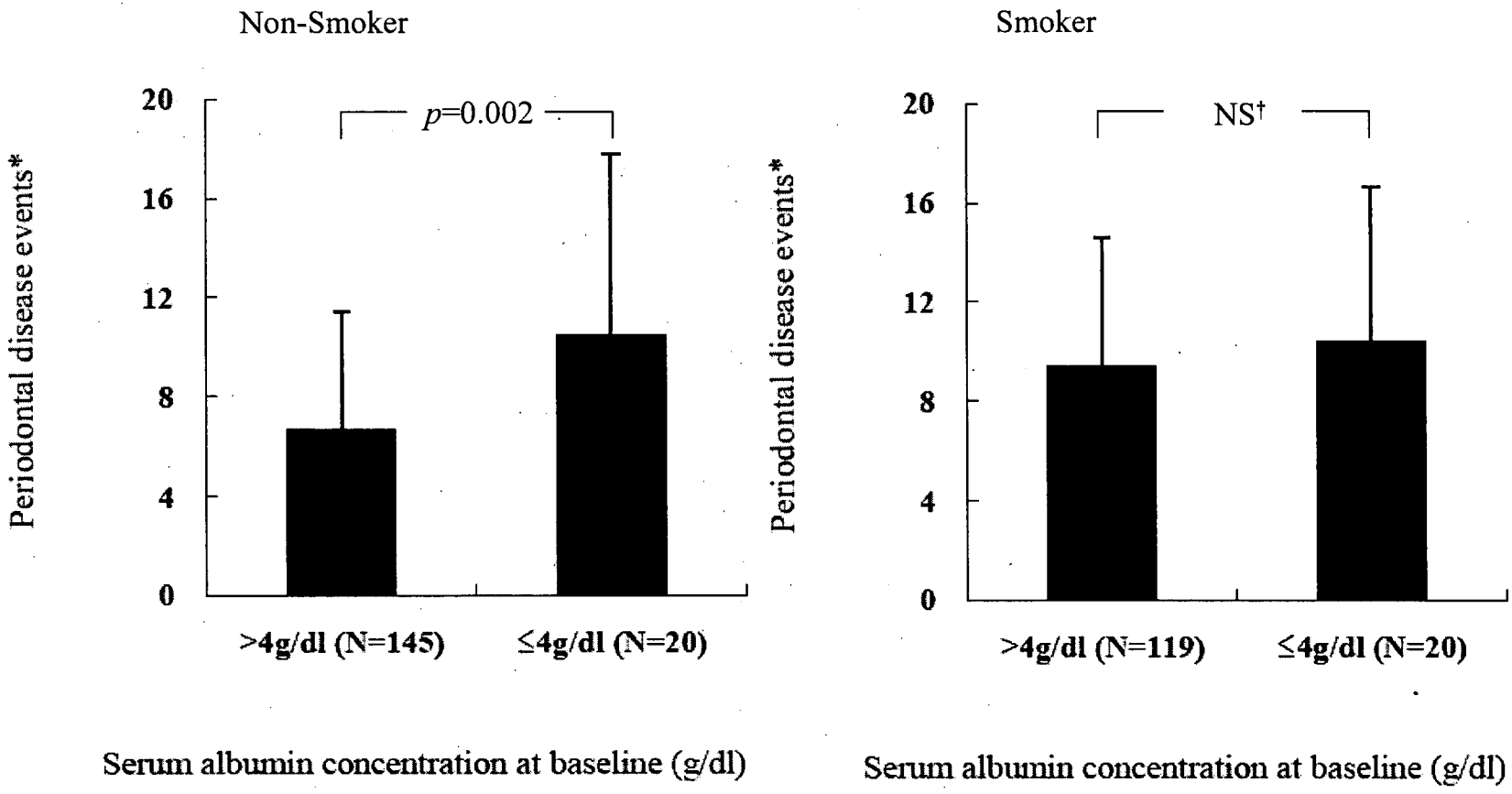
[†]Number of teeth with periodontal disease progression during 4 years.

[‡]Body mass index.

[§]Clinical attachment level.

*Not significant.

Fig. 1.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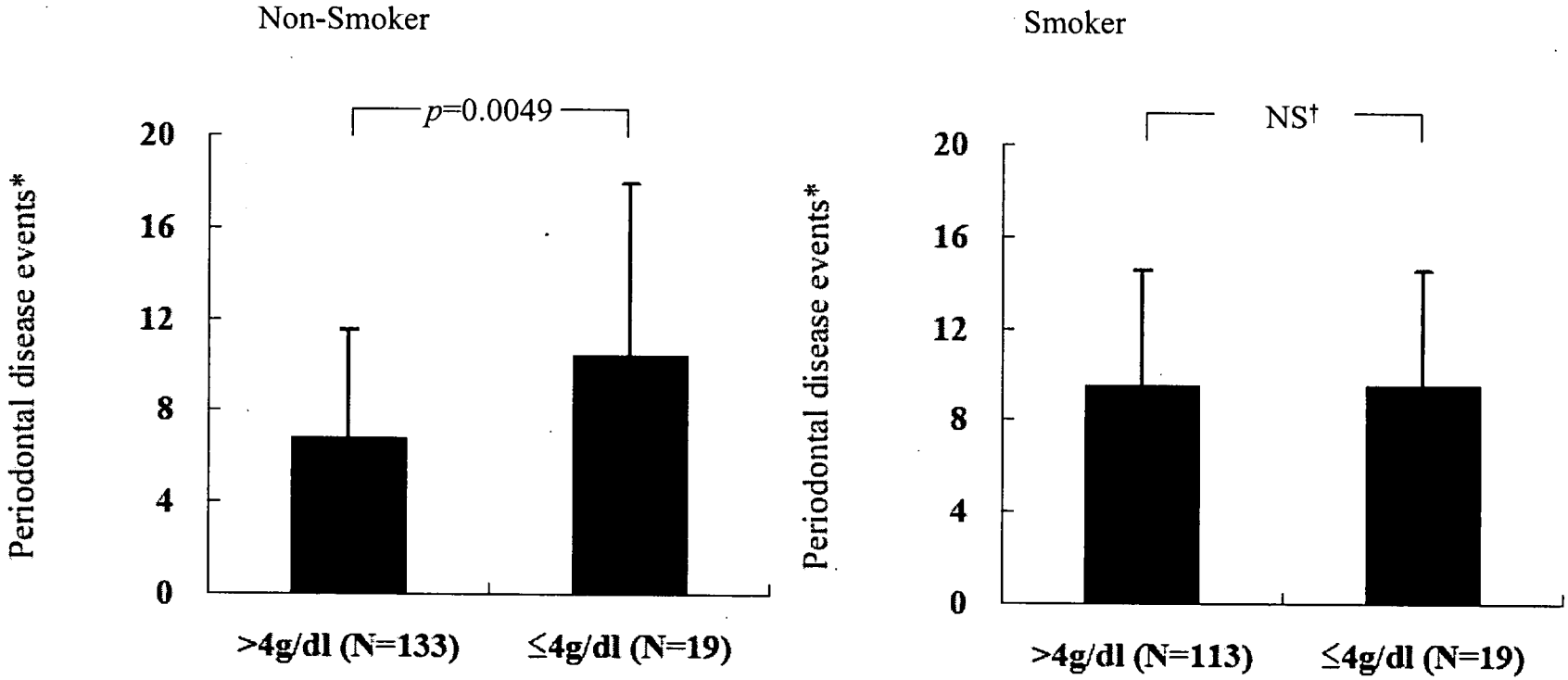
Serum albumin concentration at baseline (g/dl)

Fig. 1. Relationship between periodontal disease events and serum albumin concentration at baseline, stratified by smoking status.

* Number of teeth with periodontal disease progression during 4 years. †Not significant

Fig. 2.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