European Journal of Preventive Cardiology

ESC European Society of Cardiology

Full research paper

European Journal of Preventive Cardiology
0(00) 1–11

DOI: 10.1177/2047487319886018
journals.sagepub.com/home/cpr

SAGE

Improved oral hygiene care is associated with decreased risk of occurrence for atrial fibrillation and heart failure: A nationwide population-based cohort study

Yoonkyung Chang[1,*], Ho Geol Woo[2,*], Jin Park[3,*], Ji Sung Lee[4] and Tae-Jin Song[1]

Abstract

Aims: Poor oral hygiene can provoke transient bacteremia and systemic inflammation, a mediator of atrial fibrillation and heart failure. This study aims to investigate association of oral hygiene indicators with atrial fibrillation and heart failure risk in Korea.

Methods: We included 161,286 subjects from the National Health Insurance System-Health Screening Cohort who had no missing data for demographics, past history, or laboratory findings. They had no history of atrial fibrillation, heart failure, or cardiac valvular diseases. For oral hygiene indicators, presence of periodontal disease, number of tooth brushings, any reasons of dental visit, professional dental cleaning, and number of missing teeth were investigated.

Results: During median follow-up of 10.5 years, 4911 (3.0%) cases of atrial fibrillation and 7971 (4.9%) cases of heart failure occurred. In multivariate analysis after adjusting age, sex, socioeconomic status, regular exercise, alcohol consumption, body mass index, hypertension, diabetes, dyslipidemia, current smoking, renal disease, history of cancer, systolic blood pressure, blood and urine laboratory findings, frequent tooth brushing ($\geq$3 times/day) was significantly associated with attenuated risk of atrial fibrillation (hazard ratio: 0.90, 95% confidence interval (0.83–0.98)) and heart failure (0.88, (0.82–0.94)). Professional dental cleaning was negatively (0.93, (0.88–0.99)), while number of missing teeth $\geq$22 was positively (1.32, (1.11–1.56)) associated with risk of heart failure.

Conclusion: Improved oral hygiene care was associated with decreased risk of atrial fibrillation and heart failure. Healthier oral hygiene by frequent tooth brushing and professional dental cleaning may reduce risk of atrial fibrillation and heart failure.

Keywords

Oral hygiene, atrial fibrillation, heart failure, disease free survival, population study

Received 4 August 2019; accepted 10 October 2019

Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia that is closely associated with risk of systemic embolism, hospitalization, and death.[1–4] It is also a well-known major risk factor for occurrence and recurrence of stroke and stroke-related mortality.[5] With the current aging population and associated increase of concomitant vascular risk factors and/or cardiovascular disease, the burden of AF is increasing in Western and Asian populations.[6–9] Heart failure

[1]Department of Neurology, Mokdong Hospital, Ewha Womans University College of Medicine, Korea
[2]Department of Neurology, Seoul Hospital, Ewha Womans University College of Medicine, Korea
[3]Department of Critical Care Medicine, Ewha Womans University Seoul Hospital, Korea
[4]Clinical Research Center, Asan Institute for Life Sciences, Asan Medical Center, University of Ulsan College of Medicine, Korea
*These authors contributed equally as first authors.

Corresponding author:
Tae-Jin Song, Department of Neurology, Mokdong Hospital, Ewha Womans University College of Medicine, 1071 Anyangcheon-ro, Yangcheon-gu, Seoul, 07985, Korea.
Email: knstar@ewha.ac.kr

(HF) is a clinical syndrome accompanied by decreased ability of cardiac contraction or pumping and/or filling with blood.[10] HF is also one of the most frequent cardiovascular diseases worldwide. The prevalence of HF is continuously increasing. Despite recent advances for treatment and prevention for HF, HF-related morbidity and mortality remain as high as ever.[11] Therefore, it is important to identify and control risk factors or causative factors of AF and HF. Up to now, risk factors such as hypertension, coronary artery occlusive disease, cardiomyopathy, alcohol consumption, and smoking have been identified.[12,13] However, information about other modifiable risk factors is lacking.[14,15]

Periodontal disease is common in the general population. It is closely related to oral hygiene behavior such as tooth brushing.[16] Indicators of oral hygiene include presence of periodontal disease, number of tooth brushing per day, professional dental cleaning, and number of missing teeth.[17–19] Poor oral hygiene can provoke transient bacteremia and systemic inflammation, an immune process known to be a mediator of AF and HF.[20,21] However, studies regarding the association of oral hygiene indicators with occurrence of AF and HF are lacking.

We hypothesized that improved oral hygiene care would be associated with decreased risk of AF and HF. Thus, the aim of this study was to investigate the association of oral hygiene indicators with risk of AF and HF in a nation-wide general population based longitudinal study.

Methods

Subjects

The National Health Insurance System (NHIS) covers demographics, socioeconomic status, type of health insurance coverage, medical database for diagnosis, and treatment modality. It provides a nation-supported health examination database and a medical care institution database through random sampling of health information for 50 m Koreans.[22] In Korea, the NHIS is the sole insurance provider. It is controlled and supported by the Korean government. It covers approximately 97% of the Korean population. The remaining 3% are supported by the Medical Aid program. Subscribers of the NHIS are recommended to receive standardized medical health examinations every two years.[23] We enrolled subjects from the National Health Insurance System-National Health Screening Cohort (NHIS-HEALS).[24] The NHIS-HEALS cohort enrolled subjects who participated in medical health screening programs. Their height, weight, laboratory tests, questionnaires on lifestyle, oral health disease, and oral hygiene behaviors were all obtained by the NHIS. The oral health disease and oral hygiene behaviors screening program was provided to subscribers aged $\geq$40 years. It consisted of a self-reported questionnaire regarding information about dental symptoms, any dental visits at last year, and oral hygiene behavior. Subjects were investigated by dentists for presence of periodontal disease and condition of teeth including number of missing teeth. If there were dental problems, oral hygiene care was recommended to participants if necessary.[23]

Our study was based on data from the NHIS-HEALS. Subjects were enrolled from 2003–2004, who were aged between 40–79 years. All subjects had routine medical examinations including previous history of medical illness, body weight, height, blood pressure measurements, laboratory tests, and lifestyle questionnaire. The total number of recruited subjects was 514,866. Among them, subjects with missing data for variables such as oral health status ($n = 343{,}037$) or variables in health examination ($n = 8094$) and subjects with previous history of AF, HF, or cardiac valvular diseases ($n = 2449$) were excluded. Finally, 161,286 subjects were analyzed in this study (Supplementary Material Figure 1). This study was approved by the Ewha Womans University of College of Medicine Institutional Review Board (approval number: EUMC 2018-01-067). Informed consent was waived because retrospective anonymized data were used.

Study variables and definitions

Information on smoking habits and alcohol consumption was obtained by questionnaire. Body mass index was defined as the participant's weight in kilograms divided by the square of the participant's height in meters. Regular physical exercise was considered to be strenuous physical activity performed for at least 20 minutes more than once per week. Economic status was dichotomized at the bottom 10% level. Hypertension was defined using the International Statistical Classification of Diseases Related Health Problems (ICD)-10 codes I10–I11 and the prescription of an antihypertensive agent with at least one claim per year.[22,25] Diabetes mellitus was defined using ICD–10 codes E10–E14 and the prescription of an antidiabetic medication with at least one claim per year. Dyslipidemia was defined using ICD-10 code E78 and the prescription of a lipid-lowering agent with at least one claim per year. Renal disease was considered as using ICD–10 codes N18.1–N18.5 and N18.9 with at least one claim per year. Malignancy was defined as using ICD-10 codes C00–D48 with at least one claim per year.

Subjects were examined by dentists as part of routine health check-up.[25] Periodontal disease was considered

as the presence of the ICD-10 codes, including acute periodontitis (K052), chronic periodontitis (K053), periodontosis (K054), other periodontal disease (K055), and unspecified periodontal disease (K056) that were diagnosed by dentists and when more than two times of claims occurred. The number of tooth brushings were categorized by: 0–1 times/day, =2 times/day, and ≥3 times/day. Any reasons of dental visit and professional dental cleaning were categorized into "yes" or "no" based on the self-reported question (Have you been to a dental clinic for any reasons for in the last year?; Have you ever had professional dental cleaning in the last year?). Lost teeth were detected by dentists during oral health examination. The number of missing teeth was classified as 0, 1–7, 8–14, 15–21, and ≥22 regardless of the causes such as periodontal disease or other dental reasons. Index date was defined as the date of the oral health status test. In case of variables with serial measurements, such as body mass index, blood pressure, risk factors, blood laboratory findings, and oral hygiene indicators, the result of the latest measurements during the period 2002–2003 was used for analysis. The outcomes were occurrence of AF (ICD-10 code: I48) and HF (ICD-10 code: I50) with at least two claims per year. These codes were validated and/or utilized from a previous study.[25,26] The diagnostic accuracy of AF (ICD-10 code: I48) was validated by reviewing electrocardiograms and the positive predictive value for diagnosis was 94.1%.[24]

Statistical analysis

Chi-squared test and independent *t*-test were performed for comparison of categorical and continuous variables, respectively. Kaplan–Meier survival curves were used to evaluate the relationship between oral hygiene indicators and the incidence of AF and HF. The statistical differences among oral hygiene indicators in Kaplan–Meier curves were assessed using log-rank tests. The Cox proportional hazard model was applied to determine the association of oral hygiene indicators and occurrence of AF and HF. The hazard ratio (HR) and 95% confidence interval (CI) were determined. Multivariable regression models were constructed with adjustment for model 1 (age, sex, socioeconomic status, regular exercise, alcohol consumption, body mass index (kg/m^2), hypertension, diabetes mellitus, dyslipidemia, smoking status, renal disease, and history of cancer), model 2 (model 1 + systolic blood pressure, fasting blood sugar, liver panel, and presence of proteinuria), and model 3 (model 2 + periodontal disease, tooth brushing, dental visit for any reasons, professional dental cleaning and number of missing teeth). All statistical analyses were performed using SAS software (version 9.2, SAS Institute, Cary, North Carolina, USA). A p value of less than 0.05 was defined as statistically significant.

Results

The mean age of subjects was 52.2 ± 8.7 years. Males accounted for 61.2%. Periodontal disease was present in 13.4% of all subjects. Subjects with hypertension, diabetes mellitus, and status of current smoker accounted for 38.9%, 9.0%, and 25.1%, respectively. Subjects with 0–1 tooth brushing per day, two times a day, and ≥3 times a day accounted for 14.6%, 44.6%, and 40.8%, respectively. Professional dental cleaning was performed for 24.1% of subjects (Table 1). Supplementary Material Table 1 shows difference between subjects with and without periodontal disease.

During a median follow-up of 10.5 years, 4911 (3.0%) cases of AF and 7971 (4.9%) cases of HF occurred. Kaplan–Meier survival curves showed that the risk for AF and HF was lower in subjects without periodontal disease. The risk of AF and HF was lower in groups with frequent tooth brushing and professional dental cleaning. In contrast, subjects with larger number of missing teeth were associated with increased risk of AF and HF (Figures 1 and 2, Tables 2 and 3).

In multivariate analysis, frequent tooth brushing (≥3 times/day) was significantly associated with attenuated risk of AF (HR: 0.89, 95% CI: 0.82–0.97, $p = 0.005$, p for trend = 0.004 in model 1; HR: 0.90, 95% CI: 0.83–0.98, $p = 0.014$, p for trend = 0.011 in model 2; HR: 0.90, 95% CI: 0.83–0.98, $p = 0.014$, p for trend = 0.011 in model 3) even after adjusting for confounding factors (Table 2). In contrast, the statistical significance for the relationship of periodontal disease, professional dental cleaning, and number of missing teeth with future occurrence of AF was diminished after adjusting for confounding factors in models 1–3 (Table 2).

Table 3 shows the risk of HF according to oral health and hygiene care. Frequent tooth brushing (≥3 times/day) was related with decreased risk of HF occurrence (HR: 0.87, 95% CI: 0.82–0.93, $p < 0.001$, p for trend <0.001 in model 1; HR: 0.88, 95% CI: 0.82–0.94, $p < 0.001$, p for trend <0.001 in model 2; HR: 0.88, 95% CI: 0.83–0.94, $p < 0.001$, p for trend <0.001 in model 3). Moreover, professional dental cleaning was associated with an attenuated risk of HF (HR: 0.93, 95% CI: 0.88–0.98, $p = 0.011$ in model 1; HR: 0.93, 95% CI: 0.88–0.99, $p = 0.015$ in model 2; HR: 0.94, 95% CI: 0.89–1.01, $p = 0.076$ in model 3). In addition, number of missing teeth ≥22 was positively associated with risk of HF occurrence (HR: 1.35, 95% CI: 1.14–1.60, $p = 0.001$, p for trend = 0.001 in model 1; HR: 1.32, 95% CI: 1.11–1.56, $p = 0.001$, p for trend = 0.002 in model 2; HR: 1.31, 95% CI: 1.11–1.55, $p = 0.001$, p for trend = 0.004 in model 3).

Table 1. Baseline characteristics of the study population.

Characteristics	Total
Number of subjects	161,286
Age (years)	52.2 ± 8.7
Male sex	98,671 (61.2)
Income levels	
Fifth quintile (highest)	64,331 (39.9)
Fourth quintile	32,793 (20.3)
Third quintile	22,101 (13.7)
Second quintile	20,028 (12.4)
First quintile (lowest)	21,796 (13.5)
Covered by medical aid	237 (0.1)
Alcohol consumption	76,288 (47.3)
Regular physical activity	15,688 (9.7)
Anthropometric measurements	
Body mass index (kg/m^2)	23.9 ± 2.9
Systolic blood pressure (mm Hg)	126.3 ± 17.1
Diastolic blood pressure (mm Hg)	79.3 ± 11.2
Comorbidities	
Hypertension	62,774 (38.9)
Diabetes mellitus	14,520 (9.0)
Dyslipidemia	25,668 (15.9)
Current smoking	40,447 (25.1)
Renal disease	12,587 (7.8)
History of cancer	274 (0.2)
Laboratory findings	
Total cholesterol (mg/dl)	198.1 ± 36.4
Fasting blood sugar (mg/dl)	97.0 ± 28.9
Aspartate aminotransferase (U/l)	26.1 ± 16.3
Alanine aminotransferase (U/l)	25.5 ± 20.2
Gamma-glutamyl transferase (U/l)	38.3 ± 53.4
Proteinuria (≥+1 in dipstick test)	4848 (3.0)
Oral health status	
Number of missing teeth	
0	122,757 (76.1)
1–7	34,577 (21.4)
8–14	2350 (1.5)
15–21	765 (0.5)
≥22	837 (0.5)
Oral hygiene care	
Dental visit for any reasons	68,537 (42.5)
Number of tooth brushings (times/day)	
0–1	23,614 (14.6)
2	71,928 (44.6)
≥3	65,744 (40.8)
Dental visit for professional cleaning	38,847 (24.1)

Values of *p* by Student's *t*-test and Chi-square test. Data are expressed as the mean ± standard deviation (SD), or *n* (%).

In the subgroup analysis, there were no statistical interactions regarding the relationship of tooth brushing number with AF and HF occurrence according to demographics or comorbidities (age (dichotomized at 50 years), sex, alcohol consumption, regular physical activity, hypertension. diabetes mellitus, dyslipidemia, and current smoking status) in multivariate models 1–3 (Supplementary Material Tables 2 and 3).

Discussion

The key findings of our study were: (a) frequent tooth brushing (≥3 times per day) was negatively associated with risk of AF and HF occurrence; and (b) professional dental cleaning was negatively associated with risk of HF occurrence while increased number of missing teeth was positively associated with such risk after adjusting for confounding factors. Our study demonstrated that frequent tooth brushing, especially frequent tooth brushing ≥3 times per day, decreased the risk of AF. Previous studies have revealed the correlation of oral hygiene and cardiovascular disease risk. Poor oral hygiene was related to increased risk of cardiovascular disease and low grade inflammation in a Scottish Health Survey.[27] Improving oral hygiene behaviors, for example, professional dental cleaning and frequent tooth brushing, attenuated the risk of future cardiovascular diseases in an Asian population.[25] A systematic review suggested that there is a general consensus for preventive screening and treatment for dental infections in the patients undergoing cardiothoracic and cardiovascular intervention.[28] Previously, one study has proposed that periodontitis is an independent factor of arrhythmic events in patients with AF and AF highly occurs in patients with severe periodontitis.[29] Considering HF, performing tooth scaling is associated with decreased risk of myocardial infarction.[30] Because coronary artery occlusive disease is an important cause of HF,[31] an association between poor oral hygiene care or periodontal disease and HF seems possible. Another study has reported that there is a high occurrence of periodontal disease in chronic heart failure patients.[32] In addition, low income, alcohol consumption, hypertension, diabetes mellitus, and smoking are common risk factors for periodontal disease and HF.[33] Owing to common risk factors shared between poor oral hygiene and HF, these facts may explain the relevance of our study.

Although our study did not suggest the exact mechanism underlying the relationship of frequent tooth brushing with AF and HF, several hypotheses can explain this association. First, subgingival biofilm in periodontal pockets enables translocation of oral

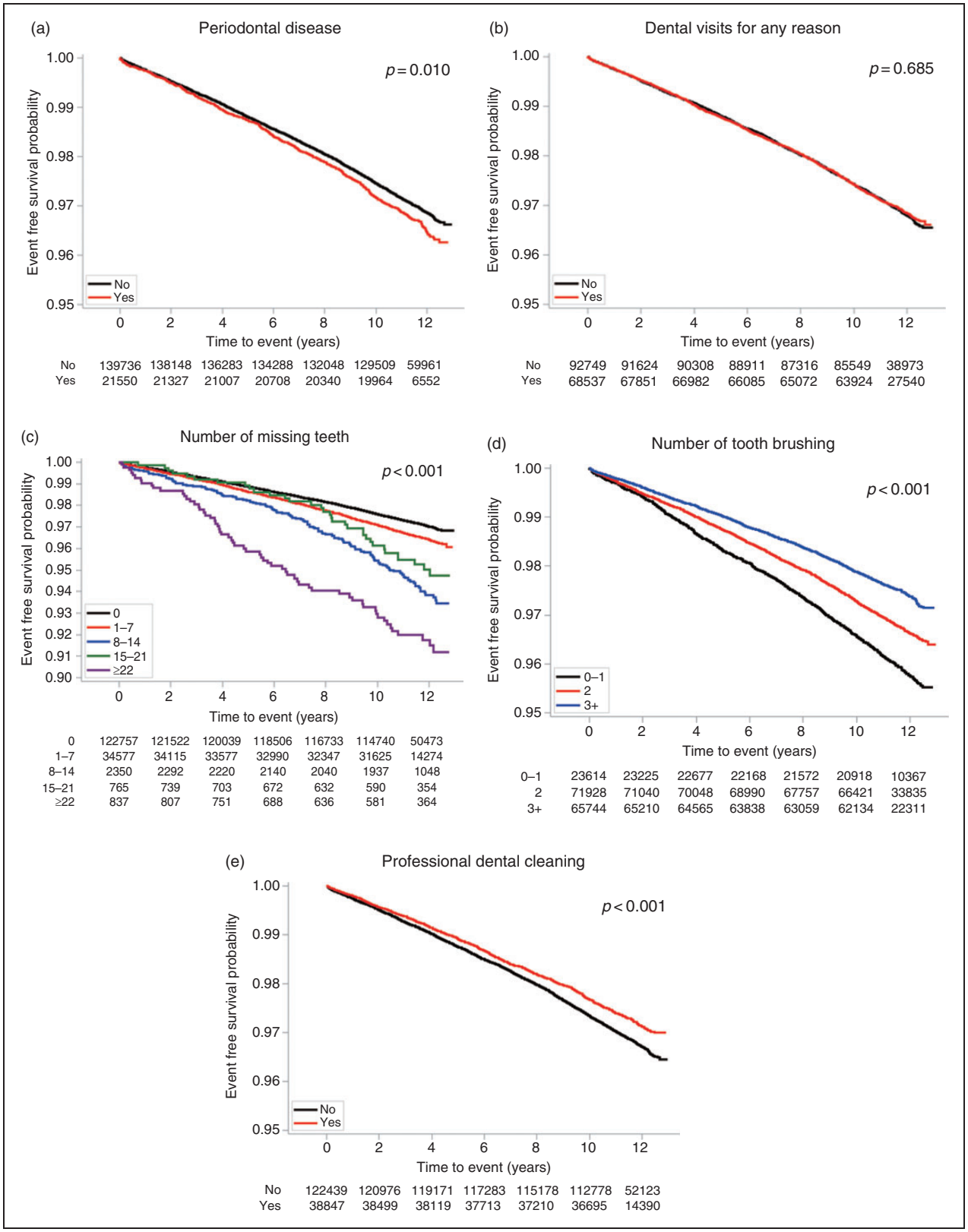

Figure 1. Kaplan-Meier survival curves associated with oral health diseases and oral hygiene behaviors for risk of atrial fibrillation occurrence. The Kaplan-Meier curve shows that risk of atrial fibrillation occurrence depends on the presence of periodontal disease (a) ($p = 0.010$), number of missing teeth (c) ($p < 0.001$), number of tooth brushing (d) ($p < 0.001$), and professional dental cleaning (e) ($p < 0.001$), but not dental visit for any reason (b) ($p = 0.685$).

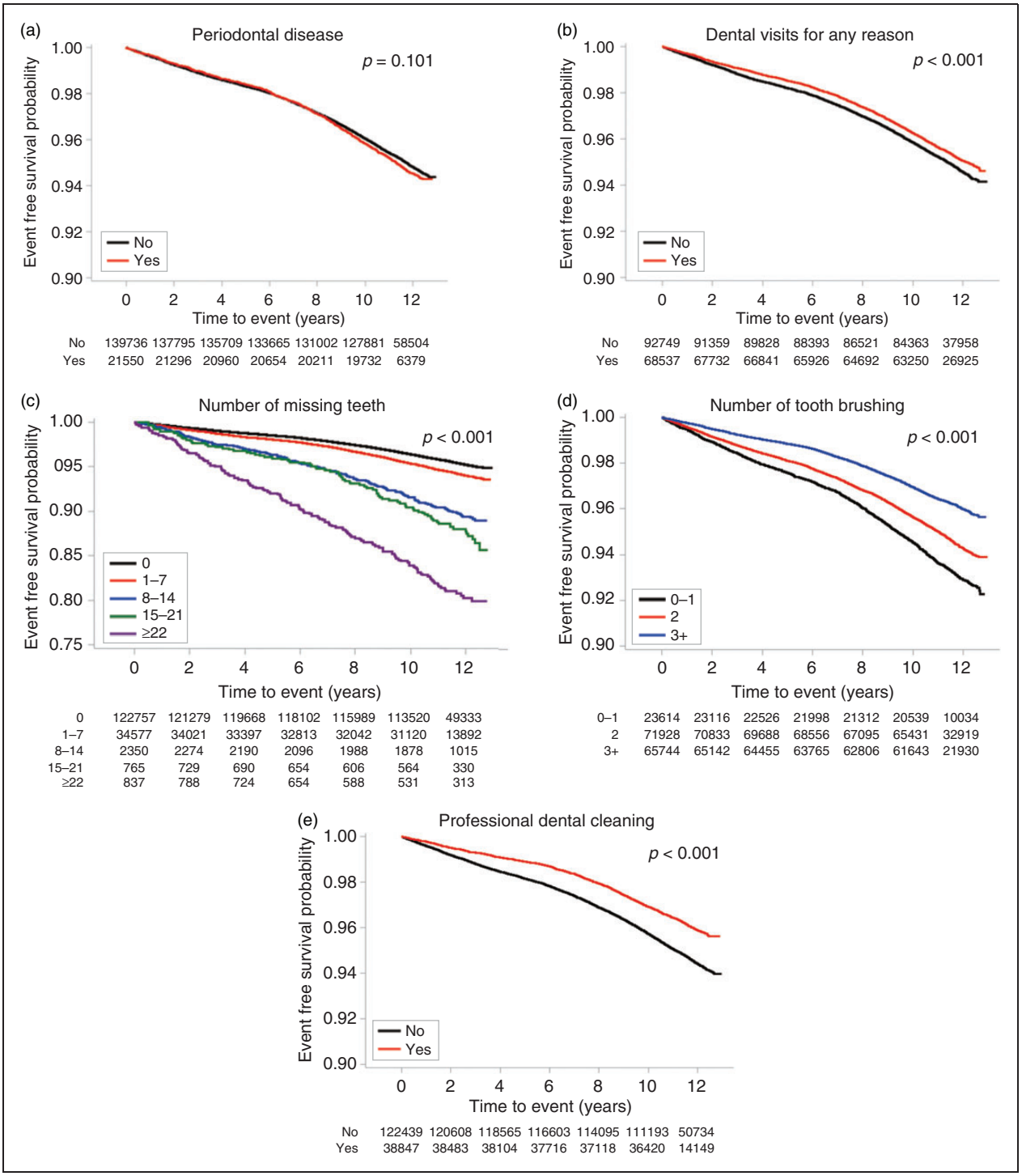

Figure 2. Kaplan-Meier survival curves associated with oral health diseases and oral hygiene behaviors for risk of heart failure occurrence. The Kaplan-Meier curve shows that risk of heart failure occurrence depends on dental visit for any reason (b) ($p < 0.001$), number of missing teeth (c) ($p < 0.001$), number of tooth brushing (d) ($p < 0.001$), and professional dental cleaning (e) ($p < 0.001$), but not the presence of periodontal disease (a) ($p = 0.110$).

bacteria into the systemic circulation. Particularly, *Porphyromonas gingivalis* can cause alteration of gut microbiota configuration and initiate indirect induction of systemic inflammation in response to secretion of many toxins.[34] Second, systemic inflammations due to poor oral hygiene care and periodontal disease are associated with AF. Serum inflammatory markers including tumor necrosis factor-α, interleukin (IL)-6,

Table 2. Risk of atrial fibrillation events according to oral health disease and oral hygiene care.

	Number of subjects	Number of events	Event rate (%, 95% CI)	Follow-up duration (person-years)	Incidence rate (per 1000 person-years)	Unadjusted model		Multivariable adjusted (1)		Multivariable adjusted (2)		Multivariable adjusted (3)	
						HR (95% CI)	*p*-value	HR (95% CI)	*p*-value	HR (95% CI)	*p*-value	HR (95% CI)	*p*-value
Periodontal disease													
No	139,736	4203	2.54 (2.45, 2.62)	1,585,949	2.65 (2.57–2.73)	1 (ref)		1 (ref)		1 (ref)		1 (ref)	
Yes	21,550	708	2.82 (2.59, 3.04)	241,556	2.93 (2.72–3.16)	1.11 (1.02–1.20)	0.010	1.02 (0.94–1.11)	0.613	1.02 (0.94–1.11)	0.577	1.02 (0.94–1.11)	0.583
Number of tooth brushings (times/day)													
0–1	23,614	942	3.42 (3.19, 3.66)	262,462	3.59 (3.37–3.83)	1 (ref)		1 (ref)		1 (ref)		1 (ref)	
2	71,928	2319	2.72 (2.60, 2.84)	817,291	2.84 (2.72–2.96)	0.79 (0.73–0.85)	<0.001	0.95 (0.88–1.02)	0.180	0.96 (0.89–1.03)	0.263	0.96 (0.89–1.03)	0.263
≥3	65,744	1650	2.12 (2.01, 2.23)	747,753	2.21 (2.10–2.32)	0.61 (0.57–0.67)	<0.001	0.89 (0.82–0.97)	0.005	0.90 (0.83–0.98)	0.014	0.90 (0.83–0.98)	0.014
p for trend						<0.001		0.004		0.011		0.011	
Dental visit for any reasons													
No	92,749	2834	2.57 (2.47, 2.68)	1,049,298	2.70 (2.60–2.80)	1 (ref)		1 (ref)		1 (ref)		1 (ref)	
Yes	68,537	2077	2.58 (2.46, 2.70)	778,207	2.67 (2.56–2.79)	0.99 (0.93–1.05)	0.685	1.00 (0.95–1.06)	0.876	1.01 (0.95–1.07)	0.739	1.00 (0.94–1.07)	0.974
Professional dental cleaning													
No	122,439	3847	2.66 (2.57, 2.75)	1,384,986	2.78 (2.69–2.87)	1 (ref)		1 (ref)		1 (ref)		1 (ref)	
Yes	38,847	1064	2.32 (2.17, 2.47)	442,519	2.40 (2.26–2.55)	0.87 (0.81–0.93)	<0.001	1.01 (0.94–1.08)	0.776	1.02 (0.95–1.09)	0.620	1.02 (0.94–1.10)	0.644
Number of missing teeth													
0	122,757	3500	2.41 (2.33, 2.50)	1,396,420	2.51 (2.42–2.59)	1 (ref)		1 (ref)		1 (ref)		1 (ref)	
1–7	34,577	1186	2.90 (2.72, 3.08)	389,370	3.05 (2.88–3.22)	1.22 (1.14–1.30)	<0.001	1.03 (0.96–1.10)	0.391	1.02 (0.95–1.09)	0.548	1.02 (0.95–1.09)	0.636
8–14	2350	130	4.57 (3.69, 5.45)	25,350	5.13 (4.32–6.09)	2.05 (1.72–2.44)	<0.001	1.09 (0.91–1.30)	0.341	1.07 (0.90–1.28)	0.439	1.07 (0.89–1.27)	0.474
15–21	765	33	3.87 (2.41, 5.33)	8015	4.12 (2.93–5.79)	1.65 (1.17–2.32)	0.004	0.74 (0.53–1.05)	0.089	0.72 (0.51–1.02)	0.064	0.72 (0.51–1.02)	0.062
≥22	837	62	7.20 (5.34, 9.06)	8349	7.43 (5.79–9.52)	2.98 (2.32–3.84)	<0.001	1.08 (0.84–1.39)	0.563	1.04 (0.80–1.34)	0.781	1.04 (0.80–1.34)	0.779
p for trend						<0.001		0.608		0.931		0.997	

CI: confidence interval; HR: hazard ratio.

Event rates were reported in 10-year event rates (%). Model 1 was adjusted for age, sex, income levels, regular exercise, alcohol consumption, body mass index (kg/m^2), hypertension, diabetes, dyslipidemia, current smoking, renal disease, and history of cancer. Model 2 was adjusted for the variables listed above as well as systolic blood pressure, fasting blood sugar, total cholesterol, aspartate aminotransferase, alanine aminotransferase, gamma glutamyl transferase, and proteinuria. Model 3 was adjusted for the variables listed above as well as periodontal disease, number of tooth brushings, dental visit for any reasons, professional dental cleaning, and number of missing teeth.

Table 3. Risk of heart failure events according to oral health disease and oral hygiene care.

	Number of subjects	Number of events	Event rate (%, 95% CI))	Follow-up duration (person-years)	Incidence rate (per 1000 person-years)	Unadjusted model		Multivariable adjusted (1)		Multivariable adjusted (2)		Multivariable adjusted (3)	
						HR (95% CI)	*p*-value	HR (95% CI)	*p*-value	HR (95% CI)	*p*-value	HR (95% CI)	*p*-value
Periodontal disease													
No	139,736	6874	3.95 (3.85, 4.06)	1,575,292	4.36 (4.26–4.47)	1 (ref)		1 (ref)		1 (ref)		1 (ref)	
Yes	21,550	1097	4.17 (3.90, 4.44)	240,263	4.57 (4.30–4.84)	1.05 (0.99–1.12)	0.104	1.01 (0.94–1.07)	0.830	1.01 (0.95–1.07)	0.809	1.03 (0.96–1.10)	0.370
Number of tooth brushings (times/day)													
0–1	23,614	1563	5.47 (5.17, 5.76)	259,811	6.02 (5.72–6.32)	1 (ref)		1 (ref)		1 (ref)		1 (ref)	
2	71,928	3913	4.36 (4.21, 4.51)	810,635	4.83 (4.68–4.98)	0.80 (0.75–0.85)	<0.001	0.94 (0.89–1.00)	0.042	0.94 (0.89–1.00)	0.058	0.95 (0.89–1.01)	0.078
≥3	65,744	2495	3.05 (2.92, 3.19)	745,109	3.35 (3.22–3.48)	0.56 (0.52–0.59)	<0.001	0.87 (0.82–0.93)	<0.001	0.88 (0.82–0.94)	<0.001	0.88 (0.83–0.94)	<0.001
p for trend						<0.001		<0.001		<0.001		<0.001	
Dental visit for any reasons													
No	92,749	4765	4.16 (4.03, 4.29)	1,041,199	4.58 (4.45–4.71)	1 (ref)		1 (ref)		1 (ref)		1 (ref)	
Yes	68,537	3206	3.75 (3.60, 3.89)	774,356	4.14 (4.00–4.29)	0.90 (0.87–0.95)	<0.001	0.96 (0.92–1.01)	0.097	0.97 (0.92–1.01)	0.125	0.98 (0.94–1.04)	0.541
Professional dental cleaning													
No	122,439	6468	4.27 (4.15, 4.38)	1,374,200	4.71 (4.59–4.82)	1 (ref)		1 (ref)		1 (ref)		1 (ref)	
Yes	38,847	1503	3.09 (2.91, 3.26)	441,355	3.41 (3.24–3.58)	0.72 (0.68–0.77)	<0.001	0.93 (0.88–0.98)	0.011	0.93 (0.88–0.99)	0.015	0.94 (0.89–1.01)	0.076
Number of missing teeth													
0	122,757	5559	3.61 (3.50, 3.71)	1,388,686	4.00 (3.90–4.11)	1 (ref)		1 (ref)		1 (ref)		1 (ref)	
1–7	34,577	1957	4.65 (4.42, 4.87)	386,268	5.07 (4.85–5.30)	1.27 (1.20–1.33)	<0.001	1.05 (1.00–1.10)	0.074	1.04 (0.99–1.10)	0.110	1.04 (0.99–1.09)	0.160
8–14	2350	227	8.43 (7.27, 9.59)	24,888	9.12 (8.01–10.39)	2.30 (2.01–2.62)	<0.001	1.07 (0.94–1.22)	0.318	1.06 (0.93–1.21)	0.388	1.05 (0.92–1.20)	0.471
15–21	765	86	9.58 (7.37, 11.79)	7790	11.04 (8.94–13.64)	2.79 (2.26–3.46)	<0.001	1.05 (0.85–1.31)	0.632	1.03 (0.83–1.28)	0.769	1.03 (0.83–1.27)	0.819
≥22	837	142	16.08 (13.42, 18.73)	7924	17.92 (15.20–21.12)	4.59 (3.89–5.43)	<0.001	1.35 (1.14–1.60)	<0.001	1.32 (1.11–1.56)	0.001	1.31 (1.11–1.55)	0.001
p for trend						<0.001		<0.001		0.002		0.004	

CI: confidence interval; HR: hazard ratio.

Event rates were reported in 10-year event rates (%). Model 1 was adjusted for age, sex, income levels, regular exercise, alcohol consumption, body mass index (kg/m^2), hypertension, diabetes, dyslipidemia, current smoking, renal disease, and history of cancer. Model 2 was adjusted for the variables listed above as well as systolic blood pressure, fasting blood sugar, total cholesterol, aspartate aminotransferase, alanine aminotransferase, gamma glutamyl transferase, and proteinuria. Model 3 was adjusted for the variables listed above as well as periodontal disease, number of tooth brushings, dental visit for any reasons, professional dental cleaning, and number of missing teeth.

IL-2, and C-reactive protein are associated with a higher risk of AF. They are elevated in patients with periodontal disease.[35,36] These pro-inflammatory conditions could promote occurrence of AF by electrical and structural remodeling. Moreover, systemic inflammation can facilitate atherosclerotic change, valve injury, and myocardial damage, consequently resulting in HF (Figure 3).

In our study, the presence of periodontal disease, professional dental cleaning, and lower number of missing teeth were related with lower risk of AF. Moreover, a dental visit for any reason was related with a lower risk for occurrence of HF even in univariate analysis. On the other hand, after adjusting for various important confounding factors, these associations became statistically insignificant. This indicates that other factors might be associated with AF and HF rather than poor oral hygiene and/or improving oral hygiene behaviors. Furthermore, in our study, professional dental cleaning and the number of missing teeth were associated with HF only but not AF. These diverse associations with oral hygiene indicators could be associated with or affect the occurrence of AF and HF to a different extent.

This study has several limitations. First, our study could not be generalized to other ethnicities because our data set consisted of only individuals in the Asian population. Second, although our study used the definition of AF and HF based on previous studies which validated or confirmed the diagnostic accuracy, no actual electrocardiography or echocardiographic findings were identified in our study. Third, we did not confirm the presence of periodontal diseases by dental X-rays. Additionally, we could not identify the exact cause of missing teeth through health examination. However, the existence of periodontal disease and lost teeth were confirmed objectively by dentists. Fourth, the educational level, marital status, and data about blood inflammatory markers, such as C-reactive protein, were not included because the NHIS-HEALS dataset did not deal with personal information and blood inflammatory markers. Fifth, since the screening was based on 2002–2003 examinations, the number of regular check-ups and dental visits cannot be checked.

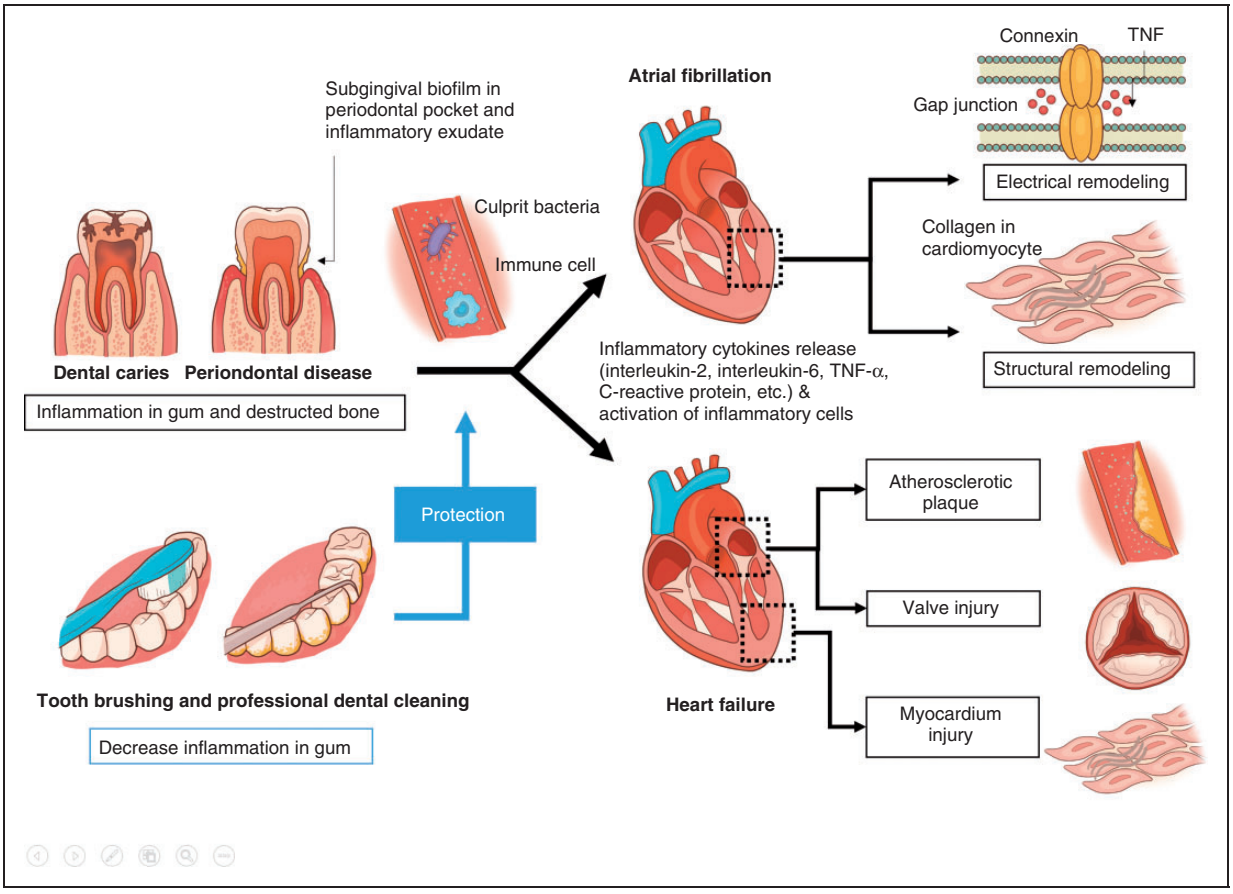

Figure 3. Possible mechanism regarding the association of oral hygiene with occurrence of atrial fibrillation and heart failure. TNF, tumor necrosis factor.

Sixth, because information about oral hygiene indicators including the number of tooth brushings, dental visit for any reasons, and professional dental cleaning and other behavioral information were acquired from the self-reported questionnaire, there may be recall bias. Seventh, although oral hygiene indicators and risk factors can be changed during follow-up, our study did not consider these time-varying factors. Finally, although it was a longitudinal study, our study was a retrospective cohort study. Therefore, a causal relationship could not be identified.

Conclusion

Our study demonstrated that improved oral hygiene care was associated with a lower risk of AF and HF. Healthier oral hygiene attained by frequent tooth brushing and professional dental cleaning may decrease risk of AF and HF.

Author contribution

YC, HW, JP, and TS contributed to conception and design of the study, data acquisition, analysis and interpretation of results, drafted, and revised the manuscript; JL contributed to design of the study, data acquisition and interpretation, and revised the manuscript.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This project was supported by a grant (2018R1D1A1B07040959) from the Basic Science Research Program through the National Research Foundation of Korea funded by the Ministry of Education.

References

1. Chugh SS, Havmoeller R, Narayanan K, et al. Worldwide epidemiology of atrial fibrillation: A Global Burden of Disease 2010 study. *Circulation* 2014; 129: 837–847.
2. Benjamin EJ, Wolf PA, D'Agostino RB, et al. Impact of atrial fibrillation on the risk of death: The Framingham Heart Study. *Circulation* 1998; 98: 946–952.
3. Bekwelem W, Connolly SJ, Halperin JL, et al. Extracranial systemic embolic events in patients with nonvalvular atrial fibrillation: Incidence, risk factors, and outcomes. *Circulation* 2015; 132: 796–803.
4. Meyre P, Blum S, Berger S, et al. Risk of hospital admissions in patients with atrial fibrillation: A systematic review and meta-analysis. *Can J Cardiol* 2019; 35: 1332–1343.
5. Lin HJ, Wolf PA, Kelly-Hayes M, et al. Stroke severity in atrial fibrillation. *The Framingham Study*. Stroke 1996; 27: 1760–1764.
6. Go AS, Hylek EM, Phillips KA, et al. Prevalence of diagnosed atrial fibrillation in adults: National implications for rhythm management and stroke prevention: The AnTicoagulation and Risk Factors in Atrial Fibrillation (ATRIA) study. *JAMA* 2001; 285: 2370–2375.
7. Guo Y, Tian Y, Wang H, et al. Prevalence, incidence, and lifetime risk of atrial fibrillation in China: New insights into the global burden of atrial fibrillation. *Chest* 2015; 147: 109–119.
8. Inoue H, Fujiki A, Origasa H, et al. Prevalence of atrial fibrillation in the general population of Japan: An analysis based on periodic health examination. *Int J Cardiol* 2009; 137: 102–107.
9. Choi EJ, Lee IH and Je NK. Inadequate stroke prevention in Korean atrial fibrillation patients in the post-warfarin era. *Int J Cardiol* 2016; 220: 647–652.
10. Tan LB, Williams SG, Tan DK, et al. So many definitions of heart failure: Are they all universally valid? A critical appraisal. *Expert Rev Cardiovasc Ther* 2010; 8: 217–228.
11. Savarese G and Lund LH. Global public health burden of heart failure. *Card Fail Rev* 2017; 3: 7–11.
12. Lau DH, Nattel S, Kalman JM, et al. Modifiable risk factors and atrial fibrillation. *Circulation* 2017; 136: 583–596.
13. Benedetto LD, Michels G, Luben R, et al. Individual and combined impact of lifestyle factors on atrial fibrillation in apparently healthy men and women: The EPIC-Norfolk prospective population study. *Eur J Prev Cardiol* 2018; 25: 1374–1383.
14. Casiglia E, Tikhonoff V, Albertini F, et al. Caffeine intake reduces incident atrial fibrillation at a population level. *Eur J Prev Cardiol* 2018; 25: 1055–1062.
15. Mourtzinis G, Schiöler L, Kahan T, et al. Antihypertensive control and new-onset atrial fibrillation: Results from the Swedish Primary Care Cardiovascular Database (SPCCD). *Eur J Prev Cardiol* 2017; 24: 1206–1211.
16. Marcenes W, Kassebaum NJ, Bernabe E, et al. Global burden of oral conditions in 1990–2010: A systematic analysis. *J Dent Res* 2013; 92: 592–597.
17. Lissowska J, Pilarska A, Pilarski P, et al. Smoking, alcohol, diet, dentition and sexual practices in the epidemiology of oral cancer in Poland. *Eur J Cancer Prev* 2003; 12: 25–33.
18. Chang JS, Lo HI, Wong TY, et al. Investigating the association between oral hygiene and head and neck cancer. *Oral Oncol* 2013; 49: 1010–1017.
19. Guha N, Boffetta P, Wunsch Filho V, et al. Oral health and risk of squamous cell carcinoma of the head and neck and esophagus: Results of two multicentric case-control studies. *Am J Epidemiol* 2007; 166: 1159–1173.
20. Andrade J, Khairy P, Dobrev D, et al. The clinical profile and pathophysiology of atrial fibrillation: Relationships among clinical features, epidemiology, and mechanisms. *Circ Res* 2014; 114: 1453–1468.

21. DuBrock HM, AbouEzzeddine OF and Redfield MM. High-sensitivity C-reactive protein in heart failure with preserved ejection fraction. *PLoS One* 2018; 13: e0201836.
22. Kim MK, Han K, Koh ES, et al. Variability in total cholesterol is associated with the risk of end-stage renal disease: A nationwide population-based study. *Arterioscler Thromb Vasc Biol* 2017; 37: 1963–1970.
23. Song SO, Jung CH, Song YD, et al. Background and data configuration process of a nationwide population-based study using the Korean national health insurance system. *Diabetes Metab J* 2014; 38: 395–403.
24. Seong SC, Kim YY, Park SK, et al. Cohort profile: The National Health Insurance Service-National Health Screening Cohort (NHIS-HEALS) in Korea. *BMJ Open* 2017; 7: e016640.
25. Park SY, Kim SH, Kang SH, et al. Improved oral hygiene care attenuates the cardiovascular risk of oral health disease: A population-based study from Korea. *Eur Heart J* 2019; 40: 1138–1145.
26. Lee SS, Ae Kong K, Kim D, et al. Clinical implication of an impaired fasting glucose and prehypertension related to new onset atrial fibrillation in a healthy Asian population without underlying disease: A nationwide cohort study in Korea. *Eur Heart J* 2017; 38: 2599–2607.
27. de Oliveira C, Watt R and Hamer M. Toothbrushing, inflammation, and risk of cardiovascular disease: Results from Scottish Health Survey. *BMJ* 2010; 340: c2451.
28. Cotti E, Arrica M, Di Lenarda A, et al. The perioperative dental screening and management of patients undergoing cardiothoracic, vascular surgery and other cardiovascular invasive procedures: A systematic review. *Eur J Prev Cardiol* 2017; 24: 409–425.
29. Pressman GS, Qasim A, Verma N, et al. Periodontal disease is an independent predictor of intracardiac calcification. *Biomed Res Int* 2013; 2013: 854340.
30. Chen ZY, Chiang CH, Huang CC, et al. The association of tooth scaling and decreased cardiovascular disease: A nationwide population-based study. *Am J Med* 2012; 125: 568–575.
31. Weinbrenner S, Langer T, Scherer M, et al. [The German national disease management guideline "chronic heart failure"]. *Dtsch Med Wochenschr* 2012; 137: 219–227.
32. Frohlich H, Herrmann K, Franke J, et al. Periodontitis in chronic heart failure. *Tex Heart Inst J* 2016; 43: 297–304.
33. Reynolds MA. Modifiable risk factors in periodontitis: At the intersection of aging and disease. *Periodontol 2000* 2014; 64: 7–19.
34. Hajishengallis G. Periodontitis: From microbial immune subversion to systemic inflammation. *Nat Rev Immunol* 2015; 15: 30–44.
35. Guo Y, Lip GY and Apostolakis S. Inflammation in atrial fibrillation. *J Am Coll Cardiol* 2012; 60: 2263–2270.
36. Loos BG. Systemic markers of inflammation in periodontitis. *J Periodontol* 2005; 76: 2106–2115.