

# BMJ Open Association between periodontitis and hypertension: cross-sectional survey from the Fourth National Oral Health Survey of China (2015–2016)

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## ABSTRACT

**Objectives** To evaluate the association between periodontitis severity and hypertension based on Chinese epidemiological data.

**Design** This cross-sectional survey enrolled adults from the Fourth National Oral Health Survey of China (2015–2016).

**Setting** The data were obtained from the Fourth National Oral Health Survey of China (2015–2016).

**Participants** The study included individuals aged 35–44 years (n=4409), 55–64 years (n=4568) and 65–74 years (n=4218).

**Primary and secondary outcome measures** Periodontal status, defined on the basis of the 2017 classification scheme, and periodontal parameters (eg, bleeding on probing (BOP)) were compared between individuals with hypertension and individuals with normotension. Smoothed scatterplots were constructed to demonstrate the associations of periodontal parameters and periodontal status with hypertension.

**Results** Severe periodontitis (stages III and IV) was present in 41.4% of individuals with hypertension and 28.0% of individuals with normotension, respectively (p<0.001). The prevalence of severe periodontitis was higher in individuals with hypertension than that in individuals with normotension among participants aged 35–44 years (18.0% vs 10.1%, p<0.001) and 55–64 years (40.2% vs 36.7%, p=0.035), but not in participants aged 65–74 years (46.4% vs 45.1%, p=0.429). Therefore, the difference in periodontal status between individuals with hypertension and individuals with normotension decreased with age. There were higher prevalences of BOP, probing depth (PD) ≥4 mm and PD ≥6 mm in individuals with hypertension than in individuals with normotension (52.1% vs 49.2%, 19.6% vs 14.7% and 1.8% vs 1.1%, respectively). Periodontitis severity and the proportion of teeth with PD ≥4 or ≥6 mm were positively associated with hypertension.

**Conclusion** Periodontitis is associated with hypertension in Chinese adults. Hypertension prevalence increased with periodontitis severity, particularly among young participants. Accordingly, it is necessary to improve the education, awareness of periodontal treatment and preventive management among individuals at risk of hypertension, particularly in the younger population.

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ The participant group was based on a large-scale national survey in China, and the sample size of the study was relatively large.
- ⇒ Periodontitis was diagnosed in accordance with the classification proposed at the 2017 World Workshop.
- ⇒ Hypertension was self-reported and not based on blood pressure measurements.

## INTRODUCTION

Hypertension, which affects 45% of the global population, is the most common cardiovascular disease (CVD) worldwide.<sup>1 2</sup> It is defined as systolic or diastolic blood pressure (BP) of ≥140 or ≥90 mm Hg, respectively. Hypertension is frequently poorly controlled and untreated.<sup>3</sup> It is a complex disease with multiple causes and a major risk factor for CVDs.<sup>4</sup> Oxidative stress, endothelial dysfunction and inflammation are associated with the development of hypertension.<sup>5</sup> The results of experimental and clinical studies suggest that inflammation has a major role in the development of hypertension.<sup>6</sup> Chronic inflammation predisposes to the development of pro-hypertensive inflammation.

Periodontal disease, an immune-inflammatory reaction to plaque biofilms,<sup>7</sup> has received substantial attention because of its association with CVDs. The Global Burden of Disease Study revealed that periodontitis was the sixth most prevalent disease worldwide. Periodontitis affects 743 million people worldwide (11.2% of the global population); the prevalence is higher in China than in other countries. The Fourth National Oral Health Survey of China showed that 90.9% of individuals aged 35–44 years had periodontal disease.<sup>8 9</sup> The low-grade inflammation associated with periodontitis has harmful effects on

endothelial function, which may result in hypertension.<sup>10</sup> A recent study revealed that individuals with periodontitis have increased risks of hypertension and antihypertensive treatment failure.<sup>11,12</sup> Previous studies have suggested that dental treatment can improve BP, although the findings have been inconclusive and further studies are needed.<sup>13–16</sup>

Periodontitis and hypertension are major health problems, and their association received considerable public health attention. Therefore, we evaluated the relationship between periodontitis and hypertension based on data from the Fourth National Oral Health Survey of China. We sought to determine whether individuals with periodontitis are more likely to have hypertension than individuals who do not have periodontitis, and whether periodontitis severity is associated with hypertension.

## MATERIALS AND METHODS

### Study design and sample

This cross-sectional study obtained data from adult participants of the Fourth National Oral Health Survey of China (2015–2016).<sup>8</sup> The planned sample size was 4230 each for the age groups 35–44, 55–64 and 65–74 years. We excluded data from edentulous participants and from those without complete information. Finally, 13 195 individuals were included (4409, 4568, and 4218 individuals aged 35–44, 55–64, and 65–74 years, respectively).

### Data collection

We collected data related to oral examination findings and questionnaire answers.

### Periodontal examination

Periodontal examinations were performed using a community periodontal index probe. A full mouth examination was performed, during which the probe was walked along the gingival crevices using a force of  $\leq 20$  g to assess bleeding on probing (BOP), the presence of calculus, probing depth (PD) and attachment loss (AL). For each parameter, each tooth was scored according to the condition of the most severely affected site. Training programmes were conducted for examiner calibration before the survey. The reliability of the results was assessed using kappa values; kappa values for periodontal pocket depth were  $\geq 0.6$ . Additionally, 5% of the participants were randomly selected for assessment of interexaminer reproducibility. The kappa values for all age groups were 0.76–0.80.

### Patient and public involvement

The study participants and the public were not involved in the design, conduct, reporting or dissemination plans of our research.

### Study parameters

Supragingival and subgingival calculus were identified by visual examination and probing, respectively (0=absent, 1=present, 9=tooth excluded and X=tooth not present).

PD was recorded as 0 (1–3 mm), 1 (4–5 mm), 2 ( $\geq 6$  mm), 9 (tooth excluded) or X (tooth not present). BOP was recorded as 0 (absent), 1 (present), 9 (tooth excluded) or X (tooth not present). AL was measured as the distance from the cemento-enamel junction to the bottom of the periodontal pocket; it was recorded as 0 (0–3 mm), 1 (4–5 mm), 2 (6–8 mm), 3 (9–11 mm), 4 ( $\geq 12$  mm), 9 (tooth excluded) or X (tooth not present).

The classification scheme proposed at the 2017 World Workshop on the Classification of Periodontal and Per-Implant Diseases and Conditions was used to classify the periodontal status as periodontally healthy ( $< 10\%$  BOP-positive sites and PD  $\leq 3$  mm) or gingivitis ( $\geq 10\%$  BOP-positive sites and PD  $\leq 3$  mm). Periodontitis was staged using the algorithm developed by Tonetti *et al.*<sup>17</sup> For each tooth, periodontitis of stages I–III was defined as AL of 1–2 mm, 3–4 mm and  $\geq 5$  mm, respectively. We also considered the number of teeth lost when classifying periodontitis: stages I and II, no tooth loss; stage III,  $\leq 4$  teeth lost; and stage IV,  $\geq 5$  teeth lost. The cause of tooth loss was not considered. Finally, we evaluated the complexity of patient management. Stage II patients were reclassified as stage III if the maximum PD was  $\geq 6$  mm. Stage III patients were reclassified as stage IV if there were  $< 10$  opposing pairs of teeth. The stages of periodontitis reflect the severity and complexity of managing the individual patient.

### Interview data from the questionnaire

Questionnaires were administered during in-person interviews to collect data regarding demographics, socioeconomic status, habits, dental history and health attitudes. The following information was collected for analysis: age (years), annual family income (in increments of ¥10 000), sex (male or female), duration of education (years), self-reported hypertension (yes or no), smoking status (current smoker, former smoker or non-smoker) and region (urban or rural).

### Statistical analyses

Statistical analyses were performed using SPSS (V.19; IBM Corp) or R (V.3.6.1; R Foundation for Statistical Computing, Vienna, Austria). The primary outcome was periodontal status (health, gingivitis and stages I–IV periodontitis). The secondary outcomes were periodontal parameters (BOP-positive teeth, teeth with PD  $\geq 4$  and  $\geq 6$  mm, and teeth with AL  $\geq 4$ ,  $\geq 6$ , and  $\geq 9$  mm, presented as the percentages and numbers of teeth affected) and missing teeth. First, descriptive analysis was performed. Quantitative data are reported as means and SDs; categorical data are reported as numbers and percentages. Periodontal parameters were compared between individuals with hypertension and individuals with normotension; subgroup analyses were conducted according to age group and smoking status. Periodontal status and parameters were analysed using the  $\chi^2$  test. Additionally, smoothed scatterplots based on generalised additive models were constructed, with adjustment for confounders (gender, smoking status, region, duration of education and annual

family income), to evaluate the relationships of hypertension prevalence with periodontal status or parameters. The level of statistical significance was set at  $p < 0.05$ .

## RESULTS

The participants were randomly selected from 31 provinces, autonomous regions and municipalities in mainland China. In total, data from 13 195 individuals were included in the analysis; invalid data from 5 participants and data from 264 edentulous patients were excluded. The mean participant age was  $56.43 \pm 12.40$  years. The sample consisted of 6575 men (49.8%) and 6620 women (50.2%). There were 3470 non-smokers (26.3%), 8405 current smokers (63.7%) and 1318 former smokers (10.0%). Hypertension was present and absent in 3154 (23.9%) and 10 041 (76.1%) participants, respectively.

### Differences in periodontal status between participants with hypertension and participants with normotension decreased with age

Table 1 presents the distributions of periodontal status according to age, gender and smoking status in participants with and without hypertension.

Significantly greater proportions of participants with hypertension had stages I–IV periodontitis (70.3% vs 61.5%,  $p < 0.001$ ) and severe periodontitis (stages III–IV, 41.4% vs 28.0%,  $p < 0.001$ ), compared with participants with normotension. Stratified analysis according to gender showed that the prevalence of periodontitis (stages I–IV) was significantly higher in participants with hypertension than in participants with normotension in women (66.5% vs 55.9%,  $p < 0.001$ ), but not in men (74.0% vs 67.1%,  $p = 0.057$ ). Severe periodontitis (stages III and IV) was more common in participants with hypertension than in participants with normotension in both men (46.1% vs 32.7%,  $p < 0.001$ ) and women (36.6% vs 23.4%,  $p < 0.001$ ). Stratified analysis according to age showed that the prevalence of periodontitis (stages I–IV) was significantly higher in participants with hypertension than in participants with normotension among individuals aged 35–44 years (59.2% vs 52.3%,  $p = 0.030$ ), 55–64 years (72.7% vs 69.1%,  $p = 0.023$ ) and 65–74 years (70.3% vs 66.2%,  $p = 0.009$ ). Severe periodontitis (stages III and IV) was more common in participants with hypertension than in participants with normotension among individuals aged 35–44 years (18.0% vs 10.1%,  $p < 0.001$ ) and 55–64 years (40.2% vs 36.7%,  $p = 0.035$ ), but not among individuals aged 65–74 years (46.4% vs 45.1%,  $p = 0.429$ ). Therefore, differences in periodontal status between participants with hypertension and participants with normotension decreased with age (table 1). Stratified analysis according to smoking status showed that the prevalence of periodontitis (stages I–IV) was significantly higher in participants with hypertension than in participants with normotension among current smokers (76.2% vs 68.1%,  $p = 0.016$ ) and non-smokers (67.3% vs 57.4%,  $p < 0.001$ ), but not in former smokers (73.8% vs

70.6%,  $p = 0.972$ ). Severe periodontitis (stages III and IV) was more common in participants with hypertension than in participants with normotension in all three subgroups: current smokers (48.4% vs 34.7%,  $p < 0.001$ ), non-smokers (36.9% vs 23.7%,  $p < 0.001$ ) and former smokers (50.2% vs 38.0%,  $p < 0.001$ ).

Due to the limitation of the published format, the percentages of hypertensive group and normotensive group and the distribution of periodontal status by smoking group are omitted in table 1. The full table is uploaded as an online supplemental table 1.

### Periodontal parameters were significantly worse in participants with hypertension than in participants with normotension

Table 2 and online supplemental tables 2 and 3 present comparisons of periodontal parameters between participants with hypertension and participants with normotension. Compared with participants with normotension, participants with hypertension had significantly increased proportions of teeth with BOP (52.1% vs 49.2%), PD  $\geq 4$  mm (19.6% vs 14.7%), PD  $\geq 6$  mm (1.8% vs 1.1%), AL  $\geq 4$  mm (23.6% vs 17.2%) and AL  $\geq 6$  mm (6.6% vs 4.4%). The differences in the percentages of teeth with each periodontal parameter between participants with hypertension and participants with normotension were consistent in men and women, and among current smokers, former smokers and non-smokers (except for BOP, which showed no significant difference in men, current smokers and former smokers; and PD  $\geq 6$  mm, which showed no significant difference in former smokers). Differences in periodontal parameters between participants with hypertension and participants with normotension decreased with age. The differences in the mean prevalence of PD  $\geq 4$  mm were consistent in all age groups. Compared with participants with normotension, participants with hypertension had significantly more teeth with PD  $\geq 4$  mm (4.5 vs 3.5), PD  $\geq 6$  mm (0.4 vs 0.2), AL  $\geq 4$  mm (5.0 vs 3.8) and AL  $\geq 6$  mm (1.2 vs 0.8). The mean number of BOP-positive teeth was not significantly different between participants with hypertension and participants with normotension (12.4 vs 12.3). Differences in the mean number of teeth with each periodontal parameter between participants with hypertension and participants with normotension were consistent in men and women, and among current smokers, former smokers and non-smokers (except for BOP, which had significant differences in women, and PD  $\geq 6$  mm, which had no significant difference in former smokers). The difference in the mean number of teeth between participants with hypertension and participants with normotension decreased with age. Furthermore, differences in the number of teeth with PD  $\geq 4$  mm and PD  $\geq 6$  mm sites were consistent in all age groups.

Due to the limitation of the published format, the comparison of the percentage of teeth with each periodontal parameter between participants with hypertension and participants with normotension according

**Table 1** Comparison of distribution of periodontal status according to the 2017 classification by age/gender group between participants with hypertension (HT) and participants with normotension (NT)

	Periodontal status	HT		NT		P value 1*	P value 2†
		N	Percentage (95% CI)	N	Percentage (95% CI)		
Male	Health	598	11.1~12.9	159	8.7~11.7	0.057	<0.001
	Gingivitis	1051	19.9~22.1	246	14.0~17.6		
	Stage I	844	15.8~17.9	171	9.5~12.6		
	Stage II	883	16.6~18.7	266	15.2~18.9		
	Stage III	906	17.0~19.2	357	20.8~25.0		
	Stage IV	730	13.6~15.6	364	21.2~25.4		
Female	Health	755	14.1~16.0	179	9.8~12.9	<0.001	<0.001
	Gingivitis	1461	27.8~30.3	355	20.3~24.4		
	Stage I	867	16.2~18.3	199	10.9~14.2		
	Stage II	770	14.3~16.3	277	15.6~19.3		
	Stage III	588	10.8~12.6	260	14.6~18.2		
	Stage IV	586	10.8~12.6	323	18.4~22.3		
35–44 years	Health	658	14.8~17.1	40	10.7~18.9	0.030	<0.001
	Gingivitis	1312	30.3~33.2	73	21.4~31.8		
	Stage I	1133	26.1~28.8	70	20.4~30.6		
	Stage II	612	13.8~15.9	44	11.9~20.5		
	Stage III	360	7.9~9.6	40	10.7~18.9		
	Stage IV	57	1.1~1.8	10	1.9~6.3		
55–64 years	Health	347	9.6~11.7	116	7.5~10.6	0.023	0.035
	Gingivitis	661	18.9~21.6	239	16.4~20.6		
	Stage I	403	11.2~13.5	174	11.7~15.4		
	Stage II	658	18.8~21.5	247	17.0~21.3		
	Stage III	659	18.8~21.5	273	18.9~23.3		
	Stage IV	544	15.4~17.9	247	17.0~21.3		
65–74 years	Health	348	12.0~14.5	182	10.0~13.1	0.009	0.429
	Gingivitis	539	18.9~22.0	289	16.4~20.2		
	Stage I	175	5.7~7.6	126	6.7~9.4		
	Stage II	383	13.2~15.9	252	14.2~17.8		
	Stage III	475	16.6~19.5	304	17.3~21.2		
	Stage IV	715	25.5~28.8	430	25.0~29.4		
Total	Health	1353	12.8~14.2	338	9.7~11.8	<0.001	<0.001
	Gingivitis	2512	24.2~25.9	601	17.7~20.4		
	Stage I	1711	16.3~17.8	370	10.6~12.9		
	Stage II	1653	15.8~17.2	543	15.9~18.6		
	Stage III	1494	14.2~15.6	617	18.2~21.0		
	Stage IV	1316	12.5~13.8	687	20.4~23.2		

\*Significant differences in the proportions of periodontitis (stages I–IV) and non-periodontitis (health and gingivitis) between participants with HT and participants with NT according to the  $\chi^2$  test.

†Significant differences in the proportions of severe periodontitis (stages III and IV) and non-severe periodontitis (health, gingivitis, stages I and II) between participants with HT and participants with NT according to the  $\chi^2$  test.

to smoking status is omitted in [table 2](#). The full table is uploaded as an online supplemental table 2.

Due to the limitation of the published format, the comparison of the number of teeth with each periodontal parameter between participants with hypertension and

**Table 2** Comparison of the percentage of teeth with each periodontal parameter between participants with hypertension (HT) and participants with normotension (NT) according to gender and age group

Group	Periodontal parameter	NT		HT		P value*
		Mean	95% CI	Mean	95% CI	
Male	BOP+	50.9	49.9~51.9	52.2	50.4~54.0	0.232
	PD ≥4 mm	17.9	17.2~18.6	22.6	21.3~24.0	<0.001
	PD ≥6 mm	1.5	1.3~1.6	2.3	1.9~2.7	<0.001
	AL ≥4 mm	20.9	20.2~21.7	27.5	26.0~28.9	<0.001
	AL ≥6 mm	5.7	5.3~6.1	8.3	7.5~9.1	<0.001
Female	BOP+	47.4	46.5~48.4	52.1	50.4~53.8	<0.001
	PD ≥4 mm	11.5	11.0~12.0	16.5	15.4~17.6	<0.001
	PD ≥6 mm	0.7	0.6~0.8	1.3	1.0~1.6	<0.001
	AL ≥4 mm	13.5	12.9~14.0	19.8	18.6~20.9	<0.001
	AL ≥6 mm	3.2	2.9~3.4	4.8	4.2~5.4	<0.001
35–44 years	BOP+	46.5	45.4~47.5	50.5	46.1~54.9	0.096
	PD ≥4 mm	10.5	9.9~11.1	15.8	12.8~18.8	0.001
	PD ≥6 mm	0.5	0.4~0.6	1.1	0.6~1.6	0.031
	AL ≥4 mm	6	5.6~6.4	10.1	7.8~12.4	0.001
	AL ≥6 mm	0.8	0.7~0.9	1.6	0.8~2.4	0.053
55–64 years	BOP+	52.5	51.3~53.7	54.0	52.1~56.0	0.188
	PD ≥4 mm	17.9	17.1~18.8	20.3	18.9~21.7	0.004
	PD ≥6 mm	1.4	1.2~1.6	1.9	1.6~2.2	0.024
	AL ≥4 mm	22.1	21.2~22.9	21.5	20.1~22.9	0.543
	AL ≥6 mm	5.3	4.9~5.8	5.5	4.8~6.2	0.722
65–74 years	BOP+	49.2	47.9~50.6	50.8	49.1~52.6	0.144
	PD ≥4 mm	17.4	16.5~18.3	19.6	18.4~20.8	0.004
	PD ≥6 mm	1.5	1.3~1.8	1.8	1.5~2.2	0.188
	AL ≥4 mm	28.7	27.6~29.8	27.6	26.3~29.0	0.239
	AL ≥6 mm	8.9	8.3~9.6	8.3	7.5~9.1	0.220
Total	BOP+	49.2	48.5~49.9	52.1	50.9~53.4	<0.001
	PD ≥4 mm	14.7	14.3~15.2	19.6	18.7~20.4	<0.001
	PD ≥6 mm	1.1	1.0~1.2	1.8	1.6~2.0	<0.001
	AL ≥4 mm	17.2	16.7~17.7	23.6	22.7~24.5	<0.001
	AL ≥6 mm	4.4	4.2~4.7	6.6	6.0~7.1	<0.001

\*Significant difference according to Student's t-test.

AL, attachment loss; BOP, bleeding on probing; PD, probing depth.

participants with normotension according to smoking status is omitted in [table 3](#). The full table is uploaded as an online supplemental table 3.

#### Hypertension prevalence increased with periodontitis severity

Multivariate regression analysis was performed to evaluate the relationship between hypertension and age stratified according to periodontal status, after adjustments for sex, smoking status, region, duration of education and annual family income ([table 4](#)). Compared with participants who did not have periodontitis, participants with stages III and IV periodontitis had a significantly increased risk of hypertension (OR=1.70, 95% CI= 1.45–1.99,

$p<0.001$ ). However, the difference between participants with stages I and II periodontitis and participants without periodontitis was not statistically significant (OR=1.03, 95% CI=0.88–1.20,  $p=0.717$ ). Therefore, hypertension prevalence increased with periodontitis severity. Notably, the OR for participants with stages III and IV periodontitis decreased with age; it was not statistically significant in participants aged 65–74 years ([table 4](#)).

#### Relationships of hypertension with periodontal parameters

[Tables 5 and 6](#) present the multivariate regression analyses of the relationships of hypertension with periodontal parameters, after adjustments for gender, smoking status,

**Table 3** Comparison of the number of teeth with each periodontal parameter between participants with hypertension (HT) and participants with normotension (NT) according to gender and age group

Group	Periodontal parameter	NT		HT		P value*
		Mean	95% CI	Mean	95% CI	
Male	BOP+	12.7	12.5~13.0	12.3	11.8~12.8	0.111
	PD ≥4 mm	4.2	4.0~4.4	5.1	4.8~5.4	<0.001
	PD ≥6 mm	0.3	0.3~0.3	0.5	0.4~0.6	<0.001
	AL ≥4 mm	4.6	4.5~4.8	5.7	5.4~6.0	<0.001
	AL ≥6 mm	1.1	1.0~1.1	1.5	1.3~1.6	<0.001
Female	BOP+	11.9	11.7~12.1	12.6	12.1~13.0	0.013
	PD ≥4 mm	2.7	2.6~2.9	3.8	3.6~4.1	<0.001
	PD ≥6 mm	0.1	0.1~0.2	0.3	0.2~0.3	<0.001
	AL ≥4 mm	2.9	2.8~3.1	4.3	4.0~4.5	<0.001
	AL ≥6 mm	0.6	0.5~0.6	0.9	0.8~1.0	<0.001
35–44 years	BOP+	12.7	12.4~13.0	13.6	12.4~14.8	0.143
	PD ≥4 mm	2.8	2.7~3.0	4.2	3.4~5.0	0.001
	PD ≥6 mm	0.1	0.1~0.2	0.3	0.1~0.4	0.036
	AL ≥4 mm	1.6	1.5~1.7	2.6	2.0~3.2	0.001
	AL ≥6 mm	0.2	0.2~0.2	0.4	0.2~0.6	0.049
55–64 years	BOP+	13.0	12.7~13.3	13.4	12.9~13.9	0.241
	PD ≥4 mm	4.2	4.0~4.4	4.8	4.4~5.1	0.005
	PD ≥6 mm	0.3	0.2~0.3	0.4	0.3~0.5	0.003
	AL ≥4 mm	5.0	4.8~5.2	4.8	4.5~5.1	0.222
	AL ≥6 mm	1.1	1.0~1.2	1.1	1.0~1.2	0.914
65–74 years	BOP+	10.9	10.6~11.3	11.5	11.0~11.9	0.051
	PD ≥4 mm	3.5	3.3~3.7	4.3	4.0~4.5	<0.001
	PD ≥6 mm	0.3	0.2~0.3	0.4	0.3~0.4	0.042
	AL ≥4 mm	5.7	5.4~5.9	5.6	5.3~5.9	0.752
	AL ≥6 mm	1.5	1.4~1.6	1.4	1.3~1.5	0.508
Total	BOP+	12.3	12.2~12.5	12.4	12.1~14.8	0.574
	PD ≥4 mm	3.5	3.4~3.6	4.5	4.2~4.7	<0.001
	PD ≥6 mm	0.2	0.2~0.2	0.4	0.3~0.4	<0.001
	AL ≥4 mm	3.8	3.7~3.9	5.0	4.8~5.2	<0.001
	AL ≥6 mm	0.8	0.8~0.9	1.2	1.1~1.3	<0.001

\*Significant difference according to Student's t-test.

AL, attachment loss; BOP, bleeding on probing; PD, probing depth.

region, duration of education and annual family income. Hypertension prevalence increased with increases in the proportions of teeth with BOP (OR=1.20, 95% CI=1.05–1.38,  $p=0.006$ ), PD ≥4 mm (OR=1.73, 95% CI=1.43–2.10,  $p<0.001$ ) and PD ≥6 mm (OR=2.44, 95% CI=1.19–5.03,  $p=0.015$ ), but it decreased with increases in the proportions of teeth with AL ≥4 mm (OR=0.87, 95% CI=0.73–1.05,  $p=0.155$ ) and AL ≥6 mm (OR=0.74, 95% CI=0.53–1.04,  $p=0.083$ ). There were significant positive associations of hypertension with the number of teeth with BOP (OR=1.01, 95% CI=1.00–1.01,  $p=0.001$ ), PD ≥4 mm (OR=1.03, 95% CI=1.02–1.04,  $p<0.001$ ) and PD ≥6 mm (OR=1.07, 95% CI=1.03–1.11,  $p<0.001$ ). There were

statistically insignificant negative associations of the presence of hypertension with the proportions of teeth with AL ≥4 mm and AL ≥6 mm (table 6).

#### Significantly more teeth were missing in participants with hypertension than in participants with normotension

Online supplemental table 4 presents a comparison of the number of missing teeth between participants with and without hypertension. Significantly more teeth were missing in participants with hypertension than in participants with normotension (4.4 vs 2.9 teeth). The difference in the number of missing teeth between participants with hypertension and participants with normotension

**Table 4** Relationships between blood pressure (hypertension vs normotension) and periodontal status (compared with non-periodontitis) according to the 2017 classification, analysed by logistic regression after adjusting for gender, smoking status, region, years of education and annual family income

Age group	Periodontal status*	OR	95% CI	P value
35–44 years	Periodontitis (stages III and IV)	1.62	1.00~2.61	0.050
	Periodontitis (stages I and II)	0.97	0.65~1.43	0.863
55–64 years	Periodontitis (stages III and IV)	1.40	1.07~1.84	0.015
	Periodontitis (stages I and II)	1.30	1.00~1.69	0.051
65–74 years	Periodontitis (stages III and IV)	1.21	0.96~1.42	0.113
	Periodontitis (stages I and II)	1.12	0.96~1.42	0.336
Total	Periodontitis (stages III and IV)	1.70	1.45~1.99	<0.001
	Periodontitis (stages I and II)	1.03	0.88~1.20	0.717

\*According to the 2017 World Workshop on the Classification of Periodontal and Per-Implant Diseases and Conditions.<sup>17</sup>

decreased with age. The differences in missing teeth between participants with hypertension and participants with normotension were generally consistent in men and women, and among current smokers, former smokers and non-smokers.

## DISCUSSION

Based on data from the Fourth National Oral Health Survey of China, periodontitis is significantly and strongly associated with hypertension among Chinese adults, independent of the effects of age, gender and smoking. The association between periodontitis and hypertension reported here is in agreement with recent reviews.<sup>11 18</sup> This association between periodontitis and hypertension has considerable importance since the high prevalence of both in the population and the serious impact on oral health and general health.<sup>19</sup>

In recent systemic reviews analysing the association between periodontitis and hypertension, the included studies had been conducted in different countries across Asia, Europe, America and Africa, but large-scale data from

China were lacking.<sup>11 18</sup> In this study, we used data from a large-scale national survey in which participants were representative of the Chinese population. In addition, the lack of consistent definitions of case and the severity of periodontitis in the retrieved studies did not allow for a relevant analysis of the extent and severity of periodontitis with hypertension. In the present study, periodontitis was diagnosed in accordance with the classification proposed at the 2017 World Workshop. The association of hypertension with periodontitis was assessed according to age and smoking status to minimise errors and the effects of confounding factors. Periodontitis was associated with a higher prevalence of hypertension among Chinese adults, independent of known confounders. In most studies, periodontal status was evaluated clinically via PD or clinical attachment level measurements.<sup>11 18</sup> Nevertheless, several definitions of periodontal disease have been used across studies, and only a few have distinguished severe forms of periodontitis. In the present study, periodontitis severity was defined using the new 2017 classification mentioned above. Participants with severe periodontal

**Table 5** Relationships between blood pressure (hypertension vs normotension) and percentage of teeth affected by different thresholds of periodontal parameters, analysed by logistic regression after adjusting for age, gender, smoking status, region, years of education and annual family income

Periodontal parameter	OR*	95% CI	P value
BOP+	1.20	1.05~1.38	0.006
PD ≥4 mm	1.73	1.43~2.10	<0.001
PD ≥6 mm	2.44	1.19~5.03	0.015
AL ≥4 mm	0.87	0.73~1.05	0.155
AL ≥6 mm	0.74	0.53~1.04	0.083

\*The OR as the periodontal parameter increased by 1% (for example, as the BOP+ % increases by 1%, the odds of hypertension increase by 20%; in other words, 1.20 minus 1).<sup>32 46</sup> AL, attachment loss; BOP, bleeding on probing; PD, probing depth.

**Table 6** Relationships between blood pressure (hypertension vs normotension) and the number of teeth affected by different thresholds of periodontal parameters, analysed by logistic regression after adjusting for age, gender, smoking status, region, years of education and annual family income

Periodontal parameter	OR*	95% CI	P value
BOP+	1.01	1.00~1.01	0.001
PD ≥4 mm	1.03	1.02~1.04	<0.001
PD ≥6 mm	1.07	1.03~1.11	<0.001
AL ≥4 mm	1.00	0.99~1.01	0.507
AL ≥6 mm	0.99	0.97~1.01	0.217

\*The OR as the periodontal parameter increased by 1% (for example, as BOP+ % increases by one tooth, the odds of hypertension increase by 1%; in other words, 1.01 minus 1).<sup>32 46</sup> AL, attachment loss; BOP, bleeding on probing; PD, probing depth

disease (stages III and IV periodontitis) had an increased risk of hypertension compared with participants who had mild or no periodontal disease.

Hypertension prevalence increased with periodontitis severity, particularly among young participants (35–44 years). Therefore, participants with risk factors, particularly young adults, should engage in healthy lifestyle habits to improve their oral health. Accordingly, there is a need to improve the education and awareness of dental treatment and preventive management among individuals at risk of hypertension, particularly in the younger population. Periodontitis and hypertension are chronic diseases; therefore, substantial exposure time may be necessary for their development. The exposure time to risk factors may be considerably shorter in younger individuals than in older individuals. The influence of the longer exposure time to the common risk factors for periodontitis and hypertension in older individuals may mask the effects of periodontitis on the development of hypertension. When the confounding effects of the risk factors were removed, a link between periodontitis and hypertension was identified. Therefore, severe periodontitis may have a greater role in the development of hypertension among younger individuals than among older individuals. The association of periodontitis with hypertension was also present in never smokers and former smokers, who had less exposure to common risk factors. The greater susceptibility to hypertension among young individuals with severe periodontitis may be attributed to periodontal inflammation. Periodontitis is a chronic infection that leads to inflammation. Previous evidence suggested the connection between periodontal disease and systemic inflammation, which in turn was associated with an increased risk of hypertension.<sup>13–16</sup> The inflammatory response with periodontal disease has been proposed as one of the factors that induces vascular inflammation leading to endothelial dysfunction and exerts an adverse effect on the regulation of hypertension.<sup>20</sup> After periodontal therapy, endothelial dysfunction is reversible in patients with hypertension.<sup>20,21</sup> Periodontal treatment can improve the endothelial function effectively.<sup>22</sup> In addition, the periodontal pathogens may directly invade the arterial wall and lead to vascular inflammation.<sup>23</sup> There is growing evidence indicating that periodontitis induces excessive production of reactive oxygen species (ROS) in periodontal tissue.<sup>24–26</sup> The production of ROS increases in response to periodontal inflammation; then ROS enters the systemic circulation.<sup>27</sup> ROS is one of the regulators for vascular inflammation and vasoconstriction.<sup>13,20</sup> It has been reported that high BP was related to the imbalance between ROS production and antioxidant.<sup>20,28,29</sup>

This study evaluated the association between periodontal status and hypertension risk among young and older adults. Hypertension prevalence increased with periodontitis severity, which was most prominent in individuals aged 35–44 years. Adults aged <65 years with hypertension had significantly greater risks of stages III and IV periodontitis, compared with individuals who did

not have hypertension. Therefore, healthcare providers should carefully monitor oral health status in their patients to prevent hypertension, particularly among adults; they should conduct regular oral examinations and engage in periodontal disease management.

This study showed the percentage of teeth of each periodontal status that reflected the extent of periodontal pathology in the oral cavity. The association between periodontitis and hypertension was also present in participants who had a greater proportion of teeth with BOP or deep periodontal pockets. The findings suggest that severe extensive periodontal inflammation, as evidenced by the depth of the inflamed periodontal pocket and the number of bleeding sites, is associated with hypertension. In particular, the presence of BOP indicates acute inflammation, which may lead to systemic effects and subsequent hypertension. The association of inflammation (ie, PD) with hypertension suggests that persistent, long-term, extensive inflammation may also underlie this relationship. Compared with AL, PD seems to be more closely related to hypertension. For example, significant differences in the percentages/numbers of teeth with PD  $\geq 4$  mm and  $\geq 6$  mm, but not AL  $\geq 4$  mm and  $\geq 6$  mm, in those 55–64 years old, were seen between individuals with hypertension and individuals with normotension (tables 2 and 3). This is because AL is more related to periodontal attachment damage, while PD is more closely related to the existing periodontal inflammation. This also indicates that the correlation between periodontitis and hypertension may be related to the increase in systemic inflammation. Our study adds to the existing literature concerning oral health parameters associated with systemic outcomes.<sup>30,31</sup> BOP and PD are the most appropriate clinical measures when the outcome of interest is an acute disease, whereas AL is more strongly correlated with chronic systemic conditions.<sup>11</sup> Our findings of an association between hypertension and the severity of periodontal inflammation (BOP and PD) are consistent with the results of previous studies.<sup>12,32</sup> Although the causality of the observed association remains unclear, several hypotheses have been proposed, including endothelial dysfunction, oxidative stress, worsening of systemic inflammation in response to bacteraemia and dissemination of inflammatory mediators from periodontal pockets, particularly BOP.<sup>33</sup> This association is further supported by the results of a randomised clinical trial that showed short-term benefits of periodontal therapy on hypertension.<sup>34</sup> Additionally, a recent study identified oral pathogens associated with high or uncontrolled BP, which supports our findings.<sup>35</sup>

Our finding of an association between the number of missing teeth and hypertension is consistent with the results reported by Taguchi *et al.*<sup>36</sup> Missing teeth are indicative of poor oral health; they presumably were lost because of caries and periodontal disease. Thus, the absence of several teeth suggests the presence of severe periodontal disease, caries or other oral health problems; these may have contributed to the increased risk of



hypertension. This association was strongest in younger adults. There were no residual confounding effects of age that may have affected our study results. Because of the high prevalence of hypertension in Chinese adults, further studies are needed to clarify the association between periodontitis and hypertension. Moreover, attention is needed concerning the prevention and treatment of periodontitis in the general population.

There is minimal knowledge concerning the natural history of the association between periodontal disease and hypertension.<sup>37–41</sup> A significant linear trend was observed between the severity of periodontal disease and hypertension in a cross-sectional study of 3352 patients with periodontal disease and 902 controls.<sup>39</sup> A recent prospective cohort study of Japanese individuals demonstrated an increased incidence of hypertension among participants with periodontal pockets  $\geq 4$  mm at baseline.<sup>40</sup> Our findings are consistent with the results in a similar study of 6617 men and 7377 women who underwent dental examinations as part of the National Health and Nutrition Examination Survey III in the USA.<sup>42</sup> In the present study, after multivariate adjustment, gingival bleeding (BOP) was associated with an increased risk of hypertension, whereas periodontitis severity (defined using the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions) and PD were positively associated with hypertension. Participants with severe periodontal disease (stages III and IV periodontitis) had a higher risk of hypertension than participants who had mild or no periodontal disease. Furthermore, there was a threshold relationship between severe periodontal disease and hypertension.

To assess the association between the two diseases accurately, several potential confounders were adjusted for, and the associations were evaluated in multiple ways, including not only periodontal severity but also several clinical parameters. The assessment of the extent of the pathological condition in periodontal disease is considered important; however, the most severe pathological condition in the oral cavity has been assessed in many studies. In this study, the extent of the pathological condition of periodontal disease in the oral cavity was assessed using the percentage of teeth of each periodontal status. In addition, we evaluated several clinical measures of periodontal disease that allowed analysis of the relationships between various aspects of periodontal disease and hypertension. We found consistent associations between PD and hypertension. PD may be indicative of poor oral health and periodontal inflammation. When the periodontal tissues are inflamed, the PD increases, allowing more bacteria to accumulate and exacerbate the inflammation.<sup>43</sup> The total surface area of the pocket epithelium in contact with subgingival bacteria and their products in patients with generalised moderate periodontitis is estimated to be approximately the size of an adult hand palm, with even larger exposure areas in cases with more advanced periodontal destruction.<sup>44</sup>

Therefore, the PD can be used as an indicator of the severity of periodontitis. It was positively associated with hypertension, suggesting a link between inflammation and hypertension.

The main limitation of our study was that hypertension was self-reported and not based on BP measurements, which is inherent in any epidemiological cohort study. However, field measurements of BP are regarded as validated tools, have been used in previous studies<sup>30 33</sup> and are considered useful for the analysis of large samples. Furthermore, although recall and reporting bias could not be excluded, the results largely reflect real-world clinical practice. First, the self-reported diagnosis was based on a face-to-face interview to ensure the validity and accuracy of the information. Second, the reliability of the study results is supported by data from the China Hypertension Survey (2012–2015),<sup>45</sup> which showed an overall hypertension prevalence of 23.2% in the adult Chinese population; this prevalence is similar to the prevalence observed in our study (23.9%).

In summary, our epidemiological analysis revealed an association between periodontitis and hypertension. We collected high-quality, large-scale clinical data related to periodontal disease and hypertension. We also collected detailed information regarding potential confounders, including variables that reflect health behaviour (eg, flossing). As this study was a cross-sectional study, we cannot draw a causal relationship between periodontitis and hypertension. Future studies should be conducted to improve the understanding of the underlying mechanisms and interactions between periodontitis and hypertension, which will further strengthen collaborations between the dental and medical communities. Preventive measures for periodontal disease in oral health promotion programmes should be emphasised to improve systemic health outcomes.

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