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Self-reported periodontal health and incident hypertension: longitudinal evidence from the NutriNet-Santé e-cohort

Maria Clotilde Carra^{a,b}, Sabine Fessi^a, Laurent Detzen^a, Christelle Darnaud^{a,c}, Chantal Julia^{d,e}, Serge Hercberg^d, Mathilde Touvier^d, Valentina A. Andreeva^{d,*}, and Philippe Bouchard^{a,f,*}

Objective: An association between periodontitis and arterial hypertension has been suggested recently. This study aimed at investigating the hypothesis that periodontal health is linked to incident arterial hypertension.

Methods: We analyzed data from the French population-based e-cohort NutriNet-Santé, selecting participants who had completed two oral health questionnaires in 2011–2012. Pregnant women, participants with diabetes, cancer, arterial hypertension and cardiovascular diseases at inclusion were excluded. Incident cases of arterial hypertension were self-reported and/or based on the use of antihypertensive therapy. Periodontal health was evaluated by estimating the modified and validated PEriodontal Screening Score (mPESS), with mPESS at least 5 corresponding to a high probability of severe periodontitis. Descriptive statistics and Cox proportional hazards regression models, taking into account sociodemographic and lifestyle confounders, were used.

Results: The study population consisted of 32 285 participants (mean age: 45.79 ± 13.87 years); 78.5% were women. Two thousand one hundred and sixteen incident cases of arterial hypertension were identified during a median follow-up of 8 years (April 2012–December 2019). In the fully adjusted model, an mPESS at least 5 [hazard ratio: 1.84; 95% confidence interval (CI): 1.66–2.03] and the presence of nonreplaced missing teeth (hazard ratio: 1.13; 95% CI: 1.03–1.23) were significantly associated with a greater risk of incident arterial hypertension, whereas a regular annual visit to the dentist was associated with a lower risk (hazard ratio: 0.88; 95% CI: 0.80–0.97).

Conclusion: Self-reported assessed periodontitis was associated with incident arterial hypertension over an 8-year period. The present results highlight the importance of considering periodontal health when assessing an individual's risk of arterial hypertension.

Trial registration: # NCT03335644

Keywords: arterial hypertension, general population, high blood pressure, oral health, periodontitis, prospective study

Abbreviations: mPESS, modified periodontal screening score; OR, odds ratio

INTRODUCTION

Periodontal health is defined as the absence of clinically detectable inflammation of the periodontium, the supporting apparatus of the tooth, including the gingiva, the alveolar bone, the periodontal ligament, and the cementum [1]. Periodontitis is a chronic, multifactorial, dysbiotic, inflammatory disease, representing one of the major causes of tooth loss in adulthood [2–4]. According to recent epidemiological data, severe periodontitis is estimated to affect 11.2% of the global adult population [5], with country-specific prevalence estimated at 8.5% in the USA [6] and 10.2% in France [7].

In addition to being a common cause of tooth loss [8], untreated severe periodontitis can adversely affect systemic health, being associated with type 2 diabetes, cardiovascular diseases (CVD), rheumatoid arthritis, and adverse pregnancy outcomes [9]. This is mainly related to the low-grade systemic inflammation associated with poor periodontal health – characterized by increased C-reactive protein (CRP), interleukin-6 (IL-6), and fibrinogen levels – which can contribute to the development of other systemic conditions [10]. In particular, the relationship between periodontal diseases and CVD has been studied extensively, with epidemiological evidence highlighting that individuals

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with periodontitis have a higher prevalence of atherosclerosis, and consequently are at higher risk of coronary heart disease and myocardial infarction [11].

Arterial hypertension is a very common chronic condition associated with increased risk of CVD [12]. On the basis of international surveys, the rate of elevated SBP (≥ 110 – 115 mmHg) increased substantially between 1990 and 2015, with approximately one in four adults being affected [13]. The 2017 Global Burden of Disease study indicated that nonoptimal blood pressure leads to 10.4 million deaths and 218 million lost healthy life-years each year, making arterial hypertension one of the leading risk factors of all-cause mortality worldwide [14]. In France, the prevalence of arterial hypertension is estimated at 30.6% [95% confidence interval (CI): 28.1–33.2] [15,16], with a global 10-year incidence of 19.9% [17,18].

Over the years, some studies have suggested an association between periodontal diseases and arterial hypertension, with the potential involvement of periodontitis as a risk factor for arterial hypertension [19,20]. In fact, as periodontitis contributes to low-grade systemic inflammation, it might provoke endothelial dysfunction, and therefore, impaired vasodilation responses that ultimately lead to increased blood pressure [21]. A recent interventional study further indicated that periodontitis may cause immune-mediated blood pressure elevation associated with endothelial dysfunction in a dose-dependent manner [22]. Moreover, the severity of periodontitis was found to be associated with increased SBP and left ventricular mass in patients with hypertension [23,24]. A relationship between arterial hypertension and poor oral hygiene, as well as gingival inflammation and tooth loss, has also been shown [25–28]. As indirect proof, an intensive periodontal treatment was found to reduce systemic inflammatory markers and SBP [29].

Due to their prevalence in the general population and their link to CVDs, both periodontitis and arterial hypertension are considered as major health problems that need to be addressed by preventive campaigns and early diagnosis and care. This is even more important in a pandemic context, during which people are refractory to visits to doctors or dentists for routine checkups or to seek treatments for nonurgent issues, with potential long-term deleterious consequences on systemic health [30–34].

The present study aimed to evaluate the association between self-reported periodontal health and incident arterial hypertension by analyzing longitudinal data of the French e-cohort NutriNet-Santé.

METHODS

The NutriNet-Santé e-cohort

NutriNet-Santé is an ongoing population-based e-cohort launched in France in 2009 (www.etude-nutrinet-sante.fr) [35]. The study was approved by the ethics committee of the French Institute for Health and Medical Research (INSERM No. 0000388FWA00005831) and the National Commission on Informatics and Liberty (CNIL No. 908450 and No. 909216). It is registered at clinicaltrials.gov (# NCT03335644). The present study is reported according to the STROBE guidelines [36].

Adult volunteers with Internet access were recruited by means of traditional strategies (e.g. flyers) and multimedia

campaigns. Participants provided informed consent and an electronic signature prior to enrollment. At inclusion, they completed a set of five questionnaires about sociodemographics/lifestyle, anthropometrics, physical activity, diet (24-h records) and health status. On a regular basis (approximately once a month), participants were asked to fill out additional questionnaires on nutrition and/or health-related topics. For the present analysis, we applied the following inclusion criteria: participants who completed two oral health questionnaires sent in November 2011 and in April 2012 (each being available for a period of 6 months); no pregnancy; no type I or type II diabetes, no cancer (any location), no CVD, and no arterial hypertension at baseline (the date of oral health questionnaire completion). Incident cases of major CVD (including myocardial infarction, acute coronary syndrome, and stroke) that may justify the use of antihypertensive medications in the absence of arterial hypertension self-report were excluded from the analyses. The present study is part of a larger investigation into the determinants and comorbidities of periodontitis at the epidemiological level [37].

Oral and periodontal health assessment

The two oral health questionnaires provided data on oral health factors that are linked to periodontal health, including information on oral hygiene, oral health habits, need for dental treatments, visit to the dentist, number of teeth, replacement of missing teeth, masticatory comfort, and chewing capacity. Periodontitis was explored through questions originally included in the questionnaire of the Centers for Disease Control and Prevention and the American Academy of Periodontology (CDC/AAP) [38], that was translated (in French) and validated against a full-mouth clinical periodontal examination [39]. On the basis of this questionnaire, Carra *et al.* recently developed and validated a user-friendly score to estimate the individual probability of suffering from severe periodontitis, namely the PEriodontal Screening Score (PESS), based on five selected self-report items, including the self-evaluation of gum and teeth health (categorized into three classes: excellent-to-good, fair, and poor), the report of root planing treatments received for gum disease (yes/no), the presence of loose teeth (yes/no), the (dentist's) report of having lost bone around teeth (yes/no), and the perception that a tooth does not look right (yes/no). To obtain the PESS, answers to each item are weighted and combined with the subject's age and smoking status (yes/no) [39]. The PESS can range from 0 to 13 with a score at least 5 having the best sensitivity/specificity balance to identify people possibly suffering from severe periodontitis. Due to a missing question in the NutriNet-Santé e-cohort about a 'tooth that does not look right', a modified version of the PESS (mPESS) was developed by calculating the score for the available four self-report questions concerning periodontitis along with age and smoking. As described in a previous study that applied the mPESS to the NutriNet-Santé data [37], the diagnostic accuracy of the mPESS showed an area under the receiver operating curve of 0.82, with a sensitivity of 71.3% and a specificity of 79.5% for a cutoff score at least 5, which was then used to identify severe periodontitis cases.

Arterial hypertension assessment

Incident cases of arterial hypertension were identified through annual follow-up health status questionnaires as those participants who reported a first-time diagnosis of arterial hypertension and/or use of antihypertensive therapy after the date of completion of the second oral health questionnaire (April 2012, considered as the study baseline) up to December 2019. Case ascertainment was based on the same criteria used in a previous study investigating arterial hypertension in the NutriNet-Santé database [40].

Sociodemographic, lifestyle, and general health assessment

Socio-demographic and lifestyle characteristics, including age, sex, height and weight (based on which BMI was estimated), smoking status, daily alcohol consumption, daily physical activity, educational level, household income, and socio-professional category, were collected at inclusion by means of self-administered validated questionnaires [41–43]. Smoking status was categorized into four categories: daily smokers, occasional smokers, former smokers, and never smokers. Alcohol intake was assessed by estimating the mean ethanol quantity consumed daily (g/day), based on at least three 24-h dietary records [37]. Physical activity was assessed with the International Physical Activity Questionnaire – Short Form (IPAQ Group. IPAQ scoring protocol. www.ipaq.ki.se), and the information reported was converted into the following categories, as previously described [38]: less than 30 min of walking per day; at least 30 min and less than 60 min of walking/day; at least 60 min of walking/day. Educational level, socio-professional category [41], and household income were self-reported by the participants, who could choose among different categories for each construct or refuse to answer the question. Information about family history of arterial hypertension (defined as having at least one hypertensive first-degree parent) was also collected.

Statistical analysis

Descriptive analyses of the whole sample and by arterial hypertension status at follow-up were carried out with chi-squared tests and Student *t* tests. Data are reported as frequency (percentages) or mean (SD), as appropriate. Responses such as ‘I don’t know’ or ‘not reported’ were kept as separate variable categories in the analyses. The association between oral/periodontal health problems at baseline (main exposure) and the incidence of arterial hypertension (main outcome) over the follow-up period (April 2012–December 2019) was investigated by Cox proportional hazards models, providing hazard ratios and a 95% CI. In addition, we used the nonparametric Kaplan–Meier estimator. Periodontal health risk factors were modeled individually and in combination through the mPESS. In particular, susceptibility to severe periodontitis, as measured by the mPESS, was modeled separately as this composite variable constitutes age and smoking, which are also known risk factors for arterial hypertension. Moreover, to increase specificity, the analysis with mPESS as the exposure variable was carried out only on dentate participants ($n = 28\,506$) who might suffer from periodontitis

(edentulous or potentially edentulous individuals were excluded from this subgroup analysis).

Multivariable Cox models were adjusted for the following sociodemographic and lifestyle variables, as follows: model 1 was adjusted for age, sex, and BMI, whereas model 2 was adjusted for age, sex, BMI, education, household income, socio-professional category, daily ethanol intake, smoking status, physical activity, and family history of arterial hypertension. The primary time-dependent variable was duration of follow-up, censored at the date of the last follow-up, after excluding the cases of death. The measured event was the self-report of arterial hypertension diagnosis or the initiation of an antihypertensive treatment. The assumption of proportionality of the hazard model was verified by plotting arterial hypertension-free survival using the Kaplan–Meier curve and a Log-rank test was used for group comparisons between individuals with high mPESS vs. low mPESS. We had no a priori hypotheses about the association being different according to sex, therefore, no interaction tests were performed [40].

Statistical analyses were carried out with SPSS (SPSS version 22.0; SPSS Inc., Chicago, Illinois, USA). A *P* value less than 0.05 was considered statistically significant.

RESULTS

From the overall NutriNet-Santé e-cohort in 2011 ($N = 118\,637$), we selected those who completed the two oral health questionnaires in the absence of pregnancy ($n = 39\,969$); then, we excluded prevalent cases of arterial hypertension, CVD, cancer (any location), and diabetes (type I or type II) ($n = 7\,684$), and incident cases of CVD (including myocardial infarction, acute coronary syndrome and stroke, all of which had been validated using hospital records) reported during the follow-up period, which may have justified the use of antihypertensive therapy in the absence of incident arterial hypertension ($n = 17$). Consequently, 32 285 participants composed the final sample included in the present analyses (Fig. 1).

During a mean follow-up of 91.5 months (median: 95 months; interquartile range: 2 months), the annual health status questionnaires enabled the identification of 2116 (6.6%) incident cases of arterial hypertension. New case ascertainment was based on self-reported diagnosis and the use of antihypertensive therapy for 85.5% of cases, and on antihypertensive therapy only, reported without having declared other disorders that may have required such medication, for the remaining 14.5% of cases. The study sample was mostly composed of women ($n = 25\,355$; 78.5% of the sample), with an overall mean age of 45.79 (SD: 13.87); 50.4% of the sample was aged between 26 and 49 years old (Table 1).

The majority of the oral/periodontal health-related variables, including number of teeth, presence of nonreplaced missing teeth, frequency of tooth brushing, self-perceived oral health, presence of a loose tooth, report of alveolar bone loss, and presence of gingival disease, were associated in the expected direction with incident arterial hypertension at the bivariate level. The mean mPESS and the frequency of mPESS at least 5 were also significantly

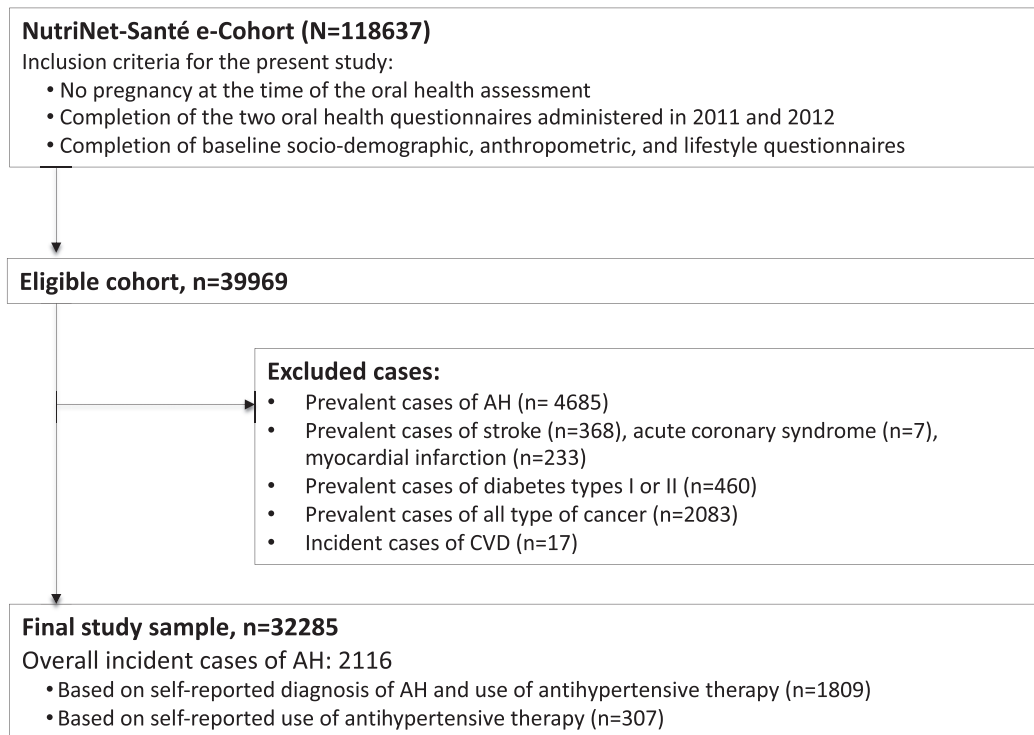


FIGURE 1 Flowchart of the study sample selection. AH, arterial hypertension.

TABLE 1. Socio-demographic characteristics of the whole study sample and by incidence of arterial hypertension

Demographic variables	Whole sample (N = 32285)	Incident AH (N = 2116)	No AH (N = 30169)	P value ^a
Age [mean (SD)]	45.79 (13.87)	56.49 (11.45)	45.04 (13.71)	<0.0001
Male sex [n (%)]	6930 (21.50)	676 (31.90)	6254 (20.70)	<0.0001
BMI [mean (SD)]	23.22 (3.95)	25.42 (4.57)	23.06 (3.86)	<0.0001
Smoking frequency [n (%)]				
Yes, every day	3164 (9.80)	168 (7.90)	2996 (9.90)	<0.0001
Yes, occasionally	1435 (4.40)	66 (3.10)	1369 (4.50)	
Former smoker	10 567 (32.70)	895 (42.30)	9672 (32.10)	
Never smoked	17 119 (53.0)	987 (46.6)	16 132 (53.50)	
Ethanol (g/day) [mean (SD)]	7.51 (11.14)	10.82 (15.67)	7.71 (12.01)	<0.0001
Physical activity				<0.0001
<30 min of walking/day	6965 (21.60)	399 (18.90)	6566 (21.80)	
≥30 min but <60 min of walking/day	6833 (21.20)	399 (18.90)	6434 (21.30)	
≥60 min of walking/day	13 775 (42.70)	1012 (47.80)	12 763 (42.30)	
Not reported	4712 (14.60)	306 (14.50)	4406 (14.60)	
Family history of AH [n (%)]	14 226 (44.10)	1306 (61.70)	12 920 (42.80)	<0.0001
Educational level [n (%)]				<0.0001
High school or less	9833 (30.50)	822 (38.80)	9011 (29.90)	
Undergraduate	11 142 (34.50)	717 (33.90)	10 425 (34.60)	
Graduate	11 095 (34.40)	562 (26.60)	10 533 (34.90)	
Other or not specified	215 (0.70)	15 (0.70)	200 (0.70)	
Household income [n (%)]				<0.0001
<1200 €/month	2985 (9.20)	107 (5.10)	2878 (9.50)	
1200–1799 €/month	4804 (14.90)	202 (9.50)	3174 (10.50)	
1800–2699 €/month	15 515 (54.30)	372 (17.60)	4432 (14.70)	
≥2700 €/month	3605 (11.20)	1241 (58.60)	16 274 (53.90)	
Not reported		194 (9.20)	3411 (11.30)	
Socio-professional category [n (%)]				<0.0001
Manual workers/farmers	880 (2.70)	77 (3.60)	803 (2.70)	
Office work/administrative/employees	8829 (27.30)	507 (24.0)	8322 (27.60)	
Intellectual professions/executive staff	11 100 (34.40)	764 (36.10)	10 336 (34.30)	
Artisan/merchant/intermediate-skill profession	9791 (30.30)	738 (34.90)	9053 (30.0)	
Not reported	1685 (5.20)	30 (1.40)	1655 (5.50)	

Significant P values are expressed in italic characters. Physical activity assessed with the International Physical Activity Questionnaire – Short Form. AH, arterial hypertension. ^aComparisons between incident AH vs. no AH groups (chi-squared tests and Student t tests).

TABLE 2. Oral and periodontal health characteristics of the whole study sample and by incidence of arterial hypertension

Oral health evaluation	Whole sample	Incident AH	No AH	P value ^a
How many natural teeth do you have? [n (%)]				<0.0001
<20 teeth	4570 (14.20)	478 (22.60)	4092 (13.60)	
≥20 teeth	26628 (82.50)	1563 (73.90)	25065 (83.10)	
I don't know	1087 (3.40)	75 (3.50)	1012 (3.40)	
Do you have missing teeth not replaced by dental prosthesis (except for wisdom teeth)? [n (%)]				<0.0001
Yes	10464 (32.40)	949 (44.80)	9515 (31.50)	
No	21684 (67.20)	1157 (54.70)	20527 (68.0)	
I don't know	137 (0.40)	10 (0.50)	127 (0.50)	
Do you have any difficulties in chewing or eating food? [n (%)]				0.002
Yes	13946 (43.20)	991 (46.80)	12955 (42.90)	
No	18182 (56.30)	1116 (52.70)	17066 (56.60)	
I don't know	157 (1.50)	9 (0.40)	148 (0.50)	
How often do you visit your dentist? [n (%)]				<0.0001
Regularly (once or twice per year)	25921 (64.80)	1464 (69.20)	19457 (64.50)	
Seldom (every two years or less)	11302 (35.0)	649 (30.70)	10653 (35.30)	
Never	62 (0.20)	3 (0.10)	59 (0.20)	
How often do you brush your teeth? [n (%)]				<0.0001
Once a day or more often	30725 (95.20)	1957 (92.50)	28768 (95.40)	
At least once per week but less than once a day	804 (2.50)	61 (2.90)	743 (2.50)	
Not reported	756 (2.30)	98 (4.60)	658 (2.20)	
Do you suffer from bleeding gums when brushing teeth, flossing or during any other moment? [n (%)]				0.035
Yes	10395 (32.20)	637 (30.10)	9758 (32.30)	
No	21890 (67.80)	1479 (69.90)	20411 (67.70)	
Periodontal health evaluation				<0.0001
How would you rate the health of your teeth and gums? [n (%)]				
Good	25031 (77.50)	1535 (72.50)	23496 (77.90)	
Fair	5976 (18.50)	470 (22.20)	5506 (18.30)	
Poor	1177 (3.60)	102 (4.80)	1075 (3.60)	
I don't know	101 (0.30)	9 (0.40)	92 (0.30)	
Have you ever received root planing treatment? [n (%)]				0.434
Yes	44 (0.10)	5 (0.20)	39 (0.10)	
No	32212 (99.80)	2109 (99.70)	30103 (99.80)	
I don't know	29 (0.10)	2 (0.10)	27 (0.10)	
Have you ever had any tooth become loose on its own, without any injury? [n (%)]				<0.0001
Yes	3137 (9.70)	320 (15.20)	2817 (9.30)	
No	28690 (88.90)	1774 (83.80)	26916 (89.30)	
I don't know	458 (1.40)	22 (1.0)	436 (1.40)	
Have you ever been told by a dental professional that you lost bone around your teeth? [n (%)]				<0.0001
Yes	2519 (7.80)	224 (10.60)	2295 (7.60)	
No	28566 (88.50)	1778 (84.0)	26788 (88.80)	
I don't know	1200 (3.70)	114 (5.40)	1086 (3.60)	
Do you think you might have a gum disease? [n (%)]				0.003
Yes	2235 (6.90)	177 (8.40)	2058 (6.80)	
No	27702 (85.80)	1764 (83.40)	25938 (86.0)	
I don't know	2348 (7.30)	175 (8.20)	2173 (7.20)	
mPESS ^b [mean (SD)]	2.71 (2.21)	3.96 (1.99)	2.62 (2.19)	<0.0001
mPESS ^b at least 5 [n (%)]	4864 (17.10)	570 (29.60)	4294 (16.20)	<0.0001

mPESS, modified and validated PEriodontal Screening Score.

^aComparisons between incident arterial hypertension (AH) vs. no AH groups (chi-squared tests).

^bAssessed among $n = 28\,506$ participants (because of exclusion of all edentulous or potentially edentulous individuals). AH: $n = 1925$; no AH: $n = 26\,581$.

different between individuals who developed arterial hypertension and those who did not (Table 2).

During the follow-up, 21 (0.1%) individuals died. After excluding these deceased cases, the Cox regression analysis was run to identify factors associated with incident arterial hypertension ($n = 32\,264$). After taking into account multiple socio-demographic and lifestyle confounders, the presence of nonreplaced missing teeth was associated with a significantly greater risk of arterial

hypertension, whereas a regular visit to the dentist was associated with a significantly lower risk (Table 3). Moreover, compared with mPESS less than 5, having an mPESS at least 5 was associated with incident arterial hypertension with a hazard ratio of 1.84 (95% CI: 1.66–2.03). Participants with mPESS at least 5 showed a significantly greater occurrence of arterial hypertension during the 8-year follow-up period, as displayed by the Kaplan–Meier curves ($P < 0.0001$) (Fig. 2).

TABLE 3. Hazard ratios of incident arterial hypertension in relation to oral/periodontal health factors

Oral/periodontal health-related variables	HR (95% CI) Model 1	HR (95% CI) Model 2
Fewer than 20 natural teeth (ref: ≥ 20 teeth)	1.01 (0.91–1.12) <i>P=0.821</i>	(0.93–1.14) <i>P=0.589</i>
Missing teeth not replaced by dental prosthesis (ref: missing teeth replaced by dental prosthesis)	1.14 (1.05–1.25) <i>P=0.002</i>	1.13 (1.03–1.23) <i>P=0.006</i>
Difficulty in chewing or eating food (ref: no difficulty)	1.02 (0.93–1.11) <i>P=0.679</i>	1.00 (0.92–1.09) <i>P=0.916</i>
Bleeding gums when brushing teeth, flossing or during any other moment (ref: no bleeding)	1.03 (0.93–1.13) <i>P=0.569</i>	0.99 (0.91–1.09) <i>P=0.971</i>
Annual visit(s) to the dentist (ref: less than once every 2 years)	0.88 (0.81–0.97) <i>P=0.011</i>	0.88 (0.80–0.97) <i>P=0.007</i>
Infrequent tooth brushing (ref: ≤ 1 /day)	1.00 (0.82–1.23) <i>P=0.940</i>	1.01 (0.82–1.24) <i>P=0.929</i>
Poor health of teeth and gum (ref: good/fair health)	1.01 (0.92–1.09) <i>P=0.910</i>	1.06 (0.85–1.31) <i>P=0.612</i>
Root planing (ref: no root planing)	1.04 (0.84–1.27) <i>P=0.703</i>	1.06 (0.86–1.30) <i>P=0.551</i>
Loose tooth (ref: no loose tooth)	1.03 (0.91–1.16) <i>P=0.658</i>	1.02 (0.91–1.13) <i>P=0.301</i>
Lost bone (ref: no bone loss)	1.13 (0.98–1.30) <i>P=0.084</i>	1.12 (0.97–1.29) <i>P=0.111</i>
Gum disease (ref: no gum disease)	1.07 (0.92–1.25) <i>P=0.357</i>	1.05 (0.90–1.23) <i>P=0.515</i>
mPES ≥ 5 (ref: mPES < 5) ^a	1.96 (1.78–2.16) <i>P<0.0001</i>	1.84 (1.66–2.03) <i>P<0.0001</i>

Significant *P* values are expressed in italic characters. HR, hazard ratio (Cox proportional hazards models); mPES, modified and validated PERiodontal Screening Score. Model 1 is adjusted for: age, sex, BMI (except for mPES, for which the model included sex and BMI). Model 2 is adjusted for: age, sex, BMI, education, household income, socio-professional category, ethanol intake, smoking status, physical activity, and family history of AH (except for mPES, for which the model included: sex, BMI, education, household income, socioprofessional category, ethanol intake, physical exercise, and family history of AH).
^aModeled separately among 28 487 individuals.

DISCUSSION

The present study, based on a large e-cohort of French adults recruited from the general population, showed that incident arterial hypertension was associated with self-reported periodontitis. The risk of having severe periodontitis (mPES ≥ 5) at baseline appeared to be an independent predictor of arterial hypertension development during an 8-year follow-up; a similar association was found for the

condition of having missing teeth that were not replaced with dental prostheses. Interestingly, these longitudinal findings also support the preventive role of visiting the dentist regularly, as individuals who reported seeing their dentist on an annual basis had a 12% lower risk of developing arterial hypertension than those who did not report such visits. To our knowledge, the present investigation is the first to explore the impact of self-reported periodontal health status on incident arterial hypertension over 8 years of follow-up in a large prospective e-cohort.

At the European level, the majority of previous reports have been cross-sectional studies that essentially explored the magnitude of the association between periodontal diseases and arterial hypertension [19], with odds ratios ranging between 1.15 and 1.67. This magnitude varies because of the heterogeneity in the definitions of periodontitis and in the methods used to assess periodontal status and arterial hypertension. Data from a Chinese population are consistent with the European findings. More specifically, arterial hypertension risk was associated with periodontal disease in both unadjusted (OR = 1.28; 95% CI: 1.14–1.47; *P* < 0.0001) and adjusted models (OR = 1.34; 95% CI: 1.14–1.58; *P* < 0.0001) [44].

Concerning previous longitudinal data, the study by Kawabata *et al.* showed a significant association between periodontitis and incident arterial hypertension, which was clinically evaluated, in a university-based sample of 2588 Japanese students (age range: 18.2–18.9 years), of whom 221 (8.5%) were identified as having periodontitis during the 3-year follow-up [45]. Conversely, another cohort study conducted in Puerto Rico failed to find a significant relationship between severe periodontitis, measured clinically,

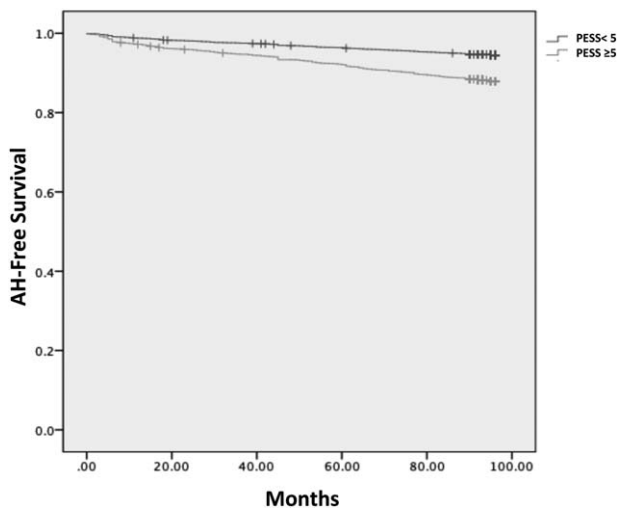


FIGURE 2 Kaplan–Meier survival curve for arterial hypertension comparing participants with modified and validated PERiodontal Screening Score at least 5 (high risk of severe periodontitis) and participants with modified and validated PERiodontal Screening Score less than 5 (low risk of severe periodontitis) (*P* < 0.0001, log-rank test).

and self-reports of high blood pressure [26]. However, as stressed by the authors, the lack of a significant relationship might have been because of insufficient statistical power, insufficient adjustments for confounding variables, and/or specific study population characteristics. Indeed, the study sample consisted of health professionals who are typically more likely to take care of their health than the general population [26]. In a cohort of 572 adult industrial workers in Japan, Morita *et al.* observed that exposure to periodontitis was significantly associated with cardiometabolic risk factors, such as obesity, dyslipidemia, hyperglycemia, and arterial hypertension, during a 9-year follow-up period. In particular, participants with periodontal pockets for at least 6 years (untreated periodontitis) had a 2.2-fold greater risk of arterial hypertension compared with participants without periodontitis [46]. Finally, data from the South Korean National Health Insurance Service–Health Examinee Cohort (2002–2013), which enrolled 200 026 individuals with periodontal disease and 154 824 individuals with a healthy oral status, showed that periodontal disease was significantly related to arterial hypertension (OR = 1.04; 95% CI: 1.01–1.07; $P < 0.014$), after adjustment for sex, age, household income, insurance status, area of residence, health status, and smoking [47].

In the present study, we assessed periodontal status from a validated self-reported questionnaire and by calculating the mPESS, which is a composite variable including several aspects related to severe periodontitis, as well as age and smoking, which are known risk factors for periodontitis [48]. The mPESS must be interpreted as a risk estimate and not as a confirmed diagnosis, yet it allows identifying individuals who may need further examinations and treatments to attain and maintain periodontal health. Within this perspective, our results suggest that individuals with a regular access to a dentist (and probably to treatments) have a lower risk of arterial hypertension, whereas those at high risk of suffering from severe periodontitis or those having lost several teeth without replacing them with dental prosthesis (corresponding to poor oral/periodontal health) are more susceptible to develop arterial hypertension. Visiting the dentist regularly is a personal choice (which is an especially salient factor in a country, such as France where access is virtually universal) that usually reveals the individual's attention and care for oral health as well as general health. It is also related to socioeconomic factors and education, which were taken into account in the multivariable analyses. Thus, it could be assumed that individuals with regular dental checkups have maintained good oral hygiene and periodontal health but they may also be more prone to seeking medical attention in the event of experiencing any symptoms or discomfort, and to follow medical advice more scrupulously. On the other hand, the present findings confirmed that a strong association exists between the status of being at risk of severe periodontitis (baseline assessment) and the risk of developing arterial hypertension over time. This has important implications for clinical practice and public health. Periodontitis is a highly prevalent chronic disease, yet it is easily diagnosable and successful treatment is available. Periodontal health can be maintained over time via basic preventive care (e.g. personal oral hygiene, regular professional scaling). Similarly,

efforts should be made to prevent tooth loss and provide oral rehabilitation to replace missing teeth, as deficits in masticatory capacity can influence nutritional habits and contribute to the inflammatory burden impacting on cardiovascular health [24,28,49–51]. To contextualize these findings to the current COVID-19 pandemic, repeated lockdowns, and general fear of infectability, the observed changes in people's behaviors, like avoiding dental care and periodontal treatments, can promote the subsequent development or evolution of noncommunicable chronic diseases, such as arterial hypertension, ultimately influencing related morbidity and mortality in the long-run [30,33,34].

The present study has strengths and limitations. One of the major strengths is the large sample of individuals recruited from the general population (>30 000 participants) who were followed-up for approximately 8 years. It is also the first study showing an association between self-reported severe periodontitis and incident arterial hypertension in a European nonclinical population. A number of potential confounding factors were taken into account in the Cox regression models, although residual confounding by additional socio-demographic factors as well as other health related factors (e.g. glycolipid profile, inflammatory status) that may impact oral health status and behaviors cannot be completely ruled out [52,53].

One can argue that the main limitation of the present study is the self-reported design, which is inherent to any epidemiological e-cohort study; exposure and outcome were both assessed via self-report questionnaires. However, the latter are nonetheless considered as validated tools and have already been used in previous studies [37,40], and proved to be useful methods for analyzing large samples [54]. Further, recall and reporting bias cannot be excluded, with a potential risk of underestimating the true incidence of arterial hypertension in the population studied [55]. Indeed, the number of incident arterial hypertension cases is somewhat lower than the rates reported in previous studies in France [17,18], partly explained by the characteristics of the studied population, composed predominantly of well educated, middle-aged women [56]. Oral health was assessed at baseline only. Changes may have occurred during the follow-up, including improvements (e.g. after treatment) or the breakdown of periodontal health. These may contribute to modulating the systemic inflammatory burden with subsequent consequences on blood pressure that could not be estimated. Notwithstanding this, the fact of being at risk of severe periodontitis in 2012 was found to be associated with self-reported incident arterial hypertension over the follow-up period. Finally, caution is needed when extrapolating these findings to the general French population as it has been shown that participants in epidemiological e-cohort studies are usually better educated and belong to higher socio-professional categories [57]. The health consciousness and nutrition consciousness of the participants in the NutriNet-Santé e-cohort may also be linked to the high proportion of women, representing over 75% of the sample, the relatively low proportion of smokers, and the generally good health status including oral health. It is worth noting that in France, the great majority of the working population has access to affordable

dental care covered by the public health system [58], although the history of oral care remains linked to socioeconomic status and should be considered when interpreting the results.

In conclusion, self-reported periodontitis was found to be associated with incident arterial hypertension over an 8-year period. It is thus important to pay attention to periodontal conditions when assessing the individual's risk of arterial hypertension, and to consider oral disease prevention as part of public health policies aimed at improving cardiovascular health.

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Conflicts of interest

There are no conflicts of interest.

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