DISCUSSION

According to the results about the difference in general health condition between EX and RE, there was a small difference in the number of cases of disease, the percentage of smokers and the percentage of people with chewing trouble. Therefore, we thought that the subjects in this study were representative of the community.

In addition, ultrasonic bone density measurements were performed to study the relationship between BMD and the progression of periodontal disease in this study. Ultrasound densitometry of the os calcis was highly reproducible and had a high correlation with BMD in different parts of the skeleton. A significant negative correlation was found between ultrasound values and age, and these values were variably affected by menopause, in the same fashion as spine or femur bone mineral density (Yamazaki *et al.*, 1994). Some researchers have evaluated BMD by ultrasonic bone density measurement (Heaney *et al.*, 1989; Resch *et al.*, 1990).

On the other hand, the R^2 by the multiple regression analysis is low (Table 3). This means that the amount of explained variance by the multiple regression analysis is low, which indicated that although two independent variables had significant probability, there are other explanatory factors. We should keep in mind the limitation of the present study.

The results sowed that the subjects in OG had a higher number of progressive sites for AAL than the subjects in NOG. This 3-year longitudinal study clearly demonstrated that BMD is a risk factor for periodontal disease progression in an elderly population.

Some systemic factors have been identified which contribute to loss of bone mass or periodontal progression (Cummings *et al.*, 1985; Genco *et al.*, 1993). There were some common factors such as smoking, nutritional deficiencies, age, corticosteroid use and immune dysfunction (Wactawski-Wende *et al.*, 1996). Therefore, it is reasonable that this study showed a significant relationship between BMD and periodontal disease progression. Maybe systemic factors of bone remodeling also modify local tissue response to periodontal disease.

However, only a weak relationship existed, although it was statistically significant, because there were many potential confounding variables. In paticular, local infection is the most outstanding feature in the origin of periodontal disease. In our previous study of an elderly population, we found significant associations between additional attachment loss during a 2 year period and smoking, and an attachment level of 6 mm or more at baseline (Ogawa *et al.*, 2000; Hirotomi *et al.*, 2002). In the same group, we also found that the subjects who had more than 20 remaining teeth were less susceptible to periodontal disease resistance

(Hirotomi *et al.*, 2002). Therefore, we evaluated the relationship between systemic bone mineral density and periodontal progression after controlling for risk factors such as gender, teeth present, diabetes mellitus and smoking habits.

According to previous reports, Kribs et al (1990) observed a significant correlation between several skeletal bone mass measurements and the number of remaining mandibular teeth in 85 osteoporotic women between 50 to 80 years of age. Some other reports showed that mandibular bone mass was significantly correlated with skeletal bone mass as well (Von Wowern *et al.*, 1994; Klemetti *et al.*, 1993). In addition, the BMD of the mandible is affected by the mineral status of the skeleton and also by general disease that cause generalized bone loss (Klemetti *et al.*, 1993). However, Mohajery and Brooks (1992) found there was no correlation between skeletal and mandibular bone measurements. According to these conflicting results, general bone mineral density might not influence the alveolar bone loss directly in some cases. The skeleton is heterogenic, and bone density, bone turnover rate and bone remodelling ability differ in different parts of the skeleton, suggesting that those regions, although related to each other, have some degree of independence. In addition, some bias such as local oral factors for alveolar bone loss might decrease the good relationship between systemic bone mineral density and periodontal progression. In the previous reports, it was difficult to control all factors which influenced the skeletal bone mineral density and periodontitis because of small sample size or not controlling for teeth present and general condition.

In conclusion, this study suggested that there was a significant relationship between periodontal disease and general bone mineral density in the well-designed, large-scale study.

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REFERENCES

Brown LF, Beck JD, Rozier RG (1994). Incidence of attachment loss in community-dwelling older adults. *J Periodontol* 65: 316-23.

Brown LJ, Brunelle JA, Kingman A (1996). Periodontal status in the United Staes, 1988-91: Prevalence, extent, and demographic variation. *J Dent Res* 75(Special issue): 672-83.

Cummings RS, Kelsey JL, Nevitt MC, O'Dowdk J (1985). Epidemiology of osteoporosis and osteoporotic fractures. *Epidemiol Rev* 7: 178-208.

Elders PJM, Habets LL, Netelenbos JC, Van der Linden LWJ, Van der Steldt PF (1992). The relation between periodontitis and systemic bone mass in women between 46 and 55 years of age. *J Clin Periodontol* 19: 492-6.

Genco RJ, Löe H (1993). The role of systemic conditions and disorders in periodontal disease. *Periodontol 2000* 2: 98-116.

Heaney RP, Avioli LV, Chesnut CH, Lappe J, Recker RR, Brandenburger GH (1989). Osteoporotic bone fragility: detection by ultrasound transmission velocity. *JAMA* 261:2986-90.

Hirotomi T, Yoshihara A, Yano M, Ando Y, Miyazaki H (2002). Longitudinal study on periodontal conditions in healthy elderly people in Japan. *Community Dent Oral Epidemiol* 30: 409-417.

Klemetti E, Collin H-L, Forss H, Markkanen H, Lassila V (1994). Mineral status of skeleton and advanced periodontal disease. *J Clin Periodontol* 21: 184-8.

Klemetti E, Vainio P, Lassila V, Alhava E (1993). Cortical bone mineral density in the mandible and osteoporosis status in postmenopausal women. *Scand J Dent Res* 101: 219-23.

Kribbs PJ, Chesnut CH, Ott SM, Kilcoyne RF (1990). Relationships between mandibular

and skeletal bone in a population of normal women. *J Prosthet Dent* 63: 86-9.

Johnson TE (1993). Factors contributing to dentists' extraction decisions in older adults. *Special Care Dent* 13: 195-9.

Langton CM, Palmer SB, Porter RW (1984). The measurement of broadband ultrasonic attenuation in cancellous bone. *Eng Med* 13: 89-91.

Lunar Corporation. Theory of ultrasound densitometry. In: Lunar Corporation, editors. Manual of Achilles ultrasound bone densitometer. Madison, Wis.: Lunar Corporation, 1991; B1-B7.

Lundstrom A, Jendle J, Stenstrom B, Toss G, Ravald N (2001). Periodontal conditions in 70-year-old women with osteoporosis. *Swed Dent J* 25: 89-96, 2001.

Miyazaki H, Hanada N, Itoh-andoh M, Yamashita Y, Saito T, Sogame A, Goto K, Shirahama R, Takehara T (1989). Periodontal disease prevalence in different age group in Japan as assessed according to the CPITN. *Community Dent Oral Epidemiol* 17: 71-4.

Miyazaki H, Ohtani I, Abe N, Ansai T, Kato Y, Sakao S, Takehara T, Shimada N, Pilot T (1995). Periodontal conditions in older cohorts aged 65 years and older in Japan, measured by CPITN and loss of attachment. *Community Dental Health* 12: 216-20.

Mohajery M, Brooks SL (1992). Oral radiographs in the detection of early signs of osteoporosis. *Oral Surg Oral Med Oral Pathol* 73: 112-7.

Mohammad AR, Bauer RL, Yeh C-K (1997). Spinal bone density and toothloss in a cohort of postmenopausal women. *Int J Prosthodont* 10: 381-5.

Offenbacher S (1996). Periodontal diseases: pathogenesis. *Ann Periodontol* 1: 821-8.

Ogawa H, Yoshihara A, Hirotomi T, Ando Y, Miyazaki H (2002). Risk factors for periodontal disease progression among elderly people. *J Clin Periodontol* 29: 592-597.

Resch H, Pietschmann P, Bernecker P, Krexner E, Willvonseder R (1990). Broadband ultrasound attenuation: a new diagnostic method in osteoporosis. *Am J Radiol* 155: 825-8.

Rossman P, Zagzebski J, Mesina C, Sorenson J, Mazess R (1989). Comparison of ultrasonic velocity and attenuation in the os calcis to photon absorptiometry measurements in the radius, femur, and lumbar spine. *Clin Phys Physiol Meas* 1989; 10: 353-60.

Slade GD, Spencer AJ (1995). Periodontal attachment loss among adults aged 60+ in South Australia. *Community Dent Oral Epidemiol* 23, 237-42.

Tezal M, Wactawski-Wende J, Grossi SG, Ho AW, Dunford R, Genco RJ (2000). The relationship between bone mineral density and periodontitis in postmenopausal women. *J Periodontol* 71: 1492-8.

Von Wowern N, Klausen B, Kollerup G (1994). Osteoporosis: A risk factor in periodontal disease. *J Periodontol* 65: 1134-8.

Wactawski-Wende J, Grossi SG, Trevisan M, Genco RJ, Tezal M, Dunford RG, Ho AW, Hausmann E, Hreshchyshyn MM (1996). The role of oseopenia in oral bone loss and periodontal disease. *J Periodontol* 67: 1076-84.

Yamazaki K, Kushida K, Ohmura A, Sano M, Inoue T (1994). Ultrasound bone densitometry of the os calcis in Japanese women. *Osteoporosis Int* 4: 220-5.

Table 1. Characteristics of subjects at baseline.

Parameters	Screened population (n=600)	Subjects included in the present analysis (n=186)
Male/Female	306/294	87/99
Smokers (%)	18.7	None
Subjects under medical treatment for diabetes (%)	5.0	None
Subjects with blood sugar ≥140mg/dl(%)	7.0	None
Edentulous subjects (%)	7.5	None
Number of teeth present (mean±SD)	17.4±0.4	25.34±2.92
Probing pocket depth, PPD mm (mean±SD)	2.03±0.03	1.90±0.50
Probing attachment level, PAL mm (mean±SD)	3.10±0.05	2.60±0.75
Number of sites (mean±SD)		
PPD 4-5mm	8.48±10.30	9.03±11.33
PPD ≥6mm	1.21±2.97	1.17±3.27
PAL 4-5mm	23.69±20.39	24.49±22.78
PAL ≥6mm	5.71±9.21	4.43±9.22

Table 2. Comparison of bone mineral density, body mass index, albumin concentration, IgG concentration and additional attachment loss between male and female.

Parameters	Subjects (n=186)		*p* value
	Male	Female	
Stiffness (%, mean±SD)[a]	74.04±10.58	59.49±8.70	<0.01
BMI (kg/m^2, mean±SD) [a]	22.53±2.58	22.61±2.82	0.852
Albumin (g/dl, mean±SD)[a]	4.30±0.27	4.33±0.24	0.350
IgG (mg/dl, mean±SD)[a]	1516.63±264.18	1553.86±338.72	0.411
Number of sites with more than ≥3mm additional attachment loss (mean±SD) [b]	6.62±10.86	5.03±8.46	0.264

a: at baseline, b: during three years (n=181).

Table 3. Multiple linear regression and associated p -values

	Dependent variable				
	Number of sites with more than ≥3mm additional attachment loss (mean±SD) [b]				
Independent variable [a]	Coef.	Std. Err.	P value	[95% CFI]	
Stiffness (%)	-0.2156	0.0776	0.006	-0.3688	-0.0625
Albumin (g/dl)	-4.3912	2.7804	0.116	-9.8786	1.0962
IgG (mg/dl)	-0.0001	0.0024	0.960	-0.0048	0.0045
Gender (1: Male, 2: Female)	-4.5760	1.8414	0.014	-8.2102	-0.9418
BMI (kg/m^2)	-0.0070	0.2711	0.980	-0.5419	0.5280
_cons	46.3782	14.5410	<0.01	17.6800	75.0764

a: at baseline, b: during three years.

p =0.028, R2=0.070

Figure ↑ Yoshihara *et al*.

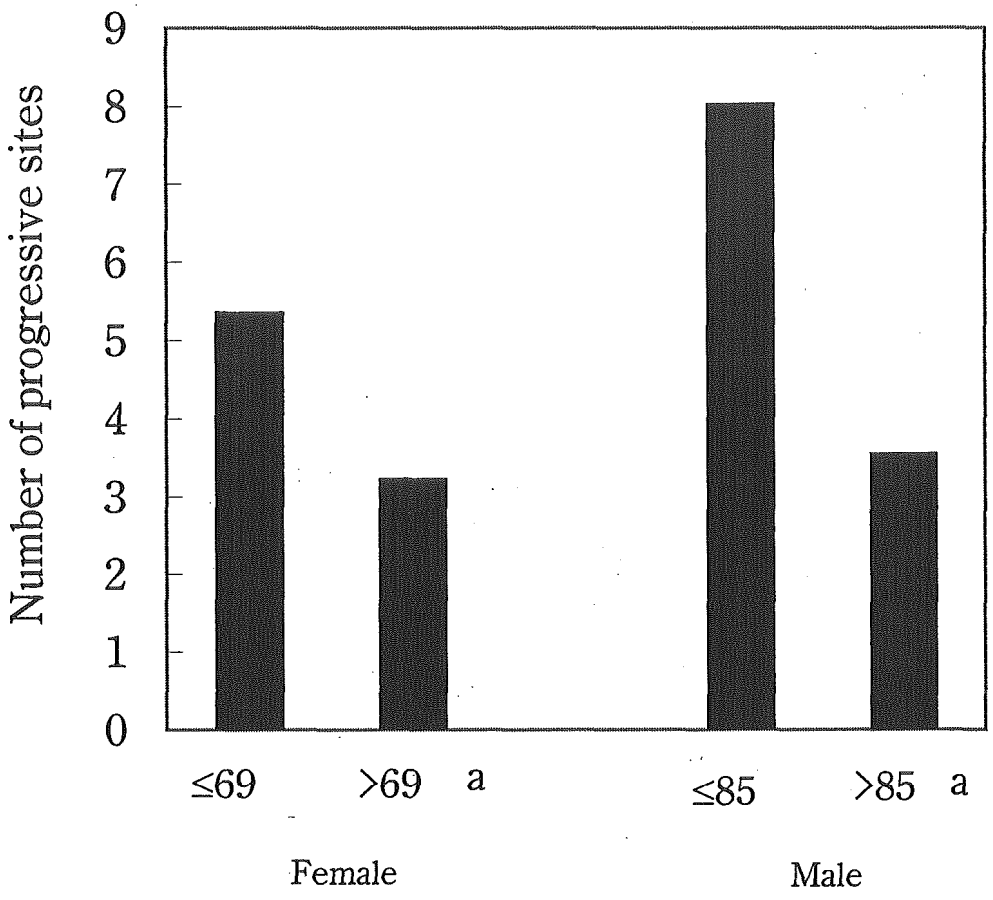

Figure legend

Fig. Relationship between number of more than ≥3mm additional attachment loss and osteopenia.

Probability=0.047, between stiffness ≤69 (n=80) and >69 (n=19) for female, ≤85 (n=65) and >85 (n=22) for male using ANOVA adjusted by gender.

a: Stiffness (%).

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「口腔保健と全身的な健康状態の関係について」

C．研究課題名：「高齢者における FcγRIIIb 遺伝子多型と喫煙経験が歯周炎の進行に及ぼす影響について」

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E．研究目的：

高齢者においてもほとんど歯周組織破壊を示さない歯周炎抵抗性の高い個体は，歯周病原性細菌に対する防御反応において歯周炎感受性の個体よりも有利な遺伝的素因を持っている可能性があると考えられる。生体防御の第一線を担う好中球は FcγR レセプターを介して IgG 免疫複合体を貪食する。FcγRIIIb は好中球に特異的に発言し２つのアレル NA1，NA2 を有する。我々はこれまでに FcγRIIIb-NA2 保有者に成人性歯周炎再発頻度が有意に高いこと，さらに FcγRIIIb-NA1 を発現する好中球は NA2 に比較して IgG1 および IgG3 を介した *Porphromonas gingivalis* 貪食能が有意に高いことを示した。本研究では FcγRIIIb-NA1/NA2 遺伝子多型が歯周炎抵抗性に関与するか否かを喫煙経験も踏まえながら評価することを目的としている。

F．研究方法：

研究への協力に合意した 70 歳の対象のうち，600 人について全検査結果が得られた。その中から糖尿病を有さない 309 人を無作為に選び FcγRIIIb-NA1/NA2 遺伝子型を決定した。その内で 20 歯以上を有する者について，FcγRIIIb-NA1NA1　(NA1)および FcγRIIIb-NA1NA2 または NA2NA2　(NA2)の２群を設定した。３年間の additional attachment loss (AAL) を測定し，喫煙経験を踏まえながら，多型２群間で相対危険度を算出した。FcγRIIIb-NA1/NA2 遺伝子型は末梢血より DNA を抽出しアレル特異的 PCR にて決定した。

G．研究結果・考察：

3年間で 4mm 以上の AL が発生した者は全体の 59.8%を占めた。4mm 以上の AL の平均部位数は 1.49 ± 4.79 で，NA1 群と NA2 群で差は認められなかった。NA1 群と NA2 群をさらに喫煙者および非喫煙者に分類し評価すると，喫煙者と非喫煙者のオッズ比は，遺伝子多型と組み合わせない場合には 2.13 であったものが，NA2 群でみると，3.03 上昇した。しかし，NA1 群においては喫煙者と非喫煙者のオッズ比に変化はみられなかった。

FcγRIIIb-NA1/NA2 遺伝子型分布が歯周病進行に影響を与えることが，高齢者においても確認でした。また，たばこは好中球の働きに影響を与えることがわかっている。それが，喫煙経験の影響が NA2 グループにおいて強くでてきたことの背景にあると考えられる。

H．結論：

8020 データバンク調査に伴い新潟市に住む 70 歳の中で，研究への協力に合意し，20 歯以上を有するものについて，FcγRIIIb-NA1NA1 (NA1)および FcγRIIIb-NA1NA2 または NA2NA2 (NA2)の2群を設定した。2年間の Additional attachment loss を測定し，喫煙経験も踏まえ評価した。その結果，FcγRIIIb-NA1 アレルは歯周炎抵抗性に関わるマーカーのひとつであることが示唆された。

I．研究発表論文：

投稿原稿

FcγRIIIb genotypes and smoking for periodontal disease progression in community-dwelling older adults

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Abstract

The purpose of this study is to determine how FcγRIIIb-NA1-NA2 polymorphism and smoking are associated with periodontal disease progression among elderly people. Among the subjects 70 years of age with more than 20 present teeth, the NA1 group was defined as FcγRIIIb-NA2 non-carrier (subjects with no FcγRIIIb-NA2 allele, n=53), whereas the NA2 group was defined as FcγRIIIb-NA2 carrier (n=111). We evaluated the progression of periodontitis by additional attachment loss during 3 years. Among the subjects, the frequency of ≥4mm additional attachment loss was 55.6% for smokers compared with 37.2% for the non-smokers. The odds ratio was 2.13 (CI: 0.92-4.76). However, there were no difference in the frequency of ≥4mm additional attachment loss.

Furthermore, we evaluated the association of the FcγRIIIb-NA1-NA2 polymorphism with smoking habit by the occurrences and odds ratios. The odds ratio of smoker increased from 2.13 for non-combination to 3.03 (CI: 1.12-8.33) for combination with FcγRIIIb-NA2 carriers (p=0.028). However, there was no increase in the odds ratio for smoker with NA2

non-carrier. Our results support the FcγRIIIb-NA1-NA2 polymorphism may be associated with periodontal progression especially in elderly smokers.

Introduction

The understanding of periodontal condition including natural history is growing rapidly (Miyazaki et al. 1989, 1995). Periodontal destruction is a frequent experience among elderly people (Slade et al. 1995, Brown et al. 1996), and it contributes to as many as 40 percent of tooth extraction (Jonson 1993). Nevertheless, elderly people who show minimum periodontal tissue destruction certainly exist (Papapanou & Lindhe 1992).

Neutrophils play an important role in the control of periodontitis, and increased disease susceptibility is observed in patients with defective neutrophil production and/or function (Hart et al. 1994, Van Dyke et al. 1994, Kinane 1999). Therefore, genetic polymorphism that affect neutrophil effector function might be relevant for disease resistance. FcγRIIIb is a neutrophil-specific receptor and bears the functional NA1-NA2 polymorphism which determines IgG1- and IgG3-mediated neutrophil effector function.

We demonstrated a role of FcγRIIIb allele as a risk factor for periodontal disease (Kobayashi et al. 1997, 1998, 2000a, 2000b, 2001, Sugita et al. 2001, Yoshihara et al. 2001). For elderly population, we found that FcγRIIIb-NA1 allotype was over-represented in the periodontitis-resistant group, compared with the priodontitis-susceptible group according to cross-sectional study (Sugita et al. 2001). However, there are many indefinite points to the role for the genetic polymorphism in pathogenesis of periodontal disease. It should be necessary to evaluate the relationship between genetic polymorphism and progression of periodontitis in the longitudinal study.

In our previous study for elderly population, we found that the subjects who had over than 20 remaining teeth were relevant for periodontal disease resistance (Hirotomi et al. 2002 in press). In the same group, we found significant associations between additional attachment loss during two years and smoking (Ogawa et al. 2002). Smoking is a major factor for periodontitis. In another study, IL-1 polymorphisms appeared to interact with smoking as significant risk factors for periodontal disease (Mesiel et al. 2002). However, the interaction of FcγRIIIb-NA1-NA2 polymorphism with smoking remain questionable.

The purpose of this study is to determine longitudinally how FcγRIIIb-NA1-NA2 polymorphism and smoking habit are associated with periodontal disease progression among healthy elderly people.

Material and methods

Subjects and Clinical Assessment

In 1998, we sent questionnaires to all 4,542 residents aged 70 years old in Niigata City (Japan) regarding their medical and dental health conditions. Among these, 599 persons 70 years of age agreed to undergo the medical and dental examinations (screened population), with signed informed consent to the protocol, which was reviewed and approved by the Ethics Committee of the Faculty of Dentistry, Niigata University. Four dentists performed clinical evaluations on the following items: (1) number of teeth present, (2) probing pocket depth (PPD), and (3) probing attachment level (PAL). PPD and PAL were assessed by means of a Williams probe at six sites per tooth and recorded to the nearest millimeter.

Among the screened population, 309 subjects with neither diabetes mellitus nor blood sugar ≥140mg/dL were randomly selected. In addition, subjects with more than 20 present teeth were included in the study and the FcγRIIIb-NA1/NA2 genotype was determined.

Among the subjects included in the study, the NA1 group was defined as FcγRIIIb-NA2 non-carrier (subjects with no FcγRIIIb-NA2 allele), whereas the NA2 group was defined as FcγRIIIb-NA2 carrier (subjects with at least one FcγRIIIb-NA2 allele). Number of the subjects for analysis in the study were 164 (NA1 group: 53, NA2 group: 111). Follow-up clinical surveys were carried out by PAL after three years.

Prior to data collection, the four examiners were calibrated with each examiner paired with all other examiners on 17 volunteer patients in the Faculty Hospital of Dentistry, Niigata University. The percentage of agreement ranged from 85.5 to 100% for PPD and from 70.0 to 100% for PAL. The kappa ranged from 0.77 to 1.00 for PPD and from 0.62 to 1.00 for PAL.

Determination of FcγRIIIb-NA1/NA2 Genotype and Smoking Habit

Genomic DNA was isolated from peripheral blood (Easy-DNA kit; Invitrogen, SanDiego, CA, USA) and genotyped for FcγRIIIb-NA1-NA2 by allele-specific polymerase chain-reaction, as previously described (de Haas et al. 1995, Kobayashi et al. 1997). Furthermore, a personal interview was performed to obtain the bulk of information regarding smoking habit.

Statistical Analysis

We used the Student's t test or χ^2 test to compare the clinical parameters between the

NA1 and NA2 groups at baseline when applicable. Moreover, the degree of association between periodontal disease progression and the genotype of FcγRIIIb or smoking habit was investigated by the risk for occurrence as the odds ratio with 95 % confidence interval (CI).

Periodontal disease progression in this study was defined as subjects exhibiting one or more sites with an additional attachment loss of 4 mm or more during 3 years. In addition, we evaluated the relationship between periodontal disease progression and smoking habit with the different genotype of FcγRIIIb by the risk for occurrence as the odds ratio with 95% CI or the number of sites with an additional attachment loss of 4mm or more per person.

Results

Table 1 shows the baseline variables in the NA1 and NA2 groups. The percentage of male or smoker in the NA1 and NA2 groups were 54.7% and 55.9% or 13.2% and 18.2 %, respectively. The difference in percentage of male or smoker between the NA1 and NA2 groups were not statistically significant. In addition, there were no significant difference in the clinical parameters such as number of teeth present, PPD and PAL between the NA1 and NA2 groups at baseline.

Among all the subjects, 98 (59.8%) exhibited additional attachment loss of 4 mm or more at one or more sites (≥4mm additional attachment loss) during 3 years. Mean number of sites per person exhibited additional attachment loss of 4 mm or more was 1.49 ± 4.79. Mean number of teeth lost per person during 3 years was 0.69 ± 1.79. There were no significant difference in mean number of sites with additional attachment loss of 4 mm or more, or mean number of teeth lost between the NA1 and NA2 groups (data not shown in Table).

Table 2 shows the occurrences and odds ratios between smoker and non-smoker or the NA1 and NA2 groups. Among the subjects, the frequency of ≥4mm additional attachment loss was 55.6% for smokers compared with 37.2% for the non-smokers. The odds ratio was 2.13 (CI: 0.92-4.76, p=0.080). There were no difference in the frequency of ≥4mm additional attachment loss between the NA1 and NA2 groups.

Furthermore, we evaluated the association of the FcγRIIIb-NA1-NA2 polymorphism with smoking habit by the occurrences and odds ratios (Table 3). The odds ratio of smoker increased from 2.13 for non-combination to 3.03 (CI: 1.12-8.33) for combination with FcγRIIIb-NA2 carriers (p=0.028). However, there was no increase in the odds ratio for smoker with NA2 non-carrier. As shown by the data of Figure 1, the smokers with NA2 non-carrier exhibit the highest proportion of the number of sites with ≥4mm addtional attachment loss per person as compared to all other groups. There was significant difference in the mean number of sites among 4 groups by ANOVA ($p<0.001$).

Discussion

Subjects for the study were selected among persons who did not refuse to participate in the examinations. According to the questionnaire survey, they were in good general health and did not require special care for their daily activities. None of the subjects had ever been hospitalized or institutionalized. It was pointed out that less mobile and less healthy people would be at a higher risk for periodontal disease compared to mobile and healthy people (Locker & Leak 1993, Beck et al. 1990). Therefore, it is mean that the present study concentrated on the healthier cohort of the elderly population.

In our previous study of an elderly population, we found significant associations between additional attachment loss during 2 years and smoking habit. In the same group, we also found that the subjects who had less than 20 remaining teeth were more susceptible to periodontal disease progression (Hirotomi et al. 2002 in press, Ogawa et al. 2002). Therefore, subjects with teeth number less than 20 were excluded in this study. In addition, we chose to restrict the age of subjects to 70 years to remove the influence of aging for periodontal disease progression.

In this study, we evaluated the genetic influence of FcγRIIIb on periodontal variables in relation to smoking habit. The odds ratio of smoker for periodontal disease progression increased from 2.13 for non-combination to 3.03 for combination with FcγRIIIb-NA2 carriers ($p=0.028$). However, there was no increase in the odds ratio for smoker with NA2 non-carrier. These findings suggested smoking habit to contribute to periodontal disease progression stronger in FcγRIIIb-NA2 carrier. That is to say that FcγRIIIb may be exerting a influence on the occurrence of periodontal disease progression through smoking habit.

The previous reports indicated a strong association between smoking and periodontal disease progression. Nicotine, the chief toxious substance found in tobaccos, and its byproducts have a vasoconstrictive effect, not only on peripheral circulation, but also on coronary, placental, and gingival blood vessels (González et al. 1996). Tobacco use may reduce the functional activity as chemotaxis and phagocytosis of blood and tissue polymorphonuclear leukocytes (Persson et al. 2000, Pabst et al. 1995). Smoking had significant systemic effect on IgG levels as well (Fredriksson et al. 2002). Furthermore, the results in this study might show that there is the connection between the condition with the positive genotype (FcγRIIIb-NA1-NA2 or FcγRIIIb-NA2-NA2 genotype) and smoking. In another study, IL-1 polymorphisms appeared to interact with smoking as significant risk factors for periodontal disease in the subjects with positive genotype (subjects bearing the