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The Role of Physiological Markers of Health in the Association between Demographic Factors and Periodontal Disease

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Abstract

Objectives—This study examines whether the association between periodontal disease and demographic factors is mediated by physiological measures of health.

Background—Age is highly related to oral health status. The higher prevalence of oral disease within sub-groups of the population may reflect a tendency towards “early aging” and dysregulation of multiple physiological systems.

Methods—Logistic regression was used to examine whether biomarkers and demographic factors, such as SES and race/ethnicity, were associated with periodontal disease, and then whether the strength of these relationships could be attributed to associations between demographic variables and physiological measures of systemic health.

Results—Periodontal disease was associated with measures of SES and race/ethnicity. Furthermore, one unit increases in CMV optical density, CRP, and HbA1c were associated with a 25% (OR=1.25; 95% CI: 1.14–1.36), 13% (OR: 1.13; 95% CI: 1.03–1.24), and 19% (OR: 1.19; 95% CI: 1.12–1.27) increased likelihood of periodontal disease, respectively. However, when biomarkers and sociodemographic variables were both included in the model, their associations with periodontal disease were significantly reduced or eliminated.

Conclusions—The risk of periodontal disease is higher among blacks and/or low income individuals; however, these associations appear to be partly due to the greater probability of elevated levels of CRP, CMV, or HbA1c among these groups.

Keywords

Periodontal disease; Cytomegalovirus; Inflammation

Introduction

With the demographic shift towards an aging society, further understanding of the relationships between age associated changes and oral disease has become an important research topic in public health. The pervasiveness of oral disease has implications for other health conditions, given its association with subsequent stroke, cardiovascular disease, diabetes, osteoporosis and mortality^{1–5}. In addition, oral disease has been shown to have negative economic, social and psychological impact, which may ultimately lead to decreases in quality of life and well being^{6,7}.

Age is an important factor in oral health status. Approximately one third of non-institutionalized adults, age 65 and over, reported edentulism in 1993 and one-third of those with natural teeth had untreated dental cavities⁸. The severity and prevalence of periodontal

disease has also been shown to increase with age⁹. While the prevalence of periodontal disease for individuals ages 25–34 is only 6%, it is over 40% for those aged 65 and over¹⁰. However, age differences are changing as younger cohorts demonstrate a transformation in our ability to prevent or combat a number of oral health problems¹¹. Nevertheless, while the prevalence of early life oral health problems has been declining over time, stark differences exist between racial and ethnic subgroups of the population as well as by socioeconomic status (SES)^{12, 13}.

The association between aging and oral health is complex and multifaceted. Declining oral health status over the lifespan may be partly attributed to physiological changes resulting from the breakdown of various biological systems and the onset of diseases. For instance, Cytomegalovirus (CMV), an indicator of immune system health and functioning at older ages, is thought to increase the risk for periodontal disease through the release of tissue-destructive cytokines, the initiation of cytotoxic events, and an overgrowth of pathogenic periodontal bacteria^{14–16}. Elevated C-reactive protein (CRP), a marker of systemic inflammation, related to cardiovascular conditions and mortality, has also been shown to increase the risk for development of periodontal disease and oral health^{17–23}. Blood glucose levels may also be related to periodontal disease. For instance, individuals with diabetes are at increased risk of periodontal disease²⁴ and the occurrence of severe periodontal disease has been shown to increase blood sugar, thus further exacerbating the negative complications associated with diabetes.

This study aims to examine how the association between demographic predictors of periodontal disease is mediated by also examining biological measures of inflammation, immune function, and glucose clearance. We hypothesize that the increased risk of periodontal disease among various racial/ethnic and SES populations may be due to physiological dysregulation and compromised function of multiple biological systems.

Materials and Methods

Study Population

The study population included adults ages 20 and over from the third National Health and Nutrition Examination Survey (NHANES III), a nationally representative, cross-sectional study conducted by the National Center for Health Statistics (NCHS)²⁵ between 1988 and 1994. NHANES III was based on a complex, multi-stage, stratified, clustered sample design of the civilian, non-institutionalized population. Individuals over age 60, African Americans, Mexican Americans and low-income white Americans were oversampled to ensure appropriate sample sizes for analysis. Data for NHANES III were collected during at-home interviews, and dentist and physician examinations taking place in a Mobile Examination Center (MEC). Further details on recruitment, procedures and study design are available through the Centers for Disease Control and Prevention²⁵. The total sample size for the adult population in NHANES III who took part in the MEC was 16,573, of which (n=11,295) had surplus sera available and were included in our analysis.

Periodontal Disease

Periodontal disease was operationalized using the definition developed by the CDC Periodontal Disease Surveillance Workgroup²⁶. Respondents with severe (≥ 2 interproximal sites with loss of attachment ≥ 6 mm and ≥ 1 interproximal sites with pocket depth ≥ 5 mm) or moderate (≥ 2 interproximal sites with loss of attachment ≥ 4 mm or ≥ 2 interproximal sites with pocket depth ≥ 5 mm) periodontitis are classified as having periodontal disease in our analysis. Reported loss of attachment values were based on two measurements taken at each site: the distance between the cement-enamel junction and the

free gingival margin, and the distance from the bottom of the sulcus (pocket depth) to the free gingival margin. Diagnostic criteria were intentionally conservative to ensure inter-rater reliability. When a classification of periodontal disease was not agreed upon, the milder one was selected²⁵.

Physiological Mechanisms

In order to examine links between oral health and physiological mechanisms, levels of three indicators of physiological status were included in the analysis—C-reactive Protein (CRP), glycated hemoglobin (HbA1c), and cytomegalovirus (CMV). Serum CRP was used as a non-specific indicator of general levels of inflammation. For NHANES III, high sensitivity CRP assays were performed on blood samples using a Behring Nephelometer²⁴. HbA1c, which is often used to screen for and measure control of diabetes, was measured using a Diamat Analyzer System. Cytomegalovirus (CMV) antibody testing was done on stored sera specimens from NHANES III, and IgG optical density values were reported. CMV optical density was top-coded at 3.01 by NHANES III.

Socio-Demographic Characteristics

Age, race/ethnicity, income, and sex were self-reported and included as independent predictors of oral health status. Age was top-coded at 90 in the data set by NHANES to protect confidentiality of respondents. Dummy variables were created to classify subjects into three race/ethnicity categories: non-Hispanic whites, non-Hispanic blacks, and Hispanics, most of whom are Mexican Americans. In analyses, Non-Hispanic whites are used as the reference category. Socioeconomic status was indicated by the poverty income ratio (PIR). The PIR is calculated as the ratio of the midpoint of a subject's reported annual family income category to the current federal poverty threshold for a family of the reported size and composition (Bureau of the Census, US Department of Commerce). It is categorized into four categories: below poverty (PIR<1), low income (PIR=1–1.99), normal income (PIR ≥ 2), and unknown income. The last category includes those who did not disclose their annual family income. This category was included in order to avoid the sample selection effect resulting from eliminating those who do not report income. Lastly, sex was indicated with a dichotomous variable, with females coded as 1 and males as 0.

Statistical Analysis

SAS statistical software package version 9.2 was used for all analyses. Three logistic regression models were used to examine whether demographic factors, including SES and race/ethnicity (Model 1), and biomarkers (Model 2) were associated with periodontal disease, and whether the power of such relationships could be attributed to associations between demographic variables and physiological measures of systemic health (Model 3). All analysis controlled for age and sex, and utilized sample weights to make results representative of the U.S. non-institutionalized population and SAS Survey procedures to account for the complex sampling procedures in NHANES III.

Results

Sample Description

Just over half the sample was female (51.2%) (Table 1). Most subjects were non-Hispanic white (79.1%); non-Hispanic blacks made up 10.8% of the sample, and Mexican Americans 10.1%. Approximately two-thirds of the sample (64.4%) had an annual family income that was at least two times the poverty level, while 18.9% were just above the poverty level (PIR between 1–1.99) and 11% were below the poverty level. Subjects ranged in age from 20–90 years, with a mean of 42 years. Periodontal disease was present in 10.1% of subjects. Mean

CRP for the sample was 3.9 mg/L (SD=0.79); mean CMV optical density was 1.66 (SD=1.65); and mean HbA1c was 5.31% (SD=1.23).

As shown in Table 2, CRP, CMV, HbA1c, and periodontal disease were highest in non-Hispanic blacks followed by Hispanics and non-Hispanic whites. Mean comparisons using a Bonferroni adjustment revealed that, for CRP and HbA1c, all three race/ethnicity groups had significantly different means. Non-Hispanic whites had significantly lower mean CMV optical density than Hispanics and non-Hispanic blacks. However, the means for the two minority groups did not significantly differ from each other.

Those below the poverty level had the highest levels of CMV optical density and periodontal disease, while those who did not disclose their income had the highest levels of CRP and HbA1c. (Table 3). Subjects with incomes at least twice the poverty limit had significantly lower mean CRP and CMV optical density than those with lower incomes or who did not disclose income. Subjects in the highest income group also had significantly lower HbA1c than both the group below the poverty limit and those with unknown income. Subjects with no PIR score also had significantly higher HbA1c than subjects with PIR between 1–1.99; however, neither of those groups differed significantly from subjects below the poverty level.

Associations between Periodontal Disease, Demographic Characteristics, and Biomarkers

Table 4 illustrates the results from the three logistic regression models. In model 1, increased age, being male, being non-Hispanic black, or having a household income that is either low or below poverty, was linked to a significantly increased likelihood of having periodontal disease. For every 10 year increase in age, subjects were 60% more likely to have periodontal disease (Odds Ratio (OR) =1.06; 95% Confidence Interval (CI)=1.06–1.07), while being female decreased the likelihood of periodontal disease by 54% (OR=0.46; 95% CI=0.39–0.56). Non-Hispanic blacks were 87% more likely than non-Hispanic whites to have periodontal disease (OR=1.87; 95% CI=1.52–2.31). Relative to individuals with higher income, low income individuals (PIR between 1–1.99) were 65% more likely to have periodontal disease (OR=1.65; 95% CI=1.34–2.03), and those below the poverty level were over two and a half times as likely to have periodontal disease (OR=2.74; 95% CI=2.16–3.47).

In model 2, having higher CRP, CMV optical density, and HbA1c was significantly related to the likelihood of having periodontal disease. One unit increases in CMV optical density, CRP, and HbA1c were associated with an increased likelihood of periodontal disease of 25% (OR=1.25; 95% CI: 1.14–1.36), 13% (OR: 1.13; 95% CI: 1.03–1.24), and 19% (OR: 1.19; 95% CI: 1.12–1.27), respectively. The effects of age and gender are only slightly reduced from the values in Model 1 with the introduction of the biological markers.

When all predictor variables were included in the model, the size of the associations between periodontal disease and race/ethnicity, CRP, CMV optical density and HbA1c were reduced (Model 3). The association between periodontal disease and being non-Hispanic black was decreased by 23.6%, while the association between periodontal disease and being below the poverty level was reduced by 10%. The association between CRP and periodontal disease decreased by 31.9% and was no longer significant. Additionally, although they remained significant, the power of CMV optical density and HbA1c to predict periodontal disease decreased by 27.9% and 19.4%, respectively.

Discussion

Our findings suggest that the risk of periodontal disease is increased in individuals who are non-Hispanic black or of low SES; however, these associations are due in part to the propensity of elevated levels of CRP, CMV optical density, and HbA1c to be more common among these sub-groups. Given the differences in the onset and prevalence of co-morbid diseases and exposures among individuals with varying socio-demographic characteristics, differences in oral health problems such as periodontal disease, may be reflective of a multitude of complex health changes.

The simultaneous presence of periodontal disease and other adverse health conditions, such as diabetes, impaired immune response, and systemic inflammation are thought to be the result of underlying physiological mechanisms, which are more adverse among racial minorities and low SES individuals^{27–29}. In addition to oral health problems, many chronic conditions such as hypertension, diabetes and stroke are significantly higher among blacks³⁰. Furthermore, individuals with lower income, lower education, and those who are black have been shown to experience earlier age at onset of biological risk factors, diseases, and mortality^{30–32}. The increased prevalence of oral disease within particular segments of the population may also be reflective of a tendency towards “earlier aging” within disadvantaged segments of the population³³.

The racial disparities in health may reflect multifactorial biological as well as environmental mechanisms. These disparities have implications for the functioning of various physiological systems that affect inflammation, immunity and insulin regulation^{34–36}. While we have emphasized the links between race and income and biological factors in this paper, differential access and utilization of healthcare and dental care, may account for the disparities in both oral and overall health among racial/ethnic and SES subpopulations.

There are limitations in the present study that should be acknowledged. First, the use of cross-sectional data hindered our ability to test for the temporality of our associations. Second, the data from NHANES III was collected between 1988–1994 and may not reflect conditions today. Nevertheless, more recent nationally representative data which incorporates the biomarker measures used in the present study is not available. Despite these limitations, the present study is strengthened by the use of reliable techniques for measuring oral health and physiological markers, and inclusion of a large representative random sample.

The current study demonstrated that differences in physiological health are important factors to be considered when examining the associations between oral health and SES or race/ethnicity. Furthermore, Blacks and individuals below the poverty level were found to have a significantly higher prevalence of periodontal disease, reaching 15%, as well as poorer overall biological health markers. Given that increased prevalence of many chronic conditions, including periodontal disease, may reflect a tendency towards early aging, more research is needed to uncover the physiological and environmental mechanisms linking differences in multiple co-morbid conditions in disadvantaged populations.

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References

1. Lamster, I.; Crawford, N. Improving oral health for the elderly (chapter 2). Springer; New York: 2008. The oral disease burden faced by older adults.
2. Appollonio I, Carabellese C, Frattola A, Trabucchi M. Dental status, quality of life, and mortality in an older community population: a multivariate approach. *J Am Geriatr Soc.* 1997 Nov; 45(11): 1315–23. [PubMed: 9361656]
3. Campus G, Salem A, Uzzau S, Baldoni E, Tonolo G. Diabetes and Periodontal Disease: A Case-Control Study. *J Periodontol.* 2005; 76:418–425. [PubMed: 15857077]
4. Tezal M, Wactawski-Wende J, Grossi SG, Ho AW, Dunford R, Genco R. The Relationship Between Bone Mineral Density and Periodontitis in Postmenopausal Women. *J Periodontol.* 2000; 71:1492–1498. [PubMed: 11022780]
5. Meurman JH, Sanz M, Janket SJ. Oral health, atherosclerosis, and cardiovascular disease. *Crit Rev Oral Biol Med.* 2004; 15(6):403–413. [PubMed: 15574681]
6. Tsakos G, Allen PF, Steele JG, Locker D. Interpreting oral health-related quality of life data. *Community Dent Oral Epidemiol.* 2011; 10.1111/j.1600-0528.2011.00651.x
7. Gerritsen AE, Allen PF, Witter DJ, Bronkhorst EM, Creugers NH. Tooth loss and oral health-related quality of life: a systematic review and meta-analysis. *Health Qual Life Outcomes.* 2010; 8:126. [PubMed: 21050499]
8. Vargas, CM.; Kramarow, EA.; Yellowitz, JA. The Oral Health of Older Americans Aging Trends, No 3. Hyattsville, MD: National Center for Health Statistics; 2001.
9. Abiko Y, Shimizu N, Yamaguchi M, Suzuki H, Takiguchi H. Effect of aging on functional changes of periodontal tissue cells. *Ann Periodontol.* 1998; 3:350–69. [PubMed: 9722719]
10. Brown L, Brunelle JA, Kingman A. Periodontal status in the United States, 1988–91: prevalence, extent, and demographic variation. *Journal of Dental Research.* 1996; 75(Spec Is):672–683. [PubMed: 8594091]
11. Ford ES, Ajan UA, Croft JB, et al. Explaining the decrease in U.S. deaths from coronary disease, 1980–2000. *N Engl J Med.* 2007; 356:2388–98. [PubMed: 17554120]
12. Vargas CM, Ronzio CR. Disparities in Early Childhood Caries. *BMC Oral Health.* 2006; 6(1):S3. [PubMed: 16934120]
13. Kim JK, Baker LA, Seirawan H, Crimmins EM. Age patterns of oral health by race/ethnicity and education. *Special Care in Dentistry.* Forthcoming.
14. Kubar A, Saygun I, Yapar M, Özdemir A, Slots J. Real-time PCR quantification of cytomegalovirus in aggressive periodontitis lesions using TaqMan technology. *Journal of Periodontal Research.* 2004; 39(2):81–86. [PubMed: 15009514]
15. Slots J. Update on human cytomegalovirus in destructive periodontal disease. *Oral Microbiology and Immunology.* 2004; 19(4):217–223. [PubMed: 15209990]
16. Slots J, Contreras A. Herpesviruses: a unifying causative factor in periodontitis? *Oral Microbiology and Immunology.* 2000; 15(5):277–280. [PubMed: 11154416]
17. Danesh J, Whincup P, Walker M, Lennon L, Thomson A, Appleby P, Gallimore JR, Pepys MB. Low grade inflammation and coronary heart disease: prospective study and updated meta-analysis. *Br Med J.* 2000; 321:199–204. [PubMed: 10903648]
18. Koenig, Sund WM, Frohlich M, Fischer HG, Lowel H, Doring A, Hutchinson WL, Pepys MB. C-reactive protein, a sensitive marker of inflammation, predicts future risk of coronary heart disease in initially healthy middle-aged men: results from the MONICA Augsburg Cohort Study, 1984–1992. *Circulation.* 1999; 99(2):237–242. [PubMed: 9892589]
19. Ridker PM, Glynn RJ, Hennekens CH. CRP adds to the predictive value of total and HDL cholesterol in determining risk of first MI. *Circulation.* 1998; 97(20):2007–2011. [PubMed: 9610529]
20. Amar S, Gokce N, Morgan S, Loukideli M, Van Dyke TE, Vita JA. Periodontal disease is associated with brachial artery endothelial dysfunction and systemic inflammation. *Arterioscler Thromb Vasc Biol.* 2003; 23:1245–1249. [PubMed: 12763762]
21. Buhlin K, Gustafsson A, Pockley AG, Frostegard J, Klinge B. Risk factors for cardiovascular disease in patients with periodontitis. *Eur Heart J.* 2003; 24:2099–2107. [PubMed: 14643270]

22. Craig RG, Yip JK, So MK, Boylan RJ, Socransky SS, Haffajee AD. Relationship of destructive periodontal disease to the acute phase response. *J Periodontol.* 2003; 74:1007–1016. [PubMed: 12931763]
23. Ebersole JL, Machen RL, Steffen MJ, Willmann DE. Systemic acute-phase reactants, C-reactive protein and haptoglobin, in adult periodontitis. *Clin Exp Immunol.* 1997; 107:347–352. [PubMed: 9030874]
24. Mealey BL, Oates TW. American Academy of Periodontology. *J Periodontol.* 2006; 77(8):1289–303. [PubMed: 16881798]
25. U.S. Department of Health and Human Services (DHHS), National Center for Health Statistics. Third National Health and Nutrition Examination Survey. 1988–1994.
26. Page RC, Eke PI. Case definitions for use in population-based surveillance of periodontitis. *J Periodontol.* 2007; 78:1387–1399. [PubMed: 17608611]
27. Carroll JE, Cohen S, Marsland AL. Early childhood socioeconomic status is associated with circulating interleukin-6 among mid-life adults. *Brain Behav Immun.* 2001; 25(7):1468–74. [PubMed: 21672624]
28. Zajacova A, Dowd JB, Aiello AE. Socioeconomic and race/ethnic patterns in persistent infection burden among U.S. adults. *J Gerontological A Biol Sci Med Sci.* 2009; 64(2):272–9.
29. Chichlowska KL, Rose KM, Diez-Roux AV, et al. Life course socioeconomic conditions and metabolic syndrome in adults: the Atherosclerosis Risk in Communities (ARIC) Study. *Ann Epidemiol.* 2009; 19(12):875–83. [PubMed: 19804985]
30. Hayward M, Crimmins E, Miles T, Yang Y. The significance of socio-economic status in explaining the race gap in chronic health conditions. *American Sociological Review.* 2000; 65:910–930.
31. Crimmins, E.; Hayward Mark, D.; Seeman, T. Race/Ethnicity, Socioeconomic Status, and Health. In: Anderson, N.; Bulatao, R.; Cohen, B., editors. *Critical Perspectives on Race and Ethnic Differences in Health in Later Life.* The National Academies Press; 2004. p. 310-352.
32. Ford PJ, Raphael SL, Cullinan MP, et al. Why should a doctor be interested in oral disease? *Expert Rev Cardiovasc Ther.* 2010; 8(10):1483–93. [PubMed: 20936934]
33. Crimmins E, Kim JK, Seeman T. Poverty and Biological Risk: The Earlier “Aging” of the Poor. *Journal of Gerontology: Medical Sciences.* 2009; 62(2):286–92.
34. Pischon N, Heng N, Bernimoulin JP, et al. Obesity, Inflammation, and Periodontal Disease. *J Dent Res.* 2007; 86:400–9. [PubMed: 17452558]
35. Nieman DC, Henson DA, Nehlsen-Cannarella SL. Influence of obesity on immune function. *Journal of the American Dietetic Association.* 1999; 99(3):294–9. [PubMed: 10076580]
36. Ogden CL, Carroll MD, Curtin LR, et al. Prevalence of Overweight and Obesity in the United States, 1999–2004. *JAMA.* 2006; 295(13):1549–55. [PubMed: 16595758]

Table 1**Weighted Sample Characteristics for Subjects**

Characteristics	
Age, Mean (SD)	42.0 (21.9)
Sex—Female, (%)	51.2%
Race/Ethnicity, (%)	
Non-Hispanic White	79.1%
Non-Hispanic Black	10.8%
Mexican American	10.1%
PIR, (%)	
Below Poverty (PIR<1)	11.0%
Low Income (PIR=1–1.99)	18.9%
Adequate Income (PIR ≥ 2)	64.5%
Non-response	5.6%
Has Periodontal Disease, (%)	10.1%
CRP, Mean (SD)	3.9 (0.78)
CMVOD, Mean (SD)	1.7 (1.6)
HbA1c, Mean (SD)	5.3 (1.2)

Note: SD=Standard Deviation; PIR=Poverty Income Ratio; CRP=C-reactive Protein (mg/l); CMV OD=Cytomegalovirus Optical Density; HbA1c=Glycated Hemoglobin (%)

Table 2

Biomarkers and Frequency of Periodontal Disease by Race/Ethnicity

Race/Ethnicity	CRP	CMVOD	HbA1c	Periodontal Disease (%)
Non-Hispanic White	3.7	1.53	5.26	9.46
Non-Hispanic Black	4.8	2.19	5.58	15.03
Hispanic	4.1	2.15	5.42	9.57

Note: CRP=C-reactive Protein (mg/l); CMVOD=Cytomegalovirus Optical Density; HbA1c=Glycated Hemoglobin (%)

Table 3

Biomarker Means and Frequency of Periodontal Disease by Poverty Income Ratio (PIR)

PIR	CRP	CMVOD	HbA1c	Periodontal Disease (%)
Below Poverty	4.5	1.92	5.40	15.17
Low Income	4.3	1.85	5.33	12.06
Income two or more times poverty	3.6	1.55	5.28	8.33
Unknown Income	4.9	1.88	5.44	13.35

Note: PIR=Poverty Income Ratio; CRP=C-reactive Protein (mg/l); CMVOD=Cytomegalovirus Optical Density; HbA1c=Glycated Hemoglobin (%)

Table 4
Regression of Periodontal Disease on Socioeconomic, Demographic and Health Indicators: Odds Ratios and 95% Confidence Intervals for

	Model 1			Model 2			Model 3		
	β Coefficient (SE)	Odds Ratio (95% CI)	β Coefficient (SE)	Odds Ratio (95% CI)	β Coefficient (SE)	Odds Ratio (95% CI)	β Coefficient (SE)	Odds Ratio (95% CI)	
Below Poverty	1.01 (.121)	2.74 (2.16–3.47)			.947 (.122)	2.58 (2.03–3.28)			
Low Income	.500 (.106)	1.65 (1.34–2.03)			.450 (.105)	1.57 (1.28–1.93)			
Unknown Income	.323 (.1935)	1.38 (0.95–2.02)			.299 (.197)	1.35 (0.92–1.98)			
Black	.628 (.106)	1.87 (1.52–2.31)			.480 (.107)	1.62 (1.31–1.99)			
Hispanic	.072 (.164)	1.08 (0.78–1.48)			–.041 (.171)	0.96 (0.69–1.34)			
Age	.060 (.003)	1.06 (1.06–1.07)	.050 (.003)	1.05 (1.05–1.06)	.054 (.003)	1.06 (1.05–1.06)			
Sex (Female)	–.772 (.093)	0.46 (0.39–0.56)	–.758 (.098)	0.47 (0.39–0.57)	–.816 (.097)	0.44 (0.37–0.53)			
CRP			.119 (.047)	1.13 (1.03–1.24)	.081 (.049)	1.08 (0.99–1.19)			
HbA1c			.175 (.033)	1.19 (1.12–1.27)	.141 (.034)	1.15 (1.08–1.23)			
CMVOD			.222 (.045)	1.25 (1.14–1.36)	.160 (.049)	1.17 (1.07–1.29)			

Note: SE=Standard Error; CI=confidence interval; CRP=C-Reactive Protein (mg/l); CMV OD=Cytomegalovirus Optical Density; HbA1c=Glycated Hemoglobin (%)