Title:

Periodontitis and health-related quality of life in hemodialysis patients

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ABSTRACT

Background and Objective: Periodontitis is common among dialysis patients. The current cross-sectional study aimed to explore associations between periodontitis and health-related quality of life (HRQoL) among hemodialysis patients.

Methods: Data from 188 dentate patients undergoing hemodialysis between May and July 2008 at a medical center in Kitakyushu city, Japan, were analyzed while applying modified Centers for Disease Control and Prevention/American Academy of Periodontology periodontitis case definitions to categorize the participants into the following three groups: severe, moderate, and no/mild periodontitis, respectively. HRQoL was assessed by the Medical Outcome Study Short-Form 36-Item Health Survey (SF-36) where a higher score indicates better health status. Associations between periodontitis groups and the eight health domains of SF-36 were evaluated using general linear models that were adjusted for age, sex, underlying cause of dialysis, duration of dialysis, comorbidities, serum biomarkers, body mass index, smoking status, and alcohol use.

Results: Among the 188 participants, 18 (9.6%) had severe, 100 (53.2%) had moderate, and the remaining 70 (37.2%) had no/mild periodontitis. Compared with the participants with no/mild periodontitis, those with severe periodontitis had worse scores in the following five of eight SF-36 health scales: physical functioning, role physical, vitality, social functioning, and mental health ($P<0.05$).

Conclusion: The findings suggest an independent relationship between severe periodontitis and decreased HRQoL among dialysis patients.

INTRODUCTION

The estimated number of dialysis patients in Japan was over three hundred thousand in 2010, and this number has continued to increase, reflecting increasing prevalence of diabetes and hypertension (1). Accumulating evidence suggests that decreased kidney function may be associated with poor oral health, including periodontitis (2, 3). Sharma *et al.* compared oral health status in people with chronic kidney disease (CKD) participating in an ongoing observational cohort study (the Renal Impairment in Secondary Care [RIISC] study) and a regional representative population-based sample of participants in the 2009 Adult Dental Health Survey (ADHS). They found that RIISC CKD patients had a significantly higher risk of periodontitis compared with ADHS participants (2). Similarly, Teratani *et al.* found that hemodialysis patients had poorer periodontal health than a regional representative population-based sample (3).

Oral diseases frequently constitute a chronic state and are directly and indirectly associated with physical, psychological, and social functioning; therefore, they can have negative impacts on patients' quality of life (QOL) (4-7). Previous studies reported that oral diseases were significantly associated with health-related QOL (HRQoL) among patients attending private dental offices (8), community-based older individuals (9, 10), or individuals with diseases related to oral health, such as diabetes (11) and chronic obstructive pulmonary disease (12). However, the impact of periodontitis on general HRQoL among dialysis patients has not yet been fully investigated. HRQoL is an important marker of how disease affects patients' lives. Because worse general HRQoL in dialysis patients was found to be associated with greater morbidity and mortality (13),

it is important to investigate the factors associated with general HRQoL. If an association between periodontal health and general HRQoL was found, such information in turn may lead to new strategies to maintain or improve patients' wellbeing through appropriate oral health education, prevention, and treatment programs. Therefore, this study was planned with the purpose of assessing whether periodontitis was associated with general HRQoL among hemodialysis patients.

METHODS

Study population and examination

This study was designed as a cross-sectional survey and conducted at a single medical institution in Kitakyushu city, Japan. Between May and July 2008, 347 sequential patients undergoing hemodialysis were invited to participate the study. Of these, 221 (63.7% [221/347]) agreed. These individuals underwent oral examination just before a session of hemodialysis therapy and were surveyed using a questionnaire about HRQoL and health behavior. All study participants gave written informed consent to being included in the study.

This study was conducted in accordance with the guidelines laid down in the Declaration of Helsinki and was approved by the Ethics Committee of Kyushu Dental University.

Periodontal examinations were performed by four calibrated dentists. The periodontal health parameters including clinical attachment loss (CAL) and periodontal probing depth (PPD) measured by placing a periodontal probe at the mesio-buccal and mid-buccal sites of each tooth, except for third molars and root remnants. The examiners were calibrated before the survey using volunteer patients in the Kyushu Dental University Hospital. The interexaminer reliabilities of CAL and PPD within 1 mm were confirmed using percentage agreement (CAL = 83.3% to 87.5%, PPD = 86.6% to 95.9%).

Using modified Centers for Disease Control and Prevention/American Academy of Periodontology (CDC/AAP) case definitions (14), study participants were categorized

into three groups: severe periodontitis was defined as ≥2 sites with CAL ≥6 mm (not on the same tooth) and ≥1 site with PD ≥5 mm; moderate periodontitis was defined as ≥2 sites with CAL ≥4 mm (not on the same tooth), or ≥2 sites with PD ≥5 mm (not on same tooth); and no/mild periodontitis was defined as no evidence of severe or moderate periodontitis. The modification was necessary because the CDC/AAP periodontitis case definitions use exactly the four proximal sites, but we only examined one proximal (mesio-buccal) and one mid-buccal site.

HRQoL was assessed using the Medical Outcome Study Short-Form 36-Item Health Survey (SF-36) version 2, which is a commonly used generic HRQoL scale. The validity of the Japanese SF-36 is reported elsewhere (15). It is designed to assess the following eight health scales: physical functioning (PF), role physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role emotional (RE), and mental health (MH). Each scale yields a score of 0 to 100, where a high score indicates better health/more favorable health state. Detailed descriptions of each SF-36 scale are presented in Appendix Table 1. The raw scores of eight health scales can be converted into Norm-Based Scores (NBSs) using Japanese norm-based scoring algorithms. A NBS is a normalized score with a mean of 50 and standard deviation (SD) of 10 (16). The use of the NBS simplifies the interpretation of the results of each subscale of the SF-36 because it eliminates the need to evaluate the difference between the raw score and national standard of each subscale.

A standardized questionnaire was used to obtain participants' health behavior including smoking status and alcohol consumption. Information on participants' age,

sex, underlying cause of hemodialysis, duration of hemodialysis, comorbidities (hypertension, diabetes, depression, ischemic heart disease, and stroke), levels of serum biomarkers (albumin and non-high-density lipoprotein cholesterol [non-HDL-C]), and body mass index (BMI) was abstracted from medical records. Hypoalbuminemia was defined as albumin < 3.6 g/dL. High non-HDL-C was defined as non-HDL-C ≥ 150 mg/dL.

Statistical Analyses

Comparisons of selected characteristics among the three clinically assessed periodontitis groups were performed using analysis of variance or Kruskal–Wallis test for continuous variables, depending on distribution, and the Chi-square test for categorical variables.

Univariable and multivariable analyses of the association between periodontitis and eight health scales of SF-36 was conducted using general linear models. The eight health scales of SF-36, which were converted into NBSs, were included as the main outcomes for the analyses. The principal exposure variable was periodontal health status based on a clinical periodontal examination. Comprehensive multivariable models for the eight health scales included adjustment for age (continuous), sex (categories: male or female), underlying cause of dialysis (categories: diabetic nephropathy, chronic glomerulonephritis, or other), duration of dialysis (continuous), comorbidities (categories: positive or negative), abnormality in serum biomarkers (categories: positive or negative), BMI (continuous), smoking status (categories: current smoker, previous smoker, or never smoked), and alcohol use (categories: ≥ 20 g/day or < 20 g/day

ethanol). Effect modifications by sex were evaluated using interaction terms. Interaction terms found not to be statistically significant were not included in the model.

The level of significance for predictor variables was set at $\alpha=0.05$. All calculations and statistical analyses were performed using the statistical software package STATA (version 14) (Stata Corp., TX, USA.).

RESULTS

Among those who entered the study (n=221), 24 individuals who had <2 teeth and 9 individuals who had incomplete data were excluded. Ultimately, 188 hemodialysis patients (age range = 28 to 93 years) were selected and included in the analyses. Among these 188 study participants, 18 (9.6%) were classified as having severe periodontitis, 100 (53.2%) had moderate periodontitis, and the remaining 70 (37.2%) had no/mild periodontitis.

The characteristics of the study population stratified by periodontal health status are presented in Table 1. Besides the lower number of teeth and poorer periodontal health parameters, age, diabetes, and smoking were seen in association with periodontitis (P<0.05).

SF-36 health profiles of study participants are presented in Figure 1. Study participants had diminished HRQoL compared with the general Japanese population. Mean SF-36 scores of study participants in this study were significantly (P<0.05) lower than Japanese norms, which were presented in the Manual of the SF-36 Japanese version (16), for all eight scales measured in this study.

Table 2 shows the association between periodontitis and the eight health scales of SF-36. There were no interactions of periodontitis with sex. Furthermore, when we performed analyses stratified by sex, the pattern of results was similar to that for the non-stratified analyses (Results not shown). Therefore, we reported the associations for both sexes combined. Significant negative associations of periodontitis was found with PF, RP, VT, SF, and MH. The regression coefficients of severe periodontitis in the

multivariable models, compared with no/mild periodontitis, were -14.2 (95% confidence interval [CI] = -24.2 to -4.3) for PF, -13.0 (95% CI = -25.2 to -0.7) for RP, -6.3 (95% CI = -12.4 to -0.2) for VT, -7.5 (95% CI = -14.3 to -0.6) for SF, and -6.8 (95% CI = -12.6 to -1.0) for MH. These results suggest that severe periodontitis was significantly and independently associated with lower scores of SF-36 for each of these five health status scales. In addition, in the multivariable model, advanced age was associated with decreases in PF and RP, longer duration of hemodialysis was associated with decreases in BP and MH, diabetes was associated with a decrease in GH and MH, depression was associated with decreases in SF and MH, ischemic heart disease was associated with decreases in RP and RE, stroke was associated with decreases in SF and MH, hypoalbuminemia was associated with decreases in PF, VT, SF, RE, and MH, and higher BMI was associated with an increase in GH (Appendix Table 2).

DISCUSSION

All eight scales of the SF-36 reported by the study participants were significantly lower than Japanese norms, which indicated hemodialysis has a negative impact on HRQoL. These findings are in line with previous studies (17-19). Diabetic nephropathy is the primary cause of end-stage renal disease (ESRD) requiring dialysis (20). Hemodialysis patients are at risk of developing other medical conditions including malnutrition, depression, and cardiovascular disease (20, 21). These health problems can adversely affect patients' activities of daily living (ADL) and HRQoL. Disability in ADL is highly prevalent in individuals with ESRD compared with the general population (22). The lower PF score of SF-36 in this study population compared with the Japanese general population indicates that they perceived limitations in physical activities.

Periodontitis was found to be significantly associated with HRQoL among hemodialysis patients, even after adjusting for other important health characteristics. Study participants with severe periodontitis, compared with those with no/mild periodontitis, had worse scores in SF-36 health scales of PF, RP, VT, SF, and MH, which suggests that hemodialysis patients with severe periodontitis perceived limitations in performing physical activities, problems with daily activities as a result of physical health, fatigue, interference with normal social activities due to physical and emotional problems, and psychological distress. To the best of our knowledge, this is the first study to demonstrate the association between clinical periodontal status and generic HRQoL measures in hemodialysis patients.

Decreased kidney function is associated with an immune dysfunction state that is

known to contribute to the high prevalence of infections among these individuals (23). Thus, decreased kidney function may predispose to periodontitis, a chronic bacterial infection/overgrowth (24). Moreover, kidney failure leads to metabolic bone disease. It is known that decreased kidney function increases osteoclast activity leading to bone turnover, and this may influence bone metabolic parameters (25). These pathophysiological changes may also explain the potential association between kidney failure and periodontitis.

Previous studies have demonstrated that poor oral health status had negative impacts on HRQoL (8, 10-12), and findings from the current study agree with these results. People with periodontitis are at increased risk of oral pain and tooth loss, which leads to limited oral function such as eating, swallowing, and speaking (26). Poor oral health is related to decreased functional ability and physical fitness and decreased dietary intakes and variety (27-29). Periodontitis also causes halitosis, which can negatively impact on daily life activities such as socializing and communication with other people (30). In addition, periodontitis and tooth loss causes embarrassment, negatively affecting appearance and self-esteem (31, 32), and can restrict social interactions. Furthermore, large epidemiological studies indicates that poor oral health could have an adverse effect on general health in people with reduced kidney function. For instance, periodontitis and tooth loss were demonstrated to be associated with higher mortality (33, 34). These problems related to periodontitis can have negative impacts on perceived general health and be reflected in deterioration in HRQoL measured by means of the SF-36. Unfortunately, our study had a cross-sectional design, which prevented us

from assessing a temporal relationship and establishing causality.

There are several other limitations to the present study. First, because other information previously recognized as relevant to HRQoL, such as education, income, and social activity (35, 36), was not collected, a number of other potentially important confounders could not be included in the analyses. Residual confounding remains a risk. Second, our study participants were recruited at a single medical institution so that extrapolation of the findings to other populations is limited. Third, even though all non-third molar teeth present were examined, periodontal health was assessed by partial mouth examination of only two buccal sites per tooth. Therefore, it is likely that the prevalence of periodontitis was underestimated, as some researchers have expressed concern over the discrepancy between a partial mouth examination and the ‘‘gold-standard’’ full-mouth examination (37). This potentially gross underestimation is due to the fact that periodontal tissue breakdown is site-specific and does not occur symmetrically within the dentition nor even around a tooth, and hence prevents any reliable statistical weighting of the measurements recorded to accurately estimate the actual presence of periodontitis. On the other hand, despite such purported underestimation and misclassification of periodontitis as cases were categorized in less severe classes, our analyses still identified significant associations that probably would have been even more pronounced with measures from a gold-standard periodontal examination. This would further support the concept of strong associations between periodontal health and HRQoL.

In summary, periodontitis, especially its severe form, is significantly associated with

decreased HRQoL among hemodialysis patients. These findings support the importance of good oral health to general HRQoL in hemodialysis patients. Future multi-center, longitudinal studies that apply the gold standard periodontal examination protocol as well as collect more information on potential confounders are needed.

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References

1. Wakasugi M, Kazama JJ, Narita I. Anticipated increase in the number of patients who require dialysis treatment among the aging population of Japan. Ther Apher Dial. 2015;19(3):201-6.
2. Sharma P, Dietrich T, Sidhu A, Vithlani V, Rahman M, Stringer S, et al. The periodontal health component of the Renal Impairment In Secondary Care (RIISC) cohort study: a description of the rationale, methodology and initial baseline results. J Clin Periodontol. 2014;41(7):653-61.
3. Teratani G, Awano S, Soh I, Yoshida A, Kinoshita N, Hamasaki T, et al. Oral health in patients on haemodialysis for diabetic nephropathy and chronic glomerulonephritis. Clin Oral Investig. 2013;17(2):483-9.
4. Kandelman D, Petersen PE, Ueda H. Oral health, general health, and quality of life in older people. Spec Care Dentist. 2008;28(6):224-36.
5. Hollister MC, Weintraub JA. The association of oral status with systemic health, quality of life, and economic productivity. J Dent Educ. 1993;57(12):901-12.
6. Chen MS, Hunter P. Oral health and quality of life in New Zealand: a social perspective. Soc Sci Med (1982). 1996;43(8):1213-22.
7. Buset S, Walter C, Friedmann A, Weiger R, Borgnakke WS, Zitzmann NU. Are periodontal diseases really silent? a systematic review of their effect on quality of life. J Clin Periodontol. 2016;43(4), 333-44.
8. Naito T, Naito M, Miyaki K, Sugiyama S, Fujiki S, Habu S, et al. Oral health on the quality of life of dental patients : a cross-sectional survey among dental patients

attending private practices in Japan. J Fkuoka Dent Coll. 2010;36(4):139-47.

9. Wang TF, Chou C, Yu S. Assessing the effects of oral health-related variables on quality of life in Taiwanese adults. Qual Life Res. 2013;22(4):811-25.
10. Ng SK, Leung WK. Oral health-related quality of life and periodontal status. Community Dent Oral Epidemiol. 2006;34(2):114-22.
11. Sandberg GE, Wikblad KF. Oral health and health-related quality of life in type 2 diabetic patients and non-diabetic controls. Acta Odontol Scand. 2003;61(3):141-8.
12. Zhou X, Wang Z, Song Y, Zhang J, Wang C. Periodontal health and quality of life in patients with chronic obstructive pulmonary disease. Respir Med. 2011;105(1):67-73.
13. Lowrie EG, Curtin RB, LePain N, Schatell D. Medical Outcomes Study Short Form-36: a consistent and powerful predictor of morbidity and mortality in dialysis patients. Am J Kidney Dis. 2003;41(6):1286-92.
14. Page RC, Eke PI. Case definitions for use in population-based surveillance of periodontitis. J Periodontol. 2007;78(7 Suppl):1387-99.
15. Fukuhara S, Ware JE, Jr., Kosinski M, Wada S, Gandek B. Psychometric and clinical tests of validity of the Japanese SF-36 health survey. J Clin Epidemiol. 1998;51(11):1045-53.
16. Fukuhara S, Suzukamo Y. Manual of SF-36v2 Japanese version. Institute for Health Outcomes & Process Evaluation Research, Kyoto, 2004.
17. Evans RW, Manninen DL, Garrison LP, Jr., Hart LG, Blagg CR, Gutman RA, et al. The quality of life of patients with end-stage renal disease. N Engl J Med.

1985;312(9):553-9.

18. Merkus MP, Jager KJ, Dekker FW, Boeschoten EW, Stevens P, Krediet RT. Quality of life in patients on chronic dialysis: self-assessment 3 months after the start of treatment. The Necosad Study Group. Am J Kidney Dis. 1997;29(4):584-92.
19. Perlman RL, Finkelstein FO, Liu L, Roys E, Kiser M, Eisele G, et al. Quality of life in chronic kidney disease (CKD): a cross-sectional analysis in the Renal Research Institute-CKD study. Am J Kidney Dis. 2005;45(4):658-66.
20. Akizawa T. Current status of dialysis therapy and related clinical guidelines in Japan. JMAJ. 2010;53(3):185-7.
21. O'Connor NR, Corcoran AM. End-stage renal disease: symptom management and advance care planning. Am Fam Physician. 2012;85(7):705-10.
22. McAdams-Demarco MA, Law A, Garonzik-Wang JM, Gimenez L, Jaar BG, Walston JD, et al. Activity of daily living disability and dialysis mortality: better prediction using metrics of aging. J Am Geriatr Soc. 2012;60(10):1981-2.
23. Kato S, Chmielewski M, Honda H, Pecoits R, Matsuo S, Yuzawa Y, et al. Aspects of immune dysfunction in end-stage renal disease. Clin J Am Soc Nephro. 2008;3(5):1526-33.
24. Fisher MA, Taylor GW, West BT, McCarthy ET. Bidirectional relationship between chronic kidney and periodontal disease: a study using structural equation modeling. Kidney Int. 2011;79(3):347-55.
25. Couttenye MM, D'Haese PC, Verschoren WJ, Behets GJ, Schrooten I, De Broe ME. Low bone turnover in patients with renal failure. Kidney Int Suppl. 1999;73:S70-6.

26. Furuta M, Yamashita Y. Oral health and swallowing problems. Curr Phys Med Rehabil Rep. 2013;1:216-22.
27. Hamalainen P, Rantanen T, Keskinen M, Meurman JH. Oral health status and change in handgrip strength over a 5-year period in 80-year-old people. Gerodontology. 2004;21(3):155-60.
28. Iwasaki M, Taylor GW, Manz MC, Yoshihara A, Sato M, Muramatsu K, et al. Oral health status: relationship to nutrient and food intake among 80-year-old Japanese adults. Community Dent Oral Epidemiol. 2014;42(5):441-50.
29. Iwasaki M, Kimura Y, Yoshihara A, Ogawa H, Yamaga T, Takiguchi T, et al. Association between dental status and food diversity among older Japanese. Community Dent Health. 2015;32(2):104-10.
30. Azodo CC, Onyeagba MI, Odai CD. Does concern about halitosis influence individual's oral hygiene practices? Niger Med J. 2011;52(4):254-9.
31. Petersen PE, Yamamoto T. Improving the oral health of older people: the approach of the WHO Global Oral Health Programme. Community Dent Oral Epidemiol. 2005;33(2):81-92.
32. Abrahamsson KH, Wennstrom JL, Hallberg U. Patients' views on periodontal disease; attitudes to oral health and expectancy of periodontal treatment: a qualitative interview study. Oral Health Prev Dent. 2008;6(3):209-16.
33. Palmer SC, Ruospo M, Wong G, Craig JC, Petruzzi M, De Benedittis M, et al. Dental health and mortality in people with end-stage kidney disease treated with hemodialysis: a multinational cohort study. Am J Kidney Dis. 2015;66(4):666-76.

34. Ricardo AC, Athavale A, Chen J, Hampole H, Garside D, Marucha P, et al. Periodontal disease, chronic kidney disease and mortality: results from the third National Health and Nutrition Examination Survey. BMC Nephrol. 2015;16:97.
35. Brennan SL, Williams LJ, Berk M, Pasco JA. Socioeconomic status and quality of life in population-based Australian men: data from the Geelong Osteoporosis Study. Aust N Z J Public Health. 2013;37(3):226-32.
36. Nilsson J, Rana AK, Kabir ZN. Social capital and quality of life in old age: results from a cross-sectional study in rural Bangladesh. J Aging Health. 2006;18(3):419-34.
37. Eke PI, Thornton-Evans GO, Wei L, Borgnakke WS, Dye BA. Accuracy of NHANES periodontal examination protocols. J Dent Res. 2010;89(11):1208-13.

Table 1. Characteristics of the study participants by periodontitis status (n = 188).

	Overall	Periodontitis category			
		No/Mild	Moderate	Severe	
	n = 188	n = 70	n = 100	n = 18	P^a
Oral health status					
Number of teeth, median (IQR)	24 (15-27)	26 (21-28)	23 (12-26)	17 (11-25)	**<0.01**
Mean PPD (mm), median (IQR)	1.7 (1.5-2.0)	1.6 (1.4-1.7)	1.8 (1.6-2.0)	2.4 (2.1-2.8)	**<0.01**
Mean CAL (mm), median (IQR)	2.4 (1.1-3.5)	1.0 (0.3-1.5)	2.8 (2.2-3.7)	4.1 (3.6-4.9)	**<0.01**
Age and sex					
Age, mean (SD)	63.6 (12.8)	60.5 (13.6)	65.9 (12.3)	63.1 (10.6)	**0.03**
Sex, n (%)					
Male	118 (62.8)	37 (52.9)	67 (67.0)	14 (77.8)	0.07
Female	70 (37.2)	33 (47.1)	33 (33.0)	4 (22.2)	
Health status and health behavior					
Underlying cause of hemodialysis, n (%)					
Diabetic nephropathy	48 (25.5)	12 (17.1)	30 (30.0)	6 (33.3)	0.24
Chronic glomerulonephritis	99 (52.7)	44 (62.9)	47 (47.0)	8 (44.4)	
Others	41 (21.8)	14 (20.0)	23 (23.0)	4 (22.2)	
Duration of hemodialysis (year), median (IQR)	7 (3-16)	8.5 (4-17)	6 (3-16)	5.5 (2-14)	0.49
Medical diagnosis, n (%)					
Hypertension	71 (37.7)	30 (42.9)	37 (37.0)	4 (22.2)	0.27
Diabetes	65 (34.6)	15 (21.4)	41 (41.0)	9 (50.0)	**0.01**
Depression	5 (2.7)	2 (2.9)	2 (2.0)	1 (5.6)	0.68
Medical history, n (%)					
Ischemic heart disease	32 (17.0)	11 (15.7)	18 (18.0)	3 (16.7)	0.93
Stroke	42 (22.3)	14 (20.0)	22 (22.0)	6 (33.3)	0.48
Serum biomarker levels					
Albumin < 3.6 g/dL	73 (38.8)	22 (31.4)	44 (44.0)	7 (38.9)	0.25
Non-high-density lipoprotein cholesterol ≥ 150 mg/dL	34 (18.1)	15 (21.4)	18 (18.0)	1 (5.6)	0.30
BMI (kg/m^2), median (IQR)	20.7	20.7 (18.8-22.3)	20.7 (19.1-22.5)	19.8 (18.4-21.3)	0.50

	(18.9-22.3)				
Smoking status, *n* (%)					
Current smoker	29 (15.4)	7 (10.0)	18 (18.0)	4 (22.2)	**0.04**
Previous smoker	73 (38.8)	21 (30.0)	43 (43.0)	9 (50.0)	
Never smoked	86 (45.7)	42 (60.0)	39 (39.0)	5 (27.8)	
Alcohol consumption, *n* (%)					
Ethanol ≥ 20 g/day	30 (16.0)	10 (14.3)	16 (16.0)	4 (22.2)	0.71

BMI = body mass index, CAL = clinical attachment loss, IQR = interquartile range, PPD = periodontal probing depth, SD = standard deviation,

[a]*P* value for the comparison among the three periodontitis groups.

Bolded = statistically significant at $P<0.05$.

Table 2. Crude and adjusted associations of periodontal health status with SF-36 health scales (n = 188).

	SF-36 health scales							
	PF		RP		BP		GH	
	Crude	Adjusted[a]	Crude	Adjusted[a]	Crude	Adjusted[a]	Crude	Adjusted[a]
Periodontitis (vs. No/Mild)								
Moderate	**-8.1**	-2.4	-7.0	-2.8	-1.7	-0.4	**-3.9**	-3.1
	(-14.5, -1.7)	(-8.5, 3.6)	(-14.1, 0.2)	(-10.3, 4.7)	(-5.2, 1.9)	(-4.2, 3.4)	**(-7.0, -0.7)**	(-6.5, 0.3)
Severe	**-16.4**	**-14.2**	**-15.5**	**-13.0**	-1.5	-1.9	-2.2	-1.2
	(-27.3, -5.6)	**(-24.2, -4.3)**	**(-27.7, -3.4)**	**(-25.2, -0.7)**	(-7.6, 4.5)	(-8.1, 4.3)	(-7.5, 3.2)	(-6.8, 4.4)

	VT		SF		RE		MH	
	Crude	Adjusted[a]	Crude	Adjusted[a]	Crude	Adjusted[a]	Crude	Adjusted[a]
Periodontitis (vs. No/Mild)								
Moderate	**-4.1**	-3.1	-2.4	-1.3	**-7.5**	-3.3	-0.9	0.4
	(-7.5, -0.7)	(-6.8, 0.7)	(-6.4, 1.6)	(-5.5, 2.9)	**(-14.0, -1.0)**	(-10.1, 3.5)	(-4.2, 2.5)	(-3.1, 4.0)
Severe	**-7.0**	**-6.3**	**-9.4**	**-7.5**	**-11.7**	-8.7	**-8.2**	**-6.8**
	(-12.9, -1.2)	**(-12.4, -0.2)**	**(-16.2, -2.7)**	**(-14.3, -0.6)**	**(-22.7, -0.6)**	(-19.9, 2.4)	**(-13.9, -2.6)**	**(-12.6, -1.0)**

[a]Adjusted for age, sex, underlying cause of hemodialysis, duration of hemodialysis, comorbidity, serum biomarkers, body mass index, smoking status, and alcohol consumption.

Numbers in the table represent parameter estimates (95% confidence intervals) for each SF-36 scale in the model.

Bold text indicates statistically significant difference (P<0.05).

SF-36 = Medical Outcome Study Short-Form 36-item health survey.

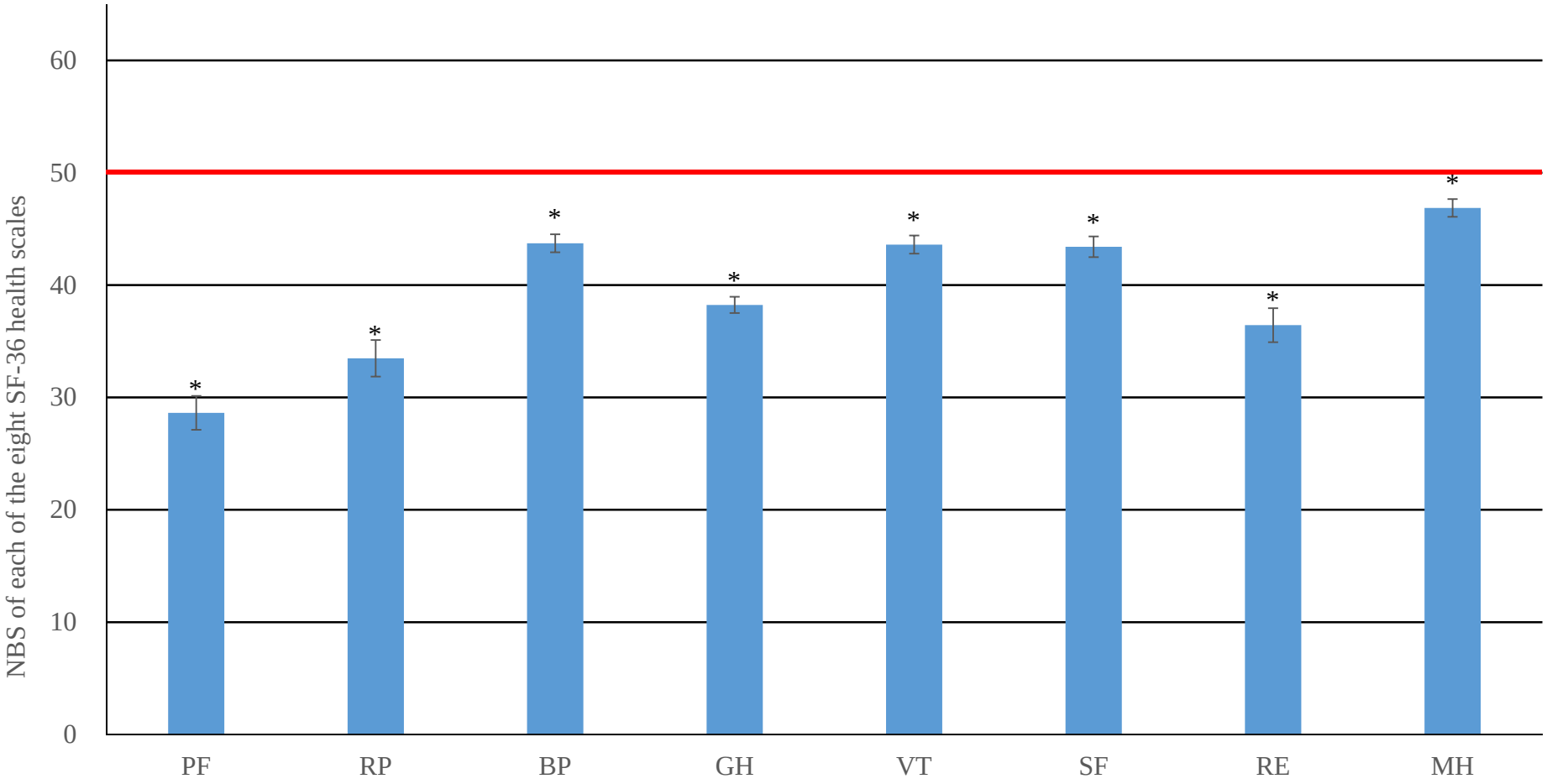
Figure legend:

Figure 1. Mean (SE) SF-36 health profile score by health domains/scales and compared to the norm of 50 in Japanese adults (*n* = 188).

BP = Bodily pain, GH = General health, MH = Mental health, PF = Physical functioning, RE = Role emotional, RP = Role physical, SE = standard error, SF = Social functioning, SF-36 = Medical Outcome Study Short-Form 36-item health survey, VT = Vitality;

Vertical bars represent SE

*significantly different from the norm of 50 in Japanese adults.



Mean	28.6	33.5	43.7	38.2	43.6	43.4	36.4	46.9
SE	1.5	1.6	0.8	0.7	0.8	0.9	1.5	0.8