

CLINICAL INVESTIGATIONS

Denture Wearing during Sleep Doubles the Risk of Pneumonia in the Very Elderly

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Abstract: *Poor oral health and hygiene are increasingly recognized as major risk factors for pneumonia among the elderly. To identify modifiable oral health-related risk factors, we prospectively investigated associations between a constellation of oral health behaviors and incident pneumonia in the community-living very elderly (i.e., 85 years of age or older). At baseline, 524 randomly selected seniors (228 men and 296 women; mean age, 87.8 years) were examined for oral health status and oral hygiene behaviors as well as medical assessment, including blood chemistry analysis, and followed up annually until first hospitalization for or death from pneumonia. During a 3-year follow-up period, 48 events associated with pneumonia (20 deaths and 28 acute hospitalizations) were identified. Among 453 denture wearers, 186 (40.8%) who wore their dentures during sleep were at higher risk for pneumonia than those who removed their dentures at night (log rank $P = 0.021$). In a multivariate Cox model, both perceived swallowing difficulties and*

*overnight denture wearing were independently associated with an approximately 2.3-fold higher risk of the incidence of pneumonia (for perceived swallowing difficulties, hazard ratio [HR], 2.31; and 95% confidence interval [CI], 1.11–4.82; and for denture wearing during sleep, HR, 2.38; and 95% CI, 1.25–4.56), which was comparable with the HR attributable to cognitive impairment (HR, 2.15; 95% CI, 1.06–4.34), history of stroke (HR, 2.46; 95% CI, 1.13–5.35), and respiratory disease (HR, 2.25; 95% CI, 1.20–4.23). In addition, those who wore dentures during sleep were more likely to have tongue and denture plaque, gum inflammation, positive culture for *Candida albicans*, and higher levels of circulating interleukin-6 as compared with their counterparts. This study provided empirical evidence that denture wearing during sleep is associated not only with oral inflammatory and microbial burden but also with incident pneumonia, suggesting potential implications of oral hygiene programs for pneumonia prevention in the community.*

Key Words: oral hygiene, very old, infection, *Candida albicans*, pneumonitis, interleukin-6.

Introduction

Pneumonia is a major morbidity and mortality risk among the elderly. The 2010 Global Burden of Disease Study reported that lower respiratory tract infections, including pneumonia, are the fourth leading cause of death globally, and the second most frequent reason for years of life lost (Lozano et al. 2012). In Japan, pneumonia has ranked as the third leading cause of death since 2011, and the second leading cause of death among nonagenarians (Ministry of Health, Labour and Welfare 2012). Aspiration is an important pathogenic mechanism for pneumonia in the elderly, and poor oral health is increasingly recognized as a predisposing factor (Janssens and Krause 2004). Indeed, randomized interventional trials demonstrated that professional oral care reduces the burden of pneumonia among the frail elderly in long-term care

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facilities (Adachi et al. 2002). It remains unknown, however, whether improving oral hygiene by altering behaviors could reduce the risk of pneumonia in community settings. With a rapid demographic shift toward the very elderly in the population and a concomitant increase in the global burden of poor oral condition (Marcenes et al. 2013), the development of a motivational and self-manageable oral health promotion program for pneumonia prevention is a matter of public health priority. To identify behavioral risk factors, modification of which could provide tangible benefits for pneumonia prevention, we prospectively investigated associations between a constellation of oral health behaviors and pneumonia events in the community-living very elderly.

Methods

Study Population

The Tokyo Oldest Old Survey on Total Health (TOOTH) is an ongoing prospective observational study organized by interdisciplinary experts, including geriatricians, dentists, psychologists, and epidemiologists. Details of its design, its recruitment, and the entire procedure have been described previously (Arai et al. 2010). Between March 2008 and November 2009, we recruited a randomly selected sample of 542 inhabitants of Tokyo aged 85 years or older for medical and dental examination. Among them, 12 subjects were excluded because they lacked oral health assessment, and 6 were excluded because they did not have information on pneumonia incidence; thus, 524 subjects were included in the analysis (228 men and 296 women; mean \pm SD age, 87.8 \pm 2.2 years; range, 85–102 years).

Oral Health Assessment

The comprehensive oral health assessment comprised a face-to-face interview including oral health-related quality of life (QOL) (Geriatric Oral Health Assessment Index [GOHAI]), the ability to eat 15 items of food, a questionnaire regarding oral health

behaviors, and dental examination by dentists (Iinuma et al. 2012). To identify behavioral risk factors, we have developed a 13-item oral health-related and hygiene-related questionnaire (Appendix Table). The questionnaire includes 4 items on denture hygiene practices modified from the study by Evren et al. (2011): frequency of denture wearing, frequency of denture cleaning, usage of denture cleanser, and denture wearing during sleep. These items were applied for 453 denture wearers only. Perceived swallowing difficulty was assessed with an item from GOHAI, “How often are you able to swallow comfortably?” After the interview, the dentist performed an oral examination to assess oral status, the presence of dental plaque, and gum inflammation according to the Standard of Dental Examination in School Health and Safety Act (Japanese School Dental Association 2007). Denture plaque was assessed using a modification of the Ambjørnsen Denture Plaque Index (Ambjørnsen et al. 1982). The presence of plaque on dentures was scored from 0 to 3 using the criteria proposed by Ambjørnsen, in which 0 is equivalent to no visible plaque, 1 is equivalent to plaque visible only by scraping on the denture base with a blunt instrument, 2 is equivalent to a moderate accumulation of dental plaque, and 3 is equivalent to an abundance of plaque. For 268 consecutive participants examined between April 2009 and November 2009, microbiological samples from the dorsal surface of the tongue were scraped 5 times with a sterilized cotton swab. The specimens were immediately inoculated onto special medium (CHROMagar Candida) for detection of *Candida*, according to a modification of the procedure of Wang et al. (2006).

Medical Assessment

At the same time as the dental examination, participants were interviewed and examined by trained geriatricians to assess medical conditions and medications, and to verify physical functional status (Barthel index). Cognitive function was evaluated according to the Mini-Mental State

Examination (MMSE). Nonfasting blood samples were obtained at baseline, and plasma concentrations of albumin, creatinine, and C-reactive protein (CRP) were measured using standard assay procedures. Plasma levels of interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF- α) were measured in duplicate using commercially available ELISA (enzyme-linked immunosorbent assay) kits (Quantikine HS [Human IL-6] and Quantikine HS [Human TNF- α], respectively; R&D Systems, Minneapolis, MN). Interassay coefficients of variation of IL-6 and TNF- α were 9.43%, and 8.72%, respectively.

Outcomes

The outcome of interest was a *serious pneumonia event*, which was defined as first hospitalization for or death from pneumonia. Participants were followed up for all-cause and cause-specific mortality and hospitalization from cancers, cardiovascular disease, pneumonia, falls and fractures, and other causes by telephone contact or mail survey conducted every 12 months. At month 36, those who remained in the cohort were examined according to the same protocol as the baseline survey, and any hospitalizations during the observational period were confirmed.

Statistical Analysis

All analyses were performed using SPSS version 19.0 (SPSS, Chicago, IL). Baseline characteristics are expressed as means and standard deviations (SD) or as percentages. Continuous variables with a skewed distribution are described as medians (interquartile ranges [IQR]) and log-transformed for statistical analyses. We characterized denture wearing during sleep as either *always* (every night) or *usually* (5–6 nights/week). Differences in continuous variables at baseline were compared using the Mann-Whitney U test. The chi-square test was used to compare categorical variables. For longitudinal analysis, we plotted Kaplan-Meier survival curves according to the risk strata. A prognostically significant result was defined as log-rank $P < 0.05$. We

then used the univariate and multivariate Cox proportional hazards model to assess the relative risk of incident pneumonia. First, biological and behavioral factors known to be associated with pneumonia mortality (age, sex, education, smoking status, low body mass index [<18.5], history of stroke, respiratory disease, diabetes mellitus, chronic kidney disease, use of angiotensin-converting enzyme inhibitors [ACEIs] and statins, and plasma levels of albumin, CRP, and IL-6) were calculated for hazard ratio (HR) in the univariate model; those with substantial associations ($P < 0.1$) were entered into the multivariate model. Because of the strong correlation between CRP and IL-6, they were entered separately in the model. Death from causes other than pneumonia was censored. In all analyses, $P < 0.05$ was taken to indicate statistical significance.

This research was approved by the Ethics Committees of Nihon University School of Dentistry (No. 2003-20, 2008) and Keio University School of Medicine (No. 20070047). The TOOTH is registered in the University Hospital Medical Information Network (UMIN)-Clinical Trial Registry (CTR) as UMIN-CTR (ID: UMIN000001842).

Results

During a 3-year follow-up period, 48 events associated with pneumonia (20 deaths and 28 acute hospitalizations) were identified, for an overall incidence of serious pneumonia of 3.1 per 100 per year. Seventy individuals died of other causes (cancer = 24; cardiovascular disease = 28; other causes = 15; and unknown causes = 3), 4 declined the follow-up survey, and 15 were censored at the time of last contact. The baseline characteristics of the participants are presented in Table 1. Those who developed pneumonia were more likely to have perceived swallowing difficulties, a habit of denture wearing during sleep, disability involving activities of daily living (ADL), cognitive impairment, lower body mass index (BMI), a history of respiratory disease and stroke, a lower level of albumin, and higher CRP and IL-6 levels. Neither remaining teeth, nor

Eichner index score (Eichner 1990), nor medication intake showed any association with pneumonia.

Because denture wearing during sleep was the only behavioral factor associated with pneumonia, we plotted Kaplan–Meier survival curves for cumulative incidence of pneumonia events according to this habit (Figure). Denture wearing during sleep was significantly associated with a higher risk of pneumonia (log rank $P = 0.021$).

In a multivariate Cox model, both swallowing difficulties and denture wearing during sleep were independently associated with an approximately 2.3-fold higher risk of incident pneumonia (for perceived swallowing difficulties, HR, 2.31; 95% CI, 1.11–4.82; and for denture wearing during sleep, HR, 2.38; 95% CI, 1.25–4.56), which were comparable with the HR attributable to cognitive impairment (HR, 2.15; 95% CI, 1.06–4.34), history of stroke (HR, 2.46; 95% CI, 1.13–5.35), and respiratory disease (HR, 2.25; 95% CI, 1.20–4.23). To test the robustness of our results, we conducted a sensitivity analysis in which we excluded ADL disability from the multivariate model. We found a consistent association between denture wearing during sleep and incident pneumonia (HR, 2.35; 95% CI, 1.23–4.51). Another sensitivity analysis excluding those who died of causes other than pneumonia during the observation period ($n = 70$) demonstrated a solid association between denture wearing during sleep and pneumonia events in the multivariate model (HR, 2.37; 95% CI, 1.21–4.65; $P = 0.012$). None of the other denture hygiene practices or factors related to oral health status, including the number of remaining teeth, Eichner index, or use of denture cleansers, were significantly associated with incident pneumonia.

To gain mechanistic insight into the association between denture wearing during sleep and incident pneumonia, we examined baseline oral and denture status as well as systemic conditions in relation to denture habits (Table 3). Those who wore dentures during sleep were more likely to have tongue and denture plaque, gum inflammation,

positive culture for *Candida albicans*, and higher levels of circulating IL-6 as compared with their counterparts. Thereafter, we incorporated each dental status item into the multivariate Cox model shown in Table 2, and we found that the associations between denture wearing during sleep and incident pneumonia were substantially attenuated and no longer statistically significant after further adjustment for gum inflammation or *C. albicans* (adjusted for gum inflammation, HR for overnight wearing, 1.45; 95% CI, 0.67–3.11; $P = 0.344$; and, adjusted for *C. albicans*, HR, 1.72; 95% CI, 0.66–4.46; $P = 0.264$), suggesting that the inflammatory and microbial burden of the oral cavity could provide a mechanistic link between denture wearing during sleep and incident pneumonia. The prevalence of ADL disability and coronary artery disease tended to be higher in nocturnal denture wearers than their counterparts; however, none of the systemic conditions had a significant impact on the relationship between denture wearing during sleep and incident pneumonia.

Discussion

In this prospective study of the community-dwelling very elderly aged 85 years or older, we found that perceived swallowing difficulties and denture wearing during sleep conferred a 2.3-fold higher risk of serious pneumonia events, which is comparable with those attributable to major predisposing factors of aspiration pneumonia, such as history of stroke and respiratory disease, and cognitive impairment. Furthermore, wearers of dentures during sleep tend to have poor denture hygiene practices, fewer dental office visits, denture and tongue plaque, and oral candidiasis, suggesting that this habit could be a sensitive marker for identifying individuals at high risk of both poor oral health and aspiration pneumonia.

There have been few previous studies regarding the association between oral health status and pneumonia outcomes in the community setting. Awano et al. reported that the number of teeth with

Table 1.

Baseline Characteristics of Participants Who Did or Did Not Develop Serious Pneumonia during 3-Year Follow-Up

Characteristics	Pneumonia	No Pneumonia	P*
	n = 48	n = 476	
Age, mean (SD)	88.4 (2.5)	87.8 (2.2)	0.039**
Female, %	45.8	57.6	0.128
Higher education, %	21.3	17.0	0.426
Smoking, %	44.4	38.7	0.523
BMI, mean (SD)	20.6 (3.2)	21.6 (3.2)	0.122**
BMI <18.5, %	25.5	17.3	0.166
ADL disability, %	36.2	25.4	0.120
Cognitive impairment, %	35.4	21.2	0.030
Oral health status			
Number of teeth, median (IQR)	5 (0–12)	7 (0–17)	0.530**
Edentulous, %	25.0	30.7	0.510
Eichner index, %^a			
A	8.3	9.8	
B	14.6	23.9	0.288
C	77.1	66.3	
Swallowing difficulty, %	21.3	12.0	0.105
Gum inflammation, % ^b	39.4	29.8	0.321
Number of chewable foods, median (IQR)	14 (13–15)	15 (13–15)	0.298**
Dental office visit in the past year, %	60.4	59.7	1.000
Denture hygiene practice (always or usually), %^c			
Frequency of denture wearing	97.7	93.8	0.498
Frequency of denture cleaning	72.7	68.9	0.731
Usage of denture cleanser	32.6	33.6	1.000
Denture wearing during sleep	58.1	39.3	0.022
Medical history, %			
Respiratory disease	45.8	32.1	0.076
Stroke	25.0	11.3	0.011
Diabetes	20.8	18.5	0.698
CAD	6.3	10.7	0.457
Hypertension	60.4	59.5	1.000
CKD	45.8	49.7	0.651
Medications, %^d			
ACEI user	2.2	4.6	0.710
ARB	26.1	29.3	0.735
Statins	10.9	16.5	0.402
PPI	19.6	13.7	0.270
Histamine H2 blockers	13.0	12.8	1.000
Biochemical			
Albumin, g/dL (SD) ^e	4.0 (0.3)	4.1 (0.3)	0.047**
CRP, mg/dL, median (IQR) ^e	0.15 (0.05–0.29)	0.08 (0.04–0.17)	0.011**
Interleukin-6, pg/ml, median (IQR) ^f	2.08 (1.45–3.11)	1.67 (1.29–2.44)	0.030**
TNF- α , pg/ml, median (IQR) ^f	2.48 (1.91–3.11)	2.19 (1.88–2.79)	0.116**

IQR, interquartile range; SD, standard deviation; BMI, body mass index; ADL, activities of daily living; CAD, coronary artery disease; CKD, chronic kidney disease; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; PPI, proton pump inhibitor; CRP, C-reactive protein; TNF- α , tumor necrosis factor- α .

^a–^fData available for ^a508, ^b355, ^c453, ^d500, ^e520, and ^f511 people, respectively.

*Chi-square test, unless otherwise indicated.

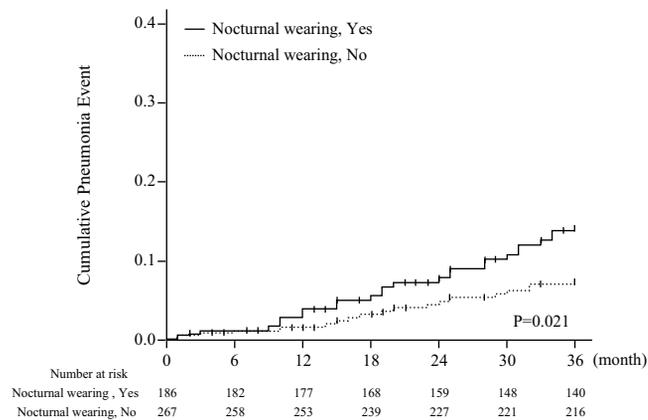
**Mann–Whitney U test.

periodontal pockets was associated with higher mortality from pneumonia in the very elderly aged 80 years or older (Awano et al. 2008). In a cohort of community-dwelling and well-functioning seniors, Jutbini-Mehta et al. identified mobility limitation and oral plaque burden as modifiable risk factors for pneumonia requiring hospitalization (Juthani-Mehta et al. 2013). Our results corroborated these studies by demonstrating an epidemiological link between denture wearing during sleep and serious pneumonia, which suggests potential implications of oral hygiene programs for the prevention of community-acquired pneumonia in the very elderly.

Elucidating the biological mechanisms by which denture wearing during sleep raises the risk of serious pneumonia is likely to provide rational information to design effective and convincing oral health programs for the very elderly, who have an increased need for removable prostheses and show loss of immune competence. First, even in a healthy older adult, aspiration of unnoticed oropharyngeal and periodontal secretions occurs during sleep, and a high incidence of silent aspiration is strongly related to pneumonia among the elderly (Kikuchi et al. 1994), particularly those with dementia or cerebrovascular disease. Denture wearing during sleep was reported to be associated with poor denture hygiene, oral candidiasis (Compagnoni et al. 2007), and denture stomatitis (Baran and Nalçaci 2009; Fenlon et al. 1998; Shulman et al. 2005; Vigild 1987), all of which may function as reservoirs of potentially infectious pathogens (Sumi et al. 2010). Our findings that denture wearers during sleep had significantly higher rates of denture and tongue plaque and oral candidiasis provide additional evidence for this suggestion. The secretion and function of saliva might have substantial influences on the relationship between denture wearing during sleep and *Candida* infection. Previous studies speculated that nocturnal denture wearing decreases the protective effects of saliva against *Candida* spp. (Compagnoni et al. 2007;

Figure.

Denture wearing during sleep and incident pneumonia. Kaplan–Meier survival curves by denture wearing during sleep ($P = 0.021$). Cumulative pneumonia events increased progressively in association with the nocturnal wearing.



Ikebe et al. 2006). Although *Candida* spp. infrequently cause pneumonia, they are an important risk factor for denture stomatitis (Pires et al. 2002), which is characterized as inflammation and erythema of the oral mucosa and its predisposal to bacterial pathogens. Therefore, the protective effect of saliva is an important factor of denture stomatitis as well as aspiration pneumonia, and it would be wise to look into patients' nocturnal denture-wearing habits and relations with oral immunity, or their salivary defense proteins such as immunoglobulin A. Second, denture wearing during sleep may be an indicator of overall poor oral hygiene practices. In the present study, denture wearers during sleep were characterized by lower frequencies of dental visits and denture cleaning, and extremely limited usage of denture cleansers compared to their counterparts. In this scenario, it remains unclear whether the physical removal of dentures during sleep is sufficiently efficient to reduce the risk of pneumonia, or if assiduous hygiene practices have preventive effects. Because of the observational nature of this study, we did not address this issue. Recently, a randomized clinical trial of institutionalized subjects demonstrated that overnight storage of dentures with alkaline peroxide-based tablets significantly decreased denture

biofilm and the amount of *C. albicans* to a greater extent than dry or water preservation (Duyck et al. 2013). There is a great deal of evidence supporting the effect of biofilm removal using a denture cleanser (Silva-Lovato et al. 2010); however, few studies have reported its practical usage, such as the dipping time (Jose et al. 2010). Future prospective and interventional studies are warranted to examine whether appropriate use of cleansers or other methods (e.g., microwave cleaning) in combination with overnight denture removal could further reduce the risk of pneumonia in the elderly.

Based on evidence supporting a mechanistic link between continuous denture wearing and *Candida*-related stomatitis, guidelines and dental professionals have recommended the overnight removal of dentures for many years. Nevertheless, a surprisingly high percentage of senior denture users do not remove their dentures during the night, for example 41.5% of patients at a university clinic in Brazil (Takamiya et al. 2011), 55.2% of complete denture wearers aged 60 years or older in Turkey (Baran and Nalçaci 2009), and 24.2% of edentulous elderly in a longitudinal cohort study in Canada (Emami et al. 2013). Therefore, to change denture wearers' behavior, exploration of contributing factors to the disparity

Table 2.
Hazard Risk from Univariate and Multivariate Cox Models for Incident Pneumonia

Characteristics	Univariate Model			Multivariate Model		
	HR	95% CI	P	HR ^a	95% CI	P
Age	1.12	(1.02–1.24)	0.024	1.09	(0.97–1.21)	0.146
Sex (female)	0.66	(0.37–1.16)	0.146			
Higher education	0.92	(0.50–1.67)	0.773			
Swallowing difficulty	1.98	(0.99–3.99)	0.055	2.31	(1.11–4.82)	0.025
Denture wearing during sleep	2.01	(1.10–3.69)	0.024	2.38	(1.25–4.56)	0.009
Smoking	1.22	(0.68–2.19)	0.516			
Cognitive impairment	2.01	(1.11–3.62)	0.021	2.15	(1.06–4.34)	0.034
ADL disability	1.73	(0.96–3.15)	0.070	0.76	(0.36–1.60)	0.467
BMI <18.5	1.59	(0.83–3.06)	0.166			
Stroke	2.47	(1.29–4.75)	0.007	2.46	(1.13–5.35)	0.024
Respiratory disease	1.68	(0.95–3.00)	0.075	2.25	(1.20–4.23)	0.011
Diabetes	1.14	(0.57–2.30)	0.706			
ACEI user	0.43	(0.06–3.11)	0.403			
Statin user	0.61	(0.24–1.55)	0.300			
CKD	0.87	(0.49–1.53)	0.625			
ALB (1 SD increase)	0.74	(0.56–0.97)	0.027	1.05	(0.75–1.46)	0.790
CRP (1 SD increase) ^b	1.29	(1.08–1.53)	0.006	1.30	(1.07–1.59)	0.009
IL-6 (1 SD increase) ^b	1.37	(1.07–1.75)	0.013	1.20	(0.92–1.58)	0.186

HR, hazard ratio; CI, confidence interval; SD, standard deviation; ADL, activity of daily living; BMI, body mass index; ACEI, angiotensin-converting enzyme inhibitor; CKD, chronic kidney disease; ALB, albumin; CRP, C-reactive protein; IL-6, interleukin-6.

^aAdjusted for age, swallowing difficulty, denture wearing during sleep, cognitive impairment, ADL disability, history of stroke, respiratory disease, and plasma levels of albumin, CRP, and IL-6. Variables with substantial association ($P < 0.1$) were entered into the multivariate model.

^bCRP and IL-6 were entered separately in the multivariate model.

between knowledge and behavior may be an effective approach. From a psychosocial viewpoint, the reasons for denture wearing during sleep may be multifactorial and vary according to age, sex, and cultural background. A study in Brazil suggested that the presence of a partner could be a reason for denture wearing during sleep (Takamiya et al. 2011); however, this may not have been the case for our participants, because those who lived alone exhibited a comparably high percentage of overnight denture wearing. Another reason the elderly do not remove their dentures at night is that the remaining teeth and denture precision attachment might hit the contralateral residual ridge in participants without opposing tooth occlusion (e.g., Eichner classifications

C1 and C2). Such elders might wear dentures to avoid sharp pain. In fact, we found that the incidence of Eichner classification C tended to be higher in nocturnal denture wearers than in nonwearers (wearers, 80.7%; nonwearers, 73.9%; $P = 0.109$), which partially supports this notion.

In contrast to previous studies, neither educational achievement nor economic status was associated with denture-wearing habits in the present study. A possible alternative is fear of denture loss in the case of an unexpected event. During the Great Hanshin-Awaji earthquake in 1995, denture loss was a serious problem encountered by many elderly disaster victims (Hyogo Dental Association 1996). In an earthquake-prone country such as Japan, innovation

of emergency interim denture technology (Kurozumi et al. 2010) and dissemination of survival manuals with appropriate information on denture storage could be effective approaches to encourage the removal of dentures during sleep at night.

Our study had several limitations. First, pneumonia in the elderly can occasionally be underdiagnosed due to its atypical presentation. In this study, we relied on death or acute hospitalization from pneumonia only, which may have resulted in underestimation of the incidence of pneumonia. We expect this effect to be approximately similar across oral health status, however, and not to affect comparisons between denture-wearing categories. Second, our sample size was relatively small, and it was limited to seniors living in the Tokyo

Table 3.
Oral Health Status and Behaviors According to Denture-Wearing Habit at Night

Characteristics	Denture Wearing During Sleep		P*
	Yes	No	
	n = 186	n = 267	
Age, mean (SD)	88.1 (2.8)	87.7 (1.9)	0.702**
Female %	58.6	57.7	0.923
Cognitive impairment, %	25.8	21.3	0.308
ADL disability, % ^a	31.9	24.8	0.109
Oral health status			
Number of teeth, median (IQR)	4 (0–10)	6 (0–14)	0.067**
Swallowing difficulty, %	12.4	13.5	0.778
Tongue plaque, % ^b	42.2	32.5	0.046
Gum inflammation, % ^c	40.0	30.5	0.101
Plaque adhesion, % ^c	47.8	40.5	0.227
Denture plaque, % ^d	57.5	39.7	0.000
Eichner index C, % ^e	80.7	73.9	0.109
Candida carriers, %^f			
<i>Candida albicans</i>	57.8	43.4	0.025
<i>Candida tropicalis</i>	18.3	11.3	0.112
<i>Candida krusei</i>	22.0	19.5	0.646
Total of 3	67.0	55.3	0.058
Denture hygiene practice (always or usually), %			
Dental office visit in the past year	52.2	66.3	0.003
Frequency of denture wearing	98.9	92.9	0.002
Frequency of denture cleaning	63.4	73.8	0.022
Usage of denture cleanser	15.1	46.4	0.000
Medical history, %			
Respiratory disease	31.7	32.6	0.919
Stroke	11.3	12.7	0.664
Diabetes	19.9	19.9	1.000
CAD	12.9	7.9	0.082
Hypertension	54.1	60.6	0.174
CKD	51.9	47.9	0.444
Biochemical			
Albumin, g/dL (SD) ^g	4.1 (0.3)	4.1 (0.3)	0.776**
CRP, mg/dL, median (IQR) ^g	0.10 (0.04–0.19)	0.09 (0.04–0.19)	0.924**
Interleukin-6, pg/ml, median (IQR) ^h	1.81 (1.38–2.66)	1.57 (1.25–2.27)	0.017**

IQR, interquartile range; SD, standard deviation; ADL, activities of daily living; CAD, coronary artery disease; CKD, chronic kidney disease; CRP, C-reactive protein.

^{a-h}Data available for ^a451, ^b446, ^c289, ^d443, ^e438, ^f268, ^g450, and ^h442 people, respectively.

*Chi-square test, unless otherwise indicated.

**Mann-Whitney U test.

Metropolitan Area. Dental resources and delivery systems vary among countries and localities. Therefore, our

findings must be validated in a larger scale, separate cohort study. Third, our sample solely comprised very

old individuals, who more frequently present with physical and cognitive disabilities and have a higher rate of

mortality from pneumonia than younger elders. Therefore, it might be difficult to generalize our findings to younger populations. In addition, we did not examine denture stomatitis precisely using measures such as the Newton scale in this study. A further study is warranted because the state of denture stomatitis could represent a mechanistic link between denture-wearing habits and the risk of pneumonia.

In conclusion, the present study provided empirical evidence that denture wearing during sleep is associated not only with oral inflammatory and microbial burden but also with incident pneumonia, a potentially life-threatening condition in the very elderly. These results suggest that simple denture care habits could reduce the risk of pneumonia in the community. To meet the widespread need for dental prostheses among the very elderly in both developed and developing countries, evidence-based guidelines (Felton et al. 2011) as well as oral health promotion programs with appropriate denture care should be urgently disseminated to dental professionals, primary care providers, and community services.

Author Contributions

T. Iinuma, Y. Arai, contributed to conception, design, data acquisition, analysis, and interpretation, drafted and critically revised the manuscript; Y. Abe, M. Takayama, M. Fukumoto, Y. Fukui, contributed to data acquisition and analysis, critically revised the manuscript; T. Iwase, contributed to data analysis, critically revised the manuscript; T. Takebayashi, N. Gionhaku, K. Komiyama, contributed to conception and data interpretation, critically revised the manuscript; N. Hirose, contributed to design, data acquisition, and interpretation, critically revised the manuscript. All authors gave final approval and agree to be accountable for all aspects of the work.

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